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Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years (Review)

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[Intervention Review]

Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years

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ABSTRACT

Background

Zinc deficiency is prevalent in low- and middle-income countries, and is considered a significant risk factor for morbidity, mortality, and linear growth failure. The effectiveness of preventive zinc supplementation in reducing prevalence of zinc deficiency needs to be assessed.

Objectives

To assess the effects of zinc supplementation for preventing mortality and morbidity, and for promoting growth, in children aged 6 months to 12 years.

Search methods

A previous version of this review was published in 2014. In this update, we searched CENTRAL, MEDLINE, Embase, five other databases, and one trials register up to February 2022, together with reference checking and contact with study authors to identify additional studies.

Selection criteria

Randomized controlled trials (RCTs) of preventive zinc supplementation in children aged 6 months to 12 years compared with no intervention, a placebo, or a waiting list control. We excluded hospitalized children and children with chronic diseases or conditions. We excluded food fortification or intake, sprinkles, and therapeutic interventions.

Data collection and analysis

Two review authors screened studies, extracted data, and assessed the risk of bias. We contacted study authors for missing information and used GRADE to assess the certainty of evidence. The primary outcomes of this review were all-cause mortality; and cause-specific mortality, due to all-cause diarrhea, lower respiratory tract infection (LRTI, including pneumonia), and malaria. We also collected information on a number of secondary outcomes, such as those related to diarrhea and LRTI morbidity, growth outcomes and serum levels of micronutrients, and adverse events.

Main results

We included 16 new studies in this review, resulting in a total of 96 RCTs with 219,584 eligible participants. The included studies were conducted in 34 countries; 87 of them in low- or middle-income countries. Most of the children included in this review were under five years of age. The intervention was delivered most commonly in the form of syrup as zinc sulfate, and the most common dose was between 10 mg and 15 mg daily. The median duration of follow-up was 26 weeks. We did not consider that the evidence for the key analyses of morbidity and mortality outcomes was affected by risk of bias.

High-certainty evidence showed little to no difference in all-cause mortality with preventive zinc supplementation compared to no zinc (risk ratio (RR) 0.93, 95% confidence interval (CI) 0.84 to 1.03; 16 studies, 17 comparisons, 143,474 participants).

Moderate-certainty evidence showed that preventive zinc supplementation compared to no zinc likely results in little to no difference in mortality due to all-cause diarrhea (RR 0.95, 95% CI 0.69 to 1.31; 4 studies, 132,321 participants); but probably reduces mortality due to LRTI (RR 0.86, 95% CI 0.64 to 1.15; 3 studies, 132,063 participants) and mortality due to malaria (RR 0.90, 95% CI 0.77 to 1.06; 2 studies, 42,818 participants); however, the confidence intervals around the summary estimates for these outcomes were wide, and we could not rule out a possibility of increased risk of mortality.

Preventive zinc supplementation likely reduces the incidence of all-cause diarrhea (RR 0.91, 95% CI 0.90 to 0.93; 39 studies, 19,468 participants; moderate-certainty evidence) but results in little to no difference in morbidity due to LRTI (RR 1.01, 95% CI 0.95 to 1.08; 19 studies, 10,555 participants; high-certainty evidence) compared to no zinc.

There was moderate-certainty evidence that preventive zinc supplementation likely leads to a slight increase in height (standardized mean difference (SMD) 0.12, 95% CI 0.09 to 0.14; 74 studies, 20,720 participants).

Zinc supplementation was associated with an increase in the number of participants with at least one vomiting episode (RR 1.29, 95% CI 1.14 to 1.46; 5 studies, 35,192 participants; high-certainty evidence). We report a number of other outcomes, including the effect of zinc supplementation on weight and serum markers such as zinc, hemoglobin, iron, copper, etc. We also performed a number of subgroup analyses and there was a consistent finding for a number of outcomes that co-supplementation of zinc with iron decreased the beneficial effect of zinc.

Authors' conclusions

Even though we included 16 new studies in this update, the overall conclusions of the review remain unchanged. Zinc supplementation might help prevent episodes of diarrhea and improve growth slightly, particularly in children aged 6 months to 12 years of age. The benefits of preventive zinc supplementation may outweigh the harms in regions where the risk of zinc deficiency is relatively high.

PLAIN LANGUAGE SUMMARY

Is zinc supplementation effective for preventing death and disease, and for promoting growth, in children aged 6 months to 12 years and does it cause unwanted effects?

Key messages

- Zinc supplementation in children aged 6 months to 12 years makes little to no difference to all-cause mortality and probably makes no difference to deaths from diarrea. Zinc supplementation probably reduces mortality due to lower respiratory tract infections and malaria but a small possibility of increased risk of mortality cannot be ruled out.

- Zinc supplementation in children aged 6 months to 12 years might prevent illness due to diarrhea, but might lead to vomiting after supplementation. It might lead to a small increase in height gain.

Why is it important to study zinc supplementation?

Zinc is an essential micronutrient. It is important to help children grow normally and to promote a healthy immune system. Lack of zinc may lead to diarrhea, pneumonia, malaria and even death. Low dietary zinc intake is often linked to poverty. As many as half of all children in low- and middle-income countries may have zinc deficiency. Meat, fish, eggs and dairy products are good natural sources of zinc, but are expensive. Lack of clean water and poor sanitation increases exposure to diseases, which zinc might help to fight. The human body cannot produce or store zinc, so giving dietary supplements is important.

What did we want to find out?

We wanted to find out if giving children zinc supplements helps prevent child death and disease, and promotes growth.

What did we do?

We searched for studies that randomly assigned children aged 6 months to 12 years to receive zinc supplementation or no zinc.

We compared and summarized the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We included 96 studies in the review, with 219,584 children. Studies took place in 34, mainly low- to middle-income countries. Most of the children in the studies were under five years old. Zinc was most commonly given as a syrup (zinc sulfate), and the most common dose was between 10 mg and 15 mg daily.

We found that giving children zinc supplementation might lead to a small to no reduction in the risk of death for any reason and the risk of death due to diarrhea. The risk of death due to lower respiratory tract infections or malaria may be reduced. Children given zinc experienced less disease due to diarrhea than children not given zinc; however, zinc does not seem to reduce children's risk of respiratory infection. Zinc supplementation may have a small positive effect on growth. Children who take zinc supplementation may experience vomiting as an unwanted effect.

What are the limitations of the evidence?

We are confident about our results on the effects of zinc supplements on reducing the risk of death due to any cause, illness due to respiratory infection, and occurrence of vomiting after supplementation. Our confidence in the results for our other outcomes was moderate because relatively few studies reported these outcomes and because studies sometimes reported different results from other studies for the same outcomes.

How up to date is this evidence?

This review updates a previous version published in 2014. The evidence is current to February 2022.

Summary of findings 1. Zinc supplementation compared to no zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age

Zinc supplementation compared to no zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age

Patient or population: otherwise healthy children aged 6 months to 12 years of age
Setting: community settings (mostly low- and middle-income countries)
Intervention: zinc supplementation
Comparison: placebo, no zinc supplementation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no zinc supplementation	Risk with zinc supplementation				
All-cause mortality Follow-up: median 26 weeks	**Study population**		RR 0.93 (0.84 to 1.03)	143,474 (16 RCTs; 17 comparisons)	⊕⊕⊕⊕ High[a,b]	Zinc supplementation results in little to no difference in all-cause mortality.
	11 per 1000	**10 per 1000** (9 to 12)				
Mortality due to all-cause diarrhea Follow-up: range 16 weeks to 48 weeks	**Study population**		RR 0.95 (0.69 to 1.31)	132,321 (4 RCTs)	⊕⊕⊕⊖ Moderate[c,d]	Zinc supplementation likely results in little to no difference in mortality due to all-cause diarrhea.
	1 per 1000	**1 per 1000** (1 to 2)				
Mortality due to LRTI Follow-up: range 16 weeks to 48 weeks	**Study population**		RR 0.86 (0.64 to 1.15)	132,063 (3 RCTs)	⊕⊕⊕⊖ Moderate[d]	Zinc supplementation likely results in a slight reduction in mortality due to LRTI.
	1 per 1000	**1 per 1000** (1 to 2)				
Mortality due to malaria Follow-up: mean 48 weeks	**Study population**		RR 0.90 (0.77 to 1.06)	42,818 (2 RCTs)	⊕⊕⊕⊖ Moderate[d]	Zinc supplementation likely results in a slight reduction in mortality due to malaria.
	15 per 1000	**13 per 1000** (11 to 15)				
Incidence of all-cause diarrhea Follow-up: median 24 weeks	**Study population**		RR 0.91 (0.90 to 0.93)	19,468 (39 RCTs)	⊕⊕⊕⊖ Moderate[e]	Zinc supplementation likely reduces the incidence of all-cause diarrhea.
	628 per 1000	**572 per 1000** (565 to 584)				

Incidence of LRTI Follow-up: median 24 weeks	**Study population**		RR 1.01 (0.95 to 1.08)	10,555 (19 RCTs)	⊕⊕⊕⊕ High[f]	Zinc supplementation results in little to no difference in the incidence of LRTI.
	228 per 1000	**233 per 1000** (219 to 246)				
Height Assessed with: cm or height-for-age z scores Follow-up: median 26 weeks	The mean height was 0 SD	SMD 0.12 SD higher (0.09 higher to 0.14 higher)	-	20,720 (74 RCTs)	⊕⊕⊕⊖ Moderate[g,h]	Zinc supplementation likely results in a slight increase in height. An SMD of 0.12 is considered small according to Cohen's value interpretation.
Participants with ≥ 1 vomiting episode Follow-up: mean 48 hours	**Study population**		RR 1.29 (1.14 to 1.46)	35,192 (5 RCTs)	⊕⊕⊕⊕ High	Zinc supplementation results in a slight increase in participants with ≥ 1 vomiting episode.
	22 per 1000	**29 per 1000** (26 to 33)				

*__The risk in the intervention group__ (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **LRTI:** lower respiratory tract infection; **RCT:** randomized controlled trial; **RR:** risk ratio; **SD:** standard deviation; **SMD:** standardized mean difference

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

[a]Even though some of the studies had concerns about selective reporting, these concerns were not related to the outcome of all-cause mortality. We, therefore, did not downgrade for the risk of bias.
[b]The analysis included a total of 143,474 participants. Even though the confidence interval around the summary estimate includes 1, the upper limit was 1.03 and the confidence interval overall was narrow. The absolute effect in the form of risk difference ranged from a reduction of 2 per 1000 to 0 per 1000. We, therefore, did not downgrade for the imprecision.
[c]Even though some of the studies had concerns about selective reporting, these concerns were not related to the outcome of diarrhea-related mortality. We, therefore, did not downgrade for the risk of bias.
[d]The confidence interval around the summary estimate was wide and included a null effect.
[e]There was substantial statistical heterogeneity in the pooled data, I^2= 79%.
[f]Even though the confidence around the summary estimate includes 1, the overall summary estimate was 1.02 and the confidence interval was narrow. So we did no downgrade for the imprecision.
[g]Even though we were concerned about the risk of bias due to selective reporting in a number of studies, data were available for meta-analysis from a significant number of studies included in this review. We did not think that selective reporting affected the outcomes of height for age.
[h]There was substantial heterogeneity in the pooled data. The $I^2$was 87%.

BACKGROUND

Description of the condition

Zinc is an essential micronutrient. Regular dietary intake of zinc is necessary because the human body cannot produce zinc and does not have an adequate mechanism for storing or releasing it (Brown 2004; Maggini 2010). Severe zinc deficiency affects numerous organ systems, including the immune, gastrointestinal, skeletal, reproductive, and central nervous systems (Tuerk 2009). Even marginal zinc deficiency may be associated with immune system dysfunction and restricted physical development (Prasad 1963; Shankar 1998). Children are especially vulnerable to deficiency because their periods of rapid growth create increased zinc needs that may remain unmet (Gibson 2006).

Intervention studies suggest that zinc deficiency may increase the risk of deaths due to diarrhea, pneumonia, and malaria, which are leading causes of mortality in this age group (Black 2008; Black 2010; Bryce 2005; Fischer Walker 2008; Wazny 2013; WHO 2009). Zinc deficiency may also impair growth and contribute to childhood stunting (Hess 2009b; Prasad 2014; Williams 1970); high stunting prevalence is used as an indicator of population-level zinc deficiency (Engle-Stone 2007; Hess 2009b). The global prevalence of zinc deficiency is approximately 9% and about 2800 deaths were attributed to zinc deficiency according to the Global Burden of Disease (GBD) study 2019 (GBD 2020). The estimate of the prevalence of micronutrient deficiencies differed in the GBD study of 2017 (GBD 2018), compared to that of 2019 (GBD 2020), and the difference in these estimates have been attributed to statistical methods used in the two studies (Hess 2021). The latest Lancet Nutrition series estimated that in some low- and middle-income countries, as many as half of all children might have zinc deficiency (Victora 2021).

At both national and individual levels, zinc deficiency and its consequences are linked to poverty. Firstly, foods from animal sources, which are rich in zinc, are often expensive. Particularly in low- and middle-income countries, poor individuals may primarily eat foods such as cereals, grains, and legumes (Brown 2004). These foods have relatively low concentrations of zinc. They also have relatively high concentrations of fiber and phytate molecules, which reduce zinc absorption by the intestine (Brown 2004; Sandstead 1995). Secondly, poor water and sanitation systems lead to frequent exposure to gastrointestinal pathogens and high rates of infectious disease and diarrhea (Brown 2004). Finally, factors such as poverty, poor nutrition and sanitation, and infectious morbidity exacerbate one another. For instance, diarrhea can compromise intestinal function and damage the gastrointestinal tract lining, thereby causing increased zinc excretion via the intestine (Aggarwal 2007; Maggini 2010). Damage to the gastrointestinal tract lining can hinder the absorption of zinc and other nutrients (Fagundes-Neto 1984; McKay 2010; Salazar-Lindo 2004). Thus, a cycle of zinc deficiency can develop, leading to infectious morbidity, in turn leading to further zinc deficiency. Similarly, since morbidity and mortality contribute to reduced economic productivity (Behrman 2004), a cycle can develop in which poverty contributes to zinc-related morbidity and mortality, which contribute to further poverty.

Description of the intervention

Zinc supplementation is a relatively easily implemented and inexpensive intervention that could help address zinc deficiency (Shrimpton 2005). Zinc supplementation comes in various physical forms, including liquid solutions, syrups, pills, tablets, capsules, powders, and pastes (Brown 2004). Supplementation also comes in various chemical forms, such as zinc sulfate and zinc acetate, with water-soluble compounds often preferred because they may be more efficiently absorbed (Brown 2004; Brown 2009). In addition, zinc is sometimes administered with other micronutrients such as vitamin A or iron (Brown 2009). Zinc supplementation has been provided at various doses, daily and weekly, for a few weeks to over a year (Brown 2009).

Recommendations for normal zinc consumption among children range between 2 mg and 11 mg per day, depending on age and diet (Brown 2004; Institute of Medicine 2001; WHO/FAO 2004). The World Health Organization (WHO) recommends a supplemental dose of 20 mg per day for 10 to 14 days to treat diarrhea in children six to 59 months of age (WHO/UNICEF 2004). Currently, there are no recommendations for preventive zinc supplementation; however, previous work has shown that a dose of 10 mg per day for six months may significantly reduce stunting in children in low- and middle-income countries who are under five years of age (Imdad 2011).

How the intervention might work

Zinc is in every cell of the human body and is required for normal functioning (Fisher 1975; Fischer Walker 2004). It plays critical catalytic, structural, and regulatory roles (Cousins 1994; Tuerk 2009). Zinc enables hundreds of enzymes to function, facilitates protein synthesis and folding, and regulates processes such as gene expression and apoptosis (Aggarwal 2007; Brown 2004; Hambidge 2007; MacDonald 2000; Stefanidou 2006; Tuerk 2009). Zinc is also important for DNA and RNA metabolism, as well as cellular replication, differentiation, and growth (MacDonald 2000; Stefanidou 2006). Zinc is involved in both non-specific and specific immune system processes, including phagocytosis, maintenance of gastrointestinal and respiratory tract linings, and development and function of T- and B-cells (Shankar 1998). Zinc is also involved in bone development, growth hormone function, taste acuity, and appetite (Salgueiro 2002). By increasing the availability of zinc for these biological processes, supplementation may improve health outcomes such as reduction in all-cause diarrhea, and promote growth (Bhutta 1999; Brown 2009). Zinc supplementation has also been shown to decrease the duration of diarrhea (Lazzerini 2016), as zinc is involved in over 300 enzymes, some of which are responsible for mechanisms protecting the integrity of the gastrointestinal tract and its regeneration after injury (IZiNCG 2004).

An important aspect of zinc supplementation is related to the interaction of zinc with other micronutrients, especially the interactions between zinc, iron, and copper. Iron supplementation may interfere with the absorption of zinc, and zinc may interfere with iron and copper absorption (Allen 1998; Maret 2006; Sandström 1985; Sandström 2001); however, the evidence is mixed as to whether supplemental zinc contributes to anemia, iron deficiency, or copper deficiency (Brown 2009; Fosmire 1990). Other potential adverse effects of zinc occur primarily when it is given in very high doses (such as 225 mg to 450 mg; Fosmire 1990).

These adverse effects include abdominal pain, nausea, vomiting, and diarrhea (Fosmire 1990; Larson 2008).

Why it is important to do this review

Several Cochrane Reviews have investigated zinc supplementation. There are reviews of zinc supplementation as an adjunct to diarrhea treatment (Lazzerini 2016), pneumonia treatment (Haider 2011), and mental and motor development in children (Gogia 2012). There are reviews of zinc supplementation in populations with HIV (Humphreys 2010; Irlam 2010). Reviews have also focused on zinc supplementation for pregnancy and infant outcomes (Carducci 2021), the common cold (Singh 2013), otitis media (Gulani 2014), and pneumonia prevention (Lassi 2016). We conducted this systematic review to assess the effect of preventive zinc supplementation in otherwise healthy children to prevent illness and death. A previous version of this review was published in 2014 (Mayo-Wilson 2014); however, additional studies have become available since the publication of the last version of this review. We, therefore, carried out an update of the evidence on preventive zinc supplementation for children aged 6 months to 12 years.

OBJECTIVES

To assess the effects of zinc supplementation for preventing mortality and morbidity, and for promoting growth, in children aged 6 months to 12 years.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) and cluster-RCTs with a parallel-group design, in which intervention and control groups were enrolled concurrently. We excluded quasi-RCTs, such as studies in which allocation was determined by alternation or date of birth.

Types of participants

Otherwise healthy children aged 6 months to 12 years (inclusive) at study baseline.

We excluded the following:

- children less than six months of age (the WHO recommends exclusive breastfeeding for children less than six months of age, and we excluded studies assessing zinc for lactating mothers);
- hospitalized children;
- children with severe protein-energy malnutrition; HIV; chronic diseases such as cystic fibrosis and sickle cell disease, or conditions such as Down syndrome, that could affect growth.

If only a subset of a study's participants were eligible for our review on the basis of age, then we asked the study authors for disaggregated data. If we were unable to obtain the appropriate disaggregated data, then we included a study if the majority (at least 51%) of its participants were eligible for our review by age criteria. If we were unable to determine the exact percent of a study's participants who were eligible, then we included the study if its participants were eligible on average (for example, the mean participant age was at least six months and less than 13 years).

Types of interventions

Intervention

Orally administered zinc given as a supplement, regardless of compound, formulation, dose, duration, or frequency.

We excluded the following:

- food fortification or intake;
- studies of mixed micronutrients that did not isolate zinc (for example, a review has already been conducted on micronutrient sprinkles (Suchdev 2020);
- studies evaluating the therapeutic effects of zinc (that is, studies in which children received zinc while they were ill with diarrhea, LRTI, or malaria, but stopped receiving zinc after recovering from illness).

Comparisons

Placebo, no intervention, and waiting list controls were included as comparators. A control comparison group could have been administered a non-zinc co-intervention (such as a vitamin A supplement), as long as both the intervention group and control group received the same co-intervention. Comparisons between two different dosages of zinc (that is, a high dose and a low dose) were not eligible, nor were comparisons between different zinc compounds, durations of supplementation, or frequencies at which doses were given. To evaluate the effect of providing zinc and iron simultaneously, we also included comparisons of zinc alone versus zinc plus iron.

Types of outcome measures

We assessed the preventive effects of zinc supplementation by extracting data for the following outcomes. Outcome definitions are outlined in Appendix 1.

Primary outcomes

- 1. All-cause mortality
- 2. Cause-specific mortality
  - 2.1 Mortality due to all-cause diarrhea
  - 2.2 Mortality due to lower respiratory tract infection (LRTI, including pneumonia)
  - 2.3 Mortality due to malaria

Secondary outcomes

- 3. All-cause hospitalization
- 4. Diarrhea
  - 4.1 Incidence of all-cause diarrhea
  - 4.2 Prevalence of all-cause diarrhea
  - 4.3 Hospitalization due to all-cause diarrhea
  - 4.4 Incidence of severe diarrhea
  - 4.5 Prevalence of severe diarrhea
  - 4.6 Incidence of persistent diarrhea
  - 4.7 Prevalence of persistent diarrhea
  - 4.8 Hospitalization due to persistent diarrhea
- 5. Lower respiratory tract infection (LRTI)
  - 5.1 Incidence of LRTI (including pneumonia)
  - 5.2 Prevalence of LRTI
  - 5.3 Hospitalization due to LRTI

- 6. Malaria
  - 6.1 Incidence of malaria
  - 6.2 Prevalence of malaria
  - 6.3 Hospitalization due to malaria
- 7. Growth
  - 7.1 Height
  - 7.2 Weight
  - 7.3 Weight-to-height ratio/height ratio
  - 7.4 Prevalence of stunting
- 8. Zinc status
  - 8.1 Serum or plasma zinc concentration
  - 8.2 Prevalence of zinc deficiency

Adverse events

- 9. Side effects
  - 9.1 Study withdrawal
  - 9.2 Participants with one or more side effects
  - 9.3 Vomiting episodes
  - 9.4 Participants with one or more vomiting episodes
- 10. Hemoglobin status
  - 10.1 Blood hemoglobin concentration
  - 10.2 Prevalence of anemia
- 11. Iron status
  - 11.1 Serum or plasma ferritin concentration
  - 11.2 Prevalence of iron deficiency
- 12. Copper status
  - 12.1 Serum or plasma copper concentration
  - 12.2 Prevalence of copper deficiency

Search methods for identification of studies

For this update we searched the databases and trial registers listed below in February 2022. Searches were limited to the period 2013 onwards, in order to identify new studies published since the previous version of the review. Details of the previous search strategies are available in Mayo-Wilson 2014.

Electronic searches

We searched the following databases without language restrictions. Appendix 2 provides details of the search strategy for each database.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2022, Issue 2), in the Cochrane Library (searched 2 February 2022)
- MEDLINE Ovid (1946 to 2 February 2022)
- MEDLINE Ovid In-Process & Other Non-Indexed Citations (1946 to 2 February 2022)
- Embase Elsevier (1974 to 2 February 2022)
- WHO International Clinical Trials Registry Platform (ICTRP; apps.who.int/trialsearch; searched 2 February 2022)
- Science Citation Index Web of Science (1970 to 2 February 2022)
- Conference Proceedings Citation Index Web of Science (1990 to 2 February 2022)
- Scopus Elsevier (2013 to 2 February 2022)
- Cochrane Database of Systematic Reviews (CDSR; 2022, Issue 2) in the Cochrane Library (searched 2 February 2022)
- Global Index Medicus (contains WPRIM, LILACS, IMSEAR, IMEMR, AIM; www.globalindexmedicus.net; searched 2 February 2022)

Searching other resources

Reference lists

We searched the reference lists of relevant review articles and included studies to identify additional studies in the published or unpublished literature.

Correspondence

We contacted the authors of included studies to identify additional studies that were ongoing or unpublished.

Data collection and analysis

Selection of studies

For this update, at least two review authors (from AI, JS, MH, AR, JR) independently screened the titles and abstracts of all reports yielded by the search to determine which were eligible for inclusion in the review. We then obtained and independently screened the full text of all potentially relevant studies to determine whether they met the inclusion criteria. If the review authors disagreed about the eligibility of a study, then they discussed the disagreement amongst themselves and with a third review author in order to reach a consensus about the study's eligibility. We sought additional information from study authors to help clarify any uncertainties regarding eligibility. During the study selection process, we were not blinded to study authors, institutions, journal of publication, or results.

Data extraction and management

We drafted a data extraction form to capture the following characteristics of each study.

General

- Year of study
- Country
- Setting (that is, urban or rural, specific region or city if provided)
- Unit of analysis (for example, individual or cluster randomization)

Participants

- Total number of study participants and clusters
- Number of study participants and clusters randomized to each included group
- Age
- Gender
- Inclusion and exclusion criteria
- Comorbidities

For each intervention or comparison group of interest

- Dose of zinc supplement
- Duration of zinc supplementation
- Frequency of zinc supplementation
- Co-interventions (if any)

For each outcome of interest

- Time points
  - collected
  - reported
- Missing data (exclusion of participants, attrition)

At least two review authors (JS, MH, AR, JR, AI) extracted the data from the included studies. We resolved any difference of opinion by discussion and with the help of the senior review author (AI).

For each study, we also rated the risk of bias (see Assessment of risk of bias in included studies).

Assessment of risk of bias in included studies

For this update, at least two authors (from JS, MH, AR, JR) coded each included study using the Cochrane tool for assessing the risk of bias (Higgins 2011). We used this tool to judge whether each study was at low, high, or unclear risk of bias relating to sequence generation, allocation concealment, blinding of study participants, blinding of personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias. If a disagreement arose concerning a risk of bias assessment, then the review authors discussed the disagreement amongst themselves and with another review author (AI) in order to reach a consensus. We were not blinded to study authors, institutions, journal of publication, or results.

Measures of treatment effect

Studies often report outcomes using multiple definitions and outcome measures. For outcome definitions pertaining to diarrhea, LRTI, malaria, growth, zinc and other micronutrient status, and adverse events, please see Appendix 1.

Multiple outcome measures

To avoid review author bias, we predetermined the order of preference for extracting outcomes when data were available in several formats.

For studies that randomized individuals, we gave preference to data that required the least manipulation by review authors or inference by review authors. We extracted raw values (for example, means and standard deviations) rather than calculated effect sizes (for example, Cohen's d). If outcomes were reported as both final values and changes from baseline, then we preferentially extracted the final values. In the case of cluster-RCTs, firstly, we used adjusted estimates reported by the study authors, or, secondly, used raw data and inflated the standard error (SE) using the procedures described below.

For mortality data, we gave preference to denominators in the following order, number with the definite outcome known (or imputed, as described in Dealing with missing data), number randomized, and child-years. For other dichotomous outcomes to which both survivors and non-survivors may have contributed data, we gave preference to denominators in the following order, child-years, number with the definite outcome known, and number randomized.

Summary measures

Whenever possible, we used a risk ratio (RR) as the effect measure for each outcome for which there were dichotomous data. For incidence data, we combined RRs (events per child) and rate ratios (events per child year), because these ratios used the same scale and could be interpreted in the same way for these studies. Since we expected the duration of studies to be short, we did not anticipate interaction between the intervention and time at risk. We estimated time at risk if appropriate, as when study authors reported incidence rate, study duration, and number of children in a group. We used Hedges' (adjusted) *g* (a standardized mean difference) for each outcome for which there were continuous data. We report all measurements of effect with a 95% confidence interval (CI).

Unit of analysis issues

Cluster-randomized trials

Cluster-randomized trials randomize groups of people rather than individuals. For each cluster-randomized trial, we first determined whether or not its data incorporated sufficient controls for clustering (such as robust SEs or hierarchical linear models). If the data did not have proper controls, then we attempted to obtain an appropriate estimate of the data's intracluster correlation coefficient (ICC). If we could not find an estimate in the report of the study, then we requested an estimate from the study authors. If the study authors did not provide an estimate, then we obtained one from a similar study. We used the ICC estimate to control the study's data for clustering, according to procedures described in Higgins 2022.

Cross-over trials

For cross-over trials, we extracted and analyzed data from the first period only.

Studies with multiple treatment groups

For factorial studies, we included all comparisons that differed only in the presence or absence of zinc. For example, in a 2 x 2 factorial study of zinc and vitamin A supplementation, we included two comparisons:

- zinc versus placebo; and
- zinc and vitamin A versus vitamin A alone.

For other studies, we combined multiple eligible intervention groups. For example, if a study had three groups and two groups compared two different doses of zinc with a third group of a placebo, we combined the two zinc groups to obtain a single comparison of zinc versus placebo.

Outcomes measured at multiple time points

For outcomes measured at multiple time points, we only included the time point that occurred the highest number of days after randomization in our meta-analyses.

Dealing with missing data

Missing data, and methods for imputing such data, may affect the magnitude and direction of a point estimate and its SE. For all analyses, we attempted to include all randomized study participants. When analyses were reported for completers as well as controlling for dropout (for example, imputed using regression methods), we extracted the latter. If data were missing for some cases, or if reasons for dropout were not reported, then we contacted study authors to request missing data and further information on dropouts.

For the primary outcome, data were likely to be missing at random. Secondary outcome data may have been missing for reasons related to group assignment (for example, early mortality in the comparison group). We reported reasons for missing data, including reasons for dropout and number of dropouts. The potential impact of missing data on review findings is discussed below.

Assessment of heterogeneity

We discussed the similarities and differences between included studies in terms of their participants, interventions, outcomes, and methods. For each meta-analysis, we used three methods to identify statistical heterogeneity: visually inspecting forest plots to see if the CIs of individual studies have poor overlap – a rough indication of statistical heterogeneity, conducting a Chi^2 test, and calculating an I^2 statistic (Higgins 2003). A rough guide to interpretation of the I^2 statistic in the context of meta-analyses of randomized trials is as follows (Deeks 2022):

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity*;
- 50% to 90%: may represent substantial heterogeneity*;
- 75% to 100%: considerable heterogeneity*.

*The importance of the observed value of I^2 depends on

- magnitude and direction of effects, and
- strength of evidence for heterogeneity (e.g. P value from the Chi^2 test, or a CI for I^2 (uncertainty in the value of I^2 is substantial when the number of studies is small).

We deemed a meta-analysis to have substantial heterogeneity if its Chi^2 P value is less than 0.10 and its I^2 statistic is greater than 50%.

Assessment of reporting biases

We created a funnel plot for each meta-analysis that included 10 or more studies and looked to see if any funnel plot appeared asymmetrical. We judged a meta-analysis with an asymmetrical funnel plot to be potentially biased by small-study effects or reporting bias.

Data synthesis

For this update, we mainly used Review Manager (RevMan) Version 5.4 software (Review Manager 2020), and RevMan Web (RevMan Web 2022), to update all meta-analyses. We used Mantel-Haenszel methods to meta-analyze dichotomous data that could be combined directly in RevMan. In the previous version of this review, if studies reported dichotomous data in multiple formats that could not be combined in RevMan, we used Comprehensive Meta-Analysis Version 2 software (Borenstein 2005), to calculate log RRs and SEs for the data, enter these log RRs and SEs into RevMan, and then meta-analyze these using inverse-variance methods (Deeks 2022). We also used the inverse-variance method to meta-analyze continuous data. We used fixed-effect methods for all meta-analyses. The reason for using the fixed-effect model was that although there may have been some differences across studies (for example, dose and population), the biological mechanism should have been similar across studies; therefore, we expected them to be estimating the same quantity. However, we conducted a sensitivity analysis in which we used random-effects methods (see Sensitivity analysis).

Subgroup analysis and investigation of heterogeneity

We conducted the following subgroup analyses for outcomes with at least 10 studies measuring the relevant characteristic. We report a Chi^2 test for each analysis to determine whether or not the effects of zinc are different for the following subgroups.

- Country income level: low- and middle-income countries versus high-income countries, as defined by the World Bank's country income classification system (World Bank 2011)
- Age: children aged six months to under one year, versus one year to under five years, versus five years to under 13 years
- Stunting: children with a height/length-for-age z-score of less than −2 versus children with a height-for-age z-score of −2 of greater (per WHO definition, as outlined in Appendix 1)
- Dose: daily dose equivalent less than 5 mg per day, versus 5 mg to under 10 mg, versus 10 mg to under 15 mg, versus 15 mg to under 20 mg, versus 20 mg or more per day
- Duration: supplementation lasting zero to five months, versus six to 11 months, versus 12 months or more
- Iron co-interventions: iron + zinc versus iron alone, versus zinc versus no zinc supplementation
- Formulation: solution versus pill and/or tablet versus capsule versus powder

We attempted all of these subgroup analysis where enough data (at least 10 studies) were available for a particular outcome.

Sensitivity analysis

We conducted the following sensitivity analysis to examine whether or not our findings were robust to certain decisions we made while conducting the review.

- We repeated the analyses using random-effects method.

We had planned other sensitivity analyses based on imputation of ICC and risk of bias, but we did not conduct them. We report the reasons and unused methods in the Differences between protocol and review section and Appendix 3 respectively.

We performed post hoc sensitivity analyses based on presentation of data from the included studies for the comparison 'zinc versus no zinc' for the following:

- all-cause hospitalization
- incidence of all-cause diarrhea
- and hospitalization due to diarrhea.

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to evaluate the certainty of evidence for the following outcomes (Schünemann 2013):

- all-cause mortality
- cause-specific mortality: all-cause diarrhea, LRTI, and malaria
- the incidence of all-cause diarrhea
- the incidence of LRTI
- length/height
- participants with one or more vomiting episode.

One review author (AI) created a summary of findings table for the main comparison, zinc versus no zinc, using GRADEpro GDT software. We graded the overall certainty of the evidence for an outcome as high, moderate, low, or very low. We downgraded the certainty of evidence if there were significant issues related to the risk of bias, inconsistency, indirectness, imprecision, or other concerns such as publication bias (Schünemann 2013). Time points of the outcomes ranged from two to 80 weeks. The section on Measures of treatment effect describes the measures reported in the Summary of findings 1 and other outcomes.

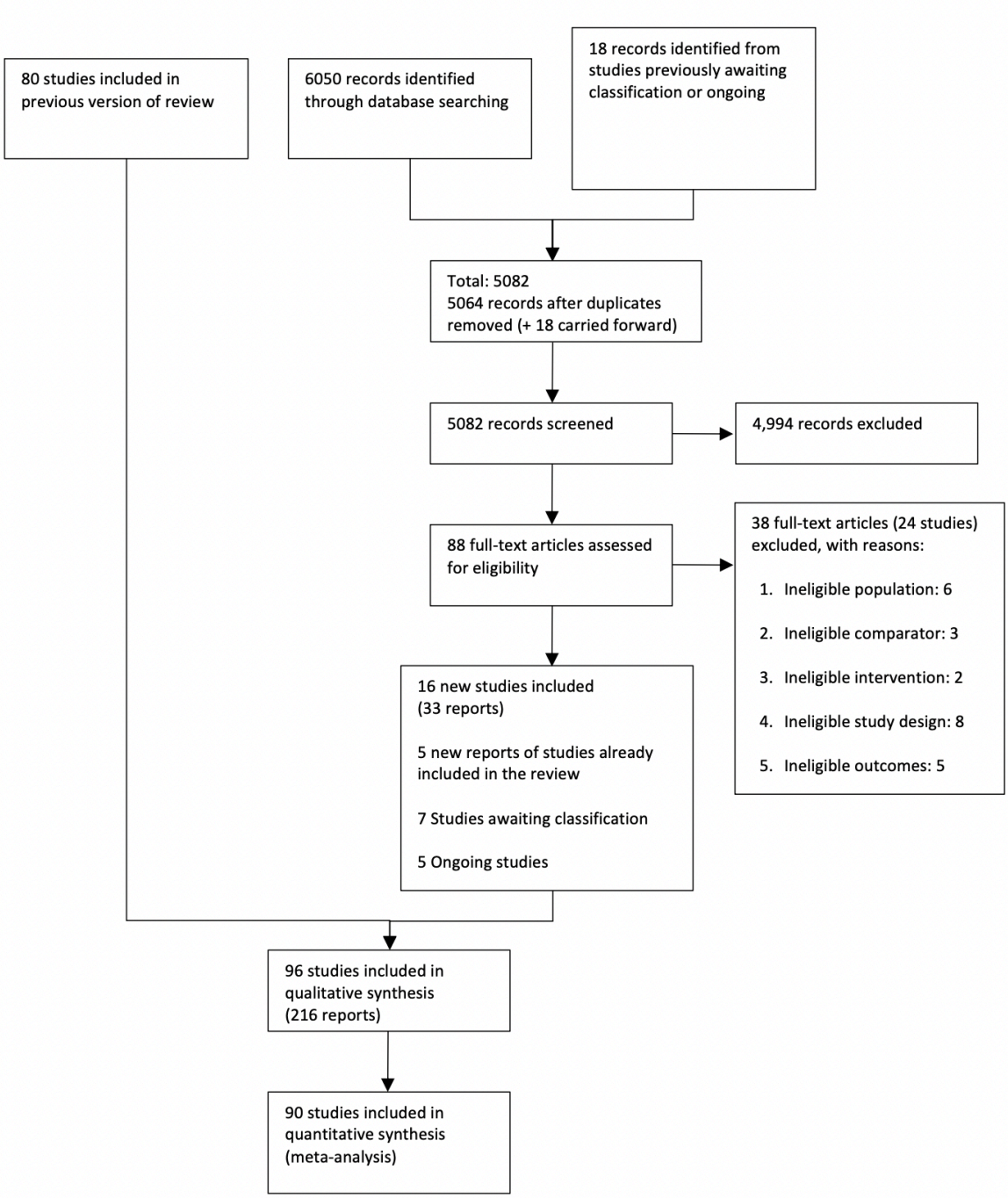
RESULTS

Description of studies

Results of the search

For this update, electronic searches identified 6050 records; 5064 records remained after duplicates were removed. From these, we identified 87 relevant citations and reviewed the full texts. We excluded 24 studies (38 reports) and included 16 new studies from 33 reports; 14 of these were identified from the updated searches and two were carried forward from the previous review in which they were ongoing. In addition, we identified four new reports of four previously included studies (Malik 2014; Sampaio 2013; Vakili 2015; Wessells 2012), five ongoing studies and seven studies awaiting classification (Figure 1). We combined these studies with those previously identified for this review, and for this update we have included a total of 96 studies (16 new) and excluded a total of 38 studies (24 new); we found 5 ongoing studies, and 7 studies awaiting classification.

Figure 1. PRISMA flow diagram



Included studies

The previous version of this review included 80 studies from 177 reports comparing zinc versus placebo or zinc with a co-intervention versus the co-intervention alone (Mayo-Wilson 2014). This update includes 16 new studies (from 33 reports) (Abdollahi 2014; Abdollahi 2019; Barffour 2019; Becquey 2016; Berger 2015; Bertinato 2013; Caulfield 2013; Fares 2021; Hess 2015; Isdiany 2021; Islam 2022; Kaseb 2013; Khodashenas 2015; Kusumastuti 2018; Mandlik 2020; Rerksuppaphol 2018), two of which were included in the previous review as ongoing (Becquey 2016; Caulfield 2013). We also found four new reports of four studies included in the previous review (Malik 2014; Sampaio 2013; Vakili 2015; Wessells 2012), bringing the total included studies in this review to 96 (215 reports). Sixteen of the 96 included studies contributed to two comparisons, resulting in 112 total comparisons.

Forty-four studies were reported in more than one publication or paper. Six studies were published in non-English languages: two studies written in Spanish, one in Chinese, and three in Portuguese.

Six studies, all of which were also included in the previous version of this review, did not contribute to any meta-analyses because they did not report any outcomes of interest to this review or because they did not report sufficient data (Ahmed 2009a; Castillo-Durán 2002; Marinho 1991; Sandstead 1998; Sanjur 1990; Shah 2011). A Characteristics of included studies table describes each included study in greater detail.

Design

In the previous version of this review, there were two cross-over trials, for which we analyzed data from the first period only (Garcia 1998; Hong 1982). This update includes no new cross-over trials.

Nine studies in the previous version of this review were cluster-RCTs (Bhandari 2007; Chen 2012; Gupta 2007; Hettiarachchi 2008; Sandstead 1998; Sazawal 2006; Soofi 2013; Tielsch 2006; Tupe 2009). This update includes four new studies that were cluster-RCTs (Becquey 2016; Hess 2015; Abdollahi 2019; Mandlik 2020). In the previous version of the review (Mayo-Wilson 2014), our team performed cluster adjustments for four studies (Bhandari 2007; Gupta 2007; Hettiarachchi 2008; Tupe 2009). All the newly added cluster trials were adjusted for cluster design with a design effect of 1.5, so we did not do any further adjustments for their data into the meta-analyses.

Sample sizes

With the addition of 16 studies, this review includes 219,584 eligible participants from a total of 96 included studies. Sample sizes of included studies ranged from 21 to 72,438 eligible participants. The five largest studies in this review accounted for 86% of the eligible participants (Bhandari 2007; Hess 2015; Islam 2022; Sazawal 2006; Tielsch 2006). Participants were approximately evenly split between zinc supplementation and control groups.

Setting

Thirty-four countries are represented amongst the studies included in this review. Eighty-seven studies (91%) were conducted in low- or middle-income countries: 47 in Asia, 27 in Latin America and the Caribbean, 12 in sub-Saharan Africa, and one in North Africa. Nine were conducted in North America or Europe. The countries in which the most studies were conducted were Bangladesh and India, with eight studies conducted in each country. The four largest studies took place in Bangladesh, India, Nepal, and Zanzibar (a semi-autonomous region of Tanzania). Among the 82 studies that described their setting, 49 were conducted in urban or peri-urban areas, 27 in rural areas, and six in both urban and rural areas.

Participants

Seventy-eight studies reported mean participant age at baseline. Most participants in this review were under five years of age. Of the 93 studies that could be classified into an age subgroup, only 31 were in the five to 13 years-of-age category. Ninety-one studies reported the gender of participants, which was usually equally divided. Five studies however included only boys (Bertinato 2013; Dehbozorgi 2007; Garcia 1998; Gibson 1989; Khodashenas 2015), and two included girls only (Berger 2015; Tupe 2009).

Fifty-nine studies reported the mean height-for-age z-score of their participants at baseline. The height-for-age z scores ranged from −2.9 to 0.577. Both stunted and non-stunted children were included in 51 studies; seven included only stunted children, 10 included only non-stunted children, and 28 did not specify whether or not their participants were stunted. Fifty-five studies reported the mean baseline plasma or serum zinc concentration.

Interventions

Studies that reported the formulation of their zinc supplementation provided zinc as a solution or syrup (51), pill or tablet (26), capsule (6), or powder (2). One study provided zinc as a syrup to one study group and as a tablet to another study group (Wessells 2012). Another two studies (Hess 2015; Islam 2022), provided zinc as either part of a paste or as a tablet, or as part of a powder or as a tablet, respectively. Studies that reported the chemical compound of their zinc supplementation provided zinc as sulfate (55), gluconate (15), acetate (6), and other compounds (9).

Studies provided zinc for less than two months (10), from two months to less than six months (27), from six months to less than 12 months (42), and for 11 months or more (17). Thirty-two studies provided zinc for six months and 13 provided zinc for 12 months. Studies that reported the frequency of zinc supplementation had frequencies ranging from twice daily to weekly. Two studies provided zinc twice daily (Bertinato 2013; Hess 2015), 63 studies provided zinc daily, and 11 weekly. One study (Islam 2022), provided zinc to one study group daily for two weeks, then not again until 12 weeks later, at which point it was once again administered daily for two weeks. Studies that could be classified based on zinc dose administered daily dose equivalents of less than 5 mg (5), 5 mg to less than 10 mg (25), 10 mg to less than 15 mg (36), 15 mg to less than 20 mg (9), and 20 mg or more (14).

Twenty studies were factorial. Among both factorial and non-factorial studies in this review, there were 119 eligible comparisons. Of these eligible comparisons, 58 (49%) included a co-intervention received by both the zinc and the control groups. Common co-interventions were iron, vitamin A, or multivitamin supplementation.

Comparators and co-interventions

Of the 96 included studies, 74 of the studies had two study arms, consisting of one group providing zinc supplementation and another group as control that either received no zinc or placebo. Twenty-two studies contained four study arms, two of which received zinc supplementation and two of which did not.

Fifty-four studies included co-interventions; in all but one of these studies, the co-intervention was identical for both the zinc and no zinc supplementation groups (in one study, (Becquey 2016), the co-interventions differed slightly, such that the zinc supplementation group received a placebo tablet for 10 days in the case of a diarrhea episode). Eighteen of these studies included two or more co-interventions. The most common co-intervention was iron, which was given in 26 of the studies. Thirteen of the studies included vitamin A as a co-intervention, while six included the use of multiple micronutrients or a micronutrient mixture and five included the use of a multivitamin. Four studies included a co-intervention containing folic acid, and two studies each included the use of vitamin B and copper.

Time points of outcome measure

Studies observed outcomes at a median time period of 26 weeks after randomization, with follow-up periods ranging between two and 80 weeks.

Excluded studies

In this update, we excluded 24 studies that came close to meeting the inclusion criteria but were ultimately deemed ineligible, resulting in a total of 39 excluded studies (see Characteristics of excluded studies). We excluded studies because of ineligible population (12), ineligible comparator (6), ineligible intervention (4), ineligible study design (11), and ineligible outcomes (6).

Ongoing studies

We identified 11 likely eligible ongoing or completed studies in the previous version of this review. Two ongoing studies were completed and are now included in this version of the review (Becquey 2016; Caulfield 2013). One previously ongoing study (NCT00967551) is now published and included as Sampaio 2013 (previously the included study Cole 2021). Overall, there are five remaining ongoing studies (NCT00228254; NCT00374023; NCT01306097; NCT01911260; NCT03098810). These studies are described in Characteristics of ongoing studies.

Studies awaiting classification

We were unable to definitively classify seven studies as eligible or ineligible (Chicourel 2001; Jimenez 2000; Long 2013; Mitter 2009; Sanchez 2014; Smith 1985; Surono 2014). These studies are described in Characteristics of studies awaiting classification.

Risk of bias in included studies

We used the Cochrane tool for assessing risk of bias to judge each included study as being at low, high, or unclear risk of bias in five domains (Higgins 2011). These judgments are summarized in Figure 2 and Figure 3. Detailed justifications for each judgment are listed in the Characteristics of included studies.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. The green circle indicatio low risk of bias, yellow circle shows the unclear risk and the red circle shows high risk of bias.

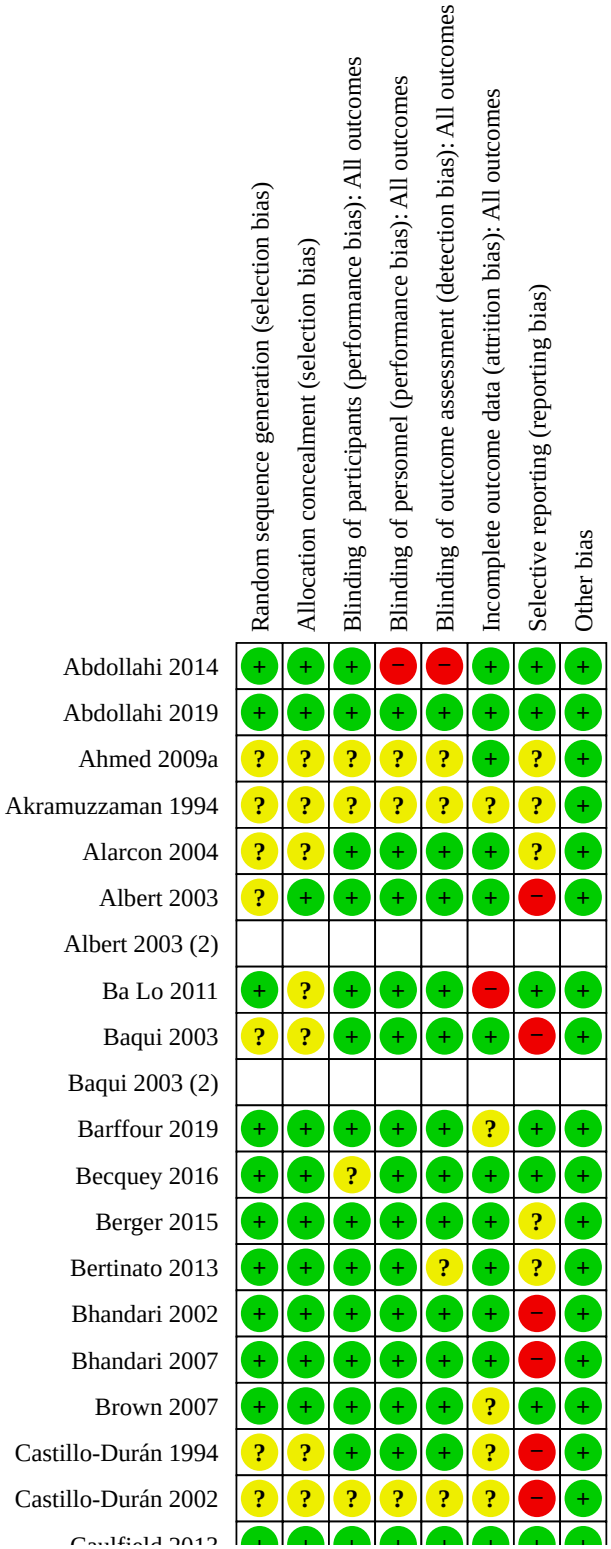
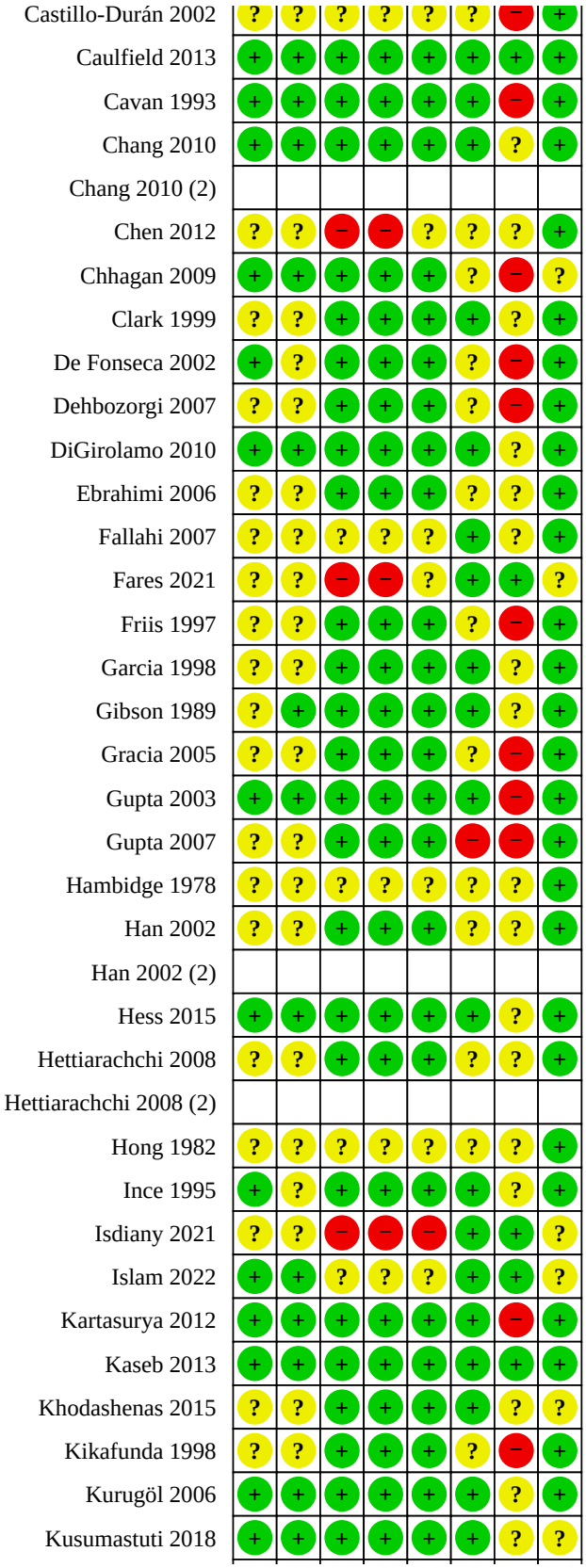


Figure 2. (Continued)



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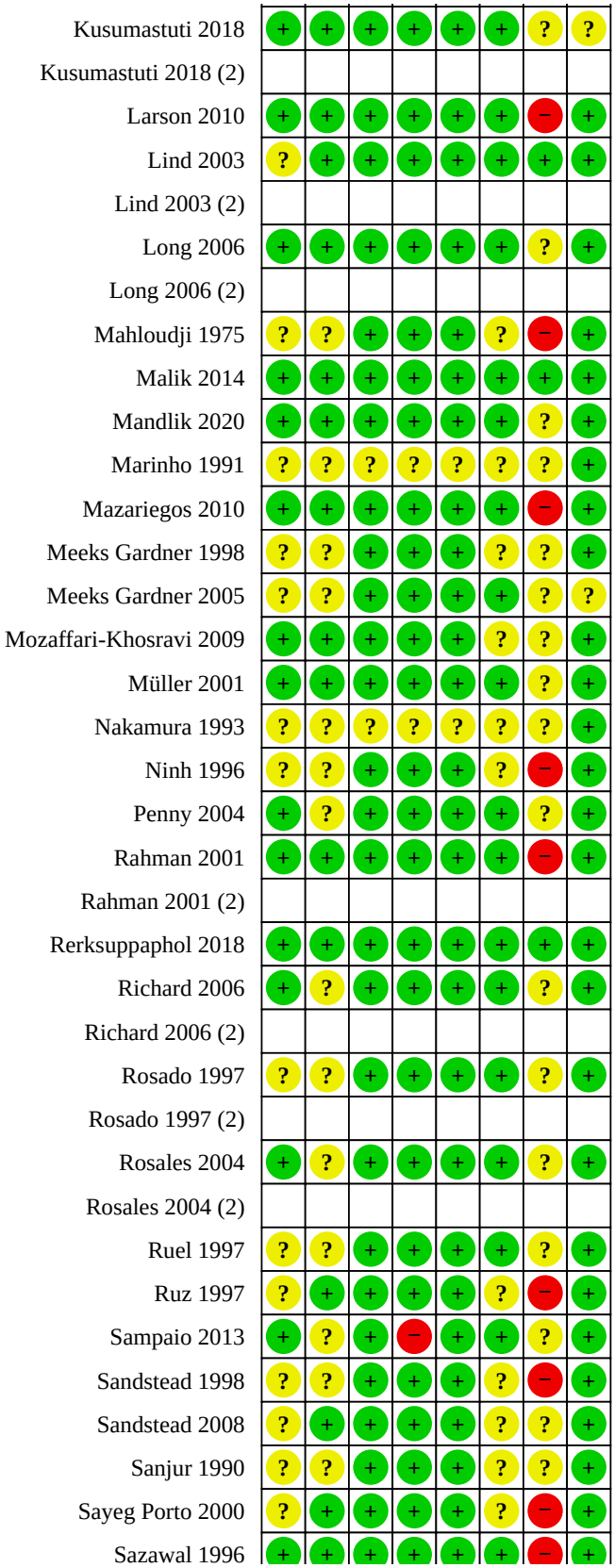

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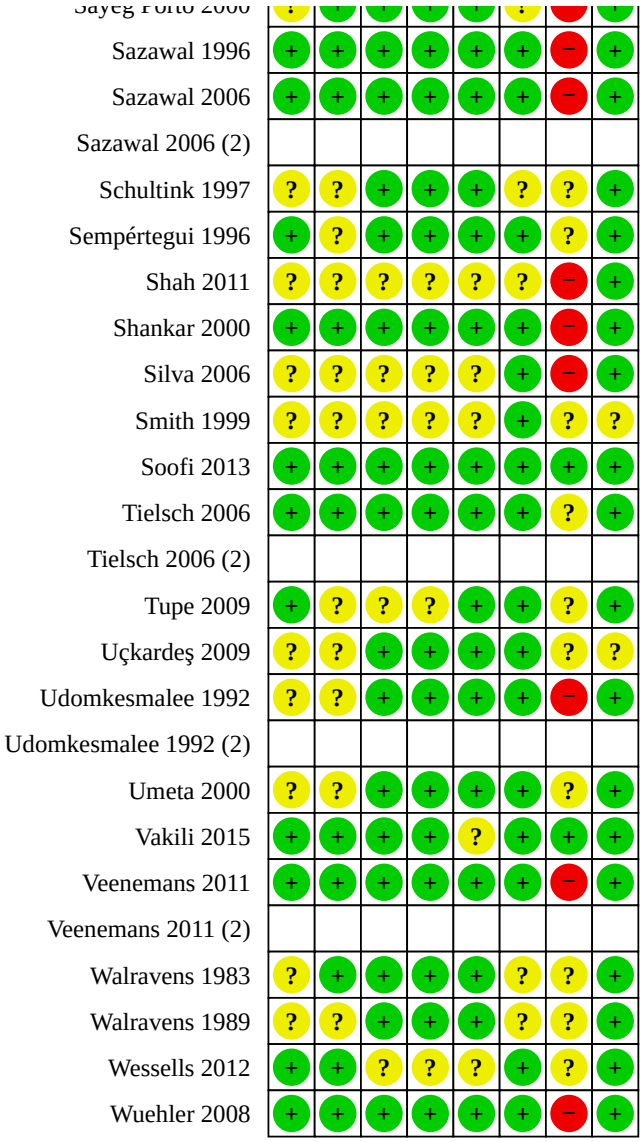
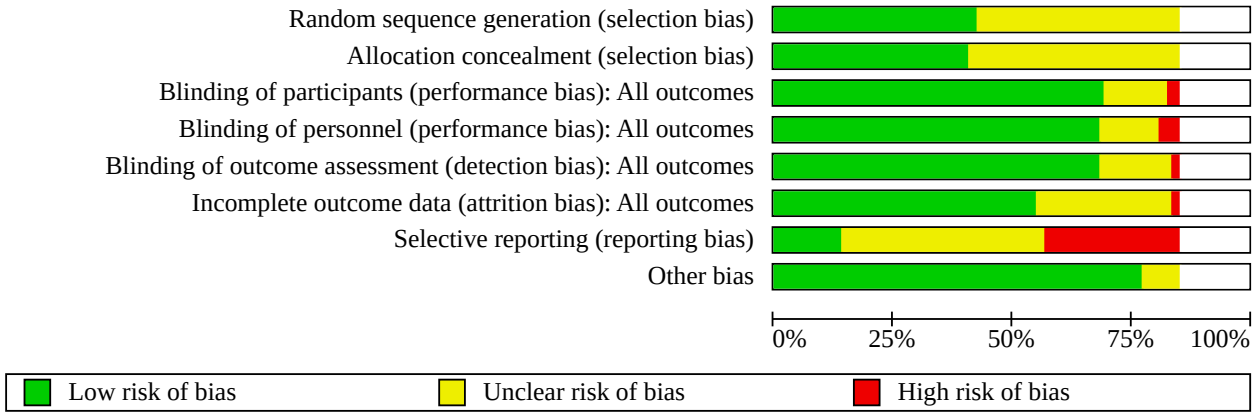


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



Allocation

Random sequence generation

Forty-eight studies were at low risk of bias for random sequence generation, and 48 were at unclear risk. Of the 48 studies at low risk of bias, 23 used a computer random number generator to randomize participants, eight used a random number table, four used drawing of lots, and one used a coin toss. Eleven of these 48 studies did not refer explicitly to any of these sequence generation methods but did report the use of permuted blocks.

Allocation concealment

Forty-six studies were at low risk of bias for allocation concealment, and 50 were at unclear risk. Among studies at low risk, methods such as central randomization (that is, randomization by someone not involved with enrolling participants) were used to conceal allocation. Furthermore, though allocation concealment and blinding are distinct bias domains, some have argued that "blinded trials of drugs are very likely to be concealed" (Devereaux 2004; Schünemann 2013). In this review, the risk of bias related to blinding did not seem substantial, nor did the risk of bias related to allocation concealment.

Blinding

Seventy-eight studies were at low risk of bias for blinding of participants, 15 were at unclear risk, and three studies were at high risk. Seventy-seven studies were at low risk of bias or blinding of personnel, 14 were at unclear risk, and five were at high risk. Seventy-seven studies were at low risk of bias for blinding of outcome assessment, 17 were at unclear risk, and two were at high risk. To ensure blinding, studies used strategies such as providing the control group with a placebo of identical appearance and taste to that of zinc.

Incomplete outcome data

Sixty-two studies were at low risk of bias for incomplete outcome data, 32 were at unclear risk, and two were at high risk. We were able to calculate an approximate percentage of study participants for 86 studies with missing data for non-mortality outcomes. Of these, 42 studies had less than 10% missing data, 27 had 10% to less than 20% missing data, and 17 studies had at least 20% missing data. Amounts of and reasons for missing data were generally balanced between groups.

Selective reporting

Sixteen studies were at low risk of bias for selective reporting, 48 were at unclear risk, and 32 were at high risk. For 35 of the studies at unclear risk, we could not obtain a study protocol and it was not possible to confirm whether their outcomes were reported as planned in their protocols. For several of the studies at high risk of bias, study reports stated that certain outcomes were measured, but no numerical data disaggregated by study group were reported for these outcomes, or insufficient data were reported to include them in a meta-analysis. Among the most common missing outcomes were biochemical, growth, and side-effect outcomes.

Other potential sources of bias

Other potential sources of bias appeared to be minimal and unlikely to impact the results of this review; 87 studies were at low risk of bias and nine were at unclear risk.

Effects of interventions

See: **Summary of findings 1** Zinc supplementation compared to no zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age

This section describes the results of the meta-analysis of each outcome in this review. We have presented updated results for outcomes that included data from newly added studies. For dichotomous outcomes, a risk ratio (RR) less than 1 favors the intervention, and for continuous outcomes, a standardized mean difference (SMD) greater than 0 favors the intervention. We have presented results as the pooled effect estimate followed by the lower and upper limits of its 95% confidence interval (CI) in brackets. Within forest plots, outcome data for each eligible comparison are in a separate row. For instance, in a factorial study, the zinc versus placebo comparison would be in one row of a forest plot, and the zinc plus vitamin A versus vitamin A comparison would be in another row. Within the Data and analyses tables, each eligible comparison is counted as a separate study. When

describing results, we report the number of studies and not the number of comparisons in a dataset.

Comparison 1: Zinc versus no zinc

Primary outcomes

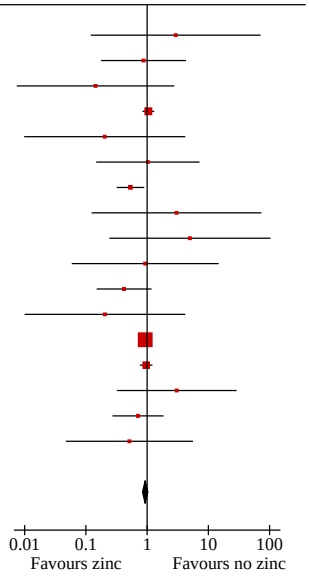
1. All-cause mortality

The analysis of all-cause mortality included 16 studies, one of which included two comparisons (total number of comparisons = 17), comprising 143,474 participants (65% of participants). High-certainty evidence showed that preventive zinc supplementation results in little to no difference on reduction of all-cause mortality compared to no zinc (RR 0.93, 95% CI 0.84 to 1.03; P = 0.15, I^2 = 0%, Figure 4; Analysis 1.1; Summary of findings 1). In this update, we included two new studies (Becquey 2016; Hess 2015).

Figure 4. Forsest plot for effect of preventive zinc supplementation all-cause mortality

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	1.07361099	1.62916074	161	157	0.1%	2.93 [0.12 , 71.29]
Becquey 2016	-0.1346	0.815	897	784	0.4%	0.87 [0.18 , 4.32]
Bhandari 2002	-1.93942189	1.51132135	1228	1236	0.1%	0.14 [0.01 , 2.78]
Bhandari 2007	0.04493755	0.11212408	36293	36145	20.3%	1.05 [0.84 , 1.30]
Chang 2010	-1.59447504	1.54597037	198	201	0.1%	0.20 [0.01 , 4.20]
Chhagan 2009	0.02643326	0.99114872	112	115	0.3%	1.03 [0.15 , 7.16]
Hess 2015	-0.6266	0.2642	1832	1387	3.7%	0.53 [0.32 , 0.90]
Larson 2010	1.10424611	1.6295395	176	177	0.1%	3.02 [0.12 , 73.56]
Lind 2003	1.60943791	1.54541389	170	170	0.1%	5.00 [0.24 , 103.38]
Malik 2014	-0.0736	1.409	141	131	0.1%	0.93 [0.06 , 14.70]
Müller 2001	-0.86670956	0.52677681	341	344	0.9%	0.42 [0.15 , 1.18]
Penny 2004	-1.58534036	1.54139551	81	83	0.1%	0.20 [0.01 , 4.20]
Sazawal 2006	-0.07257069	0.06862114	21274	21272	54.3%	0.93 [0.81 , 1.06]
Sazawal 2006 (2)	-0.03756725	0.11932628	8120	7950	18.0%	0.96 [0.76 , 1.22]
Shankar 2000	1.11321109	1.14836145	136	138	0.2%	3.04 [0.32 , 28.90]
Soofi 2013	-0.342704984498532	0.490437295227866	853	865	1.1%	0.71 [0.27 , 1.86]
Veenemans 2011	-0.6670019	1.2193957	151	155	0.2%	0.51 [0.05 , 5.60]
Total (95% CI)			**72164**	**71310**	**100.0%**	**0.93 [0.84 , 1.03]**

Heterogeneity: Chi² = 15.14, df = 16 (P = 0.51); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)
Test for subgroup differences: Not applicable



A funnel plot appeared symmetrical (Appendix 4).

Sensitivity and subgroup analyses

The effects of zinc supplementation on all-cause mortality did not differ among subgroups based on age (test for subgroup difference: Chi^2 = 0.83, P = 0.36; Analysis 2.1), dose (test for subgroup differences: Chi^2 = 3.63, P = 0.30; Analysis 2.2), duration (test for subgroup differences: Chi^2 = 5.1, P = 0.08 ; Analysis 2.3), iron co-intervention (test for subgroup differences: Chi^2 = 2.01, P = 0.16; Analysis 2.4), formulation (test for subgroup differences: Chi^2 = 0.49, P = 0.92; Analysis 2.5) but did differ for subgroup of duration (test for subgroup differences: Chi^2 = 5.17, P = 0.08).

A sensitivity analysis based on the choice of the model showed similar results for the random-effects model (RR 0.93, 95% CI 0.84 to 1.03).

2. Cause-specific mortality

2.1. Mortality due to all-cause diarrhea

Four studies, involving 132,321 participants (60% of participants in the review), showed moderate-certainty evidence that preventive zinc supplementation has little to no effect on mortality due to diarrhea (RR 0.95, 95% CI 0.69 to 1.31; P = 0.75, I^2 = 0%; Analysis 1.2). We downgraded the certainty of the evidence for imprecision as the confidence interval around the summary estimate was wide and included a null effect (Summary of findings 1). We did not add any new studies to this analysis in this update.

- We did not perform any subgroup analysis for this outcome as there were fewer than 10 studies in the analysis.
- A sensitivity analysis based on a random-effects model showed similar results (RR 0.95, 95% CI 0.69 to 1.31).

2.2. Mortality due to lower respiratory tract infection (LRTI)

Three studies including 132,063 participants (60% of participants in the review), showed moderate-certainty evidence that preventive zinc supplementation probably decreases mortality due to LRTI, however, the confidence interval was wide and a possible increased risk of mortality cannot be excluded (RR 0.86, 95% CI 0.64 to 1.15; P = 0.31, I^2 = 0%; Analysis 1.3). We downgraded the certainty of the evidence for imprecision because the confidence interval around the summary estimate was wide and included a null effect (Summary of findings 1). We did not add any new studies to this analysis in this update.

- We did not perform any subgroup analysis for this outcome as there were fewer than 10 studies in the analysis.
- A sensitivity analysis based on a random-effects model showed similar results (RR 0.86, 95% CI 0.64 to 1.15).

2.3. Mortality due to malaria

Two studies (Sazawal 2006; Shankar 2000), including 42,818 participants (19% of participants in the review), showed moderate-certainty evidence that preventive zinc supplementation probably reduces mortality due to malaria, however, the confidence intervals around the summary estimates were wide and we could not rule out possible increased risk of mortality due to malaria (RR 0.90, 95% CI 0.77 to 1.06; P = 0.20, I^2 = 0%; Analysis 1.4). We downgraded the certainty of the evidence due to imprecision of the summary estimate as the confidence interval around the summary estimate was wide and included a null effect (Summary of findings 1). We did not include any new studies in this analysis in this update.

- We did not perform any subgroup analysis for this outcome as there were fewer than 10 studies in the analysis.
- A sensitivity analysis based on a random-effects model showed similar results (RR 0.90, 95% CI 0.77 to 1.06).

Secondary outcomes

3. All-cause hospitalization

We included seven studies, three of which contributed two comparisons (total number of comparisons = 10) including a total of 93,817 participants (43% of participants in the review) and reported little to no overall effect of zinc supplementation on all-cause hospitalization (RR 1.03, 95% CI 0.96 to 1.10; P = 0.41, I^2 = 48%; Analysis 1.5). One new study added data to this outcome in this update of the review (Islam 2022).

Sensitivity analyses

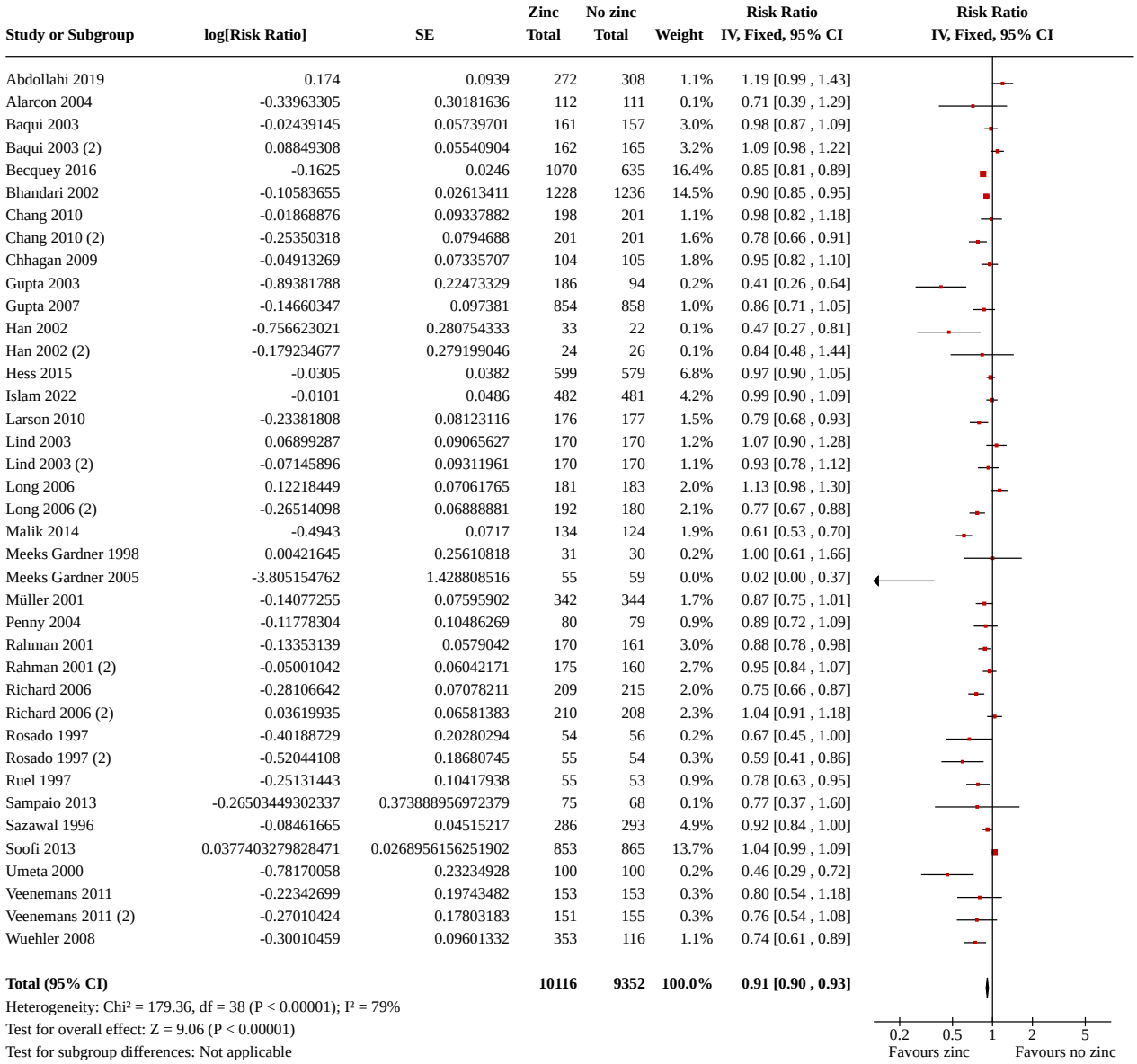
In the previous analysis, three studies reported hospitalization data as the number of participants ever hospitalized rather than as the number of hospitalizations (Bhandari 2002; Chhagan 2009; Meeks Gardner 1998). A post-hoc sensitivity analysis by excluding these from the analysis did not change the result (RR 1.04, 95% CI 0.96 to 1.11). The result also remained similar when calculated using a random-effects model (RR 0.94, 95% CI 0.80 to 1.11).

4. Diarrhea

4.1. Incidence of all-cause diarrhea

Thirty studies, nine of which included two comparisons (total number of comparisons = 39), comprising 19,468 participants (9% of participants) were included in this analysis. moderate-certainty evidence showed that preventive zinc supplementation reduced incidence of diarrhea by 9% compared to control (RR 0.91, 95% CI 0.90 to 0.93; P < 0.00001, I^2 = 79%; Analysis 1.6, Figure 5). We downgraded the certainty of evidence due to substantial statistical heterogeneity (Summary of findings 1). We included four new studies in the analysis in this update (Abdollahi 2019; Becquey 2016; Hess 2015; Islam 2022).

Figure 5. Forest plot for effect of preventive zinc supplementation on inccidence of all-cause diarrhea



- Sensitivity and subgroup analyses
  - there was some evidence of funnel plot asymmetry (Appendix 4), with several smaller studies reporting unusually large reductions in all-cause diarrhea incidence. However, the result of this meta-analysis was similar when we used a random-effects model (RR 0.88, 95% CI 0.83 to 0.92), which suggests that the result was not strongly influenced by small-study effects.
  - Three studies in this meta-analysis had reported data as medians. We calculated the number of events considering the medians as means. A post hoc sensitivity analysis by excluding studies that reported medians did not change the result (RR 0.92, 95% CI 0.90 to 0.93; Meeks Gardner 1998; Meeks Gardner 2005; Ruel 1997).
  - Effects did not differ based on age (test for subgroup differences: Chi^2 = 2.24, P = 0.33) and duration (test for subgroup differences: Chi^2 = 0.54, P = 0.76).
  - Dose subgroups were different (test for subgroup differences: Chi^2 = 194.02, P < 0.00001), but there did not appear to be a coherent pattern of increasing or decreasing effect across doses: 0 mg to 5 mg (RR 0.95, 95% CI 0.89 to 1.01); 5 mg to 10 mg (RR 0.88, 95% CI 0.85 to 0.91); 10 mg to 15 mg (RR 0.96, 95% CI 0.93 to 1.00); 15 mg to 20 mg (RR 0.61, 95% CI 0.58 to 0.65); 20 mg or more (RR 0.90, 95% CI 0.87 to 0.94).
  - Formulation subgroups were different (test for subgroup differences: Chi^2 = 49.69, P < 0.00001), but most studies used a solution and effects generally favored intervention for solution (RR 0.85, 95% CI 0.82 to 0.87), pill/tablet (RR 0.90, 95% CI 0.87 to 0.93), and capsule (RR 0.78, 95% CI 0.60 to

1.01). There was no difference in effect in two studies using micronutrient powder (RR 1.04, 95% CI 0.98 to 1.09).

- Iron co-intervention subgroups were different (test for subgroup differences: Chi^2 = 50.00, P < 0.00001), with no benefit for the group that received iron (RR 1.00, 95% CI 0.96 to 1.05) and a reduction in all-cause diarrhea for the group that did not receive iron (RR 0.85, 95% CI 0.83 to 0.87).

4.2. Prevalence of all-cause diarrhea

Thirteen studies, two of which included two comparisons (total number of comparisons = 15) including 8519 participants (4% of participants in the review), revealed a 12% reduction in the prevalence of all-cause diarrhea (RR 0.88, 95% CI 0.86 to 0.90; P < 0.00001), though heterogeneity was considerable (P < 0.00001, I^2 = 88%; Analysis 1.7). Two studies in this meta-analysis reported data as medians rather than means, but excluding these from the analysis had no effect on the result (RR 0.88, 95% CI 0.87 to 0.90; Chhagan 2009; Ruel 1997).

- Sensitivity analyses
  - The result was robust when we used a random-effects model (RR 0.87, 95% CI 0.81 to 0.93). We created a funnel plot, which appeared symmetrical (Appendix 4).
- Subgroup analyses
  - Age subgroups were different (test for subgroup differences: Chi^2 = 30.52, P < 0.00001), with greater benefit in the older age group, but both effects favored the intervention: between 6 and 12 months (RR 0.96, 95% CI 0.93 to 1.00); between one and five years (RR 0.85, 95% CI 0.83 to 0.87).
  - Dose subgroups were different (test for subgroup differences: Chi^2 = 61.69, P < 0.00001), with potentially larger effects at higher doses: 0 mg to 5 mg (RR 1.00, 95% CI 0.92 to 1.08); 5 mg to 10 mg (RR 1.17, 95% CI 0.60 to 2.28); 10 mg to 15 mg (RR 0.93, 95% CI 0.90 to 0.96); 15 mg to 20 mg (RR 0.61, 95% CI 0.54 to 0.69), 20 mg or more (RR 0.85, 95% CI 0.82 to 0.87).
  - Duration subgroups were different: Chi^2 = 13.98, P < 0.00001, but there did not appear to be a coherent pattern of results; between zero and six months (RR 0.85, 95% CI 0.82 to 0.87); between 6 and 12 months (RR 0.92, 95% CI 0.89 to 0.95); 12 months or more (RR 0.88, 95% CI 0.74 to 1.03).
  - The subgroup analysis based on formulation showed a different effect (test for subgroup differences: Chi^2 = 13.99, P < 0.0009), but most studies used a solution and effects generally favored the intervention for solution (RR 0.88, 95% CI 0.85 to 0.90) and pill/tablet (RR 0.86, 95% CI 0.81 to 0.92). There was little to no effect in one study that used micronutrient powder (RR 1.03, 95% CI 0.95 to 1.12). The solution and tablet groups were consistent when the powder study was removed from the analysis.
  - Iron co-intervention subgroups were different (test for subgroup differences: Chi^2 = 3.97, P = 0.05), with little to no difference for the group that received iron (RR 0.96, 95% CI 0.88 to 1.05) and a moderate benefit for the group that did not receive iron (RR 0.88, 95% CI 0.86 to 0.90), but only three studies contributed to the first group.

4.3. Hospitalization due to all-cause diarrhea

Four studies, one of which reported two comparisons (total number of comparisons = 5), including 74,039 participants (34% of participants in the review) found no effect on hospitalization due to all-cause diarrhea (RR 1.03, 95% CI 0.87 to 1.22; P = 0.69), and there was moderate heterogeneity (P = 0.14, I^2 = 42%; Analysis 1.8).

- Sensitivity analysis
  - Excluding data from one study that reported hospitalization data as the number of participants ever hospitalized did not change the result (RR 1.03, 95% CI 0.87 to 1.22; Chhagan 2009).

4.4. Incidence of severe diarrhea

Nine studies, one of which reported two comparisons (total number of comparisons = 10), comprising 8810 participants (4% of participants in the review) revealed a 9% reduction compared to no zinc in incidence of severe diarrhea (RR 0.91, 95% CI 0.86 to 0.96; P = 0.0007, I^2 = 51%; Analysis 1.9). We added three new studies in this update (Becquey 2016; Hess 2015; Islam 2022).

4.5. Incidence of persistent diarrhea

Eight studies, two of which reported two comparisons (total number of comparisons = 10), comprising 7161 participants (3% of participants in the review) revealed that zinc supplementation was associated with a 28% decrease in the incidence of persistent diarrhea (RR 0.72, 95% CI 0.62 to 0.85; P < 0.0001, I^2 = 56%; Analysis 1.10). We included one new study in this update for this analysis (Islam 2022).

4.6. Prevalence of persistent diarrhea

Only one study was included in the previous version of the review, which reported two comparisons (Rahman 2001/Rahman 2001 (2); the total number of comparisons = 2), with 665 participants (< 1% of participants in this review), revealing a 30% reduction in the prevalence of persistent diarrhea (RR 0.70, 95% CI 0.64 to 0.76; P < 0.00001; Analysis 1.11).

5. Lower respiratory tract infection (LRTI)

5.1. Incidence of LRTI

Fourteen studies, six of which made two comparisons (total number of comparisons = 20), contributing 10,555 participants (5% of participants in this review) to a meta-analysis found no effect on LRTI incidence (RR 1.01, 95% CI 0.95 to 1.08; P = 0.74, I^2 = 11%; Analysis 1.12). We added two new studies to this analysis (Islam 2022; Sampaio 2013b. The certainty of the evidence was moderate; we downgraded the certainty of evidence due to the imprecision of the summary estimate. A funnel plot appeared symmetrical (Appendix 4).

- Subgroup analyses
  - Effects were not significantly heterogeneous across different ages (test for subgroup differences: Chi^2 = 0.84, P = 0.66), doses (test for subgroup differences: Chi^2 = 0.70, P = 0.70), durations (test for subgroup differences: Chi^2 = 0.45, P = 0.80), iron co-intervention (test for subgroup differences: Chi^2 = 0.18, P = 0.67), or formulations (test for subgroup differences: Chi^2 = 6.25, P = 0.10) subgroups.

5.2. Prevalence of LRTI

Three studies, one reporting two comparisons (total number of comparisons = 4), included 1955 participants (1% of participants in the review) and found that zinc supplementation was associated with a 20% increase in the prevalence of LRTI (RR 1.20, 95% CI 1.10 to 1.30; P < 0.0001, I^2 = 97%; Analysis 1.13).

- Sensitivity analysis
  - This increase in prevalence was similar when we used a random-effects model (RR 1.13, 95% CI 0.71 to 1.81). However, given that the three studies in this meta-analysis had sample sizes of 603, 666, and 686, it seems unlikely that small-study effects influenced the results. LRTI outcome criteria were similar across these studies, so LRTI criteria would not likely explain the difference between the random-effects and fixed-effect models. One possible explanation for this difference is that baseline population characteristics were different among the studies included in this meta-analysis, and some results were due to chance. For example, Rahman 2001/Rahman 2001 (2) had a lower average baseline height-for-age z-score (−2.41) than that of Müller 2001 (−1.6). Baseline risk of LRTI was different across the studies: Sazawal 1996 2.11 days per child-year, Müller 2001 1.56 days per child-year, Rahman 2001 2.94 days per child-year, and Rahman 2001 (2) 3.58 days per child-year.

5.3. Hospitalization due to LRTI

Three studies, one making two comparisons (total number of comparisons = 4), included 74,743 participants (34% of participants in this review) and found no effect on hospitalization due to LRTI (RR 1.10, 95% CI 0.93 to 1.30; P = 0.28). There was no heterogeneity (P = 0.95, I^2 = 0%; Analysis 1.14; Bhandari 2007; Chang 2010/Chang 2010 (2); Soofi 2013).

6. Malaria

6.1. Incidence of malaria

Six studies, two of which made two comparisons (total number of comparisons = 8), comprising 5290 participants (2% of participants in this review) found no effect on malaria incidence (RR 0.99, 95% CI 0.94 to 1.04; P = 0.68); heterogeneity was not significant (Chi^2 = 5.24, df = 7; P = 0.63, I^2 = 0%; Analysis 1.15). We added two new studies to this analysis in this update (Becquey 2016; Hess 2015).

6.2. Prevalence of malaria

One study with 661 participants (< 1% of participants in this review) reported no effect on malaria prevalence (RR 0.88, 95% CI, 0.47 to 1.64; P = 0.69; Analysis 1.16; Müller 2001).

7. Growth

7.1. Height

A total of 64 studies, 10 of which made two comparisons (total number of comparisons = 74), reported height for 20,720 participants (9% of participants in this review). Moderate-certainty evidence showed that preventive zinc supplementation led to a small increase in height (SMD 0.12, 95% CI 0.09 to 0.14; P < 0.00001, I^2 = 87%; Analysis 1.17; Figure 6). We downgraded the certainty of evidence due to substantial heterogeneity (Summary of findings 1). We added 13 new studies to this analysis in this update (Abdollahi 2014; Abdollahi 2019; Barffour 2019; Becquey 2016; Bertinato 2013; Hess 2015; Isdiany 2021; Islam 2022; Kaseb 2013; Khodashenas 2015; Kusumastuti 2018; Mandlik 2020; Rerksuppaphol 2018) and additional data were available from one of the previously included studies (Vakili 2015).

Figure 6. Forest plot for effect of zinc supplementation on height

Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No Zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2014	0.081207	0.082178	291	302	2.5%	0.08 [-0.08 , 0.24]
Abdollahi 2019	0.2262	0.0835	272	308	2.5%	0.23 [0.06 , 0.39]
Akramuzzaman 1994	0	0.14216714	93	104	0.8%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.175624	0.13685249	109	104	0.9%	0.18 [-0.09 , 0.44]
Baqui 2003	-0.03691	0.11899992	141	140	1.2%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.03759	0.11833	135	150	1.2%	-0.04 [-0.27 , 0.19]
Barffour 2019	0	0.052	740	739	6.4%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	751	704	19.7%	0.09 [0.04 , 0.15]
Bertinato 2013	-0.60195	0.377514	27	10	0.1%	-0.60 [-1.34 , 0.14]
Bhandari 2002	-0.04597	0.04238854	1093	1133	9.6%	-0.05 [-0.13 , 0.04]
Bhandari 2007	0.142734	0.0697166	448	427	3.5%	0.14 [0.01 , 0.28]
Brown 2007	0.028317	0.15073647	83	92	0.8%	0.03 [-0.27 , 0.32]
Castillo-Durán 1994	0.35835	0.313	19	21	0.2%	0.36 [-0.26 , 0.97]
Cavan 1993	-0.19094	0.15976556	76	80	0.7%	-0.19 [-0.50 , 0.12]
Chen 2012	0.152273	0.148307705	88	93	0.8%	0.15 [-0.14 , 0.44]
Clark 1999	-0.49205	0.295419	25	21	0.2%	-0.49 [-1.07 , 0.09]
De Fonseca 2002	-0.16854	0.19990018	51	48	0.4%	-0.17 [-0.56 , 0.22]
Dehbozorgi 2007	0.308	0.2598	30	30	0.3%	0.31 [-0.20 , 0.82]
DiGirolamo 2010	-0.09681	0.07476273	360	355	3.1%	-0.10 [-0.24 , 0.05]
Ebrahimi 2006	1.261145	0.07721922	386	418	2.9%	1.26 [1.11 , 1.41]
Friis 1997	0.038991	0.12009587	141	135	1.2%	0.04 [-0.20 , 0.27]
Garcia 1998	0.105848	0.34006946	16	17	0.1%	0.11 [-0.56 , 0.77]
Gibson 1989	0.075924	0.25493989	30	30	0.3%	0.08 [-0.42 , 0.58]
Gracia 2005	-0.01896	0.13144479	115	115	1.0%	-0.02 [-0.28 , 0.24]
Hambidge 1978	0.313559	0.24369413	36	31	0.3%	0.31 [-0.16 , 0.79]
Han 2002	0.977632	0.26685037	34	28	0.2%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.03792	0.26134196	28	29	0.3%	-0.04 [-0.55 , 0.47]
Hess 2015	0.0098	0.0573	617	602	5.2%	0.01 [-0.10 , 0.12]
Hettiarachchi 2008	0.43865	0.21702312	99	40	0.4%	0.44 [0.01 , 0.86]
Hettiarachchi 2008 (2)	0.139306	0.23580261	113	30	0.3%	0.14 [-0.32 , 0.60]
Hong 1982	1.094003	0.18644996	64	67	0.5%	1.09 [0.73 , 1.46]
Ince 1995	0.450283	0.40793136	16	9	0.1%	0.45 [-0.35 , 1.25]
Isdiany 2021	-0.2724	0.3671	15	15	0.1%	-0.27 [-0.99 , 0.45]
Islam 2022	0.9992	0.071	441	453	3.4%	1.00 [0.86 , 1.14]
Kaseb 2013	-0.12359	0.205411	48	47	0.4%	-0.12 [-0.53 , 0.28]
Khodashenas 2015	-0.00828	0.298217	23	22	0.2%	-0.01 [-0.59 , 0.58]
Kikafunda 1998	-0.02126	0.18705861	59	54	0.5%	-0.02 [-0.39 , 0.35]
Kusumastuti 2018	-1.1518	0.3738	17	17	0.1%	-1.15 [-1.88 , -0.42]
Kusumastuti 2018 (2)	-1.1878	0.3757	17	17	0.1%	-1.19 [-1.92 , -0.45]
Lind 2003	0.044824	0.11052917	162	164	1.4%	0.04 [-0.17 , 0.26]
Lind 2003 (2)	-0.26456	0.11134035	161	163	1.4%	-0.26 [-0.48 , -0.05]
Long 2006	0.158402	0.11813857	144	142	1.2%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016	0.11663237	149	144	1.3%	-0.10 [-0.33 , 0.13]
Mandlik 2020	-0.1172	0.1284	124	119	1.0%	-0.12 [-0.37 , 0.13]
Mazariegos 2010	-0.04455	0.10189635	188	196	1.7%	-0.04 [-0.24 , 0.16]
Meeks Gardner 1998	0.117835	0.26252076	31	26	0.2%	0.12 [-0.40 , 0.63]
Meeks Gardner 2005	-0.23589	0.18682894	55	59	0.5%	-0.24 [-0.60 , 0.13]
Mozaffari-Khosravi 2009	0.884532	0.22577077	40	45	0.3%	0.88 [0.44 , 1.33]
Müller 2001	0.099886	0.07775177	332	329	2.8%	0.10 [-0.05 , 0.25]
Nakamura 1993	0.960095	0.44484717	10	11	0.1%	0.96 [0.09 , 1.83]
Ninh 1996	0.346345	0.16590035	73	73	0.6%	0.35 [0.02 , 0.67]
Penny 2004	0.137246	0.16491512	71	75	0.6%	0.14 [-0.19 , 0.46]
Rahman 2001	-0.00867	0.11069586	165	160	1.4%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.20323	0.11056287	171	157	1.4%	-0.20 [-0.42 , 0.01]
Rerksuppaphol 2018	0.437487	0.177583	66	64	0.5%	0.44 [0.09 , 0.79]
Richard 2006	0.124046	0.10262789	190	189	1.6%	0.12 [-0.08 , 0.33]
Richard 2006 (2)	0.011477	0.10286111	195	182	1.6%	0.01 [-0.19 , 0.21]
Rosado 1997	0.078132	0.20362659	31	47	0.4%	0.08 [-0.32 , 0.48]
Rosado 1997 (2)	0.118125	0.19963612	49	50	0.4%	0.12 [-0.27 , 0.51]
Ruel 1997	0.05884	0.21022626	45	44	0.4%	0.06 [-0.35 , 0.47]
Ruz 1997	0.258665	0.20129773	49	49	0.4%	0.26 [-0.14 , 0.65]
Sayeg Porto 2000	0.466375	0.45563575	9	9	0.1%	0.47 [-0.43 , 1.36]

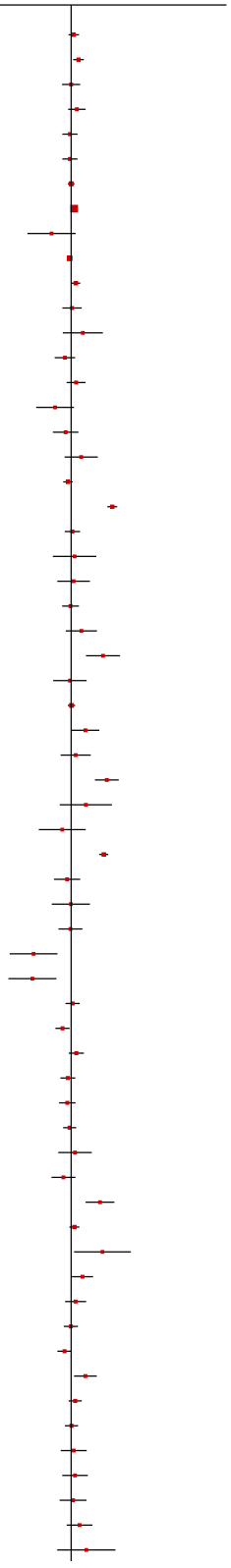
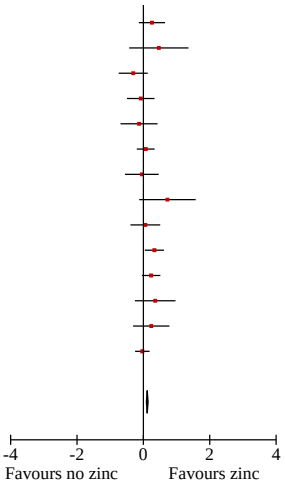


Figure 6. (Continued)

Ruz 1997	0.258665	0.20129773	49	49	0.4%	0.26 [-0.14 , 0.65]
Sayeg Porto 2000	0.466375	0.45563575	9	9	0.1%	0.47 [-0.43 , 1.36]
Sazawal 2006	-0.30538	0.22312277	44	58	0.3%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.07944	0.21183638	56	54	0.4%	-0.08 [-0.49 , 0.34]
Sempértegui 1996	-0.13048	0.28450141	23	25	0.2%	-0.13 [-0.69 , 0.43]
Shankar 2000	0.070551	0.13696712	103	109	0.9%	0.07 [-0.20 , 0.34]
Silva 2006	-0.04607	0.25926942	28	30	0.3%	-0.05 [-0.55 , 0.46]
Smith 1999	0.725292	0.43412761	10	11	0.1%	0.73 [-0.13 , 1.58]
Tupe 2009	0.058646	0.22908102	43	40	0.3%	0.06 [-0.39 , 0.51]
Umeta 2000	0.332226	0.14785133	92	92	0.8%	0.33 [0.04 , 0.62]
Vakili 2015	0.23296	0.14191	100	100	0.9%	0.23 [-0.05 , 0.51]
Walravens 1983	0.356412	0.31249613	20	20	0.2%	0.36 [-0.26 , 0.97]
Walravens 1989	0.237554	0.27941182	25	25	0.2%	0.24 [-0.31 , 0.79]
Wuehler 2008	-0.03193	0.11140371	313	108	1.4%	-0.03 [-0.25 , 0.19]
Total (95% CI)			**10514**	**10206**	**100.0%**	**0.12 [0.09 , 0.14]**

Heterogeneity: Chi² = 568.20, df = 73 (P < 0.00001); I² = 87%
Test for overall effect: Z = 8.85 (P < 0.00001)
Test for subgroup differences: Not applicable



A funnel plot appeared generally symmetrical (Appendix 4).

- Sensitivity and subgroup analyses
  - The result was not different when analyzed using random-effects model (SMD 0.11, 95% CI 0.03 to 0.19).
  - The effect was not different in the subgroup analyses for country income level (test for subgroup differences: Chi^2 = 0.20, P = 0.66), formulation (test for subgroup differences: Chi^2 = 2.22, P = 0.33) and stunting (test for subgroup differences: Chi^2 = 1.42, P = 0.23).
  - Age subgroups were heterogeneous (test for subgroup differences: Chi^2 = 29.77, P < 0.00001), with greater benefit in older age groups: between 6 and 12 months (SMD −0.02, 95% CI −0.07 to 0.03; between one and five years (SMD 0.08, 95% CI 0.05 to 0.11); between 5 and 13 years (SMD 0.20, 95% CI 0.14 to 0.26).
  - Dose subgroups were different (test for subgroup differences: Chi^2 = 30.13, P < 0.00001). There did not appear to be a coherent pattern of increasing or decreasing effect across increasing doses: 0 mg to 5 mg (SMD 0.02, 95% CI −0.10 to 0.13); 5 mg to 10 mg (SMD 0.14, 95% CI 0.10 to 0.18); 10 mg to 15 mg (SMD 0.18, 95% CI 0.13 to 0.23); 15 mg to 20 mg (SMD 0.13, 95% CI −0.07 to 0.32); 20 mg or more (SMD −0.01, 95% CI −0.07 to 0.04).
  - Duration subgroups were different (test for subgroup differences: Chi^2= 33.48, P < 0.0001). There did not appear to be a coherent pattern of increasing or decreasing effect across increasing durations: between zero and six months (SMD −0.02, 95% CI −0.08 to 0.03); between six and 12 months (SMD 0.16, 95% CI 0.13 to 0.19); 12 months or more (SMD 0.10, 95% CI 0.02 to 0.17).
  - Iron co-intervention subgroups were different (test for subgroup differences: Chi^2 = 13.41, P = 0.0003), with a small benefit in the group without iron (SMD 0.14, 95% CI 0.12 to 0.17) but no effect in the group with iron (SMD −0.00, 95% CI −0.08 to 0.07).

7.2. Weight

We pooled a total of 57 studies, nine of which reported two comparisons (total number of comparisons = 66), including 19,891 participants (9% of participants in this review). The analysis showed that zinc was associated with a small increase in weight (SMD 0.12, 95% CI 0.10 to 0.15; P < 0.00001, I^2 = 94%; Analysis 1.18). We included 12 new studies in this update for this analysis (Abdollahi 2014; Abdollahi 2019; Barffour 2019; Becquey 2016; Bertinato 2013; Hess 2015; Islam 2022; Kaseb 2013; Khodashenas 2015; Kusumastuti 2018; Mandlik 2020; Rerksuppaphol 2018), and additional data were available from one of the previously included studies (Vakili 2015).

- Sensitivity and subgroup analyses
  - There was some visual asymmetry in the funnel plot for this analysis (Appendix 4), suggesting that small-study effects or reporting bias might have influenced the result, however, the result was not different when analyzed using a random-effects model (SMD 0.13, 95% CI 0.01 to 0.25).
  - Effects did not differ in subgroup analyses for country income level (test for subgroup differences: Chi^2 = 1.13, P = 0.29), iron co-intervention (test for subgroup differences: Chi^2 = 3.40, P = 0.07), stunting (test for subgroup differences: Chi^2 = 2.47, P = 0.12), and duration (test for subgroup differences: Chi^2 = 4.69, P = 0.10) subgroups.
  - The effects of zinc on weight were different based on age subgroups (test for subgroup differences: Chi^2 = 299.16, P < 0.00001), with greater benefit in older age groups: between 5 and 13 years (SMD 0.22, 95% CI 0.15 to 0.28) compared to between 6 and 12 months (SMD −0.45, 95% CI −0.51 to −0.40); and between one and five years (SMD 0.03, 95% CI -0.00 to 0.07). The apparent harmful effect in the youngest subgroup is explained by the result of subgroup analysis from one study (Bhandari 2002).
  - Dose subgroups were different (test for subgroup difference ss: Chi^2 = 40.53, P < 0.00001), but there did not appear to be a coherent pattern of increasing or decreasing effect across increasing doses: 0 mg to 5 mg (SMD 0.00, 95% CI −0.11 to 0.12); 5 mg to 10 mg (SMD 0.07, 95% CI 0.03 to 0.10); 10 mg to 15 mg (SMD −0.15, 95% CI −0.21 to −0.09); 15 mg to 20 mg (SMD −0.06, 95% CI −0.26 to 0.15); 20 mg or more (SMD 0.03, 95% CI −0.03 to 0.09).
  - Formulation subgroups were not significantly different (test for subgroup differences: Chi^2 = 67.14, P < 0.00001) with an increased risk with pill/tablet (SMD −0.09, 95% CI −0.12 to

−0.05) but benefit with solution (SMD 0.12, 95% CI 0.08 to 0.16), and capsule (SMD 0.41, 95% CI 0.12 to 0.71).

7.3. Weight-to-height ratio

A total of 28 studies, five of which reported two comparisons (total number of comparisons = 33), including 12,948 participants (6% of participants in the review) reported the data for weight-to-height ratio. The analysis found that zinc supplementation was associated with a small increase in weight-to-height ratio (SMD 0.14, 95% CI 0.10 to 0.17; P <0.00001, I^2 = 95%; Analysis 1.19). The funnel plot appeared symmetrical.

- Subgroup analyses
  - Subgroups were not different based on country income level (test for subgroup differences: Chi^2 = 0.24, P = 0.62), age (test for subgroup differences: Chi^2 = 0.37, P = 0.83), dose (test for subgroup differences: Chi^2 = 51.3, P = 0.27), duration (test for subgroup differences: Chi^2 = 2.71, P = 0.26), iron co-interventions (test for subgroup differences: Chi^2 = 3.86, P = 0.05), and formulation (test for subgroup differences: Chi^2 = 2.05, P = 0.15). We included four new studies in this update for this analysis (Barffour 2019; Becquey 2016; Hess 2015; Islam 2022).

7.4 Prevalence of stunting

We pooled results from a total of 10 studies, three of which included two comparisons (total number of comparisons = 13), comprising 8009 participants (4% of participants in this review). Meta-analysis revealed no effect on the prevalence of stunting (RR 1.00, 95% CI, 0.94 to 1.07; P = 0.90, I^2 = 60%; Analysis 1.20). We included four new studies in this update for this analysis (Abdollahi 2019; Barffour 2019; Hess 2015; Islam 2022).

- Sensitivity analysis
  - The average effect was not different when calculated using a random-effects model (RR 0.98, 95% CI 0.86 to 1.07).

8. Zinc status

8.1 Serum or plasma zinc concentration

Pooled results from 54 studies, 10 of which had two comparisons (total number of comparisons = 64), including 12,644 participants (6% of participants randomized) found that zinc supplementation was associated with a medium to large increase in zinc concentration compared with no zinc (SMD 0.60, 95% CI 0.56 to 0.63; P < 0.00001), though heterogeneity was considerable (Chi^2 = 769.87, df = 63; P < 0.00001, I^2 = 92%; Analysis 1.21). The funnel plot did not appear to have any substantive asymmetry (Appendix 4). We included eight new studies in this update for this outcome (Abdollahi 2019; Becquey 2016; Berger 2015; Bertinato 2013; Caulfield 2013; Hess 2015; Kaseb 2013; Mandlik 2020).

- Sensitivity and subgroup analyses
  - The result was not different when analyzed using a random-effects model (SMD 0.58, 95% CI 0.44 to 0.71).
  - Age subgroups were significantly heterogeneous (test for subgroup differences: Chi^2 = 14.81, P = 0.0006), with the greatest benefit in the one-to-five-year age group: between 6 and 12 months (SMD 0.66, 95% CI 0.59 to 0.73); between one and five years (SMD 0.63, 95% CI 0.57 to 0.68); between 5 and 13 years (SMD 0.46, 95% CI 0.38 to 0.54).
  - Country income level subgroups were significantly different (test for subgroup differences: Chi^2=11.28, P= 0.0008), with moderate to large benefit in the low- and middle-income subgroups (SMD 0.61, 95% CI 0.57 to 0.65), and a smaller benefit in the high-income subgroup (SMD 0.27, 95% CI, 0.07 to 0.46).
  - Dose subgroups were significantly different (test for subgroup differences: Chi^2= 49.33, P < 0.00001), with larger doses associated with larger increases in zinc concentration: 0 mg to 5 mg (SMD 0.35, 95% CI 0.21 to 0.49); 5 mg to 10 mg (SMD 0.55, 95% CI 0.48 to 0.62); 10 mg to 15 mg (SMD 0.57, 95% CI 0.51 to 0.63); 15 mg to 20 mg (SMD 0.76, 95% CI 0.58 to 0.94); 20 mg or more (SMD 0.88, 95% CI 0.78 to 0.98).
  - Duration subgroups were different (test for subgroup differences: Chi^2 = 22.98, P < 0.00001). Shorter durations were associated with larger increases in zinc concentration: between zero and six months (SMD 0.75, 95% CI 0.68 to 0.82); between 6 and 12 months (SMD 0.54, 95% CI 0.49 to 0.59); 12 months or more (SMD 0.59, 95% CI 0.50 to 0.67).
  - Formulation subgroups were different (test for subgroup differences: Chi^2 = 99.29, P < 0.00001), with greatest benefit in the capsule subgroup (SMD 1.07, 95% CI 0.94 to 1.21), then the solution group (SMD 0.65, 95% CI 0.60 to 0.71), and least benefit in the pill/tablet subgroup (SMD 0.54, 95% CI 0.48 to 0.59).
  - Iron co-intervention subgroups were different (test for subgroup differences: Chi^2= 24.96, P < 0.00001), with greater benefit in the subgroup not given iron: no iron (SMD 0.68, 95% CI 0.64 to 0.73); iron (SMD 0.47, 95% CI 0.39 to 0.54).

8.2 Prevalence of zinc deficiency

We included a total of 18 studies, six of which reported two comparisons each (total number of comparisons = 24), including 7518 participants (3% of participants in the review) in this analysis. Zinc supplementation was associated with a 44% reduction in the prevalence of zinc deficiency (RR 0.56, 95% CI 0.52 to 0.60; P < 0.00001) compared to control, but heterogeneity was substantial (Chi^2 = 167.52, df = 23; P < 0.00001, I^2 = 86%; Analysis 1.22). We included three new studies in this update for this analysis (Abdollahi 2019; Barffour 2019; Hess 2015).

The funnel plot for publication bias appeared to be skewed (Appendix 4).

- Sensitivity and subgroup analyses
  - There was a larger effect when calculated using a random-effects model (RR 0.44, 95% CI 0.35 to 0.55)
  - Age subgroups were different (test for subgroup differences: Chi^2 = 11.57, P = 0.003), with greater benefit in older age groups: between 6 and 12 months (RR 0.62, 95% CI 0.55 to 0.70); between one and five years (RR 0.52, 95% CI 0.47 to 0.56); between five and 13 years (RR 0.31, 95% CI 0.20 to 0.49).
  - Dose subgroups were different (test for subgroup differences: Chi^2 = 67.27, P < 0.00001). There did not appear to be a coherent pattern of increasing or decreasing effect across increasing doses: 5 mg to 10 mg (RR 0.45, 95% CI 0.37 to 0.56); 10 mg to 15 mg (RR 0.57, 95% CI 0.52 to 0.63); 15 mg to 20 mg (RR 0.46, 95% CI 0.24 to 0.89); 20 mg or more (RR 0.14, 95% CI 0.10 to 0.19).

- Duration subgroups were different (test for subgroup differences: Chi^2 = 67.82,P < 0.00001). There did not appear to be a coherent pattern of increasing or decreasing effect across increasing durations: between zero and six months (RR 0.27, 95% CI 0.22 to 0.33); between 6 and 12 months (RR 0.64, 95% CI 0.59 to 0.71); 12 months or more (RR 0.55, 95% CI 0.48 to 0.64).
- Iron co-intervention subgroups were different (test for subgroup differences: Chi^2 = 25.05, P < 0.00001), with greater benefit in the subgroup not given iron (RR 0.40, 95% CI 0.36 to 0.45) compared with the group given iron (RR 0.62, 95% CI 0.55, 0.69).
- Formulation subgroups were different (test for subgroup differences: Chi^2 = 36.75, P < 0.00001), with greatest benefit in the capsule subgroup (RR 0.29, 95% CI 0.23 to 0.37), then the solution group (RR 0.50, 95% CI 0.45 to 0.56), and then the pill/tablet group (RR 0.64, 95% CI 0.58 to 0.71).

Adverse events

9. Side effects

Two studies reported no adverse events, including vomiting, in either group (Alarcon 2004; Mazariegos 2010).

9.1 Study withdrawal

Pooled data from seven studies, which included data for 5226 participants (2% of participants in this review) revealed an increase in study withdrawal (RR 1.81, 95% CI 1.11 to 2.95; P = 0.02). Heterogeneity was not significant (Chi^2 = 5.18, df = 5; P = 0.39, I^2 = 3%; Analysis 1.23). There were only 43 events in total.

9.2 Participants with more than one side effect

Three studies, which included data for 850 participants (< 1% of participants in this review), found some evidence of increased side effects (RR 1.13, 95% CI 1.00 to 1.27; P = 0.04, I^2 = 0%; Analysis 1.24).

9.3 Vomiting episodes

Five studies, one of which made two comparisons (total number of comparisons = 6), included 4095 participants (2% of participants in this review). Zinc supplementation was associated with an increase in vomiting episodes (RR 1.68, 95% CI 1.61 to 1.75; P < 0.00001, I^2 = 85%; Analysis 1.25).

- Sensitivity analysis
  - This effect appears to be slightly larger when analyzed using a random-effects model (RR 1.85, 95% CI 1.30 to 2.63).

9.4 Participants with more than one vomiting episode

Five studies, which included data for 35,192 participants (16% of participants in this review) found evidence of increased vomiting associated with supplementation (RR 1.29, 95% CI 1.14 to 1.46; P < 0.0001), with some heterogeneity (P = 0.18, I^2 = 37%; Analysis 1.26). The certainty of the evidence for this outcome was high.

10. Hemoglobin status

10.1 Blood hemoglobin concentration

A total of 30 studies, 10 of which made two comparisons (total number of comparisons = 40), including 12,946 participants (6% of participants in the review) were included in this analysis. The analysis showed a similar blood hemoglobin concentration between the two groups (SMD −0.02, 95% CI −0.05 to 0.02; P = 0.27, I^2 = 78%; Analysis 1.27). In this update, four new studies provided data on blood hemoglobin concentration (Barffour 2019; Becquey 2016; Caulfield 2013; Hess 2015). The funnel plot was generally symmetrical (Appendix 4).

- Sensitivity and subgroup analyses
  - This effect estimate remained small when estimated using random-effects methods (SMD −0.05, 95% CI −0.14 to 0.04).
  - Studies did not differ in the subgroup analyses for age (test for subgroup differences: Chi^2 = 0.12, P= 0.94), dose (Chi^2 = 2.73, P = 0.60), or formulation (test for subgroup differences: Chi^2 = 1.54, P = 0.67), duration (test for subgroup differences: Chi^2 = 1.70, P = 0.43).
  - The iron co-interventions subgroups were different (test for subgroup differences: Chi^2 = 5.89, P = 0.02), with little to no difference in blood hemoglobin (SMD −0.01, 95% CI −0.08 to 0.07) compared to when zinc was supplemented without iron co-intervention (SMD 0.10, 95% CI 0.05 to 0.14).

10.2 Prevalence of anemia

We pooled data from a total of 14 studies, six of which made two comparisons (total number of comparisons = 20), including 5762 participants (3% of participants in this review). The analysis found no overall effect on the prevalence of anemia (RR 1.01, 95% CI 0.96 to 1.06; P = 0.74, I^2 = 34%; Analysis 1.28). We included one new study in this update for this outcome (Barffour 2019).

There was evidence of some funnel plot asymmetry.

- Sensitivity and subgroup analyses
  - The estimate was not different when estimated using random-effects methods (RR 0.99, 95% CI 0.92 to 1.07).
  - Effects were not different across age (test for subgroup differences: Chi^2 = 2.19, P = 0.34), iron co-intervention (test for subgroup differences: Chi^2 = 0.01, P = 0.93), or formulation (test for subgroup differences: Chi^2 = 3.21, P = 0.36) subgroups.
  - Dose subgroups were different (test for subgroup differences: Chi^2 = 12.82, P = 0.01), despite the inclusion of one high-dose study that reported a large effect (Alarcon 2004). There did not appear to be a coherent pattern otherwise: 0 mg to 5 mg (RR 1.01, 95% CI 0.94 to 1.09); 5 mg to 10 mg (RR 1.04, 95% CI 0.93 to 1.16); 10 mg to 15 mg (RR 1.01, 95% CI 0.92 to 1.11); 15 mg to 20 mg (RR 0.76, 95% CI 0.40 to 1.46); 20 mg or more (RR 0.17, 95% CI 0.06 to 0.46).
  - Duration subgroups were different (test for subgroup differences: Chi^2 = 11.55, P = 0.003), despite the inclusion of one study that demonstrated a strong effect (Alarcon 2004): between zero and six months (RR 0.18, 95% CI 0.06 to 0.48); between 6 and 12 months (RR 1.02, 95% CI 0.96 to 1.08); 12 months or more (RR 1.00, 95% CI 0.90 to 1.12).

11. Iron status

11.1 Serum or plasma ferritin concentration

A total of 23 studies, five of which included two comparisons (total number of comparisons = 27), including 5339 participants (2% of participants in this review) contributed to this analysis. Zinc supplementation was associated with a slight increase in ferritin concentration (SMD 0.06, 95% CI 0.01 to 0.12; P = 0.02, I^2 = 95%;

Analysis 1.29). In this update, three new studies provided data for this outcome (Abdollahi 2014; Abdollahi 2019; Becquey 2016).

There was no evidence of funnel plot asymmetry (Appendix 4).

- Sensitivity and subgroup analyses
  - One study in this meta-analysis reported data as medians, but excluding this study from the analysis did not affect the result (SMD 0.10, 95% CI 0.04 to 0.16; Tielsch 2006 (2)).
  - The average effect was not different when calculated using random-effects methods (SMD 0.13, 95% CI −0.12 to 0.38).
  - Studies did not differ in the subgroup analyses for age (test for subgroup differences: Chi^2 = 0.95, P = 0.62) and iron co-intervention (test for subgroup differences: Chi^2 = 2.72, P = 0.10).
  - Country income level subgroups were significantly different (test for subgroup differences: Chi^2 = 9.96, P = 0.002), but only one study in a high-income country reported the outcome (Sandstead 2008), and it was inconsistent with the others (SMD −0.88, 95% CI −1.47 to −0.29). This inconsistency may arise from differing prevalences of zinc deficiency in high-income versus low-income countries.
  - Dose subgroups were significantly different (test for subgroup differences: Chi^2 = 24.34, P < 0.0001). There did not appear to be a coherent pattern of results: 0 mg to 5 mg (SMD 0.07, 95% CI −0.14 to 0.28); 5 mg to 10 mg (SMD −0.05, 95% CI −0.17 to 0.08); 10 mg to 15 mg (SMD 0.20, 95% CI 0.13 to 0.28); 15 mg to 20 mg (SMD 0.14, 95% CI −0.08 to 0.36); 20 mg or more (SMD −0.17, 95% CI −0.33 to −0.02).
  - Duration subgroups were significantly different (test for subgroup differences: Chi^2=31.06, P < 0.00001), with some evidence of harm at increasing doses: between zero and six months (SMD -0.06, 95% CI -0.07 to 0.20); between six and 12 months (SMD 0.03, 95% CI -0.10 to 0.05); 12 months or more (SMD 0.34, 95% CI -0.45 to 0.24).
  - Formulation subgroups were significantly different (test for subgroup differences: Chi^2 = 35.33, P < 0.00001) due to the inclusion of one outlier in the capsule group (Veenemans 2011; Veenemans 2011 (2)).

11.2. Prevalence of iron deficiency

Ten studies (comprising a total of 15 comparisons) included 3149 participants (1% of those included in the review) and found that there was an effect on the prevalence of iron deficiency (RR 0.99, 95% CI 0.89 to 1.10; P = 0.79), with no significant heterogeneity (P = 0.29, I^2 = 15%; Analysis 1.30). The funnel plot appeared generally symmetrical (data not shown).

- Subgroup analyses
  - Effects were not different across subgroups based on age (test for subgroup differences: Chi^2 = 3.56, P = 0.17), dose (test for subgroup differences: Chi^2 = 5.86, P = 0.12), duration (test for subgroup differences: Chi^2 = 4.12, P = 0.13), iron co-intervention (test for subgroup differences: Chi^2 = 0.51, P = 0.48), or formulation (test for subgroup differences: Chi^2 = 1.87, P = 0.39) subgroups.

12. Copper status

12.1. Serum or plasma copper concentration

We included a total of 13 studies (comprising a total of 15 comparisons), reporting data for 3317 participants (1% of participants in this version of the review) in this analysis. Zinc supplementation was associated with a small decrease in copper concentration compared to no zinc (SMD −0.20, 95% CI −0.27 to −0.13; P < 0.00001, I^2 = 66%; Analysis 1.31). In this update, two new studies provided data for this outcome (Abdollahi 2014; Caulfield 2013).

There was evidence of funnel plot asymmetry (Appendix 4).

- Sensitivity and subgroup analyses
  - The estimate was reduced when calculated using random-effects methods (SMD −0.10, 95% CI −0.23 to 0.03).
  - Effects did not differ among country income level (test for subgroup differences: Chi^2 = 3.44, P = 0.06), age (test for subgroup differences: Chi^2 = 5.83, P = 0.02), or iron co-intervention (test for subgroup differences: Chi^2 = 2.79, P = 0.09) subgroups.
  - Dose subgroups differed significantly (test for subgroup differences: Chi^2= 32.06, P < 0.00001), but there was not a coherent pattern of results: 0 mg to 5 mg (SMD −0.08, 95% CI −0.27 to 0.12); 5 mg to 10 mg (SMD −0.31, 95% CI −0.48 to −0.13); 10 mg to 15 mg (SMD 0.00, 95% CI −0.10 to 0.10); 20 mg or more (SMD −0.46, 95% CI −0.59 to −0.33).
  - Duration subgroups differed significantly (test for subgroup differences: Chi^2 = 33.21, P < 0.00001). There was statistically significant harm when zinc was given for between zero and six months (SMD −0.44, 95% CI −0.54 to −0.33); but little no effect when given between 6 and 12 months (SMD −0.06, 95% CI −0.17 to 0.05); 12 months or more (SMD 0.06, 95% CI −0.11 to 0.24). However, few studies were included in each group.
  - Formulation subgroups were significantly different (test for subgroup differences: Chi^2 = 24.76, P < 0.00001), with greater harm in the pill/tablet subgroup: solution (SMD −0.34, 95% CI −0.42 to −0.26); pill/tablet (SMD −0.83, 95% CI −1.01 to −0.65). The exact reason for this difference is not clear; however, bioavailability might be better with pills compared to the solution form.

12.2. Prevalence of copper deficiency

Three studies including 1337 participants (1% of participants in this review) showed that zinc supplementation was associated with an increase in the prevalence of copper deficiency compared to no zinc (RR 2.64, 95% CI 1.28 to 5.42; P = 0.008, I^2 = 59%; Analysis 1.32). The estimate became imprecise when analyzed using a random-effects model (RR 2.72, 95% CI 0.73 to 10.18).

Comparison 2: Zinc alone versus zinc plus iron

In addition to comparing zinc to no intervention, several studies included in this review compared zinc alone with zinc plus iron.

Primary outcomes

1. All-cause mortality

One study reported all-cause mortality for 323 participants. The results showed a decrease in mortality in groups given zinc alone compared to those given zinc plus iron; however, the

confidence interval around the summary estimate was very wide and imprecise, therefore no solid conclusion can be drawn from these data (RR 0.33, 95% CI 0.01 to 8.39; Analysis 3.1).

Secondary outcomes

2. Hospitalization

One study reported all-cause hospitalization for 399 participants. The results showed no clear evidence of a difference and the CI is imprecise (RR 1.09, 95% CI 0.53 to 2.24; Analysis 3.2).

3. Diarrhea

3.1. Incidence of all-cause diarrhea

Five studies reported the incidence of all-cause diarrhea for 1530 participants. The difference favored zinc alone over zinc plus iron (RR 0.91, 95% CI 0.84 to 0.97), but there was considerable heterogeneity (P = 0.002, I^2 = 76%; Analysis 3.3). The effect became imprecise when analyzed using a random-effects model (RR 0.94, 95% CI 0.80 to 1.10).

3.2. Prevalence of all-cause diarrhea

One study reported the prevalence of all-cause diarrhea for 399 participants and showed a small to no effect in favor of zinc plus iron supplementation versus zinc alone, however, the confidence interval around the summary estimate was imprecise (RR 1.11, 95% CI 0.94 to 1.31; Analysis 3.4).

3.3. Incidence of severe diarrhea

One study reported the incidence of severe diarrhea for 323 participants. The result showed that zinc plus iron supplementation reduced severe diarrhea, however, the confidence interval around the summary estimate was imprecise (RR 1.28, 95% CI 0.96 to 1.69; Analysis 3.5).

3.4. Hospitalization due to all-cause diarrhea

One study reported hospitalization due to diarrhea for 399 participants and showed little no difference in this outcome (RR 1.02, 95% CI 0.26 to 4.00; Analysis 3.6).

4. Incidence of lower respiratory tract infection (LRTI)

Three studies reported the prevalence of LRTI for 1065 participants. Results showed little to no difference in the incidence of LRTI, however, the confidence interval around the summary estimate was wide (RR 1.08, CI 0.97 to 1.20), with no important heterogeneity (P = 0.28, I^2 = 21%; Analysis 3.7).

5. Incidence of malaria

One study reported the incidence of malaria for 419 participants. The results showed no clear evidence of a difference (RR 1.17, 95% CI 0.81 to 1.69; Analysis 3.8).

6. Growth

6.1. Height

Six studies reported height for 1551 participants. The pooled results showed little to no difference between the two groups, even though the CI around the summary estimate was imprecise (SMD 0.06, 95% CI −0.04 to 0.16), with no heterogeneity (P = 0.49, I^2 = 0%; Analysis 3.9). We added one study to this update for this outcome (Kusumastuti 2018).

6.2. Weight

We analyzed a total of five studies with 944 participants. The pooled results showed a small effect in favor of zinc alone versus zinc plus iron (SMD 0.12, 95% CI -0.01 to 0.25), with no heterogeneity (P = 0.68, I^2 = 0%; Analysis 3.10).

6.3. Weight-to-height ratio

Four studies reported weight-to-height ratio for 933 participants. There was no clear difference (SMD 0.06, 95% CI −0.07 to 0.19), with no heterogeneity (P = 0.71, I^2 = 0%; Analysis 3.11).

6.4. Prevalence of stunting

Two studies reported stunting for 462 participants. The results showed a small increase in the prevalence of stunting in the zinc plus iron group versus the zinc-alone group (RR 1.09, 95% CI 1.01 to 1.17), but the studies appeared to be inconsistent (P = 0.18, I^2 = 45%; Analysis 3.12).

7. Zinc status

7.1. Serum or plasma zinc concentration

Eight studies reported serum zinc concentration for 1337 participants. The difference favored zinc alone (SMD 0.16, 95% CI 0.05 to 0.27), but there was considerable heterogeneity (P = 0.01, I^2 = 61%; Analysis 3.13), and the difference between groups became imprecise when analyzed using a random-effects model (SMD 0.14, 95% CI −0.05 to 0.33).

7.2. Prevalence of zinc deficiency

Three studies reported the prevalence of zinc deficiency for 350 participants. The results favored the zinc alone versus zinc plus iron even though the confidence interval around the summary estimate was imprecise (RR 0.70, 95% CI 0.37 to 1.33; Analysis 3.14).

Adverse events

8. Study withdrawal

Two studies reported study withdrawal for 557 participants. The difference was imprecise (RR 0.71, 95% CI 0.46 to 1.10; Analysis 3.15).

9. Hemoglobin status

Eight studies reported blood hemoglobin concentration for 1341 participants. The difference favored zinc with iron (SMD −0.23, 95% CI −0.34 to −0.12), but there was considerable heterogeneity (P < 0.00001, I^2 = 79%; Analysis 3.16), and the difference between groups became imprecise when analyzed using a random-effects model (SMD −0.21, 95% CI −0.47 to 0.05).

10. Iron status

10.1. Serum or plasma ferritin concentration

Six studies studies reported serum ferritin concentration for 945 participants. The difference showed that ferritin levels were lowered with zinc plus iron (SMD −1.78, 95% CI −1.99 to −1.56). There was considerable heterogeneity (P < 0.00001, I^2 = 99%; Analysis 3.17), and the range of possible effects appears wider (less certain) when analyzed using a random-effects model (SMD −3.28, 95% CI −6.27 to −0.30).

10.2. Prevalence of iron deficiency

Two studies reported the prevalence of iron deficiency for 434 participants. The difference favored zinc with iron (RR 5.23, 95% CI 3.10 to 8.83; Analysis 3.18).

10.3. Prevalence of anemia

Three studies reported the prevalence of anemia for 482 participants. The difference favored zinc with iron (RR 1.27, 95% CI 1.09 to 1.49; Analysis 3.20).

11. Copper status

Two studies reported serum copper concentration for 353 participants. There was no clear evidence of a difference between the two groups (SMD 0.06, 95% CI −0.15 to 0.27), with no heterogeneity (P = 0.74, I^2 = 0%; Analysis 3.19).

DISCUSSION

Summary of main results

We added 16 new studies to this update; however, not all of the new studies contributed to all the outcomes pre-specified in this review. Overall, the results of almost all the analyses remain the same as they were at the end of completion of the last version of the review, as relatively large studies with significantly different results compared to previously published studies would have been necessary to alter the conclusion of the last review (Mayo-Wilson 2014).

In summary, the effect of preventive zinc supplementation on all-cause mortality had little to no effect and the confidence interval around the summary estimate includes a possibility of a small increase in mortality. Zinc supplementation had little to no effect on mortality due to all-cause diarrhea; however, there was a likely decrease in mortality due to LRTI, and malaria, even though the confidence interval around the summary estimates for these outcomes included a possible increased risk with zinc supplementation. Supplementation resulted in small improvements in most growth-related outcomes. Serum zinc status also reflects significant medium to large improvements as a result of supplementation. Supplementation did not significantly affect reported hospitalization outcomes. There were no significant effects on morbidity due to LRTI or malaria incidence and prevalence. Preventive zinc supplementation may be associated with increased vomiting in the first 48 hours after supplementation. Supplementation had no important effect on hemoglobin or iron status, but it may have a negative effect on copper status. Most studies provided supplementation as zinc sulfate and it is unclear if the chemical formulation may relate to side effects. We completed a number of subgroup analyses, and iron co-supplementation seems to decrease the beneficial effects of zinc supplementation.

Overall completeness and applicability of evidence

Overall, the external validity of this review is strong. With the addition of 16 new studies, this review now includes 96 studies, including 219,584 participants and studies conducted in a large number of countries. Almost all outcomes of interest were reported in multiple trials and almost all meta-analyses included over 1000 participants. Non-stunted and stunted children of both genders and all eligible ages were represented in the included trials and numerous types of preventive zinc supplementation characteristics are examined. Clinical outcomes were investigated, as well as side effects and biochemical outcomes (such as zinc status). Furthermore, there was no important heterogeneity among studies for the primary outcomes of this review. Given these strengths, there may be no need for further placebo-controlled trials of the effects of preventive zinc supplementation for the population and outcomes of this review.

Most of the studies in this review were conducted in low- or middle-income countries, and a wide range of such countries are represented. The evidence of this review may not be as applicable in high-income countries, as the risk of zinc deficiency is a greater problem in low- and middle-income countries.

Among low- and middle-income countries, there is inter- and intra-country variation. For instance, zinc supplementation may be more effective in settings with relatively low levels of meat intake, high levels of undernutrition, and a high population-level risk of zinc deficiency. The impact of supplementation may also vary with varying levels of fiber and phytate consumption (Black 2010; Hess 2017).

The effectiveness of zinc supplementation might also be influenced by differing disease prevalence and pathogen profiles among low- and middle-income countries. For instance, particular micronutrient supplementation interventions may have differing levels of benefit or harm when delivered in malaria-endemic versus non-endemic areas (Sazawal 2006). The impact of supplementation might also be influenced by the particular infectious, disease-causing pathogens in a given area (Patel 2011).

The full range of eligible ages was represented among participants in this review. However, the majority of studies – including the largest four trials – did not include children over five years of age (Bhandari 2007; Hess 2015; Islam 2022; Sazawal 2006; Tielsch 2006). Most of the age subgroup analyses, including the analysis for all-cause mortality, did not indicate that the effects of zinc supplementation were significantly different for different age groups. However, of those that did indicate a difference, supplementation was generally more effective in the one-to-five-years age group than in the 6-to-12-months group. This possible association must be interpreted with caution; trials may be more likely to report disaggregated data for participant subgroups when these groups are significantly different, and subgroup analyses in systematic reviews often yield false-positive results (Guyatt 2008; Schünemann 2013).

Stunted children were also represented in this review, as illustrated by the number of studies that included stunted children and the median baseline height-for-age z scores across trials. Most stunting subgroup analyses indicated that the effects of supplementation for stunted children were similar to those for non-stunted children. However, due to a relative lack of data reported separately for stunted versus non-stunted children, this review might have been underpowered to detect any meaningful effect modification by stunting status.

The evidence from this review seems applicable to preventive zinc supplementation programs with a variety of doses, durations, co-interventions, and formulations. Furthermore, there was no strong evidence of meaningful effect modification based on dose, duration, and formulation. Significant subgroup differences were generally inconsistent across outcomes, heterogeneity was often

high even within individual subgroups, and subgroup differences often lacked a coherent directionality (for example, higher doses leading to greater effects).

For many subgroup analyses, a few studies contributed most of the weight and the tests for subgroup differences were underpowered. Furthermore, certain types of effect modification, such as a gradient of effectiveness based on dose, might be more conducive to meta-regression analysis than categorical subgroup analysis. There could have been a relationship between effect estimates and dose or effect estimates and duration that the subgroup analyses in this review were unable to detect.

Furthermore, though we analyzed studies of zinc with an iron co-intervention versus those without an iron co-intervention, this review was not primarily designed to explore this relationship fully. It has been shown previously that co-supplementation of iron and zinc may reduce the efficacy of zinc for growth (Imdad 2011). This aspect is very important as there are existing programs of iron supplementation for the prevention of anemia using multiple micronutrients or additional zinc, and co-supplementation with iron might decrease the desired preventive effect of zinc supplementation. Our subgroup analyses identified few statistically significant differences between subgroups receiving an iron co-intervention versus subgroups not receiving an iron co-intervention; however, there were relatively few studies in most analyses. Within trials that made multiple comparisons, effects for groups receiving an iron co-intervention were not consistently different from effects for groups without an iron co-intervention (Comparison 2: Zinc versus zinc plus iron). We think this reaction can be further explored in meta-regression and a possible network meta-analysis.

Quality of the evidence

This review included 96 studies with approximately 219,584 children, who were evaluated for mortality, morbidity, growth, and adverse event outcomes. We used the GRADE framework to assess the certainty of the evidence for primary outcomes and certain secondary outcomes reported in the summary findings table in this review, based on the following factors: indirectness of evidence, unexplained heterogeneity, publication bias, risk of bias due to study design limitations, and imprecision of results (Schünemann 2013).

The meta-analysis of all-cause mortality included outcomes for 143,474 participants in 16 studies. For all-cause and cause-specific mortality outcomes, the certainty of evidence was moderate to high. Thus, there may be no need for further placebo-controlled trials analyzing the effects of preventive zinc supplementation on mortality in the population of this review. As discussed above, the indirectness of evidence did not seem to be a significant problem for this review, because it did not have to use proxies for its populations.

The three largest studies in this review, which accounted for almost all of the effects in each mortality meta-analysis, were at low risk of bias for sequence generation, allocation concealment, blinding, and incomplete outcome data. Many studies in this review were at high risk of bias due to selective outcome reporting. However, it seems unlikely that selective reporting substantially biased the results of the mortality meta-analyses given that the three largest studies in this review all reported mortality outcomes. Thus, even if mortality outcome data were selectively withheld from the trial reports of certain studies, these studies would not likely be numerous or large enough to influence the results of the primary analysis.

In terms of imprecision, the 95% confidence interval for all-cause mortality suggests that the intervention is highly unlikely to cause appreciable harm, so we did not downgrade the certainty of evidence. The confidence intervals for mortality due to diarrhea or LRTI included the possibility of harm and there were also few cause-specific deaths observed due to diarrhea, LRTI, or malaria. We thus downgraded the latter outcomes and considered them to be moderate- rather than high-certainty evidence.

Compared to the primary outcomes of this review, the certainty of evidence for the secondary outcomes of incidence of diarrhea, LRTI, height, and adverse events was more mixed. Heterogeneity was significant for the incidence of diarrhea and this heterogeneity remained largely unexplained even after subgroup analyses were undertaken. Due to unexplained heterogeneity, we downgraded the evidence for incidence of all-cause diarrhea and height from high to moderate certainty. Selective reporting was also more likely to influence secondary outcomes with meta-analyses involving relatively small numbers of participants.

Inverse variance methods may yield biased results for rare events, but the overall effects are small and many are not significant; small biases in the methods may have minimal consequences for the results and interpretation.

Potential biases in the review process

This review had several strengths in terms of preventing bias. Its search was comprehensive and yielded both unpublished and non-English language trial reports. Two review authors independently extracted data to reduce the possibility of introduction of errors and bias by a single extractor, except for the summary of findings table, for which only one author (AI) completed the GRADE analysis. For future updates the GRADE analysis might be completed by two review authors, which will decrease the risk of reviewer bias. Numerous trials presented at least some baseline, outcome, or risk of bias data that were unclear, incomplete, discrepant, or reported for some trial participants outside of the age range of this review. Whenever we were able to obtain the relevant contact information, we contacted the authors of such trials at least twice to obtain clarification or disaggregated data (or both). This comprehensive process of contacting study authors improved the completeness of data in this review.

However, as with any systematic review, we had to make subjective judgments and decisions during the research process. We attempted to be transparent about any such judgment calls in the text of this review as well as in the Characteristics of included studies and Characteristics of excluded studies.

We used SMDs to pool the continuous data. This approach helped us pool the studies irrespective of whether the data were presented in the form of standardized scores, such as z-scores for growth outcomes, or whether the studies reported data in original units, such as kg for weight-for-age. We preferred to pool the final values at the longest follow-up; however, some studies only reported changes from baseline, and we pooled those accordingly. Even though this approach is not advised in the *Cochrane Handbook for*

Systematic Reviews of Interventions (Deeks 2022), we think that this approach should not have a major effect on the final summary estimate, as all the studies were RCTs and the baseline values should be similar in both the intervention and control groups. Furthermore, a meta-epidemiological study showed similar results when the end values and changes from baseline were pooled together (da Costa 2013). Having said that, the SMD is difficult to interpret in absolute terms, and effect sizes less than 0.2 are considered small (Schünemann 2022). We therefore think the data on the effect of zinc for growth should be interpreted with caution and that the effect is likely small in magnitude.

Following the published protocol, we used the fixed-effect model for our primary meta-analyses. The fixed-effect model assumes that studies are estimating the same true effect (Deeks 2022). In our review, studies conducted at different times in different countries might be estimating different true effects, and the addition of new studies to this review could potentially reduce or increase true heterogeneity. We conducted sensitivity analyses using the random-effects model, which assumes that the true effect varies between studies. Although some point estimates differed between analyses, results using both models were consistent with our interpretation that zinc supplementation has clinically meaningful benefits for children at risk of deficiency in terms of growth and prevention of diarrheal diseases.

Agreements and disagreements with other studies or reviews

The results of this review were generally consistent with those of past systematic reviews of zinc supplementation. This was true of mortality outcomes, previously investigated by Brown 2009, Patel 2011 and Yakoob 2011, and diarrhea morbidity outcomes, previously investigated by Aggarwal 2007, Bhutta 1999, Brown 2009, Patel 2011 and Yakoob 2011.

Previously, reviews have generally found a beneficial impact of zinc supplementation on LRTI (Aggarwal 2007; Bhutta 1999; Brown 2009; Lassi 2016; Patel 2011; Roth 2010; Yakoob 2011). The results of this review do not support this finding. However, this discrepancy might be due to slightly differing inclusion criteria and eligible LRTI outcome definitions. For example, Lassi 2016 included studies with children infected with HIV, while we excluded them. Similarly, Brown 2009 included studies with children younger than six months of age, while we excluded them. However, differing age criteria did not seem to account for all of the differences in results. Zinc supplementation may be more beneficial for severe LRTI or LRTI that meets more specifically defined clinical criteria (Roth 2010). While this review indicates a slight, statistically insignificant harm in terms of malaria incidence, one other review indicated a statistically insignificant benefit (Yakoob 2011).

Previously, reviews have disagreed on whether supplementation has a significant positive effect on growth outcomes (Brown 2002; Brown 2009; Imdad 2011; Liu 2018), or not (Gera 2019; Ramakrishnan 2009). Though this review does not fully explain this disagreement, it does support the hypothesis that supplementation may have a small but positive effect on growth. As shown by the age subgroup analysis for height and weight, zinc may be more effective at improving growth outcomes in the 5-to-13-years subgroup. Thus, one potential reason for the disagreement between previous reviews is the fact that Brown 2002 and Brown 2009 included participants older than five years of age, and Ramakrishnan 2009 did not.

The results of this review are also generally consistent with past investigations of zinc (Brown 2002; Brown 2009), hemoglobin (Brown 2009; Dekker 2010), and iron status (Brown 2009). However, while this review indicates that supplementation has a negative effect on copper status, one past review indicated no effect (Brown 2009).

Finally, previous reviews have attempted to explain heterogeneity related to the impact of zinc supplementation. Three reviews have suggested that age may modify the impact of supplementation, with benefits limited to children one year of age or older (Brown 2009; Liu 2018; Patel 2011). Subgroup analyses for some outcomes in this review were consistent with this hypothesis. However, this potential association could be spurious; indeed, Patel 2011 notes that studies in their review with older age groups also appeared to be at higher risk of bias.

AUTHORS' CONCLUSIONS

Implications for practice

The benefits, harms, and costs of preventive zinc supplementation should be carefully considered when deciding whether or not to use this intervention. On the one hand, supplementation positively impacted zinc status and diarrhea morbidity, and there were beneficial effects for growth outcomes, albeit small. Supplementation may have had a small positive impact on all-cause mortality, though the effects of zinc on this outcome, and on most hospitalization, lower respiratory tract infection (LRTI), and malaria outcomes, were not significant. On the other hand, supplementation was associated with increased vomiting and worsened copper status, though it was not associated with any important effect on hemoglobin or iron status. Balancing these factors, the benefits of zinc supplementation would outweigh the harms in low- and middle-income countries where the risk of zinc deficiency is relatively high. It has been argued that zinc supplementation, as part of a package of interventions to reduce undernutrition among preschoolers, is among the most cost-effective interventions for advancing human welfare (Horton 2008).

However, preventive zinc supplementation may not be a sufficient or long-term solution to the nutrition and health challenges facing children in resource-limited settings. Children ultimately need well-balanced diets, and poverty is often a risk factor for undernutrition and pathogen exposure. Unfortunately, until these issues are effectively addressed, zinc deficiency (and the mortality, morbidity, and growth deficits associated with it) will likely remain. The evidence suggests that preventive zinc supplementation offers a short-term intervention to help alleviate these problems in resource-scarce settings. It may also be pragmatic and effective to deliver zinc supplementation along with other public health interventions such as growth monitoring. Furthermore, fortification may be beneficial in areas where food production and processing systems could enrich foods with zinc (Brown 2004; Hess 2009a).

On the basis of our review findings, policymakers may wish to consider preventive zinc supplementation as one of the public health and nutrition interventions offered to children at risk of zinc deficiency in low- and middle-income countries. Where zinc

supplements are locally available, clinicians in such settings could provide them to children under their care, who likely lack sufficient dietary zinc intake. However, the evidence also suggests that monitoring for side effects, such as vomiting, may be required. Finally, families can be encouraged to recognize the importance of adequate dietary zinc for their children.

Implications for research

Finding ways to improve the delivery of zinc to hard-to-reach populations (for example, the poorest of the poor) is one of the most important priorities in reducing mortality and morbidity due to childhood diarrheal disease (Wazny 2013).

Children with severe protein-energy malnutrition were excluded from this review, as well as children with chronic diseases such as cystic fibrosis and sickle cell disease. The effects of zinc in populations with co-morbidities such as these could be examined in future systematic reviews. As mentioned above, two Cochrane Reviews have already addressed the effects of zinc supplementation in populations with HIV (Humphreys 2010; Irlam 2010).

This review has not confirmed the optimal range of doses, durations, frequencies or formulations necessary for zinc supplementation to achieve clinically meaningful improvements in mortality, morbidity, or growth outcomes. Future studies could try to clearly specify these optimal intervention characteristics. In addition, the timing of when preventive supplementation should be initiated in children could be further investigated. For instance, a few studies in this review started several months of preventive supplementation immediately after participants received therapeutic supplementation for an episode of diarrhea (Larson 2010; Sazawal 1996).

In addition, future studies could further evaluate fortification and dietary change interventions as alternative means of addressing zinc deficiency. These could be compared to a zinc supplementation intervention.

Overall, this review presents strong evidence for the effectiveness of preventive zinc supplementation on most of the outcomes analyzed. Many of the conclusions of this review would be robust to the results of further preventive zinc supplementation trials. Further updates of this review are unlikely to come to different conclusions in the absence of extremely large trials with different results.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abdollahi 2014

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: the districts of Damavand and Varamin, Iran; urbanicity: rural Inclusion criteria: children aged 6-24 months old; covered under health houses Exclusion criteria: N/A **Baseline characteristics** Avg age (months): Group 1: 14.5 ± 5.4, Group 2: 14.6 ± 5.4; min age (months): N/A; max age (months): N/A; % female: 48 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height in cm (SD): Group 1: 77.4 (± 6.2), Group 2: 77.5 (± 6.2); avg zinc concentration (µg/dL): N/A Total N: 593; Group 1 N: 291; Group 2 N: 302
Interventions	**Group 1:** zinc Formulation: syrup; compound: sulfate; frequency: daily; duration (months): 1; dose (mg): 5; co-intervention(s): multivitamin **Group 2:** no zinc No placebo given; co-intervention(s): multivitamin
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 12
Notes	**Study dates:** August-November 2009 **Funding source(s):** WHO

Abdollahi 2014 *(Continued)*

Comment(s): none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Minimization - Quote: "multistage randomized sampling deign was used, with HH [household] as the unit of randomization and children 6-24 months of age as the unit of analysis" ..."HHs were then randomly allocated to intervention (n=8) and control (n=9) arms within both districts. This type of randomization ensured the similarity of participants in both arms in terms of climate, socio-economic status, and access to health services."
Allocation concealment (selection bias)	Low risk	The randomization was done based on clusters and the allocation concealment was not of a major concern
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "To minimize potential bias, mothers were informed about the aim of this study, but not about the intervention or control groups"
Blinding of personnel (performance bias) All outcomes	High risk	Quote: "Behvarzes [a community health worker who delivered the intervention] could not be blinded to the intervention because of the required training." "Behvarzes replaced the vials at each visit and monitored the intake by parent recall and recorded the compliance with supplementation as well as symptoms of illness."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Anthropometric measurements were performed at baseline and followed-up on a monthly basis during the study period by Behvarzes in both intervention and control groups" "Behvarzes could not be blinded to the intervention because of the required training."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall there was low attrition. No reason for 3 excluded participants (1 intervention, 2 control) was provided i.e. Figure 1 all participants lost to follow-up were accounted for (moved, travel, did not attend at least one of monthly visits)
Selective reporting (reporting bias)	Low risk	Authors seems to report all the pre-specified outcomes.
Other bias	Low risk	No other risk of bias was noted

Abdollahi 2019

Study characteristics

Methods	CRCT; non-cross-over
Participants	Country: Iran; setting: Damavand, Pishva and Varamin, rural villages; urbanicity: rural Inclusion criteria: children 6-24 months old under the coverage of a rural health center Exclusion criteria: serious underlying disease; prescribed contraindications of taking zinc **Baseline characteristics** Avg age (months): 15.9; min age (months): N/A; max age (months): N/A; % female: 49.0

Abdollahi 2019 *(Continued)*

	Avg height-for-age z score: −0.1; stunting: both - separate data not given; avg height (cm): 78.7; avg zinc concentration (µg/dL): 83.6 Total N: 580; Group 1 N: 272; Group 2 N: 308
Interventions	**Group 1:** zinc Formulation: suspension/syrup; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency **Time point (week):** 24
Notes	**Study dates:** September 2014-May 2015 **Funding source(s):** UNICEF **Comment(s):** the study was registered at the Iranian Registry of Clinical Trials, under the registration number IRCT2014111519951N1.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Three boxes were numbered, each for one county and the names of all health centers of that county were put into its box. We drew the calculated number of the health centers from each box assigning the first draw to group one, the second to group two, the third to group one, the fourth to group two and so on."
Allocation concealment (selection bias)	Low risk	This was a CRCT, so issues with allocation concealment were less likely.
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "complete masking scheme of the investigators, health workers (service delivery and outcome assessment), staff of laboratories and the families was carried out (double blinded design)."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote, "complete masking scheme of the investigators, health workers (service delivery and outcome assessment), staff of laboratories and the families was carried out (double blinded design)."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote, "complete masking scheme of the investigators, health workers (service delivery and outcome assessment), staff of laboratories and the families was carried out (double blinded design)."

Abdollahi 2019 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Even though the Zinc group had 20% loss to follow up and control group had 8%. The loss to follow up in the Zinc group was due to administrative reasons. Also, the baseline characteristics were similar in both groups.
Selective reporting (reporting bias)	Low risk	Study authors seem to report all the relevant outcomes.
Other bias	Low risk	No other risk of bias was noted.

Ahmed 2009a

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh Setting: Mirpur, a slum area in Dhaka; urbanicity: urban Inclusion criteria: healthy Exclusion criteria: history of gastrointestinal disorder; suffered from any diarrheal disease in the past 2 weeks; febrile illness in the preceding week; received antibiotic treatment at least 7 d prior to enrollment; ≤ 2 SD (weight/length as NCHS); stool that was positive for common enteric pathogens **Baseline characteristics** Avg age (months): 14; min age (months): 10; max age (months): 18; % female: 53 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): 74.3; avg zinc concentration (µg/dL): 73 Total N: 40; Group 1 N: 20; Group 2 N: 20
Interventions	**Group 1:** zinc Formulation: solution; compound: acetate; frequency: daily; duration (months): 1.5; dose (mg): 20; Co-intervention(s): oral inactivated cholera vaccine **Group 2:** no zinc Placebo not given; Co-intervention(s): oral inactivated cholera vaccine
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** December 2007-April 2008 **Funding source(s):** Swedish Agency for International Development and Cooperation (Sida/SAREC); Marianne and Markus Wallenberg Foundation, through support to the Gothenburg University Vaccine Research Institute (GUVAX); ICDDR, B **Comment(s)** • In addition to the study groups mentioned in this table, there was a group of participants who received zinc only, but there was no placebo group to which this zinc group could be compared in this review. So, baseline characteristics reported in this table are weighted averages of all groups except this zinc group, since this group is not included in any meta-analyses in this review. • The trial authors might have meant to report "≤ -2 SD (weight/length as NCHS)" rather than "≤ 2 SD (weight/length as NCHS)" as part of this study's exclusion criteria.

Ahmed 2009a *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The children were randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "...no zinc placebo was administered…" Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "...no zinc placebo was administered…" Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...no zinc placebo was administered…" Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 5 Reasons/details: N/A Comment: 5% of the randomised participants eligible for our review had data missing; this 5% missing figure includes all groups except the zinc group, since this group is not included in any meta-analyses in this review. 2 children, both in the vaccine + zinc group, did not complete the study. Reasons for missing data were not given. However, the amount of missing data seems too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Akramuzzaman 1994

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: N/A; urbanicity: peri-urban

Akramuzzaman 1994 *(Continued)*

	Inclusion criteria: undernourished Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 34.8; min age (months): N/A; max age (months): N/A; % female: N/A Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 256; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: acetate; frequency: daily; duration (months): 15; dose (mg): 20; co-intervention(s): vitamins A, D, and C **Group 2:** no zinc Placebo given; co-intervention(s): vitamins A, D, and C
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 60
Notes	**Study dates:** N/A **Funding source(s):** Wellcome Trust/UK **Comment(s):** Though "both baseline and final measurements of weight and height were available in 197 (93 and 104 in zinc and placebo groups respectively) children", the numbers of children initially randomized to each group is not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…randomized clinical trial…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "...double blind…clinical trial..." Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "...double blind…clinical trial..." Comment: insufficient details available to make a judgement

Akramuzzaman 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...double blind…clinical trial..." Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Quote: "Of 256 children, both baseline and final measurements of weight and height were available in 197 (93 and 104 in zinc and placebo groups respectively) children." Comment: so, no more than 59 participants (23% of the original 256 randomised) were missing. However, the number randomised to each study group was not reported; nor was the exact number of participants missing in the zinc group, the exact number of participants missing in the placebo group, or reasons for missing data
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Alarcon 2004

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Peru; setting: Collique, a shanty town of Lima, Peru; urbanicity: peri-urban Inclusion criteria: moderately anemic (hemoglobin concentration between 70 and 99.9 g/L) Exclusion criteria: severe anemia (hemoglobin < 70.0 g/L); mild anemia (hemoglobin 100.0-109.9 g/L); chronic disease; any dietary restrictions; received treatment with one of the micronutrients in the study in the previous 6 months; measles; received a measles vaccine in the preceding 2 months; severe malnutrition (defined as weight-for-height < −3 SDs, HAZ < −3 SDs, or both) **Baseline characteristics** Avg age (months): 17.4; min age (months): 6; max age (months): 35; % female: N/A Avg height-for-age z score: −1.04; stunting: unclear; avg height (cm): 76.8; avg zinc concentration (µg/dL): N/A Total N: 223; Group 1 N: 112; Group 2 N: 111
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 6 d/week; duration (months): 4.5; dose (mg): 3 mg/kg; co-intervention(s): 3 mg/kg iron **Group 2:** no zinc Placebo given; co-intervention(s): 3 mg/kg iron
Outcomes	**Primary** • N/A **Secondary**

Alarcon 2004 *(Continued)*

- Incidence of all-cause diarrhea
- Prevalence of all-cause diarrhea
- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Study withdrawal
- Participants with ≥ 1 side effect
- Blood hemoglobin concentration (g/L)
- Prevalence of anemia
- Serum or plasma ferritin concentration (µg/L)
- Prevalence of iron deficiency

Time point (week): 18

Notes

Study dates: December 2001-April 2002

Funding source(s): N/A

Comment(s): in addition to the study groups mentioned in this table, there was a group of 112 participants who received zinc, iron, and vitamin A. Baseline characteristics reported in this table are weighted averages of all groups except the group that received zinc, iron, and vitamin A, since this group is not included in any meta-analyses in this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The children were...allocated by block randomization…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "This was a...double-blind trial…Supplements, prepared as syrup, were individually bottled and coded according to treatment group. The code was known only to the pharmacist and was not broken until the data analyses were completed. The placebos were tested before the study started, and no visual or organoleptic differences in the preparations could be detected." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "This was a...double-blind trial…Supplements, prepared as syrup, were individually bottled and coded according to treatment group. The code was known only to the pharmacist and was not broken until the data analyses were completed. The placebos were tested before the study started, and no visual or organoleptic differences in the preparations could be detected." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "This was a...double-blind trial…Supplements, prepared as syrup, were individually bottled and coded according to treatment group. The code was known only to the pharmacist and was not broken until the data analyses were completed. The placebos were tested before the study started, and no visual or organoleptic differences in the preparations could be detected." Comment: sufficient blinding seems likely

Alarcon 2004 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4 Reasons/details: in the zinc + iron group: 2 "moved", and 1 withdrew because their mothers "believed after 5-7 wk of treatment that their children were 'healthy' and refused further treatment." In the iron group: 2 "moved", 2 withdrew because their mothers "believed after 5-7 wk of treatment that their children were 'healthy' and refused further treatment", 1 was "absent at last sampling", and 2 "stopped treatment for perceived side effects (constipation, stomachaches, and staining of the teeth)." Comment: 4% of the randomised participants eligible for our review had data missing; this 4% missing figure includes all groups except the group that received zinc, iron, and vitamin A, since this group is not included in any meta-analyses in this review. Missing data seem too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Albert 2003

Study characteristics	
Methods	RCT
Participants	Country: Bangladesh; setting: Dhaka; urbanicity: urban Inclusion criteria: vitamin A deficiency (serum retinol level < 20 µg/dL, determined by testing of a blood sample obtained for pre-enrollment screening); nutritional status corresponding to a WAZ ≥ 61% of the median NCHS standard Exclusion criteria: received vitamin A supplementation during the preceding 6 months; history of night blindness or sickness due to underlying illnesses such as diarrhea, respiratory tract infections, or other infections **Baseline characteristics** Avg age (months): N/A; min age (months): 24; max age (months): 60; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): 62 Total N: 256; Group 1 N: N/A; Group 2 N: N/A; Group 3 N: N/A; Group 4 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: acetate; frequency: daily; duration (months): 1.5; dose (mg): 20; co-intervention(s): killed oral cholera vaccine **Group 2:** no zinc Placebo given; co-intervention(s): killed oral cholera vaccine **Group 3:** zinc Co-intervention(s): killed oral cholera vaccine; 200,000 IU vitamin A syrup 2 weeks after the start of zinc supplementation **Group 4:** no zinc

Albert 2003 *(Continued)*

	Placebo given; co-intervention(s): killed oral cholera vaccine; 200,000 IU vitamin A syrup 2 weeks after the start of zinc supplementation
Outcomes	**Secondary** • Prevalence of zinc deficiency **Time point (week):** 6
Notes	**Study dates:** June 1998-May 2000 **Funding source(s):** Thrasher Research Fund **Comment(s)** • At the end of the study, 61, 63, 62, and 63 children remained in the vitamin A, zinc, vitamin A + zinc, and placebo groups, respectively; however, the number of children randomized to each study group is not reported. • Though the percentage of trial participants who were female is approximately 44%, the reported ratio of boys to girls did not add up in the zinc group. • Though the unit of baseline zinc concentration was reported to be mg/dL, it seems that the unit should be µg/L. Assuming that the intended unit of zinc concentration was actually mg/L, then the average baseline zinc concentration was 62 µg/dL.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…children were randomly assigned…The randomization code…" Comment: though a "randomization code" was used, there are insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "The randomization code was broken after completion of the study. Bottles of syrup were serially numbered according to the randomization list, and this numbering corresponded to the study serial numbers. Enrolled children were assigned numbered bottles in the order in which they were recruited." Comment: indicates sequentially numbered drug containers of identical appearance to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind trial…" "The zinc syrup and its placebo syrup looked very similar…The randomization code was broken after completion of the study. " Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind trial…" "The zinc syrup and its placebo syrup looked very similar…The randomization code was broken after completion of the study. " Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind trial…" "The zinc syrup and its placebo syrup looked very similar…The randomization code was broken after completion of the study. " Comment: sufficient blinding seems likely

Albert 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3 Reasons/details: N/A Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: serum zinc concentration was measured, but is not reported in a way that can be meta-analyzed.
Other bias	Low risk	Comment: appears to be free of other bias.

Albert 2003 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Secondary** • Prevalence of zinc deficiency **Time point (week):** 6
Notes	As Albert 2003 above

Ba Lo 2011

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Senegal; setting: neighborhood of Dakar; urbanicity: urban Inclusion criteria: LAZ and WLZ > −2.0 with respect to the WHO growth standard; hemoglobin concentration > 80 g/L; no consumption of zinc-fortified foods or zinc-containing vitamin-mineral supplements; no symptomatic infections within the preceding 2 weeks Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 13.2; min age (months): 9; max age (months): 17; % female: 52.6 Avg height-for-age z score: −0.44; stunting: non-stunted; avg height (cm): 75; avg zinc concentration (µg/dL): 63.3 Total N: 97; Group 1 N: 50; Group 2 N: 47
Interventions	**Group 1:** zinc

Ba Lo 2011 *(Continued)*

	Formulation: solution; compound: sulfate; frequency: daily; duration (months): 0.5; dose (mg): 6; co-intervention(s): 200 mg albendazole as a single oral dose at enrollment; 30 g dry weight iron-fortified cereal porridge; a liquid multivitamin supplement **Group 2:** no zinc Placebo given; co-intervention(s): 200 mg albendazole as a single oral dose at enrollment; 30 g dry weight iron-fortified cereal porridge; a liquid multivitamin supplement
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 2
Notes	**Study dates:** July 2008-September 2009 **Funding source(s):** Global Alliance for Improved Nutrition **Comment(s):** in addition to the study groups mentioned in this table, there was a group of 40 participants who received 30 g dry weight iron-fortified cereal porridge with added zinc to provide 6 mg zinc per 25 g dry weight of porridge, but who did not receive any zinc supplement. Baseline characteristics reported in this table are weighted averages of all groups except this "ZnFort group", since this group is not included in any meta-analyses in this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Eligible children were randomly assigned to 1 of 3 treatment groups for a 15-d period by using a computer-generated block randomization scheme, with a varied block length of 3, 6, or 9 (www.randomization.com)." Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "A double-blind intervention trial…Group assignments remained masked until all biochemical and statistical analyses were completed." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "A double-blind intervention trial…Group assignments remained masked until all biochemical and statistical analyses were completed." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A double-blind intervention trial…Group assignments remained masked until all biochemical and statistical analyses were completed." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	High risk	% Missing: 32 Reasons/details: in the zinc group: 2 participants were missing due to illness, 6 due to travel, 7 due to "insufficient consumption of porridge", and 1 due to

Ba Lo 2011 *(Continued)*

		withdrawn consent. In the control group: 1 participant was missing due to illness, 6 due to travel, 5 due to "insufficient consumption of porridge", and 3 due to withdrawn consent. Comment: 32% of the randomised participants eligible for our review had data missing; this 32% missing figure includes all groups except the "ZnFort group", since the ZnFort group is not included in any meta-analyses in this review. A large proportion of data is missing. Different proportions of each study group were missing due to "insufficient consumption of porridge" and withdrawn consent. Those who were randomised, but not analyzed also had slightly different anthropometric data at baseline.
Selective reporting (reporting bias)	Low risk	Comment: length, weight, and hemoglobin concentration were measured at baseline and at the end of the supplementation period, but are not reported as post-intervention outcomes. Diarrhoea prevalence was measured, but is not reported in a way that can be meta-analyzed. All of these outcomes were prespecified in the protocol for this study. However, the authors of this study explained that there was probably not sufficient time to allow for detectable differences in morbidity or growth, and that these outcomes were included in the measurements simply to control for any baseline differences or possible confounding Protocol identifier: NCT0094398
Other bias	Low risk	Comment: appears to be free of other bias

Baqui 2003

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: Matlab subdistrict; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: fed infant formula; severe malnutrition (MUAC < 110 mm); severe anemia (hemoglobin concentration < 90 g/L); signs of neurological disorders, physical disability, or chronic illness that might affect feeding, activity, and cognitive development; family not planning to stay in the trial area for 6 months **Baseline characteristics** Avg age (months): 6; min age (months): 6; max age (months): 6; % female 47.2 Avg height-for-age z score: −1.2; stunting: both - separate data not given; avg height (cm): 64.1; avg zinc concentration (µg/dL): 67.6 Total N: 645; Group 1 N: 161; Group 2 N: 157; Group 3 N: 162; Group 4 N: 165
Interventions	**Group 1:** zinc Formulation: solution; compound: acetate; frequency: weekly; duration (months): 6; dose (mg): 20; co-intervention(s): 1 mg riboflavin **Group 2:** no zinc Placebo given; co-intervention(s): 1 mg riboflavin **Group 3:** zinc

Baqui 2003 *(Continued)*

	Co-intervention(s): 20 mg iron, 1 mg riboflavin **Group 4:** no zinc Placebo given; co-intervention(s): 20 mg iron, 1 mg riboflavin
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of severe diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (mg/L) • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) • Serum or plasma copper concentration (mg/L) **Time point (week):** 24
Notes	**Study dates:** N/A **Funding source(s):** USAID; Nutricia Foundation through ICDDR,B; International Centre for Health and Population Research, Dhaka, Bangladesh **Comment(s)** • In addition to the 645 participants mentioned in this table, there was a group of 154 participants who received a MM. Baseline characteristics reported in this table were obtained from the Baqui 2003 trial report and are weighted averages of all groups except the MM group, because the MM group is not included in any meta-analyses in this review. • Vitamin A was not directly provided in this study, "Because vitamin A supplementation is a national program in Bangladesh, infants in all groups received 100,000 IU of vitamin A...at the beginning of the study."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Block randomization was done within strata to ensure equivalent enrollment…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, randomized, controlled community trial...Each study infant received a weekly dose of the assigned supplement, which was presented in the same type of capsules and labeled in such a way that the various types of supplements could not be differentiated." "The supplements were prepared as capsules, which were mixed with flavored syrup and fed to the infants. The mixtures were similar in taste and appearance."

Baqui 2003 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, randomized, controlled community trial...Each study infant received a weekly dose of the assigned supplement, which was presented in the same type of capsules and labeled in such a way that the various types of supplements could not be differentiated." "The supplements were prepared as capsules, which were mixed with flavored syrup and fed to the infants. The mixtures were similar in taste and appearance." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, randomized, controlled community trial...Each study infant received a weekly dose of the assigned supplement, which was presented in the same type of capsules and labeled in such a way that the various types of supplements could not be differentiated." "The supplements were prepared as capsules, which were mixed with flavored syrup and fed to the infants. The mixtures were similar in taste and appearance." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 12 Reasons/details: 14, 19, 30, and 12 participants "refused continued participation" in the iron, zinc, iron-zinc, and control group, respectively; in the zinc group, 2 migrated out and 1 died; in the control group, 1 migrated out. "6% in the iron + zinc group dropped out due to vomiting. In contrast, 0–2% of the infants in other groups dropped out due to vomiting", though it is unclear whether or not these participants who dropped out due to vomiting are included in the number of participants who "refused continued participation." For the subset of participants contributing zinc, hemoglobin, ferritin, and copper concentration data, "It was not possible to obtain 2 blood samples from all children and some samples were found to be hemolyzed or insufficient in quantity." For the sub-set of participants contributing height, weight, and height-to-rate ratio data, "Staff availability, transportation, and inclement weather were the primary reasons for missing data." Comment: 12% of the 645 randomised participants eligible for our review had data missing for diarrhea and LRTI outcomes; this 12% missing figure includes all groups except the micronutrient mix (MM) group, since the MM group is not included in any meta-analyses in this review. "The baseline characteristics of the children who were excluded or lost to follow up were comparable to those of the children who continued in the study", and missing data seem unlikely to bias results
Selective reporting (reporting bias)	High risk	Comment: number of participants who dropped out due to vomiting was measured, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Baqui 2003 (2)

Study characteristics
Methods
Participants

Baqui 2003 (2) *(Continued)*

Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of severe diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (mg/L) • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) • Serum or plasma copper concentration (mg/L) **Time point (week):** 24
Notes	As Baqui 2003 above

Barffour 2019

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Laos; setting: rural communities in Khammouane Province, central Lao People's Democratic Republic; urbanicity: rural Inclusion criteria: children 6–23 months of age; children's families accepted weekly visits; planned residency within the study area for the duration of the study; signed informed consent Exclusion criteria: severe anemia (Hb < 70 g/L); WLZ < 3; presence of bipedal edema; severe illness warranting hospital referral; congenital abnormalities potentially interfering with growth; chronic medical condition (e.g. malignancy) requiring frequent medical attention; known HIV infection of index child or child's mother; currently consuming zinc supplements; current participation in another clinical trial **Baseline characteristics** Avg age (months): 14.3 ± 5.0; min age (months): N/A; max age (months): N/A; % female 48.9 Avg height-for-age z score: −1.75 ± 1.08; stunting: both - separate data not given; avg height (cm): 7.25 ± 5.5; avg zinc concentration (µg/dL): 54.2 ± 14.2 Total N: 1478; Group 1 N: 738; Group 2 N: 740
Interventions	**Group 1:** zinc Formulation: tablet; compound: gluconate; frequency: daily; duration (months): 8-10; dose (mg): 7; co-intervention(s): placebo therapeutic tablets for diarrhea **Group 2:** control: no zinc, placebo Placebo given; co-intervention(s): placebo therapeutic tablets for diarrhea

Barffour 2019 *(Continued)*

Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Prevalence of stunting • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) **Time point (week):** 36
Notes	**Study dates:** September 2015-April 2017 **Funding source(s):** Mathile Institute for the Advancement of Human Nutrition and Nutrition International (formerly the Micronutrient Initiative); Bill & Melinda Gates Foundation **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: the randomization scheme was generated by UC Davis statisticians using a computer-generated block randomization scheme, with randomly selected block lengths of 4 or 8.
Allocation concealment (selection bias)	Low risk	Comment: the identity of the treatment codes is stored in sealed envelopes held by the co-principal investigators (PIs) and the statistician.
Blinding of participants (performance bias) All outcomes	Low risk	Comment: the specific nutrient contents of the combinations of products in each of the 4 study arms were not explicitly detailed during fieldworker training or provided descriptions of the study. A UC Davis faculty member, unaffiliated with the study, was responsible for assigning each of the 4 study codes to an intervention product and communicating this information directly to the product manufacturers.
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: the specific nutrient contents of the combinations of products in each of the four study arms were not explicitly detailed during fieldworker training or provided descriptions of the study. A UC Davis faculty member, unaffiliated with the study, was responsible for assigning each of the 4 study codes to an intervention product and communicating this information directly to the product manufacturers.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: the envelopes will be opened only after statistical analyses of primary outcomes are completed and consensus on the interpretation of results is reached, unless required by one of the Institutional Review Boards or the data safety and monitoring board (DSMB)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: from a total of 529 children who provided hair samples at both baseline and endline assessments, hair zinc concentration was successfully assessed in 512 children. Unclear what happened to the remaining 17 children.

Barffour 2019 *(Continued)*

Selective reporting (reporting bias)	Low risk	Quote: "In particular, the investigators plan to compare the impact on physical growth, morbidity, micronutrient status, immune function, environmental enteric dysfunction, parasite burden and hair cortisol concentration of: 1) daily preventive zinc supplementation as a micronutrient powder (MNP); 2) placebo powders; 3) daily preventive zinc supplementation as dispersible tablets; 4) therapeutic zinc supplementation as dispersible tablets given in relation to episodes of diarrhea. In addition to the major outcomes mentioned above, the investigators will monitor adherence to the interventions, neuro-behavioral development, and the occurrence of any adverse events."
Other bias	Low risk	Comment: no evidence of other bias noted.

Becquey 2016

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Burkina Faso; setting: the Orodara Health District in southwestern Burkina Faso; urbanicity: rural Inclusion criteria: children 6–27 months of age; residence within the study communities; not supplemented with zinc Exclusion criteria: weight-for-height Z-score < 70% of the NCHS/WHO growth reference median; presence of bipedal edema, hemoglobin < 50 g/L, acute illnesses requiring inpatient treatment, or known congenital abnormalities or chronic diseases that may affect growth or risk of infection; once enrolled, failure to consume supplements or provide morbidity surveillance information for > 14 consecutive days (considered a dropout) **Baseline characteristics** Avg age (months): 14 ± 6 at enrolment; min age (months): N/A; max age (months): N/A; % female 47 Avg height-for-age z score: zinc: −1.35 (± 0.602), control: −1.41 (± 0.0598); stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 4689; Group 1 N: 2679; Group 2 N: 2010
Interventions	**Group 1:** zinc Formulation: tablet; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 7; co-intervention(s): oral rehydration salts + placebo tablet x 10 d for treatment of diarrhea episodes **Group 2:** no zinc Placebo not given; co-intervention(s): oral rehydration salts for treatment of diarrhea episodes
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Incidence of severe diarrhea

Becquey 2016 *(Continued)*

- Incidence of malaria
- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µg/dL)
- Prevalence of zinc deficiency

Time point (week): 48

Notes

Study dates: December 2010- February 2012

Funding source(s): Thrasher Research Fund; Canadian International Development Agency; Nutricia Research Foundation; Nutriset

Comment(s)

- We included the data for the comparison of daily preventive zinc supplementation vs morbidity surveillance control.
- The data for all-cause mortality were taken from Figure 2 of the paper published in the Journal of Nutrition. We considered mortality only during the first round, as we could not calculate the cumulative risk of mortality over time, as new participants were recruited.
- The data for incidence of diarrhea were taken from Table 4 of the paper published in the Journal of Nutrition. We first calculated the rate ratio by considering the incidence rate per 100 d for the given child periods. We then pooled the rate ratio in a meta-analysis using the generic inverse variance method. The denominators in the meta-analysis are total number of participants at the end of trial and not child period (though the calculations for rate ratios were done with child period).
- The data for growth outcome were taken from Table 5 of the published manuscript. We considered data at 16 weeks. We converted the SE to SD. The denominators in the calculation were child period followed for weight and height and total participants at the end of 16-week period for weight for height.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: the study area was divided into 36 geographically defined clusters stratified by selected characteristics. The statistician randomly assigned clusters within a stratum to 1-3 schedules for initiation of supplementation. For supplementation, nurses randomly assigned children to 1-3 supplementation regimes at level of concession with use of block randomization scheme with block length of 6.
Allocation concealment (selection bias)	Low risk	Comment: once supplementation was scheduled to start, study nurses randomly assigned eligible children to 1 of the 3 supplementation regimens at the level of concession (extended family compound) with the use of a block randomization scheme with a block length of 6.
Blinding of participants (performance bias) All outcomes	Unclear risk	Comment: there was not enough information from the published article to make an accurate assessment for blinding of participants.
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: partially masked
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: partially masked

Becquey 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: a total of 7907 children in 36 clusters were screened for eligibility. Of these, 7641 children were enrolled, and they contributed 11,456 16-week child–periods of observation and 10,029 follow-up anthropometric assessments over the whole study. During the course of the study, 1743 children received IPZS; 1743 received DPZS; and 1766received TZS for durations that ranged from 1 to 50 week. A total of 2339children were included in the MSC group, and 1216 children were included in the NIC group. The proportion of participants who completed the study (87%) did not differ between study groups. Reported adherence to the preventive supplements was very high (98%–100%), but lower for therapeutic supplementation (47%). The guardians sought treatment from the CHW during just 61.8% of reported diarrhea episodes, although among those who visited the CHW, reported adherence was fairly high at 72% of scheduled doses. Reported adherence to either form of supplement did not differ by supplementation group.
Selective reporting (reporting bias)	Low risk	Comment: gave different interpretations of the results
Other bias	Low risk	Comment: no other risk of bias was noted.

Berger 2015

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Athens–Clarke County area in northeast Georgia; urbanicity: unclear Inclusion criteria: girls of non-Hispanic white or non-Hispanic black/African American race; aged 9–11 years Exclusion criteria: taking medications; any medical condition that could affect growth, pubertal maturation, nutritional status, or metabolism; having experienced menses **Baseline characteristics** Avg age (months): 126; min age (months): N/A; max age (months): N/A; % female: 100 Avg height-for-age z score: N/A; stunting: non-stunted; avg height (cm): 148.5; avg zinc concentration (µg/dL): 1.2 Total N: 147; Group 1 N: 75; Group 2 N: 72
Interventions	**Group 1:** zinc Formulation: tablet; compound: sulfate; frequency: daily; duration (months): 1; dose (mg): 9; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary**

Berger 2015 *(Continued)*

	• Serum or plasma zinc concentration (μmol/L) **Time point (week):** 4
Notes	**Study dates:** summer 2009-spring 2010 **Funding source(s):** NIH **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: participant identification numbers were used to randomly assign children by following simple randomization procedures to either zinc or control groups.
Allocation concealment (selection bias)	Low risk	Comment: a laboratory technician labeled tablet bottles with the appropriate corresponding treatment code. All investigators, research personnel, and participants remained blinded to these codes until statistical analyses were complete.
Blinding of participants (performance bias) All outcomes	Low risk	Comment: all investigators, research personnel, and participants remained blinded to these codes until statistical analyses were complete.
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: all investigators, research personnel, and participants remained blinded to these codes until statistical analyses were complete.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: all investigators, research personnel, and participants remained blinded to these codes until statistical analyses were complete.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: low attrition. Outcomes less likely to be affected because of incomplete outcome data
Selective reporting (reporting bias)	Unclear risk	Comment: study authors seem to report all the relevant outcomes.
Other bias	Low risk	Comment: no evidence of other sources of bias.

Bertinato 2013

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Canada; setting: Ontario; urbanicity: unclear Inclusion criteria: healthy boys aged 6-8 years; had not taken a mineral supplement in the past 3 months; agreed to not take mineral supplements, sodium fluoride, or aspirin during the study; normal baseline results for routine blood and urine tests, including complete blood count, electrolytes, and indicators of renal and hepatic function Exclusion criteria: girls; childhood illness of diarrhea and infections; chronic medical conditions

Bertinato 2013 *(Continued)*

	Baseline characteristics Avg age (months): placebo: 95.7 ± 3.0, Zn5: 92.7 ± 3.4, Zn10: 96.7 ± 2.5, Zn15: 94.8 ± 3.2; min age (months): N/A; max age (months): N/A; % female: 0 Avg height-for-age z score: N/A; stunting: non-stunted; avg height in centimeters (SD): placebo: 133.0 (± 1.9), Zn5: 130.3 (± 1.6), Zn10: 129.5 (± 2.3), Zn15: 129.4 (± 1.5); avg zinc concentration (µmol/L): 14.8 Total N: 37; Group 1 N: 27 (Zn5: 10, Zn10: 9, Zn15: 8); Group 2 N: 10 Zn5: received 5 mg zinc/d; Zn10: received 10 mg zinc/d; Zn15: received 15 mg zinc/d
Interventions	**Group 1:** zinc Formulation: tablet; compound: gluconate; frequency: twice daily; duration (months): 4; dose (mg/d): 5 (Zn5), 10 (Zn10), or 15 (Zn15); co-intervention(s): copper and iron **Group 2:** no zinc Placebo given; co-intervention(s): copper and iron
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) • Serum or plasma copper concentration (µmol/L) **Time point (week):** 16
Notes	**Study dates:** Feburary 2007-March 2010 **Funding source(s):** Bureau of Nutritional Sciences, Health Canada **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Permuted blocks of 4 were used for randomization of participants to treatment groups."
Allocation concealment (selection bias)	Low risk	Quote: "Jamieson Laboratories prepared and masked (with a letter code) the placebo and zinc tablets. The code was concealed until all data were ready for statistical analyses. The zinc and placebo tablets were visually indistinguishable"
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Jamieson Laboratories prepared and masked (with a letter code) the placebo and zinc tablets. The code was concealed until all data were ready for statistical analyses. The zinc and placebo tablets were visually indistinguishable"
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Jamieson Laboratories prepared and masked (with a letter code) the placebo and zinc tablets. The code was concealed until all data were ready for

Bertinato 2013 *(Continued)*

		statistical analyses. The zinc and placebo tablets were visually indistinguishable"
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: the study did not report this.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no missing outcome data, exclusions were reported with reason
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information available to permit a judgement of 'low risk' or 'high risk'
Other bias	Low risk	Comment: the study appears to be free of other sources of bias.

Bhandari 2002

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: India; setting: the urban slum of Dakshinpuri, New Deli; urbanicity: urban Inclusion criteria: in a family that did not intend to emigrate Exclusion criteria: likely to move out of the study area within the next 4 months; required urgent hospitalization on the scheduled enrollment; received massive dose of vitamin A (100,000 IU [30 mg] for infants and 200,000 IU [60 mg] for older children) within the last 2 months **Baseline characteristics** Avg age (months): 15.3; min age (months): 6; max age (months): 30; % female: 47.7 Avg height-for-age z score: −1.82; stunting: both - separate data not given; avg height (cm): 72.7; avg zinc concentration (µg/dL): 62 Total N: 2482; Group 1 N: 1241; Group 2 N: 1241
Interventions	**Group 1:** zinc Formulation: solution; compound: gluconate; frequency: daily; duration (months): 4; dose (mg): 10 mg to children 6-12 months of age, 20 mg to children 12-30 months of age; co-intervention(s): 100,000 IU vitamin A at enrollment for infants, 200,000 IU vitamin A at enrollment for older children **Group 2:** no zinc Placebo given; co-intervention(s): 100,000 IU vitamin A at enrollment for infants, 200,000 IU vitamin A at enrollment for older children
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea

Bhandari 2002 *(Continued)*

- Incidence of severe diarrhea
- Incidence of persistent diarrhea
- Incidence of LRTI
- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µg/dL)
- Prevalence of zinc deficiency
- Study withdrawal
- Vomiting episodes
- Serum or plasma copper concentration (µg/dL)
- Prevalence of copper deficiency

Time point (week): 16-17

Notes	**Study dates:** February 1998-September 2000 **Funding source(s):** European Union; Norwegian Council of Universities' Committee for Development Research and Education; Department of Child and Adolescent Health and Development, WHO **Comment(s):** "…all included subjects were given a massive dose of vitamin A...at enrollment in addition to zinc or placebo as required by the national program policy"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A simple randomization scheme in blocks of 8 was generated...using the SAS software…" Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "A simple randomization scheme...was generated by a person at Statens Serum Institut, who was not involved in the field work or the data analysis…The zinc and placebo syrups were prepared and packaged in unbreakable bottles by GK Pharma ApS (Køge, Denmark), which also labeled the bottles with unique identification numbers according to the randomization code. The zinc and placebo syrups were similar in...packaging." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) and sequentially numbered drug containers of identical appearance to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "A double-blind, randomized, placebo-controlled trial was conducted...The zinc and placebo syrups were similar in appearance, taste, and packaging." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "A double-blind, randomized, placebo-controlled trial was conducted...The zinc and placebo syrups were similar in appearance, taste, and packaging." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A double-blind, randomized, placebo-controlled trial was conducted...The zinc and placebo syrups were similar in appearance, taste, and packaging."

Bhandari 2002 *(Continued)*

		Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 10 Reasons/details: in the zinc group, 13 participants "refused further participation on the first weekly visit", 35 "refused further participation" after the first weekly visit, and 100 moved. In the placebo group, 5 participants "refused further participation on the first weekly visit", 16 "refused further participation" after the first weekly visit, and 84 moved. "Eight children in the zinc group and none in the placebo group discontinued the intervention because of vomiting." It seems that these 8 children are probably included among those who refused further participation. "Three children, all in the placebo group, died." Comment: reasons for missing data were similar between study groups. Migration was the most common reason for missing data, and this reason is unlikely to bias results.
Selective reporting (reporting bias)	High risk	Comment: plasma ferritin was measured, but is not reported. Plasma ferritin was not pre-specified in the protocol for this study. All-cause hospitalization was reported, but was not pre-specified in the protocol for this study Protocol identifier: NCT00272116
Other bias	Low risk	Comment: appears to be free of other bias

Bhandari 2007

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: India; setting: north and northwest New Delhi; urbanicity: urban Inclusion criteria: local residents; unlikely to move away over the next 6 months; unlikely to be absent from the study area for ≥ 3 months over the subsequent year Exclusion criteria: major congenital anomalies, severe malnutrition, or any serious condition that affected the ability of the child to consume the supplement; children with visible severe wasting were enrolled after rehabilitation; children with illnesses requiring hospitalization were excluded temporarily and screened again after recovery **Baseline characteristics** Avg age (months): 14.88; min age (months): 6; max age (months): 23; % female: 47.1 Avg height-for-age z score: −1.95; stunting: both - separate data not given; avg height (cm): 72.35; avg zinc concentration (µg/dL): 64.27 Total N: 72,438; Group 1 N: 36,293; Group 2 N: 36,145 Total clusters: 68,146; Group 1 clusters: 34,201; Group 2 clusters: 33,945
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): 12.5 mg iron, 50 µg folic acid **Group 2:** no zinc Placebo given; co-intervention(s): 12.5 mg iron, 50 µg folic acid

Bhandari 2007 *(Continued)*

Outcomes	**Primary** • All-cause mortality • Mortality due to all-cause diarrhea • Mortality due to LRTI **Secondary** • All-cause hospitalization • Hospitalisation due to all-cause diarrhea • Hospitalization due to LRTI • Height (cm) • Weight (kg) • Prevalence of stunting, serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency • Participants with ≥ 1 vomiting episode • Serum or plasma ferritin concentration (ng/mL) • Prevalence of iron deficiency • Serum or plasma copper concentration (µg/dL) **Time point (week):** 52
Notes	**Study dates:** February 2002-August 2003 **Funding source(s):** Department of Child and Adolescent Health and Development, WHO; United Nations Foundation **Comment(s):** all baseline and outcome data from this study included in this review apply only to the subset of this study's participants who were at least 6 months of age at baseline.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Two randomization lists were computer generated (one for each stratum)...Each list had permuted blocks of 16 participants randomly allocated to 16 letter codes. Half of the 16 letter codes were randomly assigned to the zinc and IFA group and the other half to the IFA group." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "…randomization lists were computer generated...by a staff member of the World Health Organization (WHO)." Participants were "randomly allocated to 16 letter codes. Half of the 16 letter codes were randomly assigned to the zinc and IFA group and the other half to the IFA group. This code was only available with the WHO and the company that prepared and packaged the supplement...Randomization lists containing only serial numbers (that represented household numbers) and respective letter codes were made available to the investigators, but they did not know which of the 16 letter codes represented the 2 study groups." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double blind cluster-randomized controlled trial…The control group tablets were similar in appearance and taste except they contained a placebo for zinc."

Bhandari 2007 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double blind cluster-randomized controlled trial…The control group tablets were similar in appearance and taste except they contained a placebo for zinc." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double blind cluster-randomized controlled trial…The control group tablets were similar in appearance and taste except they contained a placebo for zinc." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4 Reasons/details: in the zinc + iron + folic acid group: 173 participants died, 31 participants "refused further participation", and 1394 "moved away before completing 12 mo follow-up." In the iron + folic acid group: 165 participants died, 17 participants "refused further participation", and 1369 "moved away before completing 12 mo follow-up." Comment: reasons for missing data were similar between study groups. Migration was the most common reason for missing data, and this reason is unlikely to bias results. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: prevalence of stunting and mean plasma copper concentration were pre-specified as secondary outcomes in the protocol for this study, but are not reported. Height and weight were measured, but were not pre-specified in the protocol for this study and are not reported. Plasma zinc concentration, prevalence of iron deficiency, hospitalization due to any cause, mortality due to diarrhea, and mortality due to LRTI were reported, but were not pre-specified in the protocol for this study; though related outcomes, such as prevalence of zinc deficiency, plasma ferritin concentration, hospitalizations due to diarrhea and pneumonia, and all-cause mortality, were pre-specified in the protocol for this study Protocol identifier: NCT00269542
Other bias	Low risk	Comment: appears to be free of other bias

Brown 2007

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Peru; setting: Trujillo, a city on the northern coast of Peru; urbanicity: peri-urban Inclusion criteria: LAZ < −0.5; WLZ > −3 (to exclude those with acute malnutrition, who were referred for treatment); hemoglobin > 8.0 g/dL Exclusion criteria: congenital abnormalities or chronic diseases affecting growth; use of infant formula providing > 1 mg Zn/d ≥ 5 times/week; a twin enrolled in the study; families that were not planning to remain in the study community for the next 7 months **Baseline characteristics** Avg age (months): 7.5; min age (months): 6; max age (months): 8; % female: 51.5

Brown 2007 *(Continued)*

	Avg height-for-age z score: −1.19; stunting: both - separate data not given; avg height (cm): 65.4; avg zinc concentration (µg/dL): 77.6 Total N: 200; Group 1 N: 101; Group 2 N: 99
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 3; co-intervention(s): 30 g dry weight of an iron-fortified cereal porridge; an aqueous multivitamin supplement **Group 2:** no zinc Placebo given; co-intervention(s): 30 g dry weight of an iron-fortified cereal porridge; an aqueous multivitamin supplement
Outcomes	**Primary** • N/A **Secondary** • Prevalence of all-cause diarrhea • Incidence of severe diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µg/dL) • Blood hemoglobin concentration (g/dL) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency • Serum or plasma copper concentration (µg/dL) **Time point (week):** 24
Notes	**Study dates:** October 2003-November 2004 **Funding source(s):** Bill & Melinda Gates Foundation **Comment(s):** in addition to the study groups mentioned in this table, there was a group of 102 participants who received 30 g dry weight of an iron- and zinc-fortified cereal porridge along with the aqueous multivitamin supplement. Baseline characteristics reported in this table are weighted averages of all groups except this zinc-fortified group, since this group is not included in any meta-analyses in this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: participants "were randomly assigned to...treatment groups by using a block randomization scheme, with a varied block length of 3 or 6." "We used the random number generator within SAS to randomly shuffle the treatments within each block." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: in response to the question, "Could you describe how you ensured that participants, and investigators enrolling participants, could not tell which group a new participant would be assigned to?" an author of this study replied

Brown 2007 *(Continued)*

		as follows: "One of the study investigators (Mary Penny) was responsible for coding and treatment assignment. She was not involved with the implementation of the study at the field site and the rest of the investigators, study personnel, and of course participants, were not aware of the coding and treatment assignment. The trial was conducted in a city 600 km north of Lima. Dr. Penny kept the code in Lima and every month sent coded porridge and supplements to the field site." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Zinc supplements were delivered in coded bottles undistinguishable from placebo. A lab technician in Lima prepared zinc supplements and placebos and placed this in the coded bottles. Zinc supplements and placebo had the same appearance, taste, etc." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Zinc supplements were delivered in coded bottles undistinguishable from placebo. A lab technician in Lima prepared zinc supplements and placebos and placed this in the coded bottles. Zinc supplements and placebo had the same appearance, taste, etc." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Zinc supplements were delivered in coded bottles undistinguishable from placebo. A lab technician in Lima prepared zinc supplements and placebos and placed this in the coded bottles. Zinc supplements and placebo had the same appearance, taste, etc." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 11 Reasons/details: N/A Comment: 11% of the randomised participants eligible for our review had data missing; this 11% missing figure includes all groups except the zinc-fortified group, since this group is not included in any meta-analyses in this review. No information was reported on reasons for dropout. Furthermore, the study authors reported that, "One possible limitation of our study was the disproportionate number of dropouts from the 2 groups that received additional zinc and the fact that those who left the study early differed slightly with regard to their initial rates of breastfeeding, anthropometric indicators of nutritional status, and prevalence of diarrhea...Nevertheless...the overall attrition rate was relatively small, as were the differences between the children who left the study early and those who completed the study, so these should not have exerted any major effect on the results."
Selective reporting (reporting bias)	Low risk	Comment: in response to an inquiry concerning the protocol for this study, a study author replied as follows: "This trial was conducted, if I am not mistaken, before trial registry was implemented. Unfortunately, I cannot share the protocol with you given we do not share these with external investigators. Nevertheless, I can tell you that all reported outcomes in the article were pre-specified before the start of the trial." Furthermore, based on the trial reports for this study, there were no outcomes of interest to this review that were: (a) measured, but (b) not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Castillo-Durán 1994

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Chile; setting: slums of Santiago; urbanicity: peri-urban Inclusion criteria: in the low-income group, defined by the Graffar scale; short stature, defined as length measurements < the 5th percentile for age according to WHO/NCHS standards Exclusion criteria: chronic diseases (e.g. Celiac disease, fetal alcohol syndrome, cardiac or chronic renal disease, genetic disorders) **Baseline characteristics** Avg age (months): 127.4; min age (months): 72; max age (months): 168; % female: 48 Avg height-for-age z score: N/A; stunting: stunted; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 114 or 113; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: capsule; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 52
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • It is unclear whether 114 or 113 participants were randomized. The number of participants randomized to the zinc group was not reported, nor was the number of participants randomized to the placebo group. • The HAZ outcome in this study was calculated, in part, based on the assumption that some height data reported in "F for difference between changes" format had a pre-post correlation of 0.5; however, assuming a pre-post correlation of 0.2 or 0.8 did not change the calculated result for this outcome.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were assigned randomly…"

Castillo-Durán 1994 *(Continued)*

		Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "For each age and gender group, children were assigned randomly to a supplement (S) or placebo (P) group in a double-blind fashion." Participants were "followed up for 12 months using a double-blind design." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "For each age and gender group, children were assigned randomly to a supplement (S) or placebo (P) group in a double-blind fashion." Participants were "followed up for 12 months using a double-blind design." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "For each age and gender group, children were assigned randomly to a supplement (S) or placebo (P) group in a double-blind fashion." Participants were "followed up for 12 months using a double-blind design." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 30 Reasons/details: "Thirty-four other subjects were left out during the initial 3 months of the study because of poor compliance with ingestion of the supplemental capsule…" Comment: a large proportion of data is missing. The number of participants randomised to the zinc group was not reported; nor was the number of participants randomised to the placebo group. Thus, it is difficult to tell whether amounts of missing data were similar between study groups
Selective reporting (reporting bias)	High risk	Comment: height (for pre-adolescent females), weight (for all participants except pre-adolescent males), and weight-for-height were measured, but are not reported in a way that can be meta-analyzed. It is unclear whether the plasma zinc concentration reported was measured at baseline or after supplementation as a post-intervention outcome
Other bias	Low risk	Comment: appears to be free of other bias

Castillo-Durán 2002

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Chile; setting: Santiago; urbanicity: urban Inclusion criteria: normal weight and length; free from chronic diseases; children of literate mothers able to understand and sign written consent Exclusion criteria: N/A **Baseline characteristics**

Castillo-Durán 2002 *(Continued)*

	Avg age (months): N/A; min age (months): 17; max age (months): 19; % female: 0 Avg height-for-age z score: N/A; stunting: non-stunted; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 42; Group 1 N: 21; Group 2 N: 21
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** N/A **Funding source(s):** The National Fund for Scientific and Technological Development (FONDECYT), Chile; International Atomic Energy Agency Comment(s): none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were randomized…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "...double blind trial…" Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "...double blind trial…" Comment: insufficient details available to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...double blind trial…" Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 19 Reasons/details: "Eight children were excluded due to non compliance with daily administration of syrup or to change of address limiting home visits." Comment: a fairly large proportion of data is missing, and neither reasons for, nor amounts of, missing data were reported separately for the zinc group versus the placebo group.
Selective reporting (reporting bias)	High risk	Comment: plasma zinc concentration, weight, and length were measured, but are not reported in a way that can be meta-analyzed. "Morbidity outcomes" were measured, but the exact types of morbidity outcomes measured were

Castillo-Durán 2002 *(Continued)*

		not defined; so, other outcomes, such as diarrhea or LRTI, might have been measured but not reported.
Other bias	Low risk	Comment: appears to be free of other bias

Caulfield 2013

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Peru; setting: Villa Salvador, an urban settlement area in the greater metropolitan area of Lima, Peru; urbanicity: urban Inclusion criteria: weight > 2500 g at birth; gestational age > 37 completed weeks; free of major malformations, genetic abnormalities, or health problems associated with developmental delays; no known vision or hearing problems; would remain in the hospital catchment area for the next 12 months Exclusion criteria: N/A **Baseline characteristics** Avg age (months): zinc: 6.3 ± 0.1, control: 6.3 ± 0.1; min age (months): N/A; max age (months): N/A; % female: 48 Avg height-for-age z score: N/A; stunting: non-stunted; avg height in cm (SD): zinc 66.0 ± 2.1, control: 65.8 ± 1.9; avg zinc concentration (µmol/L): 11 Total N: 209; Group 1 N: 101; Group 2 N: 108
Interventions	**Group 1:** zinc Formulation: syrup; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): iron and copper **Group 2:** no zinc Placebo given; co-intervention(s): iron and copper
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/dL) • Serum or plasma ferritin concentration (µmol/L) • Serum or plasma copper concentration (µmol/L) **Time point (week):** 144
Notes	**Study dates:** January 2006-March 2007 **Funding source(s):** National Institutes of Child Health and Development **Comment(s):** none
Risk of bias	

Caulfield 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: Minimization - "Random assignment to supplement type was carried out in blocks of 2 within strata based on sex."
Allocation concealment (selection bias)	Low risk	Quote: "At enrollment, the infants were assigned a unique identification number, which corresponded to the correct supplement type to be taken by the next infant recruited within that stratum. The correspondence between ID number and supplement type was sealed in a document and kept with the manufacturer and the director of the Instituto de Investigacion Nutricional. The investigators, the families of study participants, and data analysts had no knowledge of treatment groups until data analyses were complete."
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The investigators, the families of study participants, and data analysts had no knowledge of treatment groups until data analyses were complete."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The investigators, the families of study participants, and data analysts had no knowledge of treatment groups until data analyses were complete."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The investigators, the families of study participants, and data analysts had no knowledge of treatment groups until data analyses were complete."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 275 infants were evaluated for eligibility and 251 were randomly assigned, 122 to the FC [copper and iron] group and 129 to the FCZ [iron plus copper and zinc] group. Overall, 13% infants left the study, leaving 108 in the FC group and 101 in the FCZ group. A consort diagram of the study is shown elsewhere (37). Of the 251 infants enrolled for the study, 227 (90.4%) were seen for habituation at 6 mo, with 220 successful completions. At 9 mo, 214 (85.4%) infants were seen, with 194 successful completions. ...."
Selective reporting (reporting bias)	Low risk	Comment: all prespecified outcomes were reported. Per introduction of paper: Quote: "Infants from this population were provided a supplement containing either copper and iron (FC8 condition) or iron plus copper and zinc (FCZ condition) from 6 to 18 mo of age, and were assessed on measures of attention, memory/inhibition, and overall sensorimotor function across that time period with the aim of determining whether zinc supplementation might sustain normative neurodevelopmental function. In keeping with the recommendation of tracking developmental trajectories in the conduct of nutritional supplement studies (32), we assessed measures in these infants repeatedly across the age range of the study."
Other bias	Low risk	Comment: no other risk of bias was noted

Cavan 1993

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Guatemala; setting: Guatemala City; urbanicity: peri-urban Inclusion criteria: N/A

Cavan 1993 *(Continued)*

	Exclusion criteria: receiving vitamin and/or mineral supplementation at home in the last 2 months **Baseline characteristics** Avg age (months): 81.5; min age (months): 68; max age (months): 96; % female: 45 Avg height-for-age z score: −1.51; stunting: both - separate data not given; avg height (cm): 112.2; avg zinc concentration (µg/dL): 93.5 Total N: 162; Group 1 N: 80; Group 2 N: 82
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: amino acid chelate; frequency: "…each school day…"; duration (months): 6.25; dose (mg): 10; co-intervention(s): vitamin-mineral supplement that contained multiple micronutrients (including iron) **Group 2:** no zinc Placebo given; co-intervention(s): vitamin-mineral supplement that contained multiple micronutrients (including iron)
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 25
Notes	**Study dates:** February-March 1989 **Funding source(s):** Natural Sciences and Engineering Research Council of Canada; Canadian Public Health Association; University of Guelph **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Children were pair matched by sex and age to constitute two groups: thereafter, a coin toss was used to assign the groups to one or the other coded treatment." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "...a coin toss was used to assign the groups to one or the other coded treatment...only the color varied between the two supplements...Only the company (Jamieson Co, Windsor, Ontario), which manufactured the supplements, was familiar with the color code; the code was broken only on completion of the project." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias)	Low risk	Quote: "…a double-blind zinc-supplementation study…The zinc and placebo supplements were indistinguishable in taste and size; only the color varied be-

Cavan 1993 *(Continued)*

All outcomes		tween the two supplements...Only the company (Jamieson Co, Windsor, Ontario), which manufactured the supplements, was familiar with the color code; the code was broken only on completion of the project." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…a double-blind zinc-supplementation study…The zinc and placebo supplements were indistinguishable in taste and size; only the color varied between the two supplements...Only the company (Jamieson Co, Windsor, Ontario), which manufactured the supplements, was familiar with the color code; the code was broken only on completion of the project." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…a double-blind zinc-supplementation study…The zinc and placebo supplements were indistinguishable in taste and size; only the color varied between the two supplements...Only the company (Jamieson Co, Windsor, Ontario), which manufactured the supplements, was familiar with the color code; the code was broken only on completion of the project." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3.7 Reasons/details: N/A Comment: though no reasons for missing data were given, missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: plasma copper concentration was measured as an outcome, but is not reported as an outcome
Other bias	Low risk	Comment: appears to be free of other bias

Chang 2010

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: Mirzapur, a sub-district (*thana*) north of Dhaka; urbanicity: rural Inclusion criteria: permanent resident of the selected villages Exclusion criteria: severe malnutrition (weight-for-height z-score < −3 SD); severe anemia (hemoglobin < 70 g/L); chronic illnesses that would impair feeding ability; planned move during the study period; active fever > 38.5 °C; a sibling enrolled in the study **Baseline characteristics** Avg age (months): 11; min age (months): 6; max age (months): 18; % female: 48.4 Avg height-for-age z score: −1.3; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 65.3 Total N: 1000; Group 1 N: 198; Group 2 N: 201; Group 3 N: 400; Group 4 N: 201
Interventions	**Group 1:** zinc

Chang 2010 *(Continued)*

	Formulation: pill/tablet; compound: sulfate; frequency: every other day; duration (months): 6; dose (mg): 5 mg to children aged < 12 months; 10 to children aged ≥ 12 months; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): for children aged < 12 months: 6.25 mg iron every other day; 25 IU folic acid every other day. For children aged ≥ 12 months: 12.5 mg iron every other day; 50 IU folic acid every other day **Group 4:** no zinc Placebo given; co-intervention(s): for children aged < 12 months: 6.25 mg iron every other day; 25 IU folic acid every other day. For children aged ≥ 12 months: 12.5 mg iron every other day; 50 IU folic acid every other day
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Hospitalization due to all-cause diarrhea • Hospitalization due to LRTI • Serum or plasma zinc concentration (µmol/L) • Vomiting episodes • Blood hemoglobin concentration (g/L) • Prevalence of anemia **Time point (week):** 26
Notes	**Study dates:** May 2007-February 2008 **Funding source(s):** USAID, through the Global Research Activity **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Block randomization in groups of 10 were computer generated." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "Sealed envelopes concealing supplement group allocation were opened sequentially only after complete determination of enrollment eligibility." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double blind, placebo-controlled factorial community trial…Placebo was identical in color, shape, taste...The manufacturer provided supplements with blinded designation. The principal investigator alone stored the code in a remote location from the study site. The code was not revealed until the time of manuscript preparation."

Chang 2010 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double blind, placebo-controlled factorial community trial…Placebo was identical in color, shape, taste...The manufacturer provided supplements with blinded designation. The principal investigator alone stored the code in a remote location from the study site. Analyses were performed in a blinded manner. The code was not revealed until the time of manuscript preparation." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double blind, placebo-controlled factorial community trial…Placebo was identical in color, shape, taste...The manufacturer provided supplements with blinded designation. The principal investigator alone stored the code in a remote location from the study site. Analyses were performed in a blinded manner. The code was not revealed until the time of manuscript preparation." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 0.3 Reasons/details: for diarrhea and hospitalization outcomes: in the placebo group, 2 participants died; in the zinc + iron group, 1 withdrew. For zinc, hemoglobin, and anemia outcomes: in the zinc group, 2 participants were lost to follow-up (LTFU) and 10 refused to have their blood drawn; in the placebo group 2 were LTFU and 10 refused to have their blood drawn; in the zinc + iron group, 7 were LTFU and 16 refused to have their blood drawn; and in the iron group, 2 were LTFU and 7 refused to have their blood drawn Comment: reasons for, and amount of, missing data were similar between study groups. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: all-cause hospitalizations, hospitalizations due to diarrhea, hospitalization due to pneumonia, and incidence of vomiting as a side effect were reported, but were not pre-specified in the protocol for this study. However, these were not reported as primary outcomes Protocol identifier: NCT00470158
Other bias	Low risk	Comment: appears to be free of other bias

Chang 2010 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization

Chang 2010 (2) *(Continued)*

- Incidence of all-cause diarrhea
- Prevalence of all-cause diarrhea
- Hospitalization due to all-cause diarrhea
- Hospitalization due to LRTI
- Serum or plasma zinc concentration (µmol/L)
- Vomiting episodes
- Blood hemoglobin concentration (g/L)
- Prevalence of anemia

Time point (week): 26

Notes	As Chang 2010 above

Chen 2012

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: China; setting: Banan District, a suburb of Chongqing; urbanicity: peri-urban Inclusion criteria: absence of any chronic infectious diseases; hemoglobin concentration ≥ 60 g/L; C-reactive protein level < 5 mg/L; parental/guardian agreement to avoid additional supplementation of vitamins and minerals during the investigation Exclusion criteria: evidence of recent acute or chronic illnesses; hemoglobin concentration < 60 g/L **Baseline characteristics** Avg age (months): 51.60; min age (months): 36; max age (months): 72; % female: 44 Avg height-for-age z score: −0.26; stunting: unclear; avg height (cm): 102; avg zinc concentration (µg/dL): 25.6% of participants had zinc serum level < 10.7 Total N: 361; Group 1 N: 122; Group 2 N: 119
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: gluconate; frequency: 5 d/week; duration (months): 6; dose (mg): 10; co-intervention(s): vitamin A **Group 2:** no zinc Placebo not given; co-intervention(s): vitamin A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µg/dL) • Blood hemoglobin concentration (g/L) **Time point (week):** 26

Chen 2012 *(Continued)*

Notes	**Study dates:** November 2008-June 2009 **Funding source(s):** Sight and Life, Switzerland; Chongqing Medical University, China **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Three kindergartens were randomly selected out of 7 in this region; and 3 classes were chosen from each of them…The selected classes in each kindergarten were randomly assigned to receive vitamin A (A group), vitamin A plus zinc (AZ group), or vitamin A combined with multiple micronutrients (contain vitamins B-1, B-2, B-6, B-12, C, D, folate, niacinamide, and calcium)."
Allocation concealment (selection bias)	Unclear risk	Quote: N/A
Blinding of participants (performance bias) All outcomes	High risk	No placebo
Blinding of personnel (performance bias) All outcomes	High risk	Intervention was continued at the weekends by sending parents a supply of sachets with instructions (doesn't state whether these sachets also had the contents on the packet, if so risk of to the blinding status of the participants)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No placebo
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 22% intervention and 28% control missing
Selective reporting (reporting bias)	Unclear risk	Trial not registered. Study authors say "We cannot share our protocol with you. It's not a public file."
Other bias	Low risk	Comment: appears to be free of other bias

Chhagan 2009

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: South Africa; setting: Northern KwaZulu-Natal Province; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: < 60% of median weight-for-age using United States NCHS standards; nutritional edema; received vitamin or micronutrient supplements in the previous month; diarrhea for > 7 d at the time of study enrollment; enrolled in another study of a clinical intervention **Baseline characteristics** Avg age (months): 6; min age (months): 6; max age (months): 6; % female: 48

Chhagan 2009 *(Continued)*

	Avg height-for-age z score: −0.45; stunting: both - separate data given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 227; Group 1 N: 112; Group 2 N: 115
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: gluconate; frequency: daily; duration (months): 18; dose (mg): 10; co-intervention(s): 1250 IU vitamin A **Group 2:** no zinc Placebo given; co-intervention(s): 1250 IU vitamin A
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Hospitalization due to all-cause diarrhea • Incidence of severe diarrhea • Incidence of persistent diarrhea • Vomiting episodes • Blood hemoglobin concentration (g/dL) • Prevalence of anemia **Time point (week):** 52 (biochemical outcomes), 72 (morbidity and mortality outcomes)
Notes	**Study dates:** 2003-2006 **Funding source(s):** NIH; Wellcome Trust; National Institute of Child Health and Human Development/Fogarty International Center; International Nutrition Foundation **Comment(s)** • In addition to the study groups mentioned in this table, there was a group of participants who received zinc along with multiple micronutrients. Baseline characteristics reported in this table are weighted averages of all groups except this zinc and multiple micronutrient group, since this group is not included in any meta-analyses in this review. • HIV-positive children are not eligible for this review, so the baseline characteristics and most outcome data that are reported in this review only apply to this trial's HIV-uninfected child participants. (For a few outcomes, separate data were not reported for HIV-uninfected participants; however, HIV-uninfected participants comprise the majority of participants in analyses of these outcomes). • 28 participants in the vitamin A group and 26 participants in the vitamin A + zinc groups "were found to have hemoglobin below 10 g/dL during the routine testing performed on all study participants" and "were given therapeutic iron as per South Africa Department of Health guidelines…" However, "Use of any other micronutrient supplements during the study was rare." • "All supplements were given daily at home from entry into the study until 24 months of age…The median duration of enrollment in the study was 447 days and did not differ significantly between groups."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An allocation list was prepared using computer-generated random numbers and a block size of six."

Chhagan 2009 *(Continued)*

		Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The manufacturer prepared numbered packs of tablets corresponding to the allocation list. Children enrolled in the study were assigned by a study physician to one of the three study cohorts after results of the HIV tests became available. The physician then allocated the next pack of tablets from the blocks assigned to that cohort to the participant." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial...All three formulations were similar in color, taste, appearance and size…participants were blind to the treatment assignments." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial...All three formulations were similar in color, taste, appearance and size…study staff...were blind to the treatment assignments." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial...All three formulations were similar in color, taste, appearance and size…Investigators...were blind to the treatment assignments." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 37 Reasons/details: among all 373 enrolled trial participants, including HIV-positive participants and participants in the multiple micronutrient group: "Thirty-seven children withdrew and one died before any home visits took place...Twelve (3.6%) of the 335 children with at least one home visit died during the study...An additional 88 (26.2%) of the 335 children who had at least one home visit did not complete the study...Fifty-seven children moved out of the area during the study. Reasons given for withdrawal in the other 31 children included lack of time by parent to participate (2 children), the child not liking the taste of the tablets (3 children), objections from grandparent or father (2 children) and unspecified reasons in 24 children." Comment: a large proportion of the data is missing, and reasons for missing data were not reported separately for each study group
Selective reporting (reporting bias)	High risk	Comment: weight and growth were pre-specified as outcomes in the protocol for this study; however, weight-for-age z-score was measured but not reported, and height-for-age z-score was measured but not reported in a way that can be meta-analyzed. All-cause hospitalizations, incidence of LRTI, hemoglobin concentration, and prevalence of anemia were reported, but were not pre-specified in the protocol for this study Protocol identifier: NCT00133419; ISRCTN39226623
Other bias	Unclear risk	Quote: "Because of a delay in shipment, 243 children enrolled in the study did not receive supplements for 11 weeks..." Comment: this lack of supplement receipt could have influenced the outcomes, if the zinc + vitamin A group had a significantly different proportion of children who did not receive supplements than the vitamin A group

Clark 1999

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: UK; setting: Sheffield; urbanicity: urban Inclusion criteria: healthy Exclusion criteria: history of metabolic disease; taking any medication known to influence bone metabolism or zinc status **Baseline characteristics** Avg age (months): 146.4; min age (months): N/A; max age (months): N/A; % female: 100 Avg height-for-age z score: N/A; stunting: non-stunted; avg height (cm): 154; avg zinc concentration (µg/dL): 80.3 Total N: 47; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: unclear; compound: citrate; frequency: daily; duration (months): 1.5; dose (mg): 15; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 10
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • The number of participants randomized to each study group is not explicitly reported. However, given the numbers of participants analyzed in the zinc and placebo groups for baseline and final outcome measures, there were at least 25 participants in the zinc group and at least 21 participants in the placebo group. • For all outcomes, "Baseline to final measure was 10 weeks; supplementation took place over the last 6 weeks."

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "These girls…were randomised…"

Clark 1999 *(Continued)*

		Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind controlled trial…identical placebo..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind controlled trial…identical placebo..." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind controlled trial…identical placebo..." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: N/A Reasons/details: N/A Comment: the exact number of participants missing for each study group was not explicitly reported, nor were reasons for missing data. However, for outcomes of interest to this review, between 42 and 46 participants were analyzed. So, between 2% and 11% of data are missing for outcomes of interest to this review. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

De Fonseca 2002

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: Vila Mariana, São Paulo; urbanicity: urban Inclusion criteria: N/A Exclusion criteria: any organic or genetic condition that was correlated with growth retardation **Baseline characteristics** Avg age (months): 91.72; min age (months): 72; max age (months): 120; % female: 47.5 Avg height-for-age z score: N/A; stunting: both - separate data given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 199; Group 1 N: 99; Group 2 N: 100
Interventions	**Group 1:** zinc Formulation: solution; compound: amino acid chelate; frequency: weekly; duration (months): 3; dose (mg): 30; co-intervention(s): N/A

De Fonseca 2002 *(Continued)*

	Group 2: no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio **Time point (week):** 24
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s):** quotes for this study are translated from Portuguese.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...Randomized…Trial…With the help of the computer program Epi Info 6.02…children were randomized through the Statcalc sub-routine." Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…Double-Blind Trial…Each container contained the name and number of the child…properly labeled by a person not part of the research, who was the only one to know who was receiving medication or placebo." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…Double-Blind Trial…Each container contained the name and number of the child…properly labeled by a person not part of the research, who was the only one to know who was receiving medication or placebo." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…Double-Blind Trial…Each container contained the name and number of the child…properly labeled by a person not part of the research, who was the only one to know who was receiving medication or placebo." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 50 Reasons/details: during the period of supplementation, 29 children were excluded due to school transfer or unexplained absence, 2 children due to refusal to continue taking the drug, and 3 due to self-reported side effects. At the end of the supplementation period, 6 children were excluded due to not having reached the minimum total of 12 doses of supplement or placebo, due to absences on the day of the week that supplementation took place. 60 children, who had ≥ 1 gaps in anthropometric measurements in December 2000 and/or

De Fonseca 2002 *(Continued)*

		March 2001, were also excluded. One hypothesis for this large loss is that some children changed neighborhoods during the semester, but had not changed schools so as not to disrupt school performance. But at the end of the school year, these children went to new schools, because of their proximity to their new dwellings Comment: a large proportion of data is missing, and neither reasons for, nor amounts of, missing data were reported separately for the zinc versus the placebo group
Selective reporting (reporting bias)	High risk	Comment: side effects, such as nausea and epigastric pain, were measured, but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Dehbozorgi 2007

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: 2 villages east of Shiraz; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: heart failure; Down syndrome **Baseline characteristics** Avg age (months): N/A; min age (months): 72; max age (months): 144; % female: 0 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 60; Group 1 N: 30; Group 2 N: 30
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 8; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 24
Notes	**Study dates:** March-September 2002 **Funding source(s):** N/A

Dehbozorgi 2007 *(Continued)*

Comment(s): the data for height were taken from Table 1 of the cited manuscript. We think there was a typo in the table for height data in the zinc group between stages 1-3. The means at the end of stage 3 should be 6.26 cm rather than 2.26 cm, as the same group gained about 4.25 cm and 2.41 cm in stages 1 to 2 and 2 to 3, respectively. We revised the data in this update (year 2022).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…randomized clinical trial…children were selected randomly and divided into two groups…One child was assigned to the experimental group and another one was placed in the control group until the total size was reached." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind…clinical trial…The syrups containing zinc sulfate and placebo were identical and the taste and smell of the solutions were the same…The placebo was provided in completely similar bottles..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind…clinical trial…The syrups containing zinc sulfate and placebo were identical and the taste and smell of the solutions were the same…The placebo was provided in completely similar bottles..." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind…clinical trial…The syrups containing zinc sulfate and placebo were identical and the taste and smell of the solutions were the same…The placebo was provided in completely similar bottles..." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: amount of, and reasons for, missing data were not reported
Selective reporting (reporting bias)	High risk	Comment: side effects were measured, but are not reported
Other bias	Low risk	Comment: appears to be free of other bias

DiGirolamo 2010

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Guatemala; setting: low-income community in Guatemala City; urbanicity: urban Inclusion criteria: in grades 1-4

DiGirolamo 2010 *(Continued)*

	Exclusion criteria: any known severe illness shown to affect zinc status such as sickle cell disease, cystic fibrosis, renal or liver disease, severe burns, or acrodermatitis enteropathica; any other severe or chronic illness not necessarily linked to zinc status (e.g. cancer, diabetes, or seizures) **Baseline characteristics** Avg age (months): 108; min age (months): 72; max age (months): 132; % female: 50 Avg height-for-age z score: −1.2; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 75.3 Total N: 750; Group 1 N: 378; Group 2 N: 372
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: oxide; frequency: 5 d/week; duration (months): 5.8; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency **Time point (week):** 24
Notes	**Study dates:** January-March 2006 **DOI(s):** 10.3945/ajcn.2010.29686 **Comment(s):** "At approximately the time our study began, the local government in the study community implemented a school-based fortified milk program. Children in 4 out of the 5 schools received 200 mL whole milk/d fortified with" approximately 1.6 mg zinc per 200 mL along with multiple micronutrients. "Children in the fifth school…received" a daily "food supplement", which contained "2.1 mg zinc" along with multiple micronutrients. However, these government-provided nutrients would have been received by both the zinc group and the placebo group, "and the randomized controlled trial design of the study makes it very unlikely that this biased" its "results, as there is no reason to believe that one group received more of these nutrients than the other group."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Individual children within each classroom were randomly assigned by using a computer-generated list on the basis of a 1:1:1:1 allocation ratio without blocking constraints." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The zinc and placebo tablets were divided into color-coded vials (2 colors assigned to zinc; 2 colors assigned to placebo) by a staff member at INCAP who was not involved in the study...All study participants and members of the study team were blinded to the treatment code, which was maintained in

DiGirolamo 2010 *(Continued)*

		sealed envelopes at INCAP and Rollins School of Public Health. The envelopes were opened at the end of the study after preliminary data analyses had been completed." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial…The placebo was similar in taste and appearance to the zinc tablet...All study participants…were blinded to the treatment code, which was maintained in sealed envelopes at INCAP and Rollins School of Public Health. The envelopes were opened at the end of the study after preliminary data analyses had been completed." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial…The zinc and placebo tablets were divided into color-coded vials (2 colors assigned to zinc; 2 colors assigned to placebo) by a staff member at INCAP who was not involved in the study…Individuals who administered the supplements (n = 7) received a list of all children in their classroom enrolled in the study and their assigned color group...The placebo was similar in taste and appearance to the zinc tablet." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, controlled trial…The placebo was similar in taste and appearance to the zinc tablet...All…members of the study team were blinded to the treatment code, which was maintained in sealed envelopes at INCAP and Rollins School of Public Health. The envelopes were opened at the end of the study after preliminary data analyses had been completed." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4.7 Reasons/details: "Of the 750 children, 30 (4.0%) children never received treatment or completed the baseline assessment. Of the children who received at least one tablet in the zinc group, 3 were lost: 1 participant was lost due to "parent refusal", 1 "did not go to final evaluation", and 1 had a change of address. Of the children who received at least one tablet in the zinc group, 2 were lost: 1 participant was lost due to a change of address, and 1 due to "parent refusal." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: weight and height were reported, but were not pre-specified in the protocol for this study. However, these were not reported as primary outcomes Protocol identifier: NCT00283660
Other bias	Low risk	Comment: appears to be free of other bias

Ebrahimi 2006

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Yasuj city, in the southwest of Iran; urbanicity: urban

Ebrahimi 2006 *(Continued)*

	Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 96; max age (months): 132; % female: 53 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 804; Group 1 N: 386; Group 2 N: 418
Interventions	**Group 1:** zinc Formulation: solution; compound: unclear; frequency: 6 d/week; duration (months): 7; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 28
Notes	**Study dates:** December 2007-April 2008 **Funding source(s):** N/A **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were randomly assigned to zinc or placebo group…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double blind placebo controlled trial...Zinc and also placebo were administrated to the children, between meals, in an identical form (syrup) and identical pre-coded containers." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double blind placebo controlled trial...Zinc and also placebo were administrated to the children, between meals, in an identical form (syrup) and identical pre-coded containers." Comment: sufficient blinding seems likely

Ebrahimi 2006 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double blind placebo controlled trial...Zinc and also placebo were administrated to the children, between meals, in an identical form (syrup) and identical pre-coded containers." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: amount of, and reasons for, missing data were not reported
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Fallahi 2007

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Khorramabad city, capital of Lorestan province in western Iran; urbanicity: urban Inclusion criteria: in 5th grade Exclusion criteria: renal failure; thalassemia; tuberculosis; parasitic diseases; infections; taking supplementary vitamins and minerals **Baseline characteristics** Avg age (months): 133.2; min age (months): 132; max age (months): 143; % female: 62 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): 139.6; avg zinc concentration (µg/dL): 71.7 Total N: 53; Group 1 N: 26; Group 2 N: 27
Interventions	**Group 1:** zinc Formulation: capsule; compound: sulfate; frequency: 6 d/week; duration (months): 4; dose (mg): 20; co-intervention(s): 20 mg iron **Group 2:** no zinc Placebo given; co-intervention(s): 20 mg iron
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) **Time point (week):** 16

Fallahi 2007 *(Continued)*

Notes	**Study dates:** N/A **Funding source(s):** Deputy of Research and Education of Management and Planning of Lorestan Province **Comment(s)** • In addition to the study groups mentioned in this table, there was a group of participants who received zinc only, but there was no placebo group to which this zinc group could be compared in this review. So, baseline characteristics reported in this table are weighted averages of all groups except this zinc group, since this group is not included in any meta-analyses in this review. • The number of participants randomized might be off by 1 person, given discrepant numbers stated in the trial report. • Though the unit of baseline height is not explicitly stated, it seems likely that the unit is cm. Assuming that the unit is cm, then the baseline height is 139.6 cm.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…children...were randomly supplemented..." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "…double-blind clinical trial…" Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "…double-blind clinical trial…" Comment: insufficient details available to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "…double-blind clinical trial…" Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: N/A Reasons/details: "Only one child dropped out of the study before the end of the 4 months." Comment: it is unclear which study group this one participant belonged to. However, even if this participant was in the iron group or the iron + zinc group, only approximately 2% of data would be missing for participants eligible for this review. The amount of missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Fares 2021

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Egypt; setting: N/A; urbanicity: both rural and urban Inclusion criteria: < 5 years of age suffering from stunted growth Exclusion criteria: children > 5 years of age; ex-premature infants; children with physical growth disabilities, mental disability, or chronic illness such as sickle cell disease, cystic fibrosis, or severe protein-energy malnutrition **Baseline characteristics** Avg age (months): 16; min age (months): 6; max age (months): 56; % female: 55 Avg height-for-age z score: N/A; stunting: stunted; avg height (cm): 70; avg zinc concentration (µg/dL): N/A Total N: 60; Group 1 N: 30; Group 2 N: 30
Interventions	**Group 1:** zinc Formulation: N/A; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): 10-12.5 mg elemental iron for children up to 2 years of age or 30 mg elemental iron for children aged 2-5 years **Group 2:** no zinc Placebo given; co-intervention(s): 10-12.5 mg elemental iron for children up to 2 years of age or 30 mg elemental iron for children aged 2-5 years
Outcomes	**Primary** • N/A **Secondary** • Height (cm) **Time point (week):** 24
Notes	**Study dates:** January 2017-2018 **Funding source(s):** N/A **Comment(s):** the data for endline height was taken from Table 6 of the study.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Cases randomly divided equally into two groups."
Allocation concealment (selection bias)	Unclear risk	Quote: "A randomized study included 60 children less than 5 years of age came to the department of clinical nutrition in a university hospital for nutritional assessment. Cases randomly divided equally into two groups." Comment: there was not enough information to make a clear judgment about the risk of inadequate allocation concealment

Fares 2021 *(Continued)*

Blinding of participants (performance bias) All outcomes	High risk	Quote: "Group A received iron supplementation only and group B received supplementation with iron and zinc."
Blinding of personnel (performance bias) All outcomes	High risk	Quote: "Group A received iron supplementation only and group B received supplementation with iron and zinc."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "MyPlate and 24-hour dietary recall assessment were used for proper assessment of food diversity and quantity. Initial anthropometric measurements (using WHO Z scores) to assess height or length/age for boys and girls. Follow up sessions for all the included cases every 2 weeks to ensure that they were compliant with the supplements. Assessment of length/height was done after 6 months using WHO Z-scores under 5 years of age."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The study included 60 children less than 5 years of age suffering from stunted growth in the period from 1/5/2017–1/5/2018."
Selective reporting (reporting bias)	Low risk	Quote: "Outcome Measures: Length/height for age and sex (birth to 5 years Z-scores, WHO, 2003). Results: On comparing the length/ height of the two groups before (p=0.472) and after supplementation (p=0.923) respectively, no statistically significant differences were found between supplementation with iron only and with iron plus zinc."
Other bias	Unclear risk	Quote: "Percentage of infants who were received exclusive breast fed in group A was 76.7% vs. 60.0% of group B. Over 23% of infants in group A were formula fed vs. 40% of group B as shown in (Table 1)."

Friis 1997

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Zimbabwe; setting: Chiredzi District in southeastern Zimbabwe; urbanicity: rural Inclusion criteria: attending grades 3-6 Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 132; min age (months): 132; max age (months): 204; % female: 54 Avg height-for-age z score: −1.18; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): 77.8 Total N: 313; Group 1 N: 156; Group 2 N: 157
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: "On school days"; duration (months): 12; dose (mg): 30 mg to children weighing < 29.5 kg; 50 mg to children weighing ≥ 29.5 kg; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A

Friis 1997 *(Continued)*

Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 52
Notes	**Study dates:** February 1992-January 1993 **Funding source(s):** Danish International Development Assistance through the Danish Bilharziasis Laboratory; Council for Development Research **Comment(s)** • "Of the 370 day long study period, school leaves, weekends and public holidays comprised 185 days. The maximum number of tablets that could be taken by a child was thus 185, equivalent to a tablet every other day." • Due to "severe drought" a "school-based food supplementation programme" was introduced "in the middle of June 1992, after completion of the three-month follow-up examination, and was still in operation at the time of cessation of the zinc/placebo supplementation. The food supplementation programme provided the children with imported maize, dried fish, sugar beans and oil."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were allocated to either zinc or placebo according to the result of simple randomization." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: "The code was not broken before the data entry, cleaning and analysis were completed." Comment: despite this statement, the method of allocation concealment is not described in sufficient detail to allow a definite judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled trial…zinc sulphate tablets or identical-looking placebo tablets...The code was not broken before the data entry, cleaning and analysis were completed." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled trial…zinc sulphate tablets or identical-looking placebo tablets...The code was not broken before the data entry, cleaning and analysis were completed." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled trial…zinc sulphate tablets or identical-looking placebo tablets...The code was not broken before the data entry, cleaning and analysis were completed."

Friis 1997 *(Continued)*

		Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 11.8 Reasons/details: "…among the 37 (11.8%) children lost to 12-months follow-up, 22 were in the placebo and 15 in the zinc group…" Comment: no information was reported on reasons for missing data
Selective reporting (reporting bias)	High risk	Comment: change in serum ferritin concentration was measured, but is not reported in a way that can be meta-analyzed. Prevalence of zinc deficiency and iron deficiency may have been measured as outcomes, but are not reported
Other bias	Low risk	Comment: appears to be free of other bias

Garcia 1998

Study characteristics	
Methods	IRCT; cross-over
Participants	Country: Chile; setting: N/A; urbanicity: unclear Inclusion criteria: idiopathic short stature; diminished growth velocity; no other pathological condition nor growth hormone deficiency; zinc intake < 10 mg/d Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 93.6; min age (months): 66; max age (months): 159.6; % female: 0 Avg height-for-age z score: −2.6; stunting: both - separate data not given; avg height (cm): 111.8; avg zinc concentration (µg/dL): 110 Total N: 33; Group 1 N: 16; Group 2 N: 17
Interventions	**Group 1:** zinc Formulation: unclear; compound: acetate; frequency: daily; duration (months): 6; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 24
Notes	**Study dates:** N/A

Garcia 1998 *(Continued)*

Funding source(s): N/A

Comment(s)

- The country in which this study took place was not explicitly stated. However, based on the trial authors' affiliations, the language in which the trial report for this study was written, and the hospital from which ethical approval for this study was obtained, it seems that the study took place in Chile.
- The trial report for this study is written in Spanish, so quotes from it are English translations.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…a study was carried out in 33 eutrophic prepubertal boys…They were randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method.
Allocation concealment (selection bias)	Unclear risk	Quote: "They were randomly assigned in a double blind fashion…Pharmaceutical preparations were not identifiable…" Comment: despite this statement, the method of allocation concealment is not described in sufficient detail to allow a definite judgement.
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…in a double blind fashion…The pharmaceutical preparations were not identifiable…" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…in a double blind fashion…The pharmaceutical preparations were not identifiable…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…in a double blind fashion…The pharmaceutical preparations were not identifiable…" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3 Reasons/details: 1 participant, who started puberty during the study, was excluded Comment: though it is unclear whether exclusion based on initiation of puberty is likely to bias results, the amount of missing data seems too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Gibson 1989

Study characteristics

Gibson 1989 *(Continued)*

Methods	IRCT; non-cross-over
Participants	Country: Canada; setting: southern Ontario; urbanicity: unclear Inclusion criteria: male; height-for-age ≤ 15th percentile according to reference data of the NCHS; mid-parent height > 25th percentile; white; full term with weight-for-height appropriate for gestational age; apparently healthy with no detectable medical reasons for poor growth Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 75.8; min age (months): 59; max age (months): 95; % female: 0 Avg height-for-age z score: -1.39; stunting: both - separate data not given; avg height (cm): 110.9; avg zinc concentration (µg/dL): 105 Total N: 60; Group 1 N: 30; Group 2 N: 30
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 52
Notes	**Study dates:** November 1985-January 1987 **Funding source(s):** Kellogg Canada Inc; Natural Sciences and Engineering Research Council of Canada **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were…pair-matched as closely as possible for initial height percentile…initial hair Zn concentrations…age…midpoint height percentile, and reported presence or absence of a picky appetite. The first member of each pair was randomly assigned..." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "The first member of each pair was randomly assigned by an investigator not involved in the project…"

Gibson 1989 *(Continued)*

		Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation.
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "A double-blind, pair-matched 12-mo study…The control children received 1 mL of a placebo solution indistinguishable from the Zn solution in color and flavor, which was administered in a similar manner." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "A double-blind, pair-matched 12-mo study…The control children received 1 mL of a placebo solution indistinguishable from the Zn solution in color and flavor, which was administered in a similar manner." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A double-blind, pair-matched 12-mo study…The control children received 1 mL of a placebo solution indistinguishable from the Zn solution in color and flavor, which was administered in a similar manner." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 0 Reasons/details: N/A Comment: N/A
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Gracia 2005

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Colombia; setting: Cali; urbanicity: urban Inclusion criteria: healthy at the moment of the examination for selecting study participants; without chronic illness or clinical manifestations of malnutrition; adequate food consumption that satisfied energy and protein requirements Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 24; max age (months): 59; % female: N/A Avg height-for-age z score: 0; stunting: both - separate data not given; avg height (cm): 95.84; avg zinc concentration (µg/dL): 72.6 Total N: 350; Group 1 N: 175; Group 2 N: 175
Interventions	**Group 1:** zinc Formulation: unclear; compound: unclear; frequency: daily; duration (months): 8; dose (mg): 12; co-intervention(s): mineral and vitamin supplement

Gracia 2005 *(Continued)*

	Group 2: no zinc Placebo given; co-intervention(s): mineral and vitamin supplement
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight-to-height ratio **Time point (week):** 32
Notes	**Study dates:** N/A **Funding source(s):** Colciencias (National Department of Science, Technology and Innovation of Colombia); Whitehall Laboratories; Cenicaña and Universidad del Valle, Cali, Colombia **DOI(s):** 10.25100/cm.v36i4%20Supl%203.397 **Comment(s)** • Though the exact numbers of participants randomized to each study group was not explicitly stated, the trial report does state that they planned to have 2 study groups of equal numbers. • In this study, all children with parasites at baseline were treated. • Though the English abstract for this trial report states that zinc and placebo were provided for nine months, the Spanish abstract and the full text of this trial report state that zinc and placebo were provided for eight months. • The trial report for this study is written in Spanish, so quotes from it are English translations.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...they were randomly divided in two groups…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...a double blind study…The packaging of the two preparations were identical…and its composition was kept secret until the end of the analysis…Neither…nor the parents knew the composition of the supplement that corresponded to each child." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...a double blind study…The packaging of the two preparations were identical…and its composition was kept secret until the end of the analysis." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...a double blind study…The packaging of the two preparations were identical…and its composition was kept secret until the end of the analysis…Neither the group of investigators nor...knew the composition of the supplement that corresponded to each child...The codes of the two supplements were only opened once the analysis was concluded."

Gracia 2005 *(Continued)*

		Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 34 Reasons/details: of the 350 children with which the study began, 22% were missing due to migration from the study area, and a few withdrew because the physician suggested it or due to the family's decision Comment: migration was the most common reason for missing data, and this reason is unlikely to bias results. However, 12% of data were missing for reasons other than migration, and reasons for, and amount of, missing data are not reported separately for either study group
Selective reporting (reporting bias)	High risk	Comment: serum zinc concentration was measured, but is not reported in a way that can be meta-analyzed. Prevalence of stunting was measured as an outcome, but is not reported as an outcome
Other bias	Low risk	Comment: appears to be free of other bias

Gupta 2003

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: India; setting: 3 adjoining villages about 10 km away from Kolkata, West Bengal; urbanicity: rural Inclusion criteria: residing permanently in these villages with their parents Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 41; % female: 53.93 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 280; Group 1 N: 186; Group 2 N: 94
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 5 d/week or weekly; duration (months): 4; dose (mg): 10 mg or 50 mg; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea **Time point (week):** 16

Gupta 2003 *(Continued)*

Notes	**Study dates:** November 1999-March 2000 **Funding source(s):** N/A **Comment(s):** 95 children received "10 mg zinc for 5 days/wk", 91 children received "50 mg zinc once weekly", and 94 children received placebo.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization was done by a statistician using random number tables." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The two zinc syrups and placebo were...prepared in identical bottles...bottles were numbered according to the random number by the pharmaceutical company, which kept the code number to maintain confidentiality." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) and sequentially numbered drug containers of identical appearance to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind…The two zinc syrups and placebo were similar in colour and taste and were prepared in identical bottles." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind…The two zinc syrups and placebo were similar in colour and taste and were prepared in identical bottles." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind…The two zinc syrups and placebo were similar in colour and taste and were prepared in identical bottles." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 0 Reasons/details: N/A Comment: though the authors did not explicitly report that there were no missing data, it seems from the text and tables that there were no missing data
Selective reporting (reporting bias)	High risk	Comment: side effects (e.g. vomiting) were measured, but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Gupta 2007

Study characteristics

Methods	CRCT; non-cross-over
Participants	Country: India; setting: 11 villages located 35 km from Kolkata; urbanicity: rural

Gupta 2007 *(Continued)*

	Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 48; % female: 51 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 1878; Group 1 N: 943; Group 2 N: 935 Total clusters: 30; Group 1 clusters: N/A; Group 2 clusters: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: unclear; frequency: weekly; duration (months): 6; dose (mg): 50; co-intervention(s): vitamin B complex **Group 2:** no zinc Placebo given; co-intervention(s): vitamin B complex
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Participants with ≥ 1 vomiting episode **Time point (week):** 52 (incidence of all-cause diarrhea), 24 (participants with ≥ 1 vomiting episode)
Notes	**Study dates:** May 2003-April 2004 **Funding source(s):** Indian Council of Medical Research **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "For distribution of the children into 2 groups, areas of 30 surveillance workers were randomly divided into 2 groups." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double blind study…The zinc and placebo syrups in vitamin B-complex base were prepared with identical color, taste, and odor. The syrups were supplied in similar sized amber colored bottles...Each bottle was labeled with a code number...For maintenance of confidentiality, the code numbers of each group were kept with a third person who was not directly associated with the study." Comment: sufficient blinding seems likely

Gupta 2007 *(Continued)*

Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double blind study…The zinc and placebo syrups in vitamin B-complex base were prepared with identical color, taste, and odor. The syrups were supplied in similar sized amber colored bottles...Each bottle was labeled with a code number...For maintenance of confidentiality, the code numbers of each group were kept with a third person who was not directly associated with the study." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double blind study…The zinc and placebo syrups in vitamin B-complex base were prepared with identical color, taste, and odor. The syrups were supplied in similar sized amber colored bottles...Each bottle was labeled with a code number...For maintenance of confidentiality, the code numbers of each group were kept with a third person who was not directly associated with the study." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	High risk	% Missing: 9 Reasons/details: "One hundred and sixty-six children were excluded from the study because the guardians of 45 children refused to accept the syrup, 67 children left the area, 50 discontinued syrup, 2 children died, 1 due to drowning and another due to snake bite and 2 children had cardiac disorders." (However, 45 + 67 + 50 + 2 + 1 + 2 = 167, not 166). Among the 50 children for whom syrup was discontinued, "In 17...it was because of vomiting and in 33...because of advice from the local doctor/guardians of the family." In addition, "Ninety-five...guardians of the study children could not be motivated", and it is unclear whether or not some, or all, of the children of these guardians were excluded and/or were among the 45 children who "refused to accept the syrup." Comment: a somewhat sizeable proportion of data is missing, and neither reasons for, nor amounts of, missing data were reported separately for the zinc versus the placebo group. It is also unclear what implications for missing data might result from the fact that "Ninety-five...guardians of the study children could not be motivated."
Selective reporting (reporting bias)	High risk	Comment: all-cause mortality was measured, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Hambidge 1978

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Denver, Colorado; urbanicity: urban Inclusion criteria: height-for-age percentiles below the 10th for McCammon's standards; hair zinc concentration < 105 µg/g Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 52.6; min age (months): 38; max age (months): 61; % female: 44

Hambidge 1978 *(Continued)*

	Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 75; Group 1 N: 38; Group 2 N: 37
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 5 d/week; duration (months): 6; dose (mg): 14; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (mm) • Weight (g) **Time point (week):** 24
Notes	**Study dates:** during the school year, precise dates N/A **Funding source(s):** National Institute of Arthritis and Metabolic Diseases; United States Department of Agriculture; NIH **Comment(s):** "At the completion of this study, parents were requested to administer the zinc sulfate (or placebo) for a further 6 month period at home. Twenty-two test children and 25 controls (including 10 of the male pairs) remained in this study, but many of them did not take the syrup regularly."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The zinc-supplemented and control children were pair-matched as closely as possible according to sex, ethnic origin, age, initial height percentile and initial hair zinc level." "The first member of each pair was assigned randomly to receive either the zinc supplement or the placebo." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "The study was designed as a double-blind controlled investigation." Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "The study was designed as a double-blind controlled investigation." Comment: insufficient details available to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The study was designed as a double-blind controlled investigation." Comment: insufficient details available to make a judgement

Hambidge 1978 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 11 Reasons/details: in the zinc group, 2 participants were missing. In the control group, 6 participants were missing. Comment: the control group had a larger amount of missing data than the zinc group, and reasons for missing data were not reported
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Han 2002

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: China; setting: Luoyang City, Henan Province; urbanicity: urban Inclusion criteria: height-for-age < −1 SD of the standard; living in their local communities for at least 2 years; without any chronic or acute diseases Exclusion criteria: absent from the kindergarten for a continuous period of > 30 d **Baseline characteristics** Avg age (months): 48.17; min age (months): 36; max age (months): 60; % female: 50 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): 95.9; avg zinc concentration (µg/dL): N/A Total N: 119; Group 1 N: 34; Group 2 N: 28; Group 3 N: 28; Group 4 N: 29
Interventions	**Group 1:** zinc Formulation: tablets or added to milk powder; compound: unclear; frequency: 5 d/week; duration (months): 12; dose (mg): 3.5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 250 mg calcium; 200 µg vitamin A **Group 4:** no zinc Placebo given; co-intervention(s): 250 mg calcium; 200 µg vitamin A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm)

Han 2002 *(Continued)*

- Weight (kg)

Time point (week): 52

Notes	**Study dates:** October 1998-October 1999 **Funding source(s):** Institute of Nutrition and Food Hygiene; Chinese Academy of Preventive Medicine **Comment(s)** • In addition to the study groups mentioned in this table, there were 2 other groups. One was a group of 37 participants who, received zinc and calcium. The other was a group of 34 participants of normal height, who received placebo. Baseline characteristics reported in this table are weighted averages of all groups except these 2 groups, since these 2 groups are not included in any meta-analyses in this review. • The trial reports for this study state that, "Micronutrients were added to milk powder or in the form of tablets and provided alternately."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...children...were randomly assigned to five groups...children were divided into five groups and randomly assigned to different supplementations…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "A double-blind placebo-controlled trial was conducted…The placebos were indistinguishable from the supplements in both appearance and taste." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "A double-blind placebo-controlled trial was conducted…The placebos were indistinguishable from the supplements in both appearance and taste." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "A double-blind placebo-controlled trial was conducted…The placebos were indistinguishable from the supplements in both appearance and taste." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 12 Reasons/details: N/A Comment: 12% of the randomized participants eligible for our review had data missing for diarrhea outcomes; this 12% missing figure includes all groups except the zinc + calcium group and the normal-height placebo group, since these 2 groups are not included in any meta-analyses in this review. For diarrhea outcomes: 1, 6, 4, and 3 participants were missing in the zinc, placebo, zinc + calcium + vitamin A, and calcium + vitamin A groups, respectively. No information was reported on reasons for missing data
Selective reporting (reporting bias)	Unclear risk	Comment: incidence and prevalence of respiratory illness, which meets the criteria of this review, may have been measured and reported; but it is unclear

Han 2002 *(Continued)*

		how respiratory illness was defined in this study. No trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Han 2002 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm) • Weight (kg) **Time point (week):** 52
Notes	As Han 2002 above

Hess 2015

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Burkina Faso; setting: rural communities of the Dandé Health District in southwestern Burkina Faso; urbanicity: rural Inclusion criteria: 8.8 to 9.9 months of age, resided permanently in the area; planned to be available during the study period; had written parental consent Exclusion criteria: Hb < 50 g/L, weight-for-length < 70% of the median of the NCHS/WHO growth reference; presence of bipedal edema; other severe illness warranting hospital referral, congenital abnormalities potentially interfering with growth; chronic medical conditions requiring frequent medical attention; known HIV infection of infant or mother; history of allergy towards peanuts; history of anaphylaxis or serious allergic reaction to any substance requiring emergency medical care; concurrent participation in any other clinical trial **Baseline characteristics** Avg age (months): 9.4; min age (months): N/A; max age (months): N/A; % female: 50 Avg height-for-age z score: −1.21; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 69 Total N: 3219; Group 1 N: 1832; Group 2 N: 1387

Hess 2015 *(Continued)*

Interventions	**Group 1:** zinc (consisting of 3 separate groups, as outlined below) 1. SQ-LNS containing 5 mg zinc, placebo tablet 2. SQ-LNS containing 10 mg zinc, placebo tablet 3. SQ-LNS with 5 mg zinc tablet Formulation: SQ-LNS, tablet; compound: N/A; frequency: twice daily; duration (months): 9; dose (mg): 5, 10; co-intervention(s): weekly morbidity surveillance (oral rehydration salts provided for reported diarrhea and antimalarial therapy for confirmed malaria) **Group 2:** no zinc (consisting of 2 separate groups, as outlined below) 1. SQ-LNS without zinc, placebo tablet 2. SQ-LNS without zinc Placebo given; co-intervention(s): weekly morbidity surveillance (oral rehydration salts provided for reported diarrhea and antimalarial therapy for confirmed malaria) for all except those in the non-intervention cohorts (n = 785)
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of severe diarrhea • Incidence of malaria • Height (cm) • Weight (kg) • Weight-to-height ratio • Prevalence of stunting • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) **Time point (week):** 36
Notes	**Study dates:** April 2010-July 2012 **Funding source(s):** Bill & Melinda Gates Foundation **Comment(s)** • We included the data for SQ-LNS plus zinc tab vs SQ-LNS without zinc. We included the data for morbidity of diarrhea and malaria from Table 2 of BMJ Open paper (PMID 26362661). We first calculated the rate ratio by using number of events per child days and then meta-analyzed the rate ratio using the generic inverse variance method. The data for growth outcomes were considered at the longest follow-up of 18 months of age. • Cluster-randomization at the level of the family compound (i.e. concession) in the intervention communities was used to prevent cross-contamination between intervention groups through food sharing.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated an assignment within strata to participate in the intervention cohort (IC; 25 communities) or in the non-intervention cohort (NIC; 9 communities). "

Hess 2015 *(Continued)*

		"generated a random allocation sequence at the level of the concession for the enrollment of eligible infants in the IC." "At enrollment, a subset of children in IC and NIC were randomly assigned to the“biochemistry sub-group ”for a venous blood draw."
Allocation concealment (selection bias)	Low risk	Quote: "A weekly ration of LNS was initially delivered to participating children in plastic cups containing 140 g (sufficient for one week) and later in seven sachets containing 20 g each." "The LNS for each treatment group were identical, except for their zinc content."
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The trial was partially masked, as all participants, field staff and researchers remained blinded to the four intervention groups until data analyses were completed, but were aware which communities were assigned to IC [intervention] and NIC [non-intervention cohorts]." "SQ-LNS and packages of tablets were labeled with one of eight color codes (two colors per intervention group)."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The trial was partially masked, as all participants, field staff and researchers remained blinded to the four intervention groups until data analyses were completed, but were aware which communities were assigned to IC [intervention] and NIC [non-intervention cohorts]." "SQ-LNS and packages of tablets were labeled with one of eight color codes (two colors per intervention group)."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: most likely done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: exclusions were well reported as shown by Figure 1 within the text. Attrition was balanced in the study groups.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information available to permit a judgement of 'low risk' or 'high risk'
Other bias	Low risk	Comment: study appears to be free of other bias

Hettiarachchi 2008

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Sri Lanka; setting: Galle District; urbanicity: multiple Inclusion criteria: Hb ≥ 80 g/L Exclusion criteria: suffering from acute or chronic diseases; inflammatory conditions; a history of any drug consumption other than paracetamol or antihistamines for minor ailments; currently consuming nutrient supplements; donated blood or received a blood transfusion within the last 4 months **Baseline characteristics** Avg age (months): 145.35; min age (months): 144; max age (months): 155; % female: 65 Avg height-for-age z score: −1.16; stunting: both - separate data not given; avg height (cm): 143.25; avg zinc concentration (µg/dL): 56.17

Hettiarachchi 2008 *(Continued)*

	Total N: 341; Group 1 N: 107; Group 2 N: 59; Group 3 N: 127; Group 4 N: 48 Total clusters: 14; Group 1 clusters: N/A; Group 2 clusters: N/A; Group 3 clusters: N/A; Group 4 clusters: N/A
Interventions	**Group 1:** zinc Formulation: capsule; compound: sulfate; frequency: 5 d/week; duration (months): 6; dose (mg): 14; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 50 mg iron **Group 4:** no zinc Placebo given; co-intervention(s): 50 mg iron
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Prevalence of stunting • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 25
Notes	**Study dates:** N/A **Funding source(s):** International Atomic Energy Agency **Comment(s)** • All baseline and outcome data from this study included in this review apply only to the subset of this study's participants who were < 13 years of age at baseline. • "All the study subjects were treated for parasites by giving mebendazole (500 mg) as a single oral dose (mass-treatment) approximately 2 weeks before the start of the study."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized into one of four groups…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: "...randomized into one of four groups...using a double-blind approach."

Hettiarachchi 2008 *(Continued)*

		Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind approach." "...All capsules (iron, zinc, combined & Placebo) were of same colour capsule in same mean weight" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind approach." "...the class teacher who gave the supplement during breakfast break were not aware about the content of the supplement...All capsules (iron, zinc, combined & Placebo) were of same colour capsule in same mean weight" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind approach." "Research assistant who distribute supplements to the class...were not aware about the content of the supplement...All capsules (iron, zinc, combined & Placebo) were of same colour capsule in same mean weight" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 16 Reasons/details: 7, 18, 13, and 18 participants from the zinc, placebo, iron + zinc, and iron groups, respectively, were "dropped for various reasons: withdrawal from the study…refusal to give blood after supplementation…and absence on the day of the post-supplementation blood collection..." Comment: a fairly large proportion of data is missing, and reasons for missing data were not reported separately for each study group
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Hettiarachchi 2008 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Prevalence of stunting • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L)

Hettiarachchi 2008 (2) *(Continued)*

- Prevalence of anemia
- Serum or plasma ferritin concentration (µg/L)
- Prevalence of iron deficiency

Time point (week): 25

Notes	As Hettiarachchi 2008 above

Hong 1982

Study characteristics	
Methods	IRCT; cross-over
Participants	Country: China; setting: villages, Anhui Province, and Shanghai City; urbanicity: multiple Inclusion criteria: weight < 10th percentile for children of equivalent height and age Exclusion criteria: hereditary, endocrine, and metabolic disorders **Baseline characteristics** Avg age (months): N/A; min age (months): 4; max age (months): 72; % female: 49.4 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 70.3 Total N: 158; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 2.4; dose (mg): unclear; co-intervention(s): vitamin B complex **Group 2:** no zinc Placebo given; co-intervention(s): vitamin B complex
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 10
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • Of the 158 participants randomized, 119 were ≥ 12 months of age. • 64 participants in the zinc group and 67 participants in the control group completed the study, but the number of participants randomized to each group was not reported.

Hong 1982 *(Continued)*

- 92 children in the trial, who were found to be anemic, were provided iron; the trial report did not state the dose or the duration of iron provided, nor did it state how many of these children were in the zinc group or the placebo group.
- The trial report for this study is written in Chinese, so quotes from it are English translations.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "…double blind…" Comment: insufficient details available
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "…double blind…" Comment: insufficient details available
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "…double blind…" Comment: insufficient details available
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 19 Reasons/details: N/A Comment: the following were not reported: number of participants randomised to each group, amount of missing data for each group, reasons for missing data in each group
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Ince 1995

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Turkey; setting: Ankara; urbanicity: urban Inclusion criteria: height between the 3rd and 10th percentiles for age; product of a term pregnancy; birth measurements appropriate for gestational age; no detectable medical reasons for poor growth Exclusion criteria: N/A **Baseline characteristics**

Ince 1995 *(Continued)*

	Avg age (months): 50; min age (months): 25; max age (months): 76; % female: 12 Avg height-for-age z score: −1.55; stunting: non-stunted; avg height (cm): 94.2; avg zinc concentration (µg/dL): N/A Total N: 25; Group 1 N: 16; Group 2 N: 9
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 52
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The participants for the study were randomized to study or control groups" by "a lottery"." Comment: it seems likely that the allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind study design." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind study design…Zinc and placebo were given to children by their kindergarten teachers…Test and control groups were not known by the kindergarten teachers…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind study design…Test and control groups were not known by…the investigator who performed anthropometry..." Comment: sufficient blinding seems likely

Ince 1995 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 0 Reasons/details: N/A Comment: N/A
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Isdiany 2021

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Indonesia; setting: North Cimahi; urbanicity: unclear Inclusion criteria: stunted child in grades 2–6; HAZ < −2 SD; willing to participate through parental consent Exclusion criteria: suffering from chronic diseases/disorders **Baseline characteristics** Avg age (months): 123; min age (months): N/A; max age (months): N/A; % female: 57 Avg height-for-age z score: −2.5; stunting: stunted; avg height (cm): 123.4; avg zinc concentration (µg/dL): N/A Total N: 30; Group 1 N: 15; Group 2 N: 15
Interventions	**Group 1:** zinc Formulation: syrup; compound: sulfate; frequency: 3 times/week; duration (months): 3; dose (mg): 20; co-intervention(s): practiced physical exercise 3 times/week (physical fitness for elementary school students using a video) **Group 2:** no zinc Placebo given; co-intervention(s): practiced physical exercise 3 times/week (physical fitness for elementary school students using a video)
Outcomes	**Primary** • N/A **Secondary** • Height (cm) **Time point (week):** 12
Notes	**Study dates:** 2020-2021 academic year **Funding source(s):** Bandung Health Polytechnic **Comment(s):** the data for HAZ were included from Table 4 of the cited study. The SDs were not given and we used SD from a similar study per our protocol.

Isdiany 2021 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This study used a randomized pre-posttest control group design."
Allocation concealment (selection bias)	Unclear risk	Quote: "The participants were divided into two groups, including the treatment group and the control group." Comment: the study authors did not provide explicit information about allocation concealment
Blinding of participants (performance bias) All outcomes	High risk	Quote: "The research assistants visited each participant's house by implementing health protocol to meet the parents to provide the zinc supplementation to their children as recommended. Supplementation of 5 ml of zinc syrup contained 20 mg of zinc in the form of zinc sulfate monohydrate syrup."
Blinding of personnel (performance bias) All outcomes	High risk	Quote: "The research assistants visited each participant's house by implementing health protocol to meet the parents to provide the zinc supplementation to their children as recommended. Supplementation of 5 ml of zinc syrup contained 20 mg of zinc in the form of zinc sulfate monohydrate syrup."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The research assistants measured the participants' height before and after the intervention at their respective houses by implementing health protocol using a microtome with an accuracy of 0.1 cm." "The dietary intake data (protein, zinc, calcium) were collected using a 24-h recall method through telephone and messages on the WhatsApp Group." "The collection of academic performance data was carried out by interviewing the participants' parents about the scores received from the school."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "...each group consisted of 15 children." Comment: overall low attrition and balanced between the groups, so overall, we had low concerns for risk of bias for attrition
Selective reporting (reporting bias)	Low risk	Quote: "The purpose of this study was to analyze the effect of zinc supplementation and physical exercise on height, H/A z-score, and academic performance of stunted children in the COVID-19 pandemic."
Other bias	Unclear risk	Quote: " Monitoring and evaluating the takings of zinc syrup supplementation were carried out online through WhatsApp Group. Physical exercise intervention in the form of physical fitness exercise was practiced online using videos sent by the sports teacher on WhatsApp Group. Each child practiced the exercise at their respective houses and sent photos during the exercise. Studying from home during the COVID-19 pandemic limits the direct meetings between the researchers and the participants to practice the physical exercise together." "However, the short length of intervention, which was 3 months, with physical exercise in the treatment group did not show a significant difference between the two groups."

Islam 2022

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: low-income area of Mirpur in Dhaka; urbanicity: peri-urban Inclusion criteria: 9–11 months of age at the time of enrolment; WLZ ≥ −3 according to the 2006 WHO Growth Standards Exclusion criteria: severe acute malnutrition, defined as WLZ < −3 and/or the presence of bipedal edema and/or MUAC < 115 mm; congenital anomalies (e.g. cardiac defects, cleft lip or palate) or any other conditions that interfere with feeding; chromosomal anomalies and other organic problems (e.g. jaundice, tuberculosis, etc.) **Baseline characteristics** Avg age (months): 9.75; min age (months): N/A; max age (months): N/A; % female: 50 Avg height-for-age z score: −1.18; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 69.9 Total N: 945; Group 1 N: 470; Group 2 N: 475
Interventions	**Group 1:** standard 15-component MNP [multiple micronutrient powder] containing 4.1 mg zinc and 10 mg iron, consumed daily **Group 2:** high-zinc (10 mg), low-iron (6 mg) (HiZn LoFe) MNPs [multiple micronutrient powder], consumed daily **Group 3:** HiZn LoFe [iron]/high-zinc (10 mg), no iron MNPs [multiple micronutrient powder], consumed on alternating days **Group 4:** dispersible tablet with 10 mg zinc; consumed daily **Group 5:** Intermittent zinc (dispersible tablet with 10 mg zinc consumed daily for 2 wk at enrollment and at 12 wk) **Group 6:** placebo powder, consumed daily
Outcomes	**Primary** • N/A **Secondary** • Incidence of diarrhea • Height (units) **Time point (week):** 24
Notes	**Study dates:** February 2018-July 2019 **Funding source(s):** Bill & Melinda Gates Foundation **Comment(s):** the study had 6 study groups. We included data from daily zinc vs placebo groups only. We included the data for morbidity from Table 3 of the main manuscript. The data were given as incidence. We calculated the number of participants with persistent diarrhea, severe diarrhea and acute LRTI by multiplying the incidence rate to total participants, assuming that a given participant did not have more than one episode for these outcomes. We could not include the data for all-cause diarrhea as the actual time of follow-up was not given. We included data for weight, height, and WLZ scores and stunting, wasting, and underweight from Table 4.

Islam 2022 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Children meeting the eligibility criteria and whose caregivers provided informed consent will be stratified by sex and then randomized into one of six groups using block randomization, in order to ensure even distribution of groups across time."
Allocation concealment (selection bias)	Low risk	Quote: "Sealed opaque envelopes bearing the subject number and containing a paper with the group assignment and any subgroup assignments will be prepared by a person not involved in any study activities and codes will be stored in a secure computer file accessible only by two persons not involved in the project working at icddr,b. At the time of allocation, the study personnel will open the envelope as per the specific child's study identification numbers in a chronological way, and will record the specific code allocation in the infant's clinical record forms and also in a register. Then, she/he will request the appropriate supplement from a person responsible for dispensing of supplements. All individuals involved in the trial (including parents, research staff and investigators) will be unaware of the intervention group assignment until the code is revealed when the data analysis is complete."
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "All individuals involved in the trial (including parents, research staff and investigators) will be unaware of the intervention group assignment until the code is revealed when the data analysis is complete. Given the distinct differences between powders and dispersible tablets, it will not be possible to blind study groups 1, 2, 3, and 6 from study groups 4 and 5. However, complete double-blinding will occur among study groups 1, 2, 3, and 6, and between study groups 4 and 5."
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "All individuals involved in the trial (including parents, research staff and investigators) will be unaware of the intervention group assignment until the code is revealed when the data analysis is complete. Given the distinct differences between powders and dispersible tablets, it will not be possible to blind study groups 1, 2, 3, and 6 from study groups 4 and 5. However, complete double-blinding will occur among study groups 1, 2, 3, and 6, and between study groups 4 and 5."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All individuals involved in the trial (including parents, research staff and investigators) will be unaware of the intervention group assignment until the code is revealed when the data analysis is complete. Given the distinct differences between powders and dispersible tablets, it will not be possible to blind study groups 1, 2, 3, and 6 from study groups 4 and 5. However, complete double-blinding will occur among study groups 1, 2, 3, and 6, and between study groups 4 and 5."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Between October 29, 2017 and July 29, 2019 5567 children were screened for eligibility and 2886 children were enrolled into the trial. All follow-up visits were completed by January 12, 2020. The detailed trial profile is shown in Figure 1. Overall, 2648 (91.8%), children completed the trial."
Selective reporting (reporting bias)	Low risk	Quote: "Incidence of diarrhea and change in length-for-age z-score (LAZ) are the primary outcomes of the trial. EZP [Exchangeable Zinc pool] size, a measure of zinc nutrition, and biomarkers of zinc and iron status will be secondary outcomes to be evaluated in subgroups of study participants. "

Islam 2022 *(Continued)*

Other bias	Unclear risk	Quote: "The study workers will visit each study participant's household twice weekly (i.e., Sunday/Wednesday or Monday/Thursday) to inquire about and record any morbidity that took place in the previous three to four days."

Kartasurya 2012

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Indonesia; setting: Semarang; urbanicity: unclear Inclusion criteria: apparently healthy children Exclusion criteria: moderately and severely malnourished children **Baseline characteristics** Avg age (months): 42.24; min age (months): 24; max age (months): 60; % female: 48% Avg height-for-age z score: −1.73; stunting: non-stunted; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 826; Group 1 N: 415; Group 2 N: 411
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 4; dose (mg): 10; co-intervention(s): vitamin A **Group 2:** no zinc Placebo given; co-intervention(s): vitamin A
Outcomes	**Primary** • All-cause mortality **Secondary** • N/A **Time point (week):** 16
Notes	**Study dates:** June-October 2003 **Funding source(s):** Nestlé Foundation **Comment(s):** none

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: "one of the physicians (not investigators) used random numbers to allocate each child"
Allocation concealment (selection bias)	Low risk	Quote: "one of the physicians (not investigators) used random numbers to allocate each child"

Kartasurya 2012 *(Continued)*

Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Supplements were prepared and labelled with alphabetic codes by the Pharmacy Department of Diponegoro University. There was no difference between the syrups in taste or appearance."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Supplements were prepared and labelled with alphabetic codes by the Pharmacy Department of Diponegoro University. There was no difference between the syrups in taste or appearance."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Supplements were prepared and labelled with alphabetic codes by the Pharmacy Department of Diponegoro University. There was no difference between the syrups in taste or appearance."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Stopped taking zinc or placebo" Comment: 3% missing
Selective reporting (reporting bias)	High risk	Registered retrospectively: ACTRN 12611000659909 Comment: only mortality reported - morbidity not reported
Other bias	Low risk	Comment: appears to be free of other bias

Kaseb 2013

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Yazd, central city of Iran; urbanicity: unclear Inclusion criteria: 9-18-year-old healthy children with normal serum zinc level (plasma level of 70-158 µg /dL) Exclusion criteria: receiving a zinc combination within the past three months; presence of any chronic systemic diseases (endocrine, cardiac, renal, metabolic, malignancy, rheumatologic, etc.); acrodermatitis enteropathica; neurodevelopmental delay; underweight (weight < 3rd percentile on a standard growth curve) and short stature (height < 2 SD below the standard) based on the third National Health and Nutrition Examination Survey (NHANES III) curves; severe malnutrition **Baseline characteristics** Avg age (months): 144; min age (months): N/A; max age (months): N/A; % female: 50.5 Avg height-for-age z score: N/A; stunting: non-stunted; avg height (cm): Group 1: 144.8, Group 2: 148.5; avg zinc concentration (µg/dL): 74 Total N: 95; Group 1 N: 48; Group 2 N: 47
Interventions	**Group 1:** zinc Formulation: tablet; compound: sulfate; frequency: daily; duration (months): 4; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary**

Kaseb 2013 *(Continued)*

	• N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg /dL) **Time point (week):** 16
Notes	**Study dates:** April-October 2011 **Funding source(s):** N/A **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: simple randomization was done by a computer-generated random numbers list which was prepared by an investigator with no clinical involvement in the trial.
Allocation concealment (selection bias)	Low risk	Comment: likely done. The list of random numbers was prepared by an investigator with no clinical involvement in the trial.
Blinding of participants (performance bias) All outcomes	Low risk	Comment: investigators, the staff and participants were all masked to outcome measurements and trial results.
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: investigators, the staff and participants were all masked to outcome measurements and trial results.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: the intervention was delivered by mothers and the primary and secondary outcomes were assessed by a researcher who was not informed of the intervention group assignment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: overall low attrition
Selective reporting (reporting bias)	Low risk	Comment: study authors seem to report all the relevant outcomes.
Other bias	Low risk	Comment: no support from the drug company

Khodashenas 2015

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Mashhad, North East of Iran; urbanicity: unclear

Khodashenas 2015 *(Continued)*

	Inclusion criteria: healthy boys aged 6-8 years with formal consent from their parents; no consumption of any micronutrient 2 weeks before the study; no micronutrient intake during the course of study Exclusion criteria: chronic infectious or inflammatory diseases; surgery; consumption of vitamin and mineral supplements **Baseline characteristics** Avg age (months): 84 ±12; min age (months): N/A; max age (months): N/A; % female: 0 Avg height-for-age z score: N/A; stunting: non-stunted; avg height (cm): 117.1; avg zinc concentration (µg/dL): N/A Total N: 45; Group 1 N: 23; Group 2 N: 22
Interventions	**Group 1:** zinc Formulation: syrup; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 24
Notes	**Study dates:** December 2010-June 2011 **Funding source(s):** Mashhad University of Medical Sciences **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: the study states multiple times that the participants were randomized, but does not state how they were randomized.
Allocation concealment (selection bias)	Unclear risk	Comment: there is not enough information to determine if there was sufficient allocation concealment
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "a randomized, double-blind, placebo controlled trial in which neither the children nor the health worker knew about the contents of the syrups" and the syrups were identical except for the zinc supplementation" Comment: It appears unlikely blinding could have been broken.
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "a randomized, double-blind, placebo controlled trial in which neither the children nor the health worker knew about the contents of the syrups" and the syrups were identical except for the zinc supplementation" Comment: It appears unlikely blinding could have been broken.

Khodashenas 2015 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: this study did not discuss this outcome bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: it seems as though no participants were excluded in this study, at an n = 45.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information available to permit a judgement of 'low risk' or 'high risk'
Other bias	Unclear risk	Comment: there appear to be no other sources of bias.

Kikafunda 1998

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Uganda; setting: a suburb of Kampala; urbanicity: peri-urban Inclusion criteria: N/A Exclusion criteria: major medical or physical problems **Baseline characteristics** Avg age (months): 55.8; min age (months): 33; max age (months): 89; % female: 46 Avg height-for-age z score: −0.7; stunting: unclear; avg height (cm): 103.4; avg zinc concentration (µg/dL): N/A Total N: 155; Group 1 N: 79; Group 2 N: 76
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: 5 d/week; duration (months): 6; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 32
Notes	**Study dates:** N/A **Funding source(s):** World Bank through the Uganda National Agricultural Research Organisation

Kikafunda 1998 *(Continued)*

Comment(s): "Because of the nature of school terms in Uganda, the treatment period was 2-phased, each phase lasting 3 mo with a 2-mo period in between with no supplements when the children were on vacation."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomization procedure was stratified according to sex…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The study was randomized, double-blind…The zinc and placebo tablets, which were indistinguishable in both color and taste..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The study was randomized, double-blind…The zinc and placebo tablets, which were indistinguishable in both color and taste..." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The study was randomized, double-blind…The zinc and placebo tablets, which were indistinguishable in both color and taste..." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 27 Reasons/details: "Two children from school 3, one from the zinc and the other from the control group, dropped out of the trial before the end of phase 1 because of insufficient funds for tuition...Forty children...did not return for phase 2 of the trial, mainly because of a change of schools or insufficient funds." "Phase 1" refers to months 0 to 3 and "phase 2" refers to months 6 to 8 Comment: a large proportion of data is missing, and no information was reported for "phase 2" on differences between study groups in numbers of participants who dropped out
Selective reporting (reporting bias)	High risk	Comment: diarrhea incidence and malaria incidence were measured, but are not reported
Other bias	Low risk	Comment: appears to be free of other bias

Kurugöl 2006

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Turkey; setting: the city of Izmir; urbanicity: urban Inclusion criteria: overall good health

Kurugöl 2006 *(Continued)*

	Exclusion criteria: known chronic disease; immunodeficiency disorder; asthma; history of sensitivity to or an idiosyncratic experience with zinc; parents who were unwilling or unable to comply with clinical study procedures **Baseline characteristics** Avg age (months): 67.2; min age (months): 24; max age (months): 120; % female: 50.5 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 200; Group 1 N: 100; Group 2 N: 100
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 7; dose (mg): 15; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Study withdrawal • Participants with ≥ 1 side effect • Participants with ≥ 1 vomiting episode **Time point (week):** 28
Notes	**Study dates:** October 2004-May 2005 **Funding source(s):** N/A **Comment(s):** the dose was increased to 2 twice/d (30 mg of zinc) at the onset of any cold, until symptoms resolved.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A statistical consultant programmed a computer-generated randomization code…" Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "A statistical consultant programmed a computer-generated randomization code and prepared the packages of medication. The packages were randomly distributed to the study personnel, all of whom were blind to the group assignments." Comment: indicates central randomization to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "This randomized, double-blind, placebo-controlled, prospective study...Placebo and active syrups were identical in appearance, texture and flavouring content, except that the placebo lacked the zinc component...All parents were also blind to the group assignments."

Kurugöl 2006 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "This randomized, double-blind, placebo-controlled, prospective study...Placebo and active syrups were identical in appearance, texture and flavouring content, except that the placebo lacked the zinc component...The packages were randomly distributed to the study personnel, all of whom were blind to the group assignments." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "This randomized, double-blind, placebo-controlled, prospective study...Placebo and active syrups were identical in appearance, texture and flavouring content, except that the placebo lacked the zinc component...The packages were randomly distributed to the study personnel, all of whom were blind to the group assignments." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3 Reasons/details: overall, 97% (n = 194) of the children (97 in the zinc group and 97 in the placebo group) completed the 7-month study period; 6 (3%) discontinued, 4 for non-compliance and 2 for adverse effects due to medication. Comment: amount of missing data was similar between study groups. Missing data seem too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Kusumastuti 2018

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Indonesia; setting: Semarang; urbanicity: unclear Inclusion criteria: aged 30-59 months; not suffering chronic disease; without a history of allergy to zinc and iron; with parents who are willing to sign the informed consent Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): N/A; max age (months): N/A; % female: 54.4 Avg height-for-age z score: −1.3; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 34; Group 1 N: 17; Group 2 N: 17
Interventions	**Group 1:** zinc Formulation: N/A; compound: N/A; frequency: daily; duration (months): 3; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc

Kusumastuti 2018 *(Continued)*

	Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 12
Notes	**Study dates:** November 2016-February 2017 **Funding source(s):** Director General of Higher Education, Ministry of Research and Technology, Indonesia **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "An independent statistician, who kept the block size, planned and prepared the randomization list."
Allocation concealment (selection bias)	Low risk	Quote: "An independent statistician, who kept the block size, planned and prepared the randomization list. Participants were randomly assigned to treatment groups by the field team according to the randomization list once eligibility have been met. Blinding the field team and participants were achieved through identical packaging with codes of 4 different supplements from the pharmaceutical company, without knowing their contents. The allocation codes for each identical packaging would be kept in safes at the administrative office of Diponegoro University, by the independent statistician, until the database ready to be revealed for analysis."
Blinding of participants (performance bias) All outcomes	Low risk	"Blinding the field team and participants were achieved through identical packaging with codes of 4 different supplements from the pharmaceutical company, without knowing their contents. The allocation codes for each identical packaging would be kept in safes at the administrative office of Diponegoro University, by the independent statistician, until the database ready to be revealed for analysis."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Blinding the field team and participants were achieved through identical packaging with codes of 4 different supplements from the pharmaceutical company, without knowing their contents. The allocation codes for each identical packaging would be kept in safes at the administrative office of Diponegoro University, by the independent statistician, until the database ready to be revealed for analysis."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Blinding the field team and participants were achieved through identical packaging with codes of 4 different supplements from the pharmaceutical company, without knowing their contents. The allocation codes for each identical packaging would be kept in safes at the administrative office of Diponegoro University, by the independent statistician, until the database ready to be revealed for analysis."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "This study began by screening 240 preschool children in Jomblang village. Among them, 80 children met the inclusion criteria and were divided ran-

Kusumastuti 2018 *(Continued)*

		domly into four groups. Overall, 68 children (17 subjects in each group) completed the trial."
Selective reporting (reporting bias)	Unclear risk	Quote: "...researchers are interested in evaluating the effects of zinc and iron on the appetite and nutritional status of children aged 2-5 years." Comment: unable to obtain study protocol to ascertain prespecified outcomes.
Other bias	Unclear risk	Quote: "In the fourth group, which received a combination of zinc and iron supplement, no significant increase in IQ score was observed. The reason could be the negative interaction between zinc and iron, which can inhibit the absorption of each nutrient. The inhibition occurs primarily if the two minerals are ingested together in the absence of food, compounds with absorptive properties different from those of iron sulfate and zinc sulfate, and if iron is present as non-heme iron in a ratio with zinc of 2: 1.(2,8) Before providing supplementation to the subject, the parents of the subjects were instructed to give both of these supplements with a time lag of at least 2 hours. This approach aims to prevent the emergence of negative interaction. However, 12 respondents were reluctant to provide the supplement simultaneously, thereby might result in a negative interaction that reduces the effect of each supplement."

Kusumastuti 2018 (2)

Study characteristics	
Methods	
Participants	
Interventions	**Group 1:** zinc Formulation: N/A; compound: N/A; frequency: daily; duration (months): 3; dose (mg): 10; co-intervention(s): iron 7.5 mg **Group 2:** no zinc Placebo given; co-intervention(s): iron 7.5 mg
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 12
Notes	As Kusumastuti 2018, unless otherwise noted

Larson 2010

Study characteristics	

Larson 2010 *(Continued)*

Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: Mirpur district, Dhaka; urbanicity: urban Inclusion criteria: an acute episode of diarrhea of 24-72 h duration Exclusion criteria: severe dehydration; suspected cholera or pneumonia; bipedal edema; currently receiving zinc; a weight-for-height z-score < −3; already participating in another study involving nutritional or therapeutic interventions **Baseline characteristics** Avg age (months): 15.4; min age (months): 6; max age (months): 24; % female: 50 Avg height-for-age z score: −1.72; stunting: unclear; avg height (cm): 73.6; avg zinc concentration (µg/dL): N/A Total N: 353; Group 1 N: 176; Group 2 N: 177
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 3; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Blood hemoglobin concentration (g/L) **Time point (week):** 6 (blood hemoglobin concentration), 36 (all-cause mortality, incidence of all-cause diarrhea)
Notes	**Study dates:** November 2004-August 2006 **Funding source(s):** Bill & Melinda Gates Foundation **Comment(s)** • All children received 10 d of zinc treatment (20 mg/d) for an episode of acute childhood diarrhea before they were divided into zinc vs placebo groups for the preventive supplementation RCT phase of this study. • It is unclear whether the maximum age of eligible trial participants at baseline was 23 or 24 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…lots were numbered and randomly assigned in permuted blocks of six (three placebo, three zinc)." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "All placebo and zinc-containing bottles of syrup…were serially numbered in lots of 100. These lots were listed and then sequentially selected

Larson 2010 *(Continued)*

		based upon random assignment…each child received a 3-month supply of syrup (five bottles) and the lot number was recorded. The randomization code was not broken until after all children had completed the trial and the data had been entered and verified." Comment: seems to indicate sequentially numbered drug containers of identical appearance to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind field trial…The randomization code was not broken until after all children had completed the trial and the data had been entered and verified." "…children received 10 mg/d zinc (zinc sulfate, syrup formulation) or placebo (placebo syrup, similar in appearance and taste)…" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind field trial…The randomization code was not broken until after all children had completed the trial and the data had been entered and verified." "…children received 10 mg/d zinc (zinc sulfate, syrup formulation) or placebo (placebo syrup, similar in appearance and taste)…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind field trial…The randomization code was not broken until after all children had completed the trial and the data had been entered and verified." "…children received 10 mg/d zinc (zinc sulfate, syrup formulation) or placebo (placebo syrup, similar in appearance and taste)…" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 6 Reasons/details: In the zinc group: 12 children were lost and 1 died. In the placebo group: 7 children were lost Comment: reasons for, and amount of, missing data were similar between study groups. Missing data seem too minimal to impact results.
Selective reporting (reporting bias)	High risk	Comment: height-for age z-score, weight-for age z-score, weight-for-height z-score, serum zinc concentration, and serum copper concentration were measured, but are not reported in a way that can be meta-analyzed. Of these outcomes, only serum zinc concentration was pre-specified in the protocol for this study. Haemoglobin concentration was reported, but was not pre-specified in the protocol for this study Protocol identifier: NCT00408356
Other bias	Low risk	Comment: appears to be free of other bias

Lind 2003

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Indonesia; setting: Purworejo district, central Java; urbanicity: rural Inclusion criteria: healthy; singleton; mother who had been monitored during pregnancy and birth

Lind 2003 *(Continued)*

	Exclusion criteria: metabolic or neurologic disorders; physical handicaps affecting development, feeding, or activity; severe or protracted illness; Hb < 90 g/L on assessment of eligibility **Baseline characteristics** Avg age (months): 6; min age (months): 6; max age (months): 6; % female: 48 Avg height-for-age z score: −0.34; stunting: both - separate data not given; avg height (cm): 65.4; avg zinc concentration (µg/dL): 60.8 Total N: 680; Group 1 N: 170; Group 2 N: 170; Group 3 N: 170; Group 4 N: 170
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): 30 mg ascorbic acid **Group 2:** no zinc Placebo given; co-intervention(s): 30 mg ascorbic acid **Group 3:** zinc Co-intervention(s): 10 mg iron; 30 mg ascorbic acid **Group 4:** no zinc Placebo given; co-intervention(s): 10 mg iron; 30 mg ascorbic acid
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Prevalence of stunting • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Participants with ≥ 1 side effect • Participants with ≥ 1 vomiting episode • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency • Serum or plasma copper concentration (µmol/L) **Time point (week):** 24
Notes	**Study dates:** July 1997-May 1999 **Funding source(s):** Swedish Agency for Research Co-operation with Developing Countries; Swedish Medical Research Council; Swedish Foundation for International Co-operation in Research and Education; Swedish Medical Society; Maud and Birger Gustavsson Foundation; Umeå University Foundation **Comment(s):** none

Lind 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization was planned and generated by an independent statistician, and was performed in blocks of 20." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was planned and generated by an independent statistician…" Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double blind, placebo-controlled trial…The pharmaceutical company marked the 4 different supplements with letter codes, blinded to...participants. Information on group assignment was kept in a safe at the administrative offices of Gadjah Mada and Umeå Universities until after the intent-to-treat analysis." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double blind, placebo-controlled trial…The pharmaceutical company marked the 4 different supplements with letter codes, blinded to researchers...Information on group assignment was kept in a safe at the administrative offices of Gadjah Mada and Umeå Universities until after the intent-to-treat analysis." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double blind, placebo-controlled trial…The pharmaceutical company marked the 4 different supplements with letter codes, blinded to researchers...Information on group assignment was kept in a safe at the administrative offices of Gadjah Mada and Umeå Universities until after the intent-to-treat analysis. The laboratory assessing the biochemical outcomes was not aware of the randomization groups." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 2 Reasons/details: for all outcomes: 1, 1, 3, and 4 participants in the zinc, placebo, zinc + iron, and iron groups, respectively, "refused supplement...discontinued intervention"; 2 from the zinc group died; and 3 from the zinc + iron group moved. For height, weight, and weight-to-height ratio outcomes: 5, 5, 3, and 3 participants in the zinc, placebo, zinc + iron, and iron groups, respectively, were "excluded from analysis" due to "incomplete anthropometric data." For serum zinc, hemoglobin, serum ferritin, and serum copper outcomes: 13, 14, 9, and 10 participants in the zinc, placebo, zinc + iron, and iron groups, respectively, were "excluded from analysis" because they "refused 2nd blood sample"; and 20, 12, 19, and 20 participants in the zinc, placebo, zinc + iron, and iron groups, respectively, were "excluded from analysis" because there was "insufficient serum volume" from them Comment: reasons for, and amount of, missing data were similar between study groups. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	Low risk	Comment: all pre-specified outcomes reported using pre-specified methods

Lind 2003 *(Continued)*

		Protocol identifier: N/A - obtained through an email from a study author
Other bias	Low risk	Comment: appears to be free of other bias

Lind 2003 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Prevalence of stunting • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Participants with ≥ 1 side effect • Participants with ≥ 1 vomiting episode • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency • Serum or plasma copper concentration (µmol/L) **Time point (week):** 24
Notes	As Lind 2003 above

Long 2006

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Mexico; setting: La Magdalena Atlicpac, a peri-urban community located on the eastern periphery of Mexico City; urbanicity: peri-urban Inclusion criteria: N/A Exclusion criteria: diseases causing immunosuppression; any congenital or acquired alteration of the digestive tract that could alter the absorption of micronutrients; taking vitamin supplements

Long 2006 *(Continued)*

	Baseline characteristics Avg age (months): 9.8; min age (months): 6; max age (months): 15; % female: 51 Avg height-for-age z score: 0.1; stunting: both - separate data not given; avg height (cm): 73.79; avg zinc concentration (µg/dL): N/A Total N: 786; Group 1 N: 196; Group 2 N: 198; Group 3 N: N/A; Group 4 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: methionine; frequency: daily; duration (months): 12; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 20,000 IU retinol every 2 months if age ≤ 12 months, 45,000 IU retinol every 2 months if age > 12 months **Group 4:** no zinc Placebo given; co-intervention(s): 20,000 IU retinol every 2 months if age ≤ 12 months, 45,000 IU retinol every 2 months if age > 12 months
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of persistent diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Prevalence of stunting **Time point (week):** 52
Notes	**Study dates:** January 2000-May 2002 **Funding source(s):** Instituto de Nutricion Danone; National Council of Science and Technology of Mexico; NIH **Comment(s)** • In the Long 2006 trial report, it is reported that 193 participants were randomized to the vitamin A + zinc group and 199 participants were randomized to the vitamin A group. In contrast, in the Long et al 2007 and Rosado et al 2009 trial reports (see secondary references under Long 2006), it is reported that 199 participants were randomized to the vitamin A + zinc group and 193 participants were randomized to the vitamin A group. • There is some discrepancy between the average, minimum, and maximum ages reported in the different trial reports for this study. However, the mean age of participants in all trial reports falls within the age range of this review.

Risk of bias

Bias	Authors' judgement	Support for judgement

Long 2006 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "The randomization sequence was generated by using a random-number table…" Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The randomization sequence was generated...by project personnel from CENSIA, a division of the Mexican Ministry of Health." "On acceptance, the child was randomly assigned to 1 of the 4 groups by the project field coordinator, who was blinded to these groups." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind randomized trial…The vitamin A, zinc, and vitamin A zinc supplements were prepared by personnel at the National Institute of Nutrition in 5-mL solutions that were similar in taste and appearance." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind randomized trial…The vitamin A, zinc, and vitamin A zinc supplements were prepared by personnel at the National Institute of Nutrition in 5-mL solutions that were similar in taste and appearance...These solutions were packaged in consecutively numbered, color-coded, opaque plastic droplet bottles to ensure that field personnel and the principal investigator were blinded." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind randomized trial…The vitamin A, zinc, and vitamin A zinc supplements were prepared by personnel at the National Institute of Nutrition in 5-mL solutions that were similar in taste and appearance...These solutions were packaged in consecutively numbered, color-coded, opaque plastic droplet bottles to ensure that field personnel and the principal investigator were blinded." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 6 Reasons/details: "Seven children migrated from the area with their families immediately after being randomly assigned…" In addition to these seven, some participants were "lost to follow-up", others "discontinued interventions", and others were "excluded from analysis." The exact numbers of participants who were lost, who discontinued interventions, or who were excluded varies slightly between trial reports. However, in the Long 2006 trial report, which reports most of the outcomes of interest to this review: in the zinc group, 5 were lost, 3 discontinued, and 5 were excluded; in the placebo group, 3 were lost, 5 discontinued, and 6 were excluded; in the vitamin A + zinc group, 5 were lost, 1 discontinued, and 4 were excluded; in the vitamin A group, 2 were lost, 2 discontinued, and 2 were excluded Comment: reasons for, and amount of, missing data were similar between study groups. Missing data seem too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: side effects may have been measured, but are not reported for the placebo group. No trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Long 2006 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of persistent diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Prevalence of stunting **Time point (week):** 52
Notes	As Long 2006 above

Mahloudji 1975

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: the village of Kherak, near Shiraz in southern Iran; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 72; max age (months): 144; % female: 8 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): 64.8 Total N: 50; Group 1 N: 25; Group 2 N: 25
Interventions	**Group 1:** zinc Formulation: capsule; compound: carbonate; frequency: 6 d/week; duration (months): 16; dose (mg): 20; co-intervention(s): 20 mg iron; vitamin and mineral supplements, which contained multiple micronutrients; egg white and corn oil supplements **Group 2:** no zinc Placebo given; co-intervention(s): 20 mg iron; vitamin and mineral supplements, which contained multiple micronutrients; egg white and corn oil supplements
Outcomes	**Primary**

Mahloudji 1975 *(Continued)*

- N/A

Secondary

- Serum or plasma zinc concentration (µg/dL)
- Blood hemoglobin concentration (g/dL)

Time point (week): 80

Notes	**Study dates:** October 1968-May 1970 **Funding source(s):** Nutrition Program; Health Services and Mental Health Administration, Center for Disease Control; Pahlavi University Research Council **Comment(s)** • The supplement and placebo were given "during the school year...Treatment was discontinued in May 1969 and resumed in October of the same year." It seems that treatment was started in October 1968, discontinued in May 1969, started again in October 1969, and ended in May 1970. • In addition to the study groups mentioned in this table, there was a group of 25 participants who received "placebo capsules containing lactose and simulated supplement", but there was no zinc group to which this placebo group could be compared. So, this group is not included in any meta-analyses in this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Care was taken to ensure that the grouping was by chance." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The supplement and simulated supplement looked and tasted alike…" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The supplement and simulated supplement looked and tasted alike…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The supplement and simulated supplement looked and tasted alike…" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: the study reported that, "Seventy-five children…were divided into three groups." However, results were reported as being out "of 59 children." Nothing (such as reasons for missing data, and number of participants with missing data, for each study group) was reported to explain this 75 versus 59 children inconsistency

Mahloudji 1975 *(Continued)*

Selective reporting (reporting bias)	High risk	Comment: height, weight, prevalence of zinc deficiency, and prevalence of anemia were measured, but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Malik 2014

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: India; setting: Delhi; urbanicity: urban Inclusion criteria: all children 6-11 months of age residing in Gokulpuri, an urban re-settlement colony in North East District of Delhi, India; likely to stay until the completion of the study; to achieve the final sample size additional children were recruited from the similar adjacent area of Gangavihar Exclusion criteria: any child receiving zinc supplement at the time of study or in the past 3 months; severely malnourished; immune-deficient or on steroid therapy; severely ill children requiring hospitalization; children of families likely to migrate from the study area **Baseline characteristics** Avg age (months): N/A; min age (months): 6 months; max age (months): 11; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 158; Group 1 N: 134; Group 2 N: 124
Interventions	**Group 1:** zinc Formulation: solution; compound: unclear; frequency: daily; duration (months): 0.46; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • Mortality due to all-cause diarrhea **Secondary** • Incidence of all-cause diarrhea • Incidence of persistent diarrhea • Prevalence of all-cause diarrhea • Vomiting episodes **Time point (week):** 22
Notes	**Study dates:** January 2011-January 2012 **Funding source(s):** Indian Council of Medical Research; Department of Health Research (Ministry of Health and Family Welfare), Government of India **Comment(s):** none

Malik 2014 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We randomized the treatment allocation; by simple randomization using computer generated random numbers."
Allocation concealment (selection bias)	Low risk	Quote: "We randomized the treatment allocation; by simple randomization using computer generated random numbers."
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The field investigator and parents were blinded to the treatment allocation and were unblinded at the end of the follow-up period."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The field investigator and parents were blinded to the treatment allocation and were unblinded at the end of the follow-up period."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The field investigator and parents were blinded to the treatment allocation and were unblinded at the end of the follow-up period."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Generalized Estimating Equations (GEE) were used to obtain an incident rate ratio (IRR) with 95% confidence intervals, in order to compare month-wise number of episodes and duration of diarrhea using Poisson log linear distribution, by intention to treat analysis...We included all children who had taken at least two doses of the intervention for the analyses. The follow-up visits for which the infant outcomes were not available were imputed using the worst case (2 episodes of diarrhea) and best case scenarios (no episodes). However this did not change the study results thus missing data was excluded from the final analysis." Comment: 7/141 and 7/131 not included in the analysis
Selective reporting (reporting bias)	Low risk	Quote: "part of a larger study taking in to account four primary outcomes, i.e. decrease in incidence of diarrhea and acute respiratory tract infections (ARI) and increase in length and weight" "We decided to adjust the IRRs for covariates which appeared to be different at baseline in the two groups. " Trial registration: CTRI/2010/091/001417
Other bias	Low risk	Comment: appears to be free of other bias

Mandlik 2020

Study characteristics

Methods	CRCT; non-cross-over
Participants	Country: India; setting: rural region 65 km east from Pune city (18°N), Western India; urbanicity: rural Inclusion criteria: apparently healthy rural Indian children between the ages of 6-12 years; not consuming any supplements or preparations containing vitamin D, calcium, or zinc Exclusion criteria: children with congenital abnormalities, chronic medical conditions, and conditions that could affect vitamin D and calcium metabolism

Mandlik 2020 *(Continued)*

	Baseline characteristics Avg age (months): 96; min age (months): N/A; max age (months): N/A; % female: 46 Avg height-for-age z score: Group 1: -0.8 (± 0.9), Group 2: -0.9 (± 0.8); stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL) and SD: 72.3 ± 28.2 Total N: 243; Group 1 N: 119; Group 2 N: 124
Interventions	**Group 1:** zinc Formulation: tablet; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 15; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 24
Notes	**Study dates:** July 2014-February 2015 **Funding source(s):** University Grants Commission, Government of India **DOI(s):** 10.4162/nrp.2020.14.2.117 **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote, "The cluster randomization method was used to randomly allocate the 435 participants to the three trial arms: vitamin D, zinc and placebo. Each class or grade in the school had 3 divisions, A, B and C, which were categorized as the designated clusters." Comment: likely done
Allocation concealment (selection bias)	Low risk	Comment: this was a cluster-randomized trial and randomization was done at once for all the clusters so allocation concealment is not applicable.
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Coding of the supplements was performed by the supplier, and the codes were revealed only after completion of the trial."
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Coding of the supplements was performed by the supplier, and the codes were revealed only after completion of the trial."
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The trial staff as well as the participants were unaware of the intervention being administered, thereby achieving double blinding."

Mandlik 2020 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	All excluded participants were accounted for. Quote: "Children whose parents had consented underwent a general medical examination by a pediatrician to rule out any medical conditions; 30 children were excluded due to pre-existing conditions including asthma, kidney stones, liver disease, growth hormone deficiency, thalassemia, and suspected neurodevelopmental delay. During blood collection, 9 children were absent. Finally, 435 children were enrolled in this trial"
Selective reporting (reporting bias)	Unclear risk	Quote: "Insufficient information available to permit a judgement of 'low risk' or 'high risk'"
Other bias	Low risk	Comment: the study appears to be free of other sources of bias.

Marinho 1991

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: a poor district of Manaus (Amazonas); urbanicity: urban Inclusion criteria: parasitized with *Ascaris lumbricoides* and/or *Giardia lamblia* Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 36; max age (months): 84; % female: 50 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 240; Group 1 N: 60; Group 2 N: 60; Group 3 N: 60; Group 4 N: 60
Interventions	**Group 1:** zinc Formulation: unclear; compound: acetate; frequency: daily; duration (months): 1; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 500 mg vitamin A **Group 4:** no zinc Placebo given; co-intervention(s): 500 mg vitamin A
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** N/A **Funding source(s):** N/A

Marinho 1991 *(Continued)*

Comment(s): "One-hundred-and-twenty of the parasitized children…were treated with mebendazol…for *A. lumbricoides* and with metronidazol…for *G. lamblia*…The efficiency of the parasitosis treatment was checked by carrying out another stool analysis." Thirty of these treated children were randomized to each study group; thus, each study group was comprised of 30 treated participants, and 30 untreated participants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The parasitized and non-parasitized groups were randomly assigned to four sub-groups…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: reasons for, and amount of, missing data were not reported for either study group.
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Mazariegos 2010

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Guatemala; setting: the town of San Juan Comalapa, in the province of Chimaltenango, in the Western Highlands of Guatemala; urbanicity: rural Inclusion criteria: living within 12 km of the township of Comalapa; apparently healthy (based on maternal history without any prenatal or natal concerns and no history of serious illness postnatally); home-cooked maize as the major family food staple

Mazariegos 2010 *(Continued)*

	Exclusion criteria: refused verbal screening; did not eat tortillas in the home; family who did not plan to stay in the geographical area for the next year **Baseline characteristics** Avg age (months): 6; min age (months): 6; max age (months): 6; % female: 49.5 Avg height-for-age z score: −2.09; stunting: both - separate data not given; avg height (cm): 62.1; avg zinc concentration (µg/dL): 110.5 Total N: 412; Group 1 N: 104; Group 2 N: 105; Group 3 N: 100; Group 4 N: 103
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: unclear; frequency: daily; duration (months): 6; dose (mg): 5; co-intervention(s): isohybrid control maize **Group 2:** no zinc Placebo given; co-intervention(s): isohybrid control maize **Group 3:** zinc Co-intervention(s): low-phytate maize **Group 4:** no zinc Placebo given; co-intervention(s): low-phytate maize
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) • Study withdrawal • Participants with ≥ 1 side effect • Vomiting episodes • Participants with ≥ 1 vomiting episode **Time point (week):** 24
Notes	**Study dates:** 2004-2006 **Funding source(s):** Global Network for Women's and Children's Health Research; Bill & Melinda Gates Foundation; Office of Dietary Supplements, NIH **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "At the time of enrolment, families were assigned to receive maize labeled with 1 of 6 randomization colors. Permuted blocks were used in the generation of the randomization list. At age 6 mo, infants were further randomized to the zinc supplementation trial. The infants were randomized to the treat-

Mazariegos 2010 *(Continued)*

		ment or control group within the family's maize group assignment, also using permuted blocks." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: in response to the question, "Could you describe how you ensured that participants, and investigators enrolling participants, could not tell which group a new participant would be assigned to?" an author of this study replied as follows: "The randomization was undertaken by RTI—totally detached from all investigators." RTI stands for "Research Triangle Institute", which was involved with data management for the study Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...doubly masked trial…" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...doubly masked trial…Quality control checks of maize…undertaken by one of the investigating team (V. R.) at the USDA [United States Department of Agriculture] facility in Aberdeen, Idaho, to verify correct delivery of the assigned maize. Apart from the members of the Data Management Center at RTI [Research Triangle Institute], V.R. was the only unmasked member of the investigating team." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...doubly masked trial…Quality control checks of maize…undertaken by one of the investigating team (V. R.) at the USDA [United States Department of Agriculture] facility in Aberdeen, Idaho, to verify correct delivery of the assigned maize. Apart from the members of the Data Management Center at RTI, V.R. was the only unmasked member of the investigating team." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 7 Reasons/details: in the zinc group: 4 were "missing" for the "12 mo visit", 4 "moved", and 8 "withdrew consent." In the placebo group, 4 were "missing" for the "12 mo visit", 4 "moved", and 4 "withdrew consent." "The small attrition rate in participant retention was primarily due to relocation from the area or withdrawal of consent because of perceived study burden." Comment: reasons for, and amount of, missing data were similar between study groups. Missing data seem too minimal to impact results.
Selective reporting (reporting bias)	High risk	Comment: diarrhea prevalence, LRTI incidence, and stunting rates were measured, but are not reported in a way that can be meta-analyzed.
Other bias	Low risk	Comment: appears to be free of other bias

Meeks Gardner 1998

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Jamaica; setting: Kingston; urbanicity: urban

Meeks Gardner 1998 *(Continued)*

	Inclusion criteria: singleton; stunted (< −2.0 SD length-for-age and less than the median weight-for-length, NCHS references) Exclusion criteria: obvious physical or mental handicap; provided vitamin-mineral supplements which contained iron and/or zinc by their carers **Baseline characteristics** Avg age (months): 14.1; min age (months): 6; max age (months): 24; % female: 57 Avg height-for-age z score: −2.9; stunting: stunted; avg height (cm): 68.7; avg zinc concentration (µg/dL): N/A Total N: 61; Group 1 N: 31; Group 2 N: 30
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 3; dose (mg): 5; co-intervention(s): multivitamin supplement (Tropivite vitamin drops) **Group 2:** no zinc Placebo given; co-intervention(s): multivitamin supplement (Tropivite vitamin drops)
Outcomes	**Primary** • N/A **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) **Time point (week):** 12 (morbidity outcomes), 52 (growth outcomes)
Notes	**Study dates:** N/A **Funding source(s):** Commonwealth Caribbean Medical Research Council, University of the West Indies, Mona **Comment(s):** "Food supplements were expected to be provided by the nutrition clinics as part of their routine care, but delivery was extremely irregular and caretakers had food supplements on average only 1 week during the 12 week supplementation period."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…children were...randomly assigned..." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias)	Low risk	Quote: "…double-blind, placebo-controlled trial...Caretakers were blind to the children's group assignment."

Meeks Gardner 1998 *(Continued)*

All outcomes		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled trial…All interviews and measurements were carried out by members of the study team who were unaware of the children's group assignments." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 7 Reasons/details: 4 children, "all from the control group, were hospitalized during the study", and "stayed in hospital for more than one night...It was necessary to exclude them since in some cases hospitalization may have included zinc supplements and the feeding regimes would have been markedly different from the situation at home." Comment: children who were hospitalized probably represented the most severe cases of illness and excluding 4 of them may have reduced the likelihood of finding significant differences between the groups in the other morbidity variables examined
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Meeks Gardner 2005

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Jamaica; setting: the parishes of Kingston, St. Andrew, and St. Catherine; urbanicity: unclear Inclusion criteria: current WAZ < −1.5 SDs of the NCHS references; WAZ < −2 SDs in the previous 3 months Exclusion criteria: twins; physical or mental impairments that could affect development **Baseline characteristics** Avg age (months): 18.8; min age (months): 9; max age (months): 30; % female: 61 Avg height-for-age z score: −1.42; stunting: unclear; avg height (cm): 77.1; avg zinc concentration (µg/dL): N/A Total N: 126; Group 1 N: 35; Group 2 N: 42; Group 3 N: 26; Group 4 N: 23
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): 0.5 mL vitamin-iron drop, which contained multiple micronutrients **Group 2:** no zinc Placebo given; co-intervention(s): 0.5 mL vitamin-iron drop, which contained multiple micronutrients

Meeks Gardner 2005 *(Continued)*

	Group 3: zinc Co-intervention(s): psychosocial stimulation; 0.5 mL vitamin-iron drop, which contained multiple micronutrients **Group 4:** no zinc Placebo given; co-intervention(s): psychosocial stimulation; 0.5 mL vitamin-iron drop, which contained multiple micronutrients
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Study withdrawal **Time point (week):** 24
Notes	**Study dates:** N/A **Funding source(s):** Thrasher Research Fund; Nestle Foundation; Grace Kennedy Foundation (Jamaica); Dr. Jeffrey Meeks; the Matalon and Melhado families **Comment(s):** "For logistic reasons, we could not extend the stimulation program. To achieve sufficient power to detect an effect of zinc, we continued enrolling children for a further 2 mo to the zinc trial only."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...children were...randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind trial…parents or guardians, who were unaware of the children's assignment to zinc or placebo..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind trial…" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind trial…testers were unaware of the assignment to interventions" Comment: sufficient blinding seems likely

Meeks Gardner 2005 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 10 Reasons/details: "Reasons for withdrawal given by the parents from the zinc-supplemented group were as follows: children became anorexic (n = 2), child would vomit after the supplement (n = 1), the fathers refused to allow participation after the mother had given consent (n = 2), and family moved away (n = 1). From the placebo group, parents reported illness (jaundice and liver problems; n = 2), families moved away (n = 2), the mother was unhappy with the doctors from the research unit (n = 1), or the mother felt that giving the supplement daily was too onerous (n = 1)." Comment: amount of missing data was similar between study groups. Reasons for missing data were varied. However, there was no reason that a large proportion of children in one study group did have but that children in the other study group did not have
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Unclear risk	Comment: "Children who received placebo were significantly taller than those who received zinc." This baseline difference could have influenced height outcomes, which were reported only as post-treatment scores, rather than as changes from baseline

Mozaffari-Khosravi 2009

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Azad-Shahr suburb of Yazd city in central Iran; urbanicity: peri-urban Inclusion criteria: below the 25th percentile of height-for-age according to NCHS data Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 38.8; min age (months): 25; max age (months): 69; % female: 55.3 Avg height-for-age z score: −1.59; stunting: both - separate data not given; avg height (cm): 91.2; avg zinc concentration (µg/dL): N/A Total N: 90; Group 1 N: 45; Group 2 N: 45
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary**

Mozaffari-Khosravi 2009 *(Continued)*

- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Prevalence of stunting

Time point (week): 52

Notes	**Study dates:** March 2005-February 2007 **Funding source(s):** Department of Research Administration, Shahid Sadoughi University of Medical Sciences **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participates were randomly allocated into one of two groups (zinc supplemented and Placebo group) using randomized numbers table." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "Vahidi pharmacy assigned codes to the different syrups and sent them to corresponding researcher, where they were kept secured until the end of the study." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled supplementation trial…" The placebo group "received the same syrup in color, odor, and taste without zinc" as the zinc group. "Vahidi pharmacy assigned codes to the different syrups and sent them to corresponding researcher, where they were kept secured until the end of the study." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled supplementation trial…" The placebo group "received the same syrup in color, odor, and taste without zinc" as the zinc group. "Vahidi pharmacy assigned codes to the different syrups and sent them to corresponding researcher, where they were kept secured until the end of the study." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, placebo-controlled supplementation trial…" The placebo group "received the same syrup in color, odor, and taste without zinc" as the zinc group. "Vahidi pharmacy assigned codes to the different syrups and sent them to corresponding researcher, where they were kept secured until the end of the study." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 6 Reasons/details: "Five children from ZG group stepped out on grounds of going on trips, illness or other reasons…" Comment: all missing data are from the zinc group and data missing due to "illness or other reasons" might impact results

Mozaffari-Khosravi 2009 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: no English language trial protocol referenced by the study. Only a Persian language trial protocol was available and this Persian language protocol could not be translated
Other bias	Low risk	Comment: appears to be free of other bias

Müller 2001

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Burkina Faso; setting: 18 villages in the Nouna district of northwestern Burkina Faso; urbanicity: rural Inclusion criteria: permanent resident of the study area Exclusion criteria: serious underlying illness **Baseline characteristics** Avg age (months): 18.1; min age (months): 6; max age (months): 30; % female: 49 Avg height-for-age z score: −1.6; stunting: both - separate data given; avg height (cm): 75.8; avg zinc concentration (µg/dL): 76.5 Total N: 709; Group 1 N: 356; Group 2 N: 353
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: 6 d/week; duration (months): 6; dose (mg): 12.5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Incidence of LRTI • Prevalence of LRTI • Incidence of malaria • Prevalence of malaria • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency **Time point (week):** 12 (biochemical outcomes), 24 (morbidity, mortality, and growth outcomes)
Notes	**Study dates:** June-December 1999

Müller 2001 *(Continued)*

Funding source(s): WHO; Deutsche Forschungsgemeinschaft

Comment(s): none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Children were allocated zinc or placebo in blocks of 30 (15 zinc, 15 placebo) by computer generated randomly permutated codes (prepared by the World Health Organization)." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The randomisation code was broken after the database was closed." "Randomization was done independently before the trial started. Investigators were not involved. Fieldworkers had to follow the randomization scheme." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Our study was designed as a...double blind efficacy trial...The tablets were identical in appearance and taste...The randomisation code was broken after the database was closed" Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Our study was designed as a...double blind efficacy trial...The tablets were identical in appearance and taste...The randomisation code was broken after the database was closed" Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Our study was designed as a...double blind efficacy trial...The tablets were identical in appearance and taste...The randomisation code was broken after the database was closed" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 6 Reasons/details: "...we excluded from the final analysis those who were absent from the study area for more than 14 consecutive days." Also, 5 children in the intervention group and 12 children in the placebo group died during the study. Comment: missing data seem too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Nakamura 1993

Study characteristics

Methods	IRCT; non-cross-over

Nakamura 1993 *(Continued)*

Participants	Country: Japan; setting: N/A; urbanicity: unclear Inclusion criteria: HAZ < −2.0 SD; apparent good health with no evidence of endocrinologic disorder; peak serum growth hormone level >10 ng/mL in insulin and clonidine stimulation tests; > 20 ng/mL in the growth hormone releasing factor loading test; mild-to-moderate zinc deficiency identified by zinc kinetic studies (zinc body clearance ≥ 20 mL/kg/h); prepubertal status (Tanner breast and genitalia growth stage) throughout the study period Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 70.3; min age (months): N/A; max age (months): N/A; % female: 47.6 Avg height-for-age z score: −2.44; stunting: stunted; avg height (cm): N/A; avg zinc concentration (µg/dL): 82 Total N: 21; Group 1 N: 10; Group 2 N: 11
Interventions	**Group 1:** zinc Formulation: unclear; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 5 mg/kg; co-intervention(s): N/A **Group 2:** no zinc Placebo not given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (kg) • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 24
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s):** study authors report that, "A total of 21 Japanese children (11 boys) with short stature were studied. They were selected by the following tests: a Tanner evaluation, growth hormone provocation test, and body zinc clearance test. The tests were performed on 220 patients with short stature hospitalized in our clinic." However, it seems that the trial participants were only in the clinic for tests, and were living in the community at the start of the trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...children were divided randomly into two groups…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement

Nakamura 1993 *(Continued)*

Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "None of the control subjects was given placebo." Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "None of the control subjects was given placebo." Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "None of the control subjects was given placebo." Comment: given that no placebo was provided, it seems likely that people involved with the study were aware of which study group participants were in. It is unclear how measured outcomes might be influenced by this lack of blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: insufficient details available to make a judgement
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Ninh 1996

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Vietnam; setting: an area near Hanoï, Vietnam; urbanicity: rural Inclusion criteria: growth retardation evidenced by WAZ < −2 and HAZ < −2 as calculated from United States NCHS reference data; otherwise healthy Exclusion criteria: obvious medical reasons for poor growth **Baseline characteristics** Avg age (months): 17.6; min age (months): 4; max age (months): 36; % female: 54 Avg height-for-age z score: −2.61; stunting: stunted; avg height (cm): 71.3; avg zinc concentration (µg/dL): N/A Total N: 210; Group 1 N: 105; Group 2 N: 105
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 5; dose (mg): 10; co-intervention(s): N/A

Ninh 1996 *(Continued)*

	Group 2: no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio **Time point (week):** 20
Notes	**Study dates:** N/A **Funding source(s):** Fund for Scientific Development, University of Louvain; National Institute of Nutrition of Vietnam; National Foundation for Scientific Research, Belgium **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The subjects were pair-matched...Each member of a pair was randomly assigned to take either a zinc supplement or a placebo." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: "The group to which the patient was assigned was unknown to the child's family and to the members of the investigation team." Comment: despite this statement, the method of allocation concealment is not described in sufficient detail to allow a definite judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind study…The group to which the patient was assigned was unknown to the child's family...The two syrups were indistinguishable in taste and color." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind study…The group to which the patient was assigned was unknown to the...members of the investigation team...The two syrups were indistinguishable in taste and color." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind study…The group to which the patient was assigned was unknown to the...members of the investigation team...The two syrups were indistinguishable in taste and color." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 30 Reasons/details: "Thirty-two pairs were excluded from analysis for various reasons: relocation (n = 3), accident (n = 2), voluntary withdrawal by parent (n = 12), poor compliance with syrup administration (n = 5), poor compliance with

Ninh 1996 *(Continued)*

		anthropometric measurements (n = 4), concurrent use of multivitamin-trace element preparations including zinc (n = 4), and hospitalization (n = 2)." Comment: amount of missing data was not reported separately for each study group. Thus, for instance, the placebo group could have more missing data for reasons such as withdrawal, non-compliance, and hospitalization, while the zinc group could have more missing data due to the fact that "pairs were excluded" and that zinc group members thus had to be excluded when their corresponding placebo group members were
Selective reporting (reporting bias)	High risk	Comment: all-cause hospitalization was measured, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Penny 2004

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Peru; setting: Canto Grande, a shanty town on the outskirts of Lima; urbanicity: peri-urban Inclusion criteria: diarrhea for ≥ 14 d; intention to remain in the study area Exclusion criteria: taking vitamins or minerals within the last 6 weeks; major congenital malformation affecting growth (e.g. Trisomy 21) **Baseline characteristics** Avg age (months): 18.9; min age (months): 6; max age (months): 35; % female: 50 Avg height-for-age z score: −1.56; stunting: both - separate data not given; avg height (cm): 76.4; avg zinc concentration (µg/dL): 70.3 Total N: 164; Group 1 N: 81; Group 2 N: 83
Interventions	**Group 1:** zinc Formulation: solution; compound: gluconate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Incidence of severe diarrhea • Incidence of LRTI • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL)

Penny 2004 *(Continued)*

- Vomiting episodes
- Blood hemoglobin concentration (g/dL)
- Serum or plasma ferritin concentration (µg/L)

Time point (week): 24

Notes

Study dates: N/A

Funding source(s): Thrasher Research Fund; WHO; University of California Pacific Rim Program

Comment(s)

- In addition to the study groups mentioned in this table, there was a group of 82 participants who received "zinc plus vitamins and other minerals at 1–2 times recommended daily intakes." Baseline characteristics reported in this table are weighted averages of all groups except this zinc + multiple micronutrient group, since this group is not included in any meta-analyses in this review.
- "The study was carried out in 2 phases. During the first phase we evaluated the effect of zinc or multiple micronutrient supplementation on the recovery from persistent diarrhea. During the second phase we assessed the effect of continued supplementation on morbidity from new infections during the following 6 mo."
- Twenty-nine children in the placebo group and 28 children in the Zn group "consumed additional iron, either as prescribed by the study team because of anemia at baseline (hemoglobin < 9.0 g/dL) or for family-determined reasons"; of these children, 22 in the placebo group and 18 in the zinc group received additional iron for ≥ 7 d. Additionally, "Children were offered a wafer biscuit and sugar candy after administration of the supplement because this had been shown in pretesting to reduce the nauseating aftertaste that was sometimes experienced with the supplement."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Children were stratified by current breast-feeding status and assigned a consecutive study number within each stratum. With the use of a computer-generated, block randomization scheme, each study number had been linked previously to 1 of 9 letter codes, each of which indicated 1 of the 3 treatment groups." Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: "The identities of the codes were not available to the field staff or investigators until after the data had been cleaned and analyzed." Comment: despite this statement, the method of allocation concealment is not described in sufficient detail to allow a definite judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled, community-based trial…Further flavoring and coloring agents and ascorbic acid were added in Lima to ensure that the supplements were indistinguishable in appearance and taste and to improve their acceptability. These additions were made by staff of the Instituto de Investigación Nutricional who had no other involvement in the study." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled, community-based trial…Further flavoring and coloring agents and ascorbic acid were added in Lima to ensure that the supplements were indistinguishable in appearance and taste and to improve their acceptability. These additions were made by staff of the Instituto de Investigación Nutricional who had no other involvement in the study." "The identities of the codes were not available to the field staff or investigators until after the data had been cleaned and analyzed."

Penny 2004 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled, community-based trial…Further flavoring and coloring agents and ascorbic acid were added in Lima to ensure that the supplements were indistinguishable in appearance and taste and to improve their acceptability. These additions were made by staff of the Instituto de Investigación Nutricional who had no other involvement in the study." "The identities of the codes were not available to the field staff or investigators until after the data had been cleaned and analyzed." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 16 Reasons/details: in the zinc group: 10 participants were lost due to "permanent departure from the area", and 4 were lost due to "parental decision to withdraw." In the placebo group: 2 participants "died", 5 were lost due to "permanent departure from the area", and 6 were lost due to "parental decision to withdraw" Comment: 16% of the randomised participants eligible for our review had data missing; this 16% missing figure includes all groups except the zinc + multiple micronutrient group, since this group is not included in any meta-analyses in this review. Numbers of participants lost due to death or parental decision to withdraw were similar between study groups. Though more participants in the zinc group moved, missing data due to migration are unlikely to bias results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Rahman 2001

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Bangladesh; setting: slums of Dhaka; urbanicity: urban Inclusion criteria: N/A Exclusion criteria: received any vitamin A supplementation within the past 4 months; severe malnutrition (weight-for-age < 60% of the NCHS median); signs or symptoms of vitamin A or zinc deficiency; any systemic illness such as diarrhea, respiratory infection, fever, or any other illness that warranted medical intervention at the time of enrollment **Baseline characteristics** Avg age (months): 23.7; min age (months): 12; max age (months): 35; % female: 47 Avg height-for-age z score: −2.41; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 72.3 Total N: 800; Group 1 N: 200; Group 2 N: 200; Group 3 N: 200; Group 4 N: 200
Interventions	**Group 1:** zinc

Rahman 2001 *(Continued)*

	Formulation: solution; compound: sulfate; frequency: daily; duration (months): 0.5; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 200,000 IU vitamin A capsule on day 14 **Group 4:** no zinc Placebo given; co-intervention(s): 200,000 IU vitamin A capsule on day 14
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Incidence of persistent diarrhea • Prevalence of persistent diarrhea • Incidence of LRTI • Prevalence of LRTI • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 12 (serum or plasma zinc concentration), 24 (morbidity and growth outcomes)
Notes	**Study dates:** October 1997-May 1998 **Funding source(s):** Thrasher Research Fund **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The children were randomly assigned by a person not involved in the study who used permuted blocks of random numbers." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The children were randomly assigned by a person not involved in the study..." "Sets of two bottles of syrup and a capsule were serially numbered according to the randomisation list and corresponding to the study serial numbers. The enrolled children were assigned the numbered bottles in the order in which they were enrolled...The zinc and placebo syrups were supplied in bottles that looked identical...The randomisation code was kept sealed until the completion of the study." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) and sequentially numbered drug containers of identical appearance to conceal allocation

Rahman 2001 *(Continued)*

Blinding of participants (performance bias) All outcomes	Low risk	Quote: "This was a randomized, double-blind, placebo-controlled trial." "The zinc and placebo syrups were supplied in bottles that looked identical, and the appearance and consistency of the syrups were similar...The randomisation code was kept sealed until the completion of the study." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "This was a randomized, double-blind, placebo-controlled trial." "The zinc and placebo syrups were supplied in bottles that looked identical, and the appearance and consistency of the syrups were similar...The randomisation code was kept sealed until the completion of the study." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "This was a randomized, double-blind, placebo-controlled trial." "The zinc and placebo syrups were supplied in bottles that looked identical, and the appearance and consistency of the syrups were similar...The randomisation code was kept sealed until the completion of the study." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 17 Reasons/details: 17% of the 800 randomized participants had data missing for diarrhea, LRTI, weight, and length outcomes: "Eighty-five children (16 in the zinc group, 31 in the A group, 14 in the ZA group, and 24 in the placebo group) were excluded from the study because they received an extra dose of vitamin A (a 60 000-RE capsule) through the Bangladesh 'National Vitamin A Week' campaign. Forty-nine children were subsequently lost to follow-up." In addition, "weight and length measurements at 6 mo were missing for 13 children." Comment: reasons for, and amount of, missing data were similar between study groups. Receiving an additional dose of vitamin A from campaigns unrelated to the study was the most common reason for missing data, and this reason is unlikely to bias results. Also, "the baseline characteristics of the excluded children were not significantly different from those of the children who continued the study."
Selective reporting (reporting bias)	High risk	Comment: vomiting was measured, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Rahman 2001 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary**

Rahman 2001 (2) *(Continued)*

- Incidence of all-cause diarrhea
- Prevalence of all-cause diarrhea
- Incidence of persistent diarrhea
- Prevalence of persistent diarrhea
- Incidence of LRTI
- Prevalence of LRTI
- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µg/dL)

Time point (week): 12 (serum or plasma zinc concentration), 24 (morbidity and growth outcomes)

Notes	As Rahman 2001 above

Rerksuppaphol 2018

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Thailand; setting: Ongkharuck district in a central Thailand; urbanicity: unclear Inclusion criteria: healthy schoolchildren studying in grades 1-6 Exclusion criteria: known history of chronic illnesses, such as chronic liver or renal diseases; congenital heart abnormalities; chronic respiratory disorders; neurological conditions and disorders; behavioral or psychiatric problem; diabetes mellitus; children regularly taking vitamin or mineral supplements and those known to be allergic to vitamin and mineral supplements were also excluded from the study **Baseline characteristics** Avg age (months): 106; min age (months): N/A; max age (months): N/A; % female: 50 Avg height-for-age z score: Group 1: −0.43, Group 2: −0.77; stunting: unclear; avg height (cm): Group 1: 127.7, Group 2: 125.4; avg zinc concentration (µg/dL): N/A Total N: 130; Group 1 N: 66; Group 2 N: 64
Interventions	**Group 1:** zinc Formulation: powder; compound: bisglycinate; frequency: daily; duration (months): 6; dose (mg): 15; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 24

Rerksuppaphol 2018 *(Continued)*

Notes	**Study dates:** June-December 2013 **Funding source(s):** Srinakharinwirot University, Thailand **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: the enrolled children were randomized to the zinc or placebo group by a computerized program (GraphPad QuickCals) using a block of two by a statistical consultant who was not involved in the implementation phase of the study.
Allocation concealment (selection bias)	Low risk	Quote, "The code to the randomization sequence was opened only after study completion." Comment: allocation likely concealed
Blinding of participants (performance bias) All outcomes	Low risk	Comment: the investigators, teachers, children and parents were masked to the intervention.
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: the investigators, teachers, children and parents were masked to the intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: the code to the randomization sequence was opened only after study completion.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: 10 children (4 in zinc, 6 in placebo) withdrew due to parental concerns. 2 children from placebo group discontinued because they moved to another school.
Selective reporting (reporting bias)	Low risk	Study seems to report all the relevant outcomes
Other bias	Low risk	Comment: No evidence of other sources of bias

Richard 2006

Study characteristics

Methods	IRCT; non-cross-over
Participants	Country: Peru; setting: the village of Santa Clara; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: chronic illness (absence of congenital diseases or major illness requiring medical care and/or medication determined by the physician at baseline evaluation); severe malnutrition (weight-for-height z-score < 2 SDs below the NCHS [Hyattsville, MD] reference population or clinical signs of marasmus or kwashiorkor) **Baseline characteristics**

Richard 2006 *(Continued)*

	Avg age (months): N/A; min age (months): 6; max age (months): 180; % female: 51.7 Avg height-for-age z score: −2.08; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 69 Total N: 855; Group 1 N: 214; Group 2 N: 215; Group 3 N: 214; Group 4 N: 212
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 7; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A Group 3*:* zinc Co-intervention(s): 15 mg iron **Group 4:** no zinc Placebo given; co-intervention(s): 15 mg iron
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Incidence of malaria • Height (cm) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/L) **Time point (week):** 28
Notes	**Study dates:** February-September 1998 **Funding source(s):** UNICEF (New York); Johns Hopkins Family Health and Child Survival Cooperative Agreement with the USAID **Comment(s):** based on the distribution of participants in the 0-4, 5-9, and 10-15 year age groups in this study, it seems extremely likely that the majority of participants in this study were between 6 months and 12 years of age.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Using an algorithm in SAS version 6...we randomized children meeting the entry criteria in blocks of four into four supplement groups…" Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement

Richard 2006 *(Continued)*

Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplements were similar in appearance and taste, bottled in similar containers, and labeled with a supplement code...The participants...were...masked throughout the study to the supplement contents." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplements were similar in appearance and taste, bottled in similar containers, and labeled with a supplement code...study personnel were...masked throughout the study to the supplement contents." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplements were similar in appearance and taste, bottled in similar containers, and labeled with a supplement code...study personnel were...masked throughout the study to the supplement contents. The data analyst was masked for the seminal analyses and was unmasked for additional analyses and sub-analyses. No data were excluded or altered after unmasking." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 12.5 Reasons/details: in the zinc group: 6, 1, and 16 participants "migrated", "refused", and were lost for "other" reasons, respectively. In the placebo group: 12, 1, and 13 participants "migrated", "refused", and were lost for "other" reasons, respectively. In the iron group: 9, 2, and 18 participants "migrated", "refused", and were lost for "other" reasons, respectively. In the iron + zinc group: 7, 5, and 17 participants "migrated", "refused", and were lost for "other" reasons, respectively. Comment: reasons for, and amount of, missing data were similar between study groups
Selective reporting (reporting bias)	Unclear risk	Comment: prevalence of stunting, zinc deficiency, anemia, and iron deficiency may have been measured as outcomes, but are not reported. No trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Richard 2006 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary**

Richard 2006 (2) *(Continued)*

- Incidence of all-cause diarrhea
- Incidence of LRTI
- Incidence of malaria
- Height (cm)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µmol/L)
- Blood hemoglobin concentration (g/L)

Time point (week): 28

Notes	As Richard 2006 above

Rosado 1997

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Mexico; setting: 5 communities in the Valley of Solís region of central Mexico; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 28.4; min age (months): 18; max age (months): 36; % female: N/A Avg height-for-age z score: −1.6; stunting: both - separate data given; avg height (cm): 83.3; avg zinc concentration (µg/dL): 96.7 Total N: 219; Group 1 N: N/A; Group 2 N: N/A; Group 3 N: N/A; Group 4 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: methionine; frequency: 6 d/week; duration (months): 12; dose (mg): 20; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 20 mg iron **Group 4:** no zinc Placebo given; co-intervention(s): 20 mg iron
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm) • Weight (kg)

Rosado 1997 *(Continued)*

- Weight-to-height ratio
- Serum or plasma zinc concentration (µmol/L)
- Prevalence of zinc deficiency
- Blood hemoglobin concentration (g/L)
- Prevalence of anemia
- Serum or plasma ferritin concentration (µg/L)
- Prevalence of iron deficiency

Time point (week): 52

Notes	**Study dates:** N/A **Funding source(s):** United States Department of Agriculture; Consejo Nacional de Ciencia y Tecnología (Spanish for National Council of Science and Technology, abbreviated CONACYT); InterHealth Co. Concord, CA **Comment(s):** Table 1 in the Rosado 1997 trial report, which reports baseline characteristics, states that the numbers of children at the beginning of the study are 54, 55, 55, and 53, for the zinc, placebo, zinc + iron, and iron groups respectively. However, these numbers do not add up to the 219 children who were reported to have enrolled in the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were…randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind, randomized community trial…Both the zinc and the iron salts were dissolved in a solution to disguise their bad taste and to ensure similar appearance...The solutions were coded...and the code was not broken until the end of data analysis." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind, randomized community trial…Both the zinc and the iron salts were dissolved in a solution to disguise their bad taste and to ensure similar appearance...The solutions were coded in such a way that their content was unknown to any of the project personnel, and the code was not broken until the end of data analysis." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind, randomized community trial…Both the zinc and the iron salts were dissolved in a solution to disguise their bad taste and to ensure similar appearance...The solutions were coded in such a way that their content was unknown to any of the project personnel, and the code was not broken until the end of data analysis." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 11

Rosado 1997 *(Continued)*

		Reasons/details: "Only 25 children were dropped from the study before the end of the 12 mo, primarily because of a changing family situation." Comment: "Changing family situation" was the primary reason for missing data, and this reason is unlikely to bias results
Selective reporting (reporting bias)	Unclear risk	Comment: LRTI (i.e. "lower respiratory disease") that meets the criteria of this review may have been measured, but is not reported in a way that can be meta-analyzed. No trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Rosado 1997 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 52
Notes	As Rosado 1997 above

Rosales 2004

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Guatemala; setting: Guatemala City; urbanicity: urban Inclusion criteria: good health; absence of chronic diseases Exclusion criteria: N/A

Rosales 2004 *(Continued)*

	Baseline characteristics Avg age (months): N/A; min age (months): 96; max age (months): 132; % female: 52 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): 65.4 Total N: 76; Group 1 N: 18; Group 2 N: 20; Group 3 N: 20; Group 4 N: 18
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 5 d/week; duration (months): 2; dose (mg): 42.5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 20 mg iron **Group 4:** no zinc Placebo given; co-intervention(s): 20 mg iron
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 8
Notes	**Study dates:** February-April 2000 **Funding source(s):** N/A **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "They were systematically blocked randomized…" In response to a question about sequence generation, an author of this study replied as follows: "I believe that at the CeSSIAM center they used a table of random numbers to generate the random allocation sequence." Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias)	Low risk	Quote: "Children were masked to the content of the mixture, which was prepared every day at the school kitchen by one of the investigators…To main-

Rosales 2004 *(Continued)*

All outcomes		tain masking,...the children had no contact with the preparation area, and the drafts were assigned by code number." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "To maintain masking...the drafts were assigned by code number." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "To maintain masking, the investigator never had direct contact with the subjects,...and the drafts were assigned by code number." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 14 Reasons/details: 2, 5, 1, and 3 children were excluded from the zinc, placebo, iron and zinc, and iron alone groups, respectively. All 11 of these children were excluded because they "missed 5 or more days of classes and did not receive at least 90% of the supplementation dosage." Comment: reasons for, and amount of, missing data were similar between study groups
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Rosales 2004 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 8
Notes	As Rosales 2004 above

Ruel 1997

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Guatemala; setting: the village of Santa Maria de Jesus; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 7.62; min age (months): 6; max age (months): 9; % female: 43 Avg height-for-age z score: −2.16; stunting: both - separate data not given; avg height (cm): 144.6; avg zinc concentration (µg/dL): N/A Total N: 108; Group 1 N: 55; Group 2 N: 53
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 7; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Height (cm) • Weight (kg) • Weight-to-height ratio **Time point (week):** 28
Notes	**Study dates:** N/A **Funding source(s):** University of California, Davis Institute of Nutrition of Central America; Panama institutional linkage project; University Development Linkage Program of the USAID; Thrasher Research Fund **Comment(s):** none

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "…randomized community trial…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A

Ruel 1997 *(Continued)*

		Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled study...The supplements were indistinguishable, and neither the families nor...were aware of the treatment group to which the infants belonged." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled study...The supplements were indistinguishable, and neither...nor the study staff were aware of the treatment group to which the infants belonged." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled study...The supplements were indistinguishable, and neither...nor the study staff were aware of the treatment group to which the infants belonged." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 18 Reasons/details: 19 children (10 from the zinc group and 9 from the placebo group) "dropped out of the study attributable to migration, or inability to comply with the project requirements because of maternal work, or late parental refusal." Comment: amount of missing data was similar between study groups. Reasons for missing data are unlikely to bias results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Ruz 1997

Study characteristics	
Methods	IRCT; non-cross-over
Participants	height-for-age z scoreCountry: Chile; setting: Santiago; urbanicity: peri-urban Inclusion criteria: apparently healthy; preschool child; of middle-to-low or low socioeconomic status Exclusion criteria: a clinical condition predisposing to growth failure **Baseline characteristics** Avg age (months): 39.8; min age (months): 27; max age (months): 50; % female: 53 Avg height-for-age z score: −0.52; stunting: both - separate data not given; avg height (cm): 95.6; avg zinc concentration (µg/dL): 114.1 Total N: 98; Group 1 N: 49; Group 2 N: 49
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 14; dose (mg): 10; co-intervention(s): N/A

Ruz 1997 *(Continued)*

	Group 2: no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/L) • Serum or plasma copper concentration (µmol/L) **Time point (week):** 24 (biochemical outcomes), 56 (height)
Notes	**Study dates:** N/A (14 calendar months, consisting of an initial 6 months, followed by 3 summer months, plus an additional 5 months thereafter) **Funding source(s):** National Fund for Scientific and Technological Development of Chile (FONDECYT) **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were pair matched according to sex and age and randomly assigned to two experimental groups…The randomization procedure was followed strictly. It yielded comparable groups for most of the variables of interest." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "The study was conducted in a doubly-blinded fashion, and the code was broken only after the project had been finished. The random allocation of each member of the pair to the experimental groups (identified as group A or B, to avoid bias) was done by a member of our staff not involved with the study...The code was only known to the pharmacist in charge." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind zinc supplementation trial…The study was conducted in a doubly-blinded fashion, and the code was broken only after the project had been finished...The zinc and placebo solutions were indistinguishable in appearance and taste." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind zinc supplementation trial…The study was conducted in a doubly-blinded fashion, and the code was broken only after the project had been finished...The zinc and placebo solutions were indistinguishable in appearance and taste." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias)	Low risk	Quote: "…double-blind zinc supplementation trial…The study was conducted in a doubly-blinded fashion, and the code was broken only after the project

Ruz 1997 *(Continued)*

All outcomes		had been finished...The zinc and placebo solutions were indistinguishable in appearance and taste." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 43 Reasons/details: "After 6 mo of intervention, 19 individuals had dropped out of the study, leaving 79; after 14 mo, the total number of children still participating was 56." Thus, 19% of data was missing for zinc, hemoglobin, ferritin, and copper concentrations (which were only measured at baseline and 6 months), and 43% of data were missing for all other outcomes. No reasons for dropout were reported Comment: a large proportion of data is missing, and no information was reported on differential dropout between study groups or reasons for dropout
Selective reporting (reporting bias)	High risk	Comment: diarrhea, weight, weight-to-height ratio, and serum ferritin were measured, but are not reported in a way that can be meta-analyzed. LRTI, which meets the criteria for this review, may have been measured; but it is not reported in a way that can be meta-analyzed, and it is unclear how LRTI was defined in this study
Other bias	Low risk	Comment: appears to be free of other bias

Sampaio 2013

Study characteristics	
Methods	IRCT; non-cross-over
Participants	height-for-age z scoreCountry: Brazil; setting: Salvador-Bahia; urbanicity: not reported Inclusion criteria: healthy children attending day care ("Institutionalized"?) Exclusion criteria: chronic medical problems including sickle cell disease and congenital heart disease **Baseline characteristics** Avg age (months): 25.63; min age (months): 6; max age (months): 48; % female: 0.42 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 143; Group 1 N: 75; Group 2 N: 68
Interventions	**Group 1:** zinc Formulation: powder/paste; compound: gluconate; frequency: daily; duration (months): 3; dose (mg): 5; co-intervention(s): sprinkles (including vitamin A and iron) **Group 2:** no zinc Placebo given; co-intervention(s): sprinkles (including vitamin A and iron)
Outcomes	**Primary** • N/A **Secondary**

Sampaio 2013 *(Continued)*

- Incidence of all-cause diarrhea

Time point (week): 13

Notes	**Study dates:** October 2001-January 2006 **Funding source(s):** NIH, Bill & Melinda Gates Foundation, Office of Health and Nutrition, United States Agency for International Development **Comment(s):** monitoring was undertaken to make sure plates were not swapped and that children ate the food. It was recorded if children did not eat the meal, or only ate half.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomização foi feita por berçários e salas, de acordo com sequência gerada por computador." - randomization was done by nursery and classroom, according to a computer-generated sequence. "The kids were randomized based on the classes that they were put in the daycare since that would make delivery of the micronutrient sprinkle package easy." (Personal communication) Comment: not clear how participants were clustered and how this was included in the analysis
Allocation concealment (selection bias)	Unclear risk	Quote: N/A
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "duplo cego" - double blind
Blinding of personnel (performance bias) All outcomes	High risk	Quote: "Os suplementos apenas eram abertos e adicionados às refeições no momento de servir, por nutricionistas não cegas para o estudo, já que os sachês estavam identificados quanto à presença de zinco" - the supplements were only opened and added to the meals at the moment of serving, by nutritionists who were not blinded to the study, since the sachets were marked as to whether they included zinc or not Comment: intervention was continued at the weekends by sending parents a supply of sachets with instructions (does not state whether these sachets also had the contents on the packet; if so a risk to the blinding status of the participants)
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Todos os médicos envolvidos estavam cegos para o estudo" - all medics involved were blinded to the study Comment: this relates to those people undertaking outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Todas completaram o estudo." - all participants completed the study
Selective reporting (reporting bias)	Unclear risk	Comment: protocol registration NCT00967551. Primary outcome reported, but unclear what other outcomes were measured.
Other bias	Low risk	Comment: appears to be free of other bias

Sandstead 1998

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: China; setting: the 3 cities of Chonqing, Qingdao, and Shanghai; urbanicity: urban Inclusion criteria: 1st grader Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 72; max age (months): 108; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Please see 'Notes' for details about number of participants
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: unclear; frequency: 6 d/week; duration (months): 2.5; dose (mg): 20; co-intervention(s): MM **Group 2:** no zinc Placebo given; co-intervention(s): MM
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** Spring-Fall 1994 **Funding source(s):** International Lead Zinc Research Organization; Research Triangle Park, North Carolina **Comment(s)** • It was reported that "Subjects were divided equally between treatments", but due to inconsistent numbers reported across the two trial reports (Penland et al 1997 (see secondary reference under Sandstead 1998) reports 372 participants and Sandstead 1998 reports 740 participants), it is unclear how many participants were in the trial. • In addition to the study groups mentioned in this table, there was a group of participants who received zinc only, but there was no placebo group to which this zinc group could be compared. So, this zinc group is not included in any meta-analyses in this review. • Baseline plasma zinc was reported as 87.25 µg/dL in Penland 1997 and 86.37 µg/dL in Sandstead 1998.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized, controlled trial…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement

Sandstead 1998 *(Continued)*

Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Double-blind randomized controlled treatment trial…Treatments were…administered double-blind for 10 weeks...identical appearing white tablets." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind randomized controlled treatment trial…Treatments were…administered double-blind for 10 weeks...identical appearing white tablets." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Double-blind randomized controlled treatment trial…Treatments were…administered double-blind for 10 weeks...identical appearing white tablets." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: numbers of participants randomized into each intervention group are not clearly reported, and different numbers of participants are reported in Penland 1997 versus Sandstead 1998
Selective reporting (reporting bias)	High risk	Comment: plasma zinc concentration, hemoglobin, anemia, serum ferritin concentration, and iron deficiency were measured, but are not reported in a way that can be meta-analyzed. The reported means and number of participants analyzed for plasma zinc concentration are different between the Penland 1997 and Sandstead 1998 trial reports
Other bias	Low risk	Comment: appears to be free of other bias

Sandstead 2008

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Brownsville, Texas; urbanicity: urban Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 72; max age (months): 84; % female: 33 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): 97.4 Total N: 54; Group 1 N: 27; Group 2 N: 27
Interventions	**Group 1:** zinc Formulation: unclear; compound: sulfate; frequency: 5 d/week; duration (months): 2.5; dose (mg): 20; co-intervention(s): multiple micronutrients

Sandstead 2008 *(Continued)*

	Group 2: no zinc Placebo given; co-intervention(s): multiple micronutrients
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/dL) • Serum or plasma ferritin concentration (µg/L) **Time point (week):** 10
Notes	**Study dates:** Spring-Fall 1994 **Funding source(s):** United States Department of Agricultural Research Service; University of Texas Medical Branch; Gerber Foundation; NIH; Labcatal, France **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were divided into 2 groups of similar composition and assigned randomly…to one of the treatments…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "The statistician assigned the treatments without specific knowledge of the subjects and held the code until completion of the trial." Comment: indicates central randomization to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…treated in double-blind fashion in equal numbers…They were divided into 2 groups of similar composition and assigned…in a double-blind fashion to one of the treatments…The statistician assigned the treatments without specific knowledge of the subjects and held the code until completion of the trial." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…treated in double-blind fashion in equal numbers…They were divided into 2 groups of similar composition and assigned…in a double-blind fashion to one of the treatments…The statistician assigned the treatments without specific knowledge of the subjects and held the code until completion of the trial." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…treated in double-blind fashion in equal numbers…They were divided into 2 groups of similar composition and assigned…in a double-blind fashion to one of the treatments…The statistician assigned the treatments without specific knowledge of the subjects and held the code until completion of the trial." Comment: sufficient blinding seems likely

Sandstead 2008 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 15 Reasons/details: N/A Comment: the amount of missing data was similar between study groups. In the zinc + micronutrients group, 2 were missing for the plasma zinc outcome, and 3 were missing for the serum ferritin outcome. In the micronutrients group, 2 were missing for the plasma zinc outcome, and 4 were missing for the serum ferritin outcome. However, a somewhat sizeable proportion of data is missing, and reasons for missing data were not stated. Also, Table 2 lists an inconsistent number of participants for the serum ferritin outcome (stating that 46 participants were analyzed for this outcome, 24 in the zinc + micronutrients group, and 23 in the micronutrients group)
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Sanjur 1990

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Denver, Colorado; urbanicity: urban Inclusion criteria: healthy; spoke English as a main language at home Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 21; min age (months): 12; max age (months): 24; % female: 51 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: N/A; Group 1 N: N/A; Group 2 N: N/A; Group 3 N: N/A; Group 4 N: N/A
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: unclear; frequency: daily; duration (months): 6; dose (mg): unclear; co-intervention(s): multivitamin **Group 2:** no zinc Placebo given; co-intervention(s): multivitamin **Group 3:** zinc Co-intervention(s): multivitamin; iron **Group 4:** no zinc Placebo given; co-intervention(s): multivitamin; iron
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** N/A

Sanjur 1990 *(Continued)*

Funding source(s): University of Colorado Health Sciences Center, Denver

Comment(s)

- "The study sample consisted of 90 healthy children...Approximately 15 to 22 children were assigned" to each study group. In addition to the study groups mentioned in this table, there was a group of participants who received placebo only, but there was no zinc group to which this placebo group could be compared in this review. The 90 participants who were randomized in this study includes this group of participants who only received placebo.
- In addition, the study authors report that "The present examination of the diet and nutrient intake of children 1 to 2 years old is part of a larger investigation undertaken by the University of Colorado Health Sciences Center. The primary objective of the larger study was to evaluate the efficacy of vitamin and mineral supplements in very young children." However, no information was available about this larger investigation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The toddlers were randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind study…Group assignment was unknown to the toddlers and their families..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind study…Group assignment was unknown to...the members of the investigating team." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind study…Group assignment was unknown to...the members of the investigating team." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: the following were not reported: number of participants randomised to each group, amount of missing data for each group, reasons for missing data in each group
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Sayeg Porto 2000

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: Rio de Janeiro; urbanicity: urban Inclusion criteria: HAZ < −2 SD according to NCHS data; attendance at the Pediatric Endocrinology Service for at least 1 year without previous treatment; normal hematological values and biochemical analysis (calcium, phosphorus, alkaline phosphatase, iron, urea, creatinine, albumin, and globulins); normal endocrine function with normal thyroid hormone levels (T3, T4, and thyroid stimulating hormone); insulin growth factor-1 level and growth hormone post-exercise > 10 ng/dL; bone age equivalent to height age Exclusion criteria: pubertal signs; family history of psychological problems; malabsorption; chronic infections; other known causes of growth failure **Baseline characteristics** Avg age (months): 118.44; min age (months): 84; max age (months): 120; % female: 24 Avg height-for-age z score: −2.67; stunting: stunted; avg height (cm): 121.6; avg zinc concentration (µg/dL): 100.7 Total N: 21; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 5 mg/kg; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) • Prevalence of zinc deficiency **Time point (week):** 24 (biochemical outcomes), 52 (growth outcomes)
Notes	**Study dates:** N/A **Funding source(s):** N/A **DOI(s):** 10.1515/jpem.2000.13.8.1121 **Comment(s):** the number of participants randomized to each study group is not reported, nor is the number of participants in either study group who completed the study, nor is any number of participants analyzed for any outcome reported. However, it is assumed that participants were split approximately evenly between study groups.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Sayeg Porto 2000 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "The study was designed as a…randomized, controlled trial…Children were randomized to two groups..." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was performed by a person not involved in the clinical management of the children." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The study was designed as a double-blind…controlled trial…In the Pharmacy Department, two syrups were made with the same color and flavor, one of which contained zinc sulfate…Assignment to the zinc or placebo group was not known by the families..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The study was designed as a double-blind…controlled trial…In the Pharmacy Department, two syrups were made with the same color and flavor, one of which contained zinc sulfate…Assignment to the zinc or placebo group was not known by the…investigators." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The study was designed as a double-blind…controlled trial…In the Pharmacy Department, two syrups were made with the same color and flavor, one of which contained zinc sulfate…Assignment to the zinc or placebo group was not known by the…investigators." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 14 Reasons/details: "During the supplementation period, three boys presented initial signs of puberty and were excluded from the study." Comment: amount of missing data is not reported separately for each study group
Selective reporting (reporting bias)	High risk	Comment: side effects were measured but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Sazawal 1996

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: India; setting: Kalkaji, New Delhi; urbanicity: urban Inclusion criteria: reported passage of at least 4 unformed stools in the previous 24 h; a diarrheal duration of < 7 d; permanent residence in the Kalkaji area Exclusion criteria: malnutrition judged clinically to be sufficiently severe to require hospitalization

Sazawal 1996 *(Continued)*

	Baseline characteristics Avg age (months): 16; min age (months): 6; max age (months): 35; % female: 47.7 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 64.8 Total N: 609; Group 1 N: 298; Group 2 N: 311
Interventions	**Group 1:** zinc Formulation: solution; compound: gluconate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): multiple micronutrients **Group 2:** no zinc Placebo given; co-intervention(s): multiple micronutrients
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Prevalence of all-cause diarrhea • Incidence of persistent diarrhea • Incidence of LRTI • Prevalence of LRTI • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/dL) • Serum or plasma copper concentration (µg/dL) • Prevalence of copper deficiency **Time point (week):** 17 (biochemical outcomes), 24 (morbidity outcomes)
Notes	**Study dates:** September 1992-November 1994 **Funding source(s):** WHO Diarrheal Disease Control Program; Thrasher Research Fund **DOI(s):** 10.1093/jn/126.2.443, 10.3329/jhpn.v27i5.3639, 10.1056/NEJM199509283331304, 10.1093/ajcn/66.2.413, 10.1542/peds.102.1.1, 10.1111/j.1651-2227.2004.tb18254.x **Comment(s):** "…a subgroup of children enrolled in a trial of the therapeutic effect of zinc supplementation…were randomly selected at the time of initial enrollment to enter a 6-mo follow-up trial after recovery from the enrollment diarrheal episode." The data in this review apply to the 6-month follow-up trial. In this follow-up trial, during episodes of diarrheal illness, the dose of zinc was doubled to provide for excess stool losses.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization schedules with permuted blocks of fixed length of 10, appropriate for double-blind studies, were used." "At WHO two separate randomization schedules were first made for long and short follow up children, then the two were combined into a single schedule such that allocation to long and short follow up was also random." Comment: N/A

Sazawal 1996 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "The company prepared bottles with labels of A, B, C, D, R, F, three of these with zinc (intervention group solution) and the other three without zinc (control group solution). The identity of codes A-F was communicated to WHO by the company and was not revealed to the investigators in Delhi until the end of the study. Both sets of bottles...were identical in all respects...The randomization schedule prepared by WHO gave serial numbers in each of the 4 strata, with letter A through F denoting which code bottle should be assigned to the child. This randomization schedule was mailed by WHO directly to clinical pharmacology at AIIMS where only the pharmacy assistant was aware of the allocation. He relabelled the bottles with stratum serial numbers and provided the bottles as required. At the clinic, on enrollment, each child was assigned a stratum serial number corresponding to a bottle of supplement, which was also labeled with the child's identification number and name. The investigators and the field staff were unaware of A-F allocation." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) and sequentially numbered drug containers of identical appearance to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind randomized trial...Both sets of bottles and solutions were identical in all respects including color and taste." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind randomized trial...The identity of codes A-F was…not revealed to the investigators in Delhi until the end of the study. Both sets of bottles and solutions were identical in all respects including color and taste." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind randomized trial...The identity of codes A-F was…not revealed to the investigators in Delhi until the end of the study. Both sets of bottles and solutions were identical in all respects including color and taste." "…duplicate blind measurements were taken by the two study physicians throughout the course of the study…" Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 7 Reasons/details: for diarrhea outcomes: "Of the 609 children, 40 (Z 12, C 28) with actual follow-up of less than 30 d were excluded from the analysis." For LRTI outcomes: "Out of 609 children...6 children (zinc, n = 1; control, n = 5)" were excluded from the analysis, because "their total surveillance was less than 15 days" due to being "absent continuously." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: height and weight were measured as outcomes, but are not reported. Prevalence of zinc deficiency was measured, but is not reported in a way that can be meta-analyzed due to different numbers reported in different trial reports
Other bias	Low risk	Comment: appears to be free of other bias

Sazawal 2006

Study characteristics

Sazawal 2006 *(Continued)*

Methods	CRCT; non-cross-over
Participants	Country: Zanzibar; setting: Pemba, an island of Zanzibar; urbanicity: both rural and urban Inclusion criteria: likely to remain resident in the study area Exclusion criteria: severe malnutrition needing rehabilitation **Baseline characteristics** Avg age (months): 18.2; min age (months): 1; max age (months): 35; % female: 50 Avg height-for-age z score: −1.5; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 78.5 Total N: 60,225; Group 1 N: 21,274; Group 2 N: 21,272; Group 3 N: 8914; Group 4 N: 8765 Total clusters: 33,899; Group 1 clusters: N/A; Group 2 clusters: N/A; Group 3 clusters: N/A; Group 4 clusters: N/A
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: daily; duration (months): 16; dose (mg): 5 mg to children aged < 12 months; 10 to children aged ≥ 12 months; co-intervention(s): 200,000 IU of vitamin A every 6 months to children aged ≥ 12 months, 100,000 IU of vitamin A every 6 months to children aged < 12 months **Group 2:** no zinc Placebo given; co-intervention(s): 200,000 IU of vitamin A every 6 months to children aged ≥ 12 months, 100,000 IU of vitamin A every 6 months to children aged < 12 months **Group 3:** zinc Co-intervention(s): 6.25 mg iron and 25 µg folic acid to children aged < 12 months; 12.5 mg iron and 50 µg folic acid to children aged ≥ 12 months; 100,000 IU of vitamin A every 6 months to children aged < 12 months; 200,000 IU of vitamin A every 6 months to children aged ≥ 12 months **Group 4:** no zinc Placebo given; co-intervention(s): 6.25 mg iron and 25 µg folic acid to children aged < 12 months; 12.5 mg iron and 50 µg folic acid to children aged ≥ 12 months; 100,000 IU of vitamin A every 6 months to children aged < 12 months; 200,000 IU of vitamin A every 6 months to children aged ≥ 12 months
Outcomes	**Primary** • All-cause mortality • Mortality due to all-cause diarrhea • Mortality due to LRTI • Mortality due to malaria **Secondary** • Height (cm) • Weight (kg) • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Prevalence of iron deficiency **Time point (week):** 24-52 (biochemical and growth outcomes), 55-69 (morbidity and mortality outcomes)

Sazawal 2006 *(Continued)*

Notes

Study dates: January 2002-August 2003

Funding source(s): WHO Department of Child Health and Adolescent Health and Development; United Nations Foundation; USAID; Bill & Melinda Gates Foundation

DOI(s): 10.1016/S0140-6736(06)67962-2, 10.1016/S0140-6736(06)68334-7, 10.1093/jn/135.4.814, 10.1016/j.earlhumdev.2007.10.007, 10.1097/DBP.0b013e31819e6a48, 10.3945/jn.107.086231, 10.1093/jn/136.9.2427, 10.1093/jn/137.12.2756, 10.1016/S0140-6736(07)60452-8

Comment(s)

- "On recommendation of the Data and Safety Monitoring Board" of the study, the iron + folic acid + zinc (IFAZ) and iron + folic acid (IFA) groups "were stopped on Aug 19, 2003 because of overwhelming evidence of increased hospital admissions and a trend for increased mortality associated with iron supplementation...Children from the IFAZ and non-zinc IFA groups were switched to the zinc and placebo groups, respectively." The numbers of participants listed in this table as being randomized to the zinc and placebo groups do not include those from the IFA and IFAZ groups who were switched to zinc or placebo.
- "Children received zinc or placebo supplements until they were 48 months of age", or, in the case of the IFAZ and IFA groups, "until the iron and folic acid-containing groups were stopped." "At the time of stopping the trial, mean duration of follow-up in the study was 383 days" in the IFAZ and IFA groups reported in the Sazawal 2006 trial report. "The mean duration of supplementation was 484.7 days" in the zinc and placebo groups reported in the Sazawal et al 2007 trial report (see secondary reference under Sazawal 2006 (2)).
- Iron deficiency was defined as zinc protoporphyrin ≥ 90 µmol/mol heme.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was by household, by an allocation sequence (permuted block randomisation with block length of 16) computer-generated by WHO." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The supplement code, which was not known to the investigators, was maintained at WHO. To ensure masking, we labeled the strips of supplements with 16 letter codes - four for each of the groups. This letter code was hidden in the batch number on each strip of tablets. On enrolment, we assigned every child a code. Labels with the child's name on were then printed from a computer database and attached by the pharmacy to the appropriate strip of supplements." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled trial…To ensure masking, we labelled the strips of supplements with 16 letter codes - four for each of the groups. This letter code was hidden in the batch number on each strip of tablets." "The halting of the IFAZ and IFA arms and switching of children to the other groups were done with the help of WHO and the DSMB statistician. The trial initially used 16-letter codes (four-letter codes assigned to the individual supplementation groups) and two-stage blinding. The four-letter codes for every group were known only to WHO and the manufacturer; the pharmacy dispensing the supplements knew only which letter code was assigned to each child, and the…family knew neither. At the time of switch, WHO and the DSMB statistician provided an alternative letter code for all of the redundant eight-letter codes...Tablets...were similar in packaging, appearance, taste, and inactive ingredients."

Sazawal 2006 *(Continued)*

		Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled trial…To ensure masking, we labelled the strips of supplements with 16 letter codes - four for each of the groups. This letter code was hidden in the batch number on each strip of tablets." "The halting of the IFAZ and IFA arms and switching of children to the other groups were done with the help of WHO and the DSMB statistician. The trial initially used 16-letter codes (four-letter codes assigned to the individual supplementation groups) and two-stage blinding. The four-letter codes for every group were known only to WHO and the manufacturer; the pharmacy dispensing the supplements knew only which letter code was assigned to each child, and the study worker…knew neither. At the time of switch, WHO and the DSMB statistician provided an alternative letter code for all of the redundant eight-letter codes...Tablets...were similar in packaging, appearance, taste, and inactive ingredients." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-masked, placebo-controlled trial…To ensure masking, we labelled the strips of supplements with 16 letter codes - four for each of the groups. This letter code was hidden in the batch number on each strip of tablets." "The halting of the IFAZ and IFA arms and switching of children to the other groups were done with the help of WHO and the DSMB statistician. The trial initially used 16-letter codes (four-letter codes assigned to the individual supplementation groups) and two-stage blinding. The four-letter codes for every group were known only to WHO and the manufacturer; the pharmacy dispensing the supplements knew only which letter code was assigned to each child, and the study worker…knew neither. At the time of switch, WHO and the DSMB statistician provided an alternative letter code for all of the redundant eight-letter codes...Tablets...were similar in packaging, appearance, taste, and inactive ingredients." Teams that assessed causes of death "were masked to supplement allocation." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 17 Reasons/details: in the zinc + iron + folic acid group reported in Sazawal 2006: 1075 participants "withdrew", 480 "outmigrated", and 146 "died". In the iron + folic acid group reported in Sazawal 2006: 1059 participants "withdrew", 445 "outmigrated", and 149 "died". In the placebo group reported in Sazawal 2007 (see secondary reference under Sazawal 2006 (2)): 865 participants "withdrew", 2018 "outmigrated", and 483 "died". In the zinc group reported in Sazawal 2007 (see secondary reference under Sazawal 2006 (2)): 1090 participants "withdrew", 2141 "outmigrated", and 401 "died". Comment: reasons for, and amount of, missing data were similar between the placebo and zinc groups. Reasons for, and amount of, missing data were similar between the iron + folic acid and zinc + iron + folic acid groups
Selective reporting (reporting bias)	High risk	Comment: all-cause hospital admissions was pre-specified as a secondary outcome in the protocol for this study and was measured, but is not reported for the study group that received zinc. Hospitalisation due to diarrhea, hospitalization due to pneumonia, and hospitalization due to malaria seem to be measured, but were not pre-specified in the protocol for this study, and are not reported; however, the related outcome of all-cause hospitalization was pre-specified as a secondary outcome in the protocol for this study. Weight-for-height z-score was measured, but was not pre-specified in the protocol for this study, and is not reported. Malaria prevalence was measured, but was not pre-specified in the protocol for this study, and is not reported in a way that can be meta-analyzed. Blood hemoglobin concentration, anemia prevalence, preva-

Sazawal 2006 *(Continued)*

		lence of iron deficiency, height, and weight were reported, but were not pre-specified in the protocol for this study. Mortality due to diarrhea, mortality due to pneumonia, and mortality due to malaria were reported, but were not pre-specified in the protocol for this study; however, the related outcome of all-cause mortality was pre-specified as a secondary outcome in the protocol for this study Protocol identifier: ISRCTN59549825
Other bias	Low risk	Comment: appears to be free of other bias

Sazawal 2006 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Height (cm) • Weight (kg) • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Prevalence of iron deficiency **Time point (week):** 24-52 (biochemical and growth outcomes), 55-69 (morbidity and mortality outcomes)
Notes	As Sazawal 2006 above

Schultink 1997

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Indonesia; setting: Tambora district of Jakarta; urbanicity: urban Inclusion criteria: pre-school children; stunted, as indicated by an HAZ < −1.5; anemic, as indicated by a hemoglobin concentration < 110 g/L Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 38; min age (months): 24; max age (months): 60; % female: 52

Schultink 1997 *(Continued)*

	Avg height-for-age z score: −2.5; stunting: both - separate data not given; avg height (cm): 85.9; avg zinc concentration (µg/dL): 87.3 Total N: 85; Group 1 N: 43; Group 2 N: 42
Interventions	**Group 1:** zinc Formulation: solution; compound: phosphate; frequency: daily; duration (months): 2; dose (mg): 15; co-intervention(s): 30 mg iron **Group 2:** no zinc Placebo given; co-intervention(s): 30 mg iron
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/L) • Serum or plasma ferritin concentration (µg/L) **Time point (week):** 8
Notes	**Study dates:** August-September 1993 **Funding source(s):** N/A **Comment(s):** "…all children received a deworming treatment (100 mg of pyrantel pamoate and 150 mg of mebendazole) before the start of the supplementation."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The children were randomly assigned to two groups." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Both syrups were similar in appearance and taste, and supplementation was double-blinded." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Both syrups were similar in appearance and taste, and supplementation was double-blinded." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Both syrups were similar in appearance and taste, and supplementation was double-blinded." Comment: sufficient blinding seems likely

Schultink 1997 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 21 Reasons/details: N/A Comment: 10 participants were missing in the zinc group, and 8 participants were missing in the control group. So, the amount of missing data was similar between study groups. However, reasons for missing data were not reported
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Sempértegui 1996

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Ecuador; setting: slum in the northeast region of the city of Quito; urbanicity: urban Inclusion criteria: attended a daycare centre (centro infantil No. 1 CAI, National Institute for the Children and the Family) for at least 6 months; malnourished according to height and weight parameters from the NCHS Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 42.3; min age (months): 12; max age (months): 59; % female: 43.8 Avg height-for-age z score: −2; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 86.5 Total N: 50; Group 1 N: 25; Group 2 N: 25
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 2; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of LRTI • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 9 (serum or plasma zinc concentration), 17 (morbidity and growth outcomes)
Notes	**Study dates:** N/A

Sempértegui 1996 *(Continued)*

Funding source(s): Universidad Central del Ecuador; Ministry of Public Health of Ecuador

Comment(s): full text could not be obtained for the Correa León et al 1992 trial report for this study (see secondary reference under Sempértegui 1996).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "…children were randomly assigned, by the Moses-Oakford algorithm..." Comment: N/A
Allocation concealment (selection bias)	Unclear risk	Quote: "The code was kept by the Ethical Committee until the end of the study." Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind placebo-controlled trial…Zinc and placebo syrups had an identical appearance and flavor...The NS group received syrup 'A' that contained placebo. The S group was given syrup 'B' that contained zinc...The code was kept by the Ethical Committee until the end of the study." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind placebo-controlled trial…Zinc and placebo syrups had an identical appearance and flavor…The NS group received syrup 'A' that contained placebo. The S group was given syrup 'B' that contained zinc…the syrups were administered…by two pediatricians...who did not know which group was the actively supplemented group until after the study was completed, and who were not involved in the daily clinical examination of the children. The code was kept by the Ethical Committee until the end of the study." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind placebo-controlled trial…Zinc and placebo syrups had an identical appearance and flavor...The NS group received syrup 'A' that contained placebo. The S group was given syrup 'B' that contained zinc...The code was kept by the Ethical Committee until the end of the study." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4 Reasons/details: "…two malnourished children from the S group were lost to follow-up when their families moved to another province." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: prevalence of zinc deficiency may have been measured, but was not reported in a way that could be meta-analyzed. No trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Shah 2011

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: India; setting: near the Jawaharlal Nehru Medical College Hospital in Aligarh, Uttar Pradesh, India; urbanicity: urban Inclusion criteria: recurrent acute LRTIs; referred to department of Pediatrics Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 59; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: N/A; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: unclear; compound: gluconate; frequency: unclear; duration (months): 2; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	No outcomes of interest reported in a way that can be meta-analyzed
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s):** though, "The final analysis included 96 children allocated equally to the two groups", the number of participants randomized is not reported, nor is the number of participants randomized to each study group.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "...double blind controlled trial…" Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "...double blind controlled trial…" Comment: insufficient details available to make a judgement

Shah 2011 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...double blind controlled trial…" Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: N/A Comment: the following were not reported: number of participants randomized, number of participants randomized to each group, amount of missing data for each group, reasons for missing data in each group
Selective reporting (reporting bias)	High risk	Comment: LRTI, which meets the criteria of this review, may have been measured and reported; but it is unclear how respiratory illness was defined in this study. Serum zinc concentration was measured, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Shankar 2000

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Papua New Guinea; setting: north Wosera District of East Sepik Province, in northwestern Papua New Guinea; urbanicity: rural Inclusion criteria: planning to reside in the Wosera for at least 1 year; no apparent chronic or debilitating condition Exclusion criteria: signs of severe zinc deficiency or malnutrition **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 60; % female: 53 Avg height-for-age z score: −1.9; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 71 Total N: 274; Group 1 N: 136; Group 2 N: 138
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: gluconate; frequency: 6 d/week; duration (months): 11.5; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • All-cause mortality • Mortality due to malaria **Secondary** • Prevalence of all-cause diarrhea

Shankar 2000 *(Continued)*

- Incidence of malaria
- Height (cm)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µg/dL)
- Prevalence of zinc deficiency
- Blood hemoglobin concentration (g/dL)
- Prevalence of anemia

Time point (week): 46

Notes	**Study dates:** November 1995-September 1996 **Funding source(s):** Johns Hopkins School of Hygiene and Public Health; Office of Health and Nutrition, USAID; Australian Agency for International Development **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Children within these strata were individually allocated to computer-generated randomly permuted 4-person blocks of two codes, Zn or placebo (PL)." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The tablets were encoded and the assignment held off-site by personnel not involved in the study...The study code was broken after closing the databases following double entry of all data." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled trial…The study code was broken after closing the databases following double entry of all data...Placebos were indistinguishable from the supplements in color, size, or taste..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled trial…The study code was broken after closing the databases following double entry of all data...Placebos were indistinguishable from the supplements in color, size, or taste..." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind placebo-controlled trial…The study code was broken after closing the databases following double entry of all data...Placebos were indistinguishable from the supplements in color, size, or taste..." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 23 Reasons/details: in the zinc group: 19 "migrated", 11 "refused", and 3 "died". In the placebo group: 19 "migrated", 9 "refused", and 1 "died" Comment: reasons for, and amount of, missing data were similar between study groups

Shankar 2000 *(Continued)*

Selective reporting (reporting bias)	High risk	Comment: side effects were measured, but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Silva 2006

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: São Sebastião, Distrito Federal (DF); urbanicity: unclear Inclusion criteria: N/A Exclusion criteria: diseased; anemic with hemoglobin levels < 9.0 g/dL; on medication or receiving supplementation; parasitic disease **Baseline characteristics** Avg age (months): 23.5; min age (months): 12; max age (months): 59; % female: 56.9 Avg height-for-age z score: −1.9; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 56.1 Total N: 60; Group 1 N: 30; Group 2 N: 30
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 4; dose (mg): 10; co-intervention(s): 2 kg iron-fortified milk **Group 2:** no zinc Placebo given; co-intervention(s): 2 kg iron-fortified milk
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Serum or plasma zinc concentration (µg/dL) • Blood hemoglobin concentration (g/dL) **Time point (week):** 16
Notes	**Study dates:** May-August 2002 **Funding source(s):** N/A **Comment(s):** none

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Silva 2006 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "...the sample consisted of 60 individuals, who were randomly placed in two groups...The children were placed in either of two groups according to the supplementation they received. Of every two mothers or surrogates who allowed their children to participate in the study, one child was assigned to the supplementation group and another one was placed in the control group..." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "A blinded randomized clinical trial was carried out…The flask containing zinc sulfate was labeled S...The flask containing the syrup was labeled C. The flasks containing placebo and zinc sulfate were identical and the taste and smell of the solutions were the same." Comment: people involved with the study might have been able to tell which solution was zinc and which was placebo based on the different letter labels on the flasks
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "A blinded randomized clinical trial was carried out…The flask containing zinc sulfate was labeled S...The flask containing the syrup was labeled C. The flasks containing placebo and zinc sulfate were identical and the taste and smell of the solutions were the same." Comment: people involved with the study might have been able to tell which solution was zinc and which was placebo based on the different letter labels on the flasks
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "A blinded randomized clinical trial was carried out…The flask containing zinc sulfate was labeled S...The flask containing the syrup was labeled C. The flasks containing placebo and zinc sulfate were identical and the taste and smell of the solutions were the same." Comment: people involved with the study might have been able to tell which solution was zinc and which was placebo based on the different letter labels on the flasks
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3 Reasons/details: "In the course of the study, two children from the supplementation group withdrew." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: side effects (i.e. "possible gastrointestinal symptoms (nausea, vomiting, diarrhea), and loss of appetite caused by zinc supplementation") were measured, but are not reported. The percentage decrease in the prevalence of anemia for the placebo group amounts to less than a single-person decrease, which seems to be an implausible result. "W/H" is reported, but it is unclear whether or not this refers to weight-for-height or weight-for-age
Other bias	Low risk	Comment: appears to be free of other bias

Smith 1999

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Belize; setting: refugee camps Los Flores and Salvapan in Cayo District; urbanicity: unclear Inclusion criteria: low/marginal concentrations of both serum vitamin A and zinc Exclusion criteria: fever; serious respiratory infection **Baseline characteristics** Avg age (months): N/A; min age (months): N/A; max age (months): N/A; % female: N/A Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 75.2 Total N: 51; Group 1 N: N/A; Group 2 N: N/A; Group 3 N: N/A; Group 4 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: gluconate; frequency: weekly; duration (months): 6; dose (mg): 70; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 3030 retinol equivalents vitamin A **Group 4:** no zinc Placebo given; co-intervention(s): 3030 retinol equivalents vitamin A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µmol/L) • Blood hemoglobin concentration (g/L) **Time point (week):** 24
Notes	**Study dates:** N/A **Funding source(s):** University of Maryland Agricultural Experiment Station **Comment(s)** • The trial reports contradictory information about the maximum age of eligible study participants. So, the minimum age was between 22 and 28 months, and the maximum age was between 66 and 72 months. • The number of participants randomized to each study group is not reported.
Risk of bias	

Smith 1999 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The children selected were randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 16 Reasons/details: "Because of relocation of residence and other causes, eight failed to complete the study…" Comment: migration was the most common reason for missing data, and this reason is unlikely to bias results
Selective reporting (reporting bias)	Unclear risk	Comment: blood hemoglobin concentration and height-for-age z score were measured for the zinc versus vitamin A + zinc comparison, but are not reported in a way that can be meta-analyzed. No trial protocol referenced by the study
Other bias	Unclear risk	Comment: "Analysis of pretreatment data indicated that children who subsequently received Zn supplementation were heavier (1.1 kg) than were non-Zn-treated subjects. The effects of these weight differences were significant variations in...weight-for-age Z score (WAZ)." This baseline difference could have influenced weight outcomes, which were reported only as post-treatment scores, rather than as changes from baseline.

Soofi 2013

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Pakistan; setting: Bilal Colony and Matiari, Sindh; urbanicity: mixed Inclusion criteria: randomized at 6 months of age Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 6; min age (months): 6; max age (months): 6; % female: 50%

Soofi 2013 *(Continued)*

	Avg height-for-age z score: not given; stunting: both - separate data not given; avg height (cm): 64.4; avg zinc concentration (µg/dL): 84.3 Total N: 1305; Group 1 N: 659; Group 2 N: 646
Interventions	**Group 1:** zinc Formulation: powder/paste; compound: gluconate; frequency: daily; duration (months): 12; dose (mg): 10; co-intervention(s): micronutrient powder **Group 2:** no zinc Placebo not given; co-intervention(s): micronutrient powder
Outcomes	**Primary** • All-cause mortality **Secondary** • Incidence of all-cause diarrhea • Incidence of severe diarrhea • Prevalence of all-cause diarrhea • Incidence of persistent diarrhea • Incidence of LRTI • Prevalence of LRTI • Hospitalization due to LRTI • Prevalence of anemia • Serum or plasma ferritin concentration (ng/mL) • Serum or plasma zinc concentration (µg/dL) • Blood hemoglobin (g/L) • Prevalence of stunting **Time point (week):** 52
Notes	**Study dates:** November 2008-December 2011 **Funding source(s):** Bill & Melinda Gates Foundation **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "randomly allocated within urban and rural strata using computer-generated random numbers"
Allocation concealment (selection bias)	Low risk	Quote: "MNPs [micronutrients] were packaged in individual daily dose sachets which were identical apart from their colour (Group B=Brown, Group C=Green). The colour coding used was known only to the Manager, Genera Pharmaceuticals, Islamabad and the Chair of the trial's Data Monitoring Committee (DMC)"
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "The investigators, field and supervisory staff were blinded to the composition of the MNP [micronutrients] preparations until after the results of the trial had been presented to the independent DMC."

Soofi 2013 *(Continued)*

Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "The investigators, field and supervisory staff were blinded to the composition of the MNP [micronutrients] preparations until after the results of the trial had been presented to the independent DMC."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: ""All data collectors were provided with refresher training at 6 monthly intervals and rotated between clusters to avoid differential interviewer bias across clusters."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Between 18 and 23.9 months of age there did not appear to be any link between treatment allocation and missingness. There was evidence to suggest that children with a high proportion of observed days with diarrhoea tended to have fewer days of completed follow-up." Comment: 18.6% missing, but no difference between groups
Selective reporting (reporting bias)	Low risk	Quote: protocol also includes "serum zinc, serum retinol, hair zinc, CRP and some immune response parameters" Comment: key clinical outcomes reported
Other bias	Low risk	Comment: appears to be free of other bias

Tielsch 2006

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Nepal; setting: Sarlahi District in southern Nepal; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 1; max age (months): 35; % female: 49 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 49,205; Group 1 N: 16,426; Group 2 N: 15,700; Group 3 N: 8951; Group 4 N: 8128 Total clusters: 425; Group 1 clusters: 107; Group 2 clusters: 106; Group 3 clusters: 107; Group 4 clusters: 105
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: sulfate; frequency: daily; duration (months): N/A; dose (mg): 5 mg to children < 1 year old; 10 mg to children ≥ 1 year of age; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 6.25 mg iron and 25 µg folic acid to children < 1 year; 12.5 mg iron and 50 µg folic acid to children ≥ 1 year

Tielsch 2006 *(Continued)*

Group 4: no zinc

Placebo given; co-intervention(s): 6.25 mg iron and 25 µg folic acid to children < 1 year old; 12.5 mg iron and 50 µg folic acid to children ≥ 1 year

Outcomes

Primary

- All-cause mortality

Secondary

- Serum or plasma zinc concentration (µmol/L)
- Prevalence of zinc deficiency
- Serum or plasma copper concentration (µmol/L)
- Prevalence of copper deficiency

Time point (week): 52 (biochemical outcomes)

Notes

Study dates: October 2001-November 2003

Funding source(s): NIH, Bill & Melinda Gates Foundation; Johns Hopkins University Office of Health and Nutrition; USAID

Comment(s)

- > 50% of participants analyzed in Tielsch 2006 are within the eligible age range for this review. So, baseline demographic data and most outcome data from this trial report are included in this review. However, Tielsch 2006 provides some outcome data for subsets of participants that potentially are not eligible for this review based on age; these data for potentially ineligible participant subsets are not included in this review. Less than 51% of participants analyzed in the (secondary reference) Tielsch 2007 article are within the eligible age range for this review. However, this trial report provides data on some outcomes for subsets of participants that are eligible for this review based on age; these data for eligible participant subsets are included in this review.
- "On the basis of recommendations from the data and safety monitoring board, the arms of the trial in which children were given iron and folic acid were stopped in November 2003, and children in those sectors were randomly reassigned to either placebo or zinc." The Tielsch 2007 trial report (see secondary reference under Tielsch 2006) analyzes a "merged set" of data, including: (a) children originally assigned to zinc or placebo, and (b) those who originally received iron/folic acid/zinc or iron/folic acid, and were then reassigned to zinc or placebo. To avoid a unit of analysis error, data from (a) the iron/folic acid/zinc and iron/folic acid groups reported in Tielsch 2006, and (b) the zinc and placebo groups reported in (secondary reference)Tielsch 2007, are not included in the same meta-analysis.
- The numbers of participants listed in this table as being randomized to the zinc and placebo groups: (a) do not include those from the iron/folic acid/zinc and iron/folic acid groups who were switched to zinc or placebo, but (b) do include "7432 children from sectors originally assigned to iron and folic acid or to iron and folic acid with zinc who were not eligible for the original allocation, but were subsequently randomly assigned to either placebo or zinc".
- Though some trial reports of this study report that 426 sectors [clusters] were randomized, Tielsch et al 2007 (see secondary reference under Tielsch 2006), which is the only trial report that provides data on the number of sectors randomized to each study group, states that 425 sectors were randomized.
- "All children older than 6 months also received vitamin A as part of a national programme or, if missed, by study staff: those aged 12 months or older were given 200 000 IU of vitamin A every 6 months and those aged 6–12 months were given 100,000 IU."
- "Children were discharged from the study when they reached 36 months of age", and most children were less than 24 months of age at baseline; the duration of supplementation seemed to be at least 12 months for most participants.

Risk of bias

Bias	Authors' judgement	Support for judgement

Tielsch 2006 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Sectors were randomly assigned to treatment groups in blocks of four…All possible orders of the four treatment groups were written on...paper slips, with roughly equal numbers of slips for each order. One slip was randomly drawn to assign treatment codes to four sectors within a VDC [Village Development Committees]. This continued until all sectors were assigned." Comment: seems likely to have used a truly random method to generate an allocation sequence
Allocation concealment (selection bias)	Low risk	Quote: "One slip was randomly drawn to assign treatment codes to...sectors...This continued until all sectors were assigned." "The Department of Child and Adolescent Health and Development at WHO, Geneva, Switzerland, kept the treatment assignment codes." Comment: sufficient allocation concealment seems likely
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "We did a...double-masked...trial…participants were unaware of assigned treatments." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "We did a...double-masked...trial…Investigators, study staff...were unaware of assigned treatments." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "We did a...double-masked...trial…Investigators, study staff...were unaware of assigned treatments." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 16 Reasons/details: besides the "7432 children from sectors originally assigned to iron and folic acid or to iron and folic acid with zinc who were not eligible for the original allocation, but were subsequently randomly assigned to either placebo or zinc", there were 12,133 participants originally assigned to the placebo group, and 12,885 participants originally assigned to the zinc group. Among these 12,133 placebo group participants: 595 refused, 917 were lost or moved, and 224 died. Among these 12,885 zinc group participants: 947 refused, 916 were lost or moved, and 225 died. Among the 8128 participants assigned to the iron + folic acid group: 952 refused, 347 moved, and 112 died before this group was stopped in November 2003. Among the 8951 participants assigned to the iron + folic acid + zinc group: 1186 refused, 354 moved, and 119 died before this group was stopped in November 2003 Comment: reasons for, and amount of, missing data were similar between the placebo and zinc groups. Reasons for, and amount of, missing data were similar between the iron + folic acid and zinc + iron + folic acid groups
Selective reporting (reporting bias)	Unclear risk	Comment: serum zinc, blood hemoglobin, serum ferritin, and serum copper concentrations; prevalence of zinc, iron, and copper deficiency; and prevalence of anemia were reported, but were not pre-specified in the trial protocol. However all of these were stated to be secondary, not primary, outcomes in the trial reports Protocol identifier: NCT00109551
Other bias	Low risk	Comment: appears to be free of other bias

Tielsch 2006 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • Mortality due to all-cause diarrhea • Mortality due to LRTI **Secondary** • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 52 (biochemical outcomes)
Notes	As Tielsch 2006 above

Tupe 2009

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: India; setting: Pune City, Maharashtra State, Western India; urbanicity: urban Inclusion criteria: N/A Exclusion criteria: current illness such as fever or respiratory or gastrointestinal infection; receiving medical treatment; suffered from any illness in the recent past; taking multivitamin mineral supplements **Baseline characteristics** Avg age (months): 144; min age (months): 120; max age (months): 155; % female: 100 Avg height-for-age z score: −1.3; stunting: both - separate data not given; avg height (cm): 142; avg zinc concentration (µg/dL): 59 Total N: 88; Group 1 N: 44; Group 2 N: 44 Total clusters: 2; Group 1 clusters: 1; Group 2 clusters: 1
Interventions	**Group 1:** zinc Formulation: pill/tablet; compound: unclear; frequency: 6 d/week; duration (months): 2.5; dose (mg): 16.6; co-intervention(s): N/A **Group 2:** no zinc

Tupe 2009 *(Continued)*

	Placebo not given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (mg/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/dL) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) **Time point (week):** 10
Notes	**Study dates:** 2005-2007 **Funding source(s):** Zensar Foundation, India **Comment(s)** • In addition to the study groups mentioned in this table, there was a group of participants who received "zinc- and micronutrient-rich food supplements." Baseline characteristics reported in this table are weighted averages of all groups except the "zinc- and micronutrient-rich food supplements" group, since this group is not included in any meta-analyses in this review. • This trial included some participants who were ≥ 13 years at baseline. However, baseline characteristics reported in this table were calculated based on data from participants < 13 years of age. Data on all outcomes (except for prevalence of zinc deficiency and prevalence of anemia) were also calculated based on data from participants < 13 years of age. Even though zinc deficiency and anemia prevalence are partially based on data from participants > 13 years, the average age of participants analyzed for these outcomes is < 13 years. • "Ayurvedic zinc tablet (jasad bhasma) was chosen as a natural elemental zinc supplement…Tablets containing 20 mg of jasad bhasma of a standard ayurvedic company were procured. Analysis of the jasad tablet in our laboratory indicated that each tablet contained 16.6 mg elemental zinc, 0.74 mg iron, and the remaining part as starch." We deemed the 0.74 mg iron to be too insignificant to have any effect on outcomes in this trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: In response to a request for further details on sequence generation, an author of this study explained that, "Three classes of 7th standard girls from the schools were randomly assigned to either of the two intervention groups or control group by the statistician", and that a "Lottery method was used to allocate a class to any one of the three treatments." Comment: it seems likely that the allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "Control group did not receive placebo but was unaware of the supplemented group."

Tupe 2009 *(Continued)*

		Comment: it is unclear how measured outcomes might be influenced by a lack of placebo
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "Control group did not receive placebo but was unaware of the supplemented group." Comment: it is unclear how measured outcomes might be influenced by a lack of placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The measurement team (both pretest and posttest observations) was blinded as to whether each girl was a member of one of the intervention groups or the control group." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 6 Reasons/details: in the zinc group: 1 participant was "excluded because of religious fasting" that she observed during the study period. In the control group: 4 participants were excluded because they were absent on the day of outcome measurement Comment: 6% of the randomized participants eligible for our review had data missing; this 6% missing figure includes all groups except the "zinc- and micronutrient-rich food supplements" group, since this group is not included in any meta-analyses in this review. In addition, this 6% missing figure only includes participants who were < 13 years of age at baseline. Though it is unclear whether being absent on the day of testing might bias results, the amount of missing data seem too minimal to impact results.
Selective reporting (reporting bias)	Unclear risk	Comment: prevalence of zinc deficiency and prevalence of anemia were reported, but were not pre-specified in the protocol for this study; though the related outcomes of plasma zinc concentration and hemoglobin concentration were pre-specified in the protocol for this study
Other bias	Low risk	Comment: appears to be free of other bias

Udomkesmalee 1992

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Thailand; setting: Pana District, Ubon Province, Northeast Thailand; urbanicity: rural Inclusion criteria: serum concentration of retinol < 1.05 µmol/L; serum concentration of zinc <12.2 µmol/L Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 112; min age (months): 72; max age (months): 156; % female: 42 Avg height-for-age z score: N/A; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 85.8 Total N: 133; Group 1 N: 33; Group 2 N: 35; Group 3 N: 32; Group 4 N: 33

Udomkesmalee 1992 *(Continued)*

Interventions	**Group 1:** zinc Formulation: capsule; compound: gluconate; frequency: 5 d/week; duration (months): 6; dose (mg): 25; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A **Group 3:** zinc Co-intervention(s): 1500 retinol equivalents vitamin A per day **Group 4:** no zinc Placebo given; co-intervention(s): 1500 retinol equivalents vitamin A per day
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 24
Notes	**Study dates:** May 1989-April 1990 **Funding source(s):** USAID **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were then randomly assigned…" Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: "The capsule code was revealed after all analyses were completed." Comment: despite this statement, the method of allocation concealment is not described in sufficient detail to allow a definite judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-blind study…All supplementary capsules were similar in appearance…The capsule code was revealed after all analyses were completed." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-blind study…All supplementary capsules were similar in appearance…The capsule code was revealed after all analyses were completed." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-blind study…All supplementary capsules were similar in appearance…The capsule code was revealed after all analyses were completed." Comment: sufficient blinding seems likely

Udomkesmalee 1992 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 5 Reasons/details: "One subject withdrew toward the end of study period; six subjects were identified with thalassemia according to abnormal blood cell morphology." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: height and weight were measured, but are not reported in a way that can be meta-analyzed. Prevalence of anemia may have been measured as an outcome, but is not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Udomkesmalee 1992 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) **Time point (week):** 24
Notes	As Udomkesmalee 1992 above

Umeta 2000

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Ethiopia; setting: Dodota Sire district, Arsi zone, central Ethiopia; urbanicity: rural Inclusion criteria: apparently healthy; looked well; exclusively breastfed for the first 4 months of life; free from intestinal parasites Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 9.4; min age (months): 6; max age (months): 12; % female: 50 Avg height-for-age z score: −1.7; stunting: both - separate data given; avg height (cm): 67.2; avg zinc concentration (µg/dL): N/A

Umeta 2000 *(Continued)*

	Total N: 200; Group 1 N: 100; Group 2 N: 100
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 6 d/week; duration (months): 6; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (mmol/L) **Time point (week):** 24
Notes	**Study dates:** August 1996-February 1997 **Funding source(s):** The Nestlé Foundation for the Study of the Problems of Nutrition in the World **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: participants were "randomly assigned to receive the zinc supplement or placebo." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplement and placebo were indistinguishable in colour and the slight metallic taste of the supplement was acceptable to the infants." Comment: the "slight metallic taste of the supplement" does not seem likely to influence outcomes. Sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplement and placebo were indistinguishable in colour and the slight metallic taste of the supplement was acceptable to the infants...Neither the field assistants nor the investigator knew the codes. The codes were revealed only after the study was completed and the data analysis was finalised." Comment: sufficient blinding seems likely

Umeta 2000 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind, placebo-controlled trial…The supplement and placebo were indistinguishable in colour and the slight metallic taste of the supplement was acceptable to the infants...Neither the field assistants nor the investigator knew the codes. The codes were revealed only after the study was completed and the data analysis was finalised." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 8 Reasons/details: N/A Comment: no reasons for dropout were reported. However, the same amount of data was missing from the zinc group and the placebo group, and missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Uçkardeş 2009

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Turkey; setting: Ankara; urbanicity: urban Inclusion criteria: 3rd grade student Exclusion criteria: any chronic systemic disease which could affect neuropsychological performance and zinc metabolism **Baseline characteristics** Avg age (months): 102; min age (months): 89; max age (months): 140; % female: 50.5 Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): 127.45; avg zinc concentration (µg/dL): 119.7 Total N: 226; Group 1 N: 113; Group 2 N: 113
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: 5 d/week; duration (months): 2.5; dose (mg): 15; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency

Uçkardeş 2009 *(Continued)*

	Time point (week): 10
Notes	**Study dates:** October 2004-January 2005 **Funding source(s):** N/A **Comment(s):** none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children in each class were randomized to one of the research groups." "Randomization was made simply by dividing the class student list into two as study and control groups." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Double-blind...placebo controlled trial." "The placebo was also manufactured by the company with same appearance." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind...placebo controlled trial...The investigators and teachers were blind until the end of the analysis." ("Zinc and placebo syrups were given by the teachers at school..." So, the teachers were the providers of the syrups.) "The placebo was also manufactured by the company with same appearance." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Double-blind...placebo controlled trial...The investigators...were blind until the end of the analysis." "The placebo was also manufactured by the company with same appearance." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4 Reasons/details: "Four children from the zinc group and four from the placebo group left the study because family moved to another district (n = 4), school absenteeism (n = 2) and vomiting (n = 2)." Comment: missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: though side effects "were monitored by teachers daily at school", "side effects were not collected numerically from all subjects" and "only the teachers' of 2 classes (45 case, 45 placebo) had documented data." No trial protocol referenced by the study.
Other bias	Unclear risk	Comment: "Serum zinc level was measured…Caloric spectrophotometery was used instead of atomic absorption spectrophotometer due to the limited budget of the study. This method may not be as sensitive as atomic absorption spectrophotometery for measuring serum zinc levels or there may be a systematic error in our chemical methodology. Although we could not detect any children with zinc deficiency in our participants most probably due to the

Uçkardeş 2009 *(Continued)*

	methodology, other studies from our region demonstrate a prevalence of zinc deficiency around 20%." Thus, an insensitive instrument for measuring prevalence of zinc deficiency may have been used, and this could have led to an under-estimation of the number of participants with zinc deficiency and/or the effect of zinc supplementation on zinc deficiency prevalence.

Vakili 2015

Study characteristics	
Methods	CRCT; non-cross-over
Participants	Country: Iran; setting: Altimor, a low-socioeconomic suburb of Mashhad city in the Northeast of Iran; urbanicity: peri-urban Inclusion criteria: children aged 78-120 months; living in Altimor Exclusion criteria: chronic disease; protein malnutrition; children receiving other mineral supplementation like zinc or iron **Baseline characteristics** Avg age (months): 93.4; min age (months): N/A; max age (months): N/A; % female: 50 Avg height-for-age z score: −0.727; stunting: unclear; avg height (cm): 122.41; avg zinc concentration (µg/dL): N/A Total N: 200; Group 1 N: 100; Group 2 N: 100
Interventions	**Group 1:** zinc Formulation: tablet; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) **Time point (week):** 24
Notes	**Study dates:** November 2004-March 2005 **Funding source(s):** Mashhad University of Medical Sciences **Comment(s):** none

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Vakili 2015 *(Continued)*

Random sequence generation (selection bias)	Low risk	Comment: most likely done
Allocation concealment (selection bias)	Low risk	Comment: likely done
Blinding of participants (performance bias) All outcomes	Low risk	Comment: health workers, children and their parents were unaware that which tablet was zinc or placebo
Blinding of personnel (performance bias) All outcomes	Low risk	Comment: health workers, children and their parents were unaware that which tablet was zinc or placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: there wasn't not enough information reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: overall low attrition
Selective reporting (reporting bias)	Low risk	Comment: authors seems to report all the relevant outcomes
Other bias	Low risk	Comment: no concerns for other risk of bias

Veenemans 2011

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Tanzania; setting: Segera and Kwedizinga wards in Handeni District of Northern Tanzania; urbanicity: rural Inclusion criteria: N/A Exclusion criteria: HAZ > −1.5 SD; weight-for-height z-score < −3 SD; Hb < 70 g/L; unlikely to remain permanently resident or comply with interventions; signs of severe or chronic disease **Baseline characteristics** Avg age (months): 32.5; min age (months): 6; max age (months): 60; % female: 51 Avg height-for-age z score: −2.43; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 612; Group 1 N: 153; Group 2 N: 153; Group 3 N: 151; Group 4 N: 155
Interventions	**Group 1:** zinc Formulation: capsule; compound: gluconate; frequency: daily; duration (months): 11; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A

Veenemans 2011 *(Continued)*

	Group 3: zinc Co-intervention(s): multi-nutrients (including iron) **Group 4:** no zinc Placebo given; co-intervention(s): multi-nutrients (including iron)
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Incidence of LRTI • Incidence of malaria • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 36 (biochemical outcomes), 47.3 (morbidity and mortality outcomes)
Notes	**Study dates:** February 2008-March 2009 **Funding source(s):** Netherlands Organisation for Scientific Research; UNICEF; Cornelis Visser Foundation and Wageningen University (Interdisciplinary Research and Education Fund); European Union's Seventh Framework Programme **Comment(s)** • Participants were enrolled between February and August 2008, and "Supplementation and follow-up continued for all children until 12 March 2009, when the trial was stopped." The primary analysis of malaria episodes had a median follow-up duration of 331 days. • "Those with Plasmodium infection at baseline were treated with artemether-lumefantrine."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We used stratified block randomisation to allocate interventions. A colleague not otherwise involved in the trial used tables with random numbers to generate the allocation sequence consisting of randomly permuted blocks with random size (4 or 8) within each of six strata defined by Plasmodium infection (yes/no infected) and age class (6–17 months, 18–35 months, and 36–60 months)." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "A colleague not otherwise involved in the trial used tables with random numbers to generate the allocation sequence…Interventions were indicated by colour code on paper slips in opaque, consecutively numbered envelopes that were prepared in advance, in excess of the expected number required…This code was not revealed to researchers, field staff, or participants, who therefore did not know who received what intervention…At the end of each screening day, when eligibility had been fully established, children

Veenemans 2011 *(Continued)*

		were individually allocated in order of their screening number to intervention groups by drawing successive envelopes from a box corresponding to the infection- and age-specific stratum for that child. The number of the envelope was then recorded on a list before the envelope was opened." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) and sequentially numbered, opaque, sealed envelopes to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "Intervention group was indicated by colour code, but neither participants…knew who received what intervention…This code was not revealed to…participants, who therefore did not know who received what intervention…All types of powder had similar appearance, smell, and taste…The randomisation code was not revealed to…participants until data collection was completed and the database had been finalised and sent to the Trial Oversight Committee." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "Intervention group was indicated by colour code, but neither…nor field staff knew who received what intervention…This code was not revealed to…field staff…who therefore did not know who received what intervention…All types of powder had similar appearance, smell, and taste…The randomisation code was not revealed to…field workers…until data collection was completed and the database had been finalised and sent to the Trial Oversight Committee." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Intervention group was indicated by colour code, but neither…researchers, nor…knew who received what intervention…This code was not revealed to researchers…, who therefore did not know who received what intervention…All types of powder had similar appearance, smell, and taste…The randomisation code was not revealed to researchers…until data collection was completed and the database had been finalised and sent to the Trial Oversight Committee…It should be noted also that the clinical outcome assessors were blinded to what intervention had been assigned to individual children." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 3 Reasons/details: in the zinc group: 5 participants emigrated from the study area, and 1 was "withdrawn by parents." In the placebo group: 4 participants emigrated from the study area. In the multi-nutrients with zinc group, 3 participants emigrated from the study area, 1 was "withdrawn by parents", and 1 died. In the multi-nutrients without zinc group, 3 participants emigrated from the study area and 2 died Comment: reasons for, and amount of, missing data were similar between study groups. Migration was the most common reason for missing data, and this reason is unlikely to bias results. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	High risk	Comment: anthropometric indices, including height-for-age z-score, were pre-specified as a secondary outcome in the protocol for this study and were measured, but are not reported as outcomes. Hospitalisations due to malaria were measured, but were not pre-specified in the protocol for this study, and are not reported in a way that can be meta-analyzed. Malaria prevalence and LRTI incidence were reported, but were not pre-specified in the protocol for this study Protocol identifier: NCT00623857

Veenemans 2011 *(Continued)*

		Online web appendix obtained from http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001125
Other bias	Low risk	Comment: appears to be free of other bias

Veenemans 2011 (2)

Study characteristics	
Methods	
Participants	
Interventions	
Outcomes	**Primary** • All-cause mortality **Secondary** • All-cause hospitalization • Incidence of all-cause diarrhea • Incidence of LRTI • Incidence of malaria • Serum or plasma zinc concentration (µmol/L) • Prevalence of zinc deficiency • Blood hemoglobin concentration (g/L) • Prevalence of anemia • Serum or plasma ferritin concentration (µg/L) • Prevalence of iron deficiency **Time point (week):** 36 (biochemical outcomes), 47.3 (morbidity and mortality outcomes)
Notes	As Veenemans 2011 above

Walravens 1983

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Denver, Colorado; urbanicity: urban Inclusion criteria: height-for-age below the 10th percentile on the NCHS grids; nutritional or biochemical evidence of zinc deficiency; products of term pregnancies; birth measurements appropriate for gestation age; ≥ 2 of the following: calculated dietary zinc intake < 2/3 of the Recommended Dietary Allowance, plasma zinc < 68 µg/dL, or hair zinc < 105 µg/g Exclusion criteria: detectable medical reasons for poor growth **Baseline characteristics** Avg age (months): 50; min age (months): 24; max age (months): 72; % female: 35

Walravens 1983 *(Continued)*

	Avg height-for-age z score: −2.07; stunting: both - separate data not given; avg height (cm): N/A; avg zinc concentration (µg/dL): 72 Total N: 57; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: twice daily; duration (months): 12; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Weight-to-height ratio • Serum or plasma zinc concentration (µg/dL) • Serum or plasma copper concentration (µg/dL) **Time point (week):** 52
Notes	**Study dates:** N/A **Funding source(s):** National Institutes of Arthritis, Metabolic and Digestive Diseases, General Clinical Research Centers Program of the Division of Research Resources, NIH; United States Department of Agriculture **Comment(s):** this was a "pair-matched" study, and at the end of the study, 20 participants remained in the zinc group and 20 participants in the placebo group. So, there might have been approximately equal numbers of participants randomized to the zinc group and the placebo group, but the exact number of participants randomized to each group was not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "These subjects were pair-matched as closely as possible...The first member of a pair was assigned randomly to either the zinc supplement or a placebo." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Low risk	Quote: "These subjects were pair-matched as closely as possible...by one of the investigators who was not involved with the clinical management of the children, and had no knowledge of the progress of the participants during the course of treatment period. The first member of a pair was assigned randomly to either the zinc supplement or a placebo." Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias)	Low risk	Quote: "…double blind…study…The two syrups were indistinguishable in appearance and were prepared at the pharmacy of the University of Colorado

Walravens 1983 *(Continued)*

All outcomes		Medical Center, where the code was kept...Test or control assignment was unknown to the children and their families..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double blind…study…The two syrups were indistinguishable in appearance and were prepared at the pharmacy of the University of Colorado Medical Center, where the code was kept...Test or control assignment was unknown to...the members of the investigating team who were responsible for clinical care, anthropometry, diet, or laboratory analysis." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double blind…study…The two syrups were indistinguishable in appearance and were prepared at the pharmacy of the University of Colorado Medical Center, where the code was kept...Test or control assignment was unknown to...the members of the investigating team who were responsible for clinical care, anthropometry, diet, or laboratory analysis." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: 30 Reasons/details: "Of the 17 (30%) who failed to complete the study, 11 moved from the area and six withdrew." Comment: a large proportion of the data is missing and the amount of missing data was not reported separately for each study group
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Walravens 1989

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: USA; setting: Denver, Colorado; urbanicity: urban Inclusion criteria: for children whose initial growth was not in the 10 lower percentiles: documented decline of ≥ 20 percentiles in weight-for-age resulting in a weight < 10th percentile; for children whose initial growth was in the 10 lower percentiles: a decline in weight percentiles, documented decline of ≥ 20 percentiles in weight for height Exclusion criteria: malabsorption; chronic infections; other known causes of growth failure; families with previous problems of neglect; disturbed family dynamics; language barriers precluding adequate communication **Baseline characteristics** Avg age (months): 15.2; min age (months): 8; max age (months): 27; % female: 48 Avg height-for-age z score: −1.35; stunting: unclear; avg height (cm): 74.61; avg zinc concentration (µg/dL): 70 Total N: N/A; Group 1 N: N/A; Group 2 N: N/A

Walravens 1989 *(Continued)*

Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: unclear; duration (months): 6; dose (mg): 25; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height (cm) • Weight (kg) • Serum or plasma zinc concentration (µg/dL) **Time point (week):** 24
Notes	**Study dates:** October 1982-February 1986 **Funding source(s):** United States Department of Agriculture; National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases, General Clinical Research Centers, NIH; Kellog Company **Comment(s):** Number of participants randomized to each study group was not reported. Instead, the following was reported: "87 families were approached regarding the zinc supplementation study. The families of 30 infants either refused participation after the introductory screening or refused to continue in the study after starting it. The remaining 57 infants completed the supplementation project...The final matching included 13 male and 12 female pairs and seven unmatched infants." It is unclear how many of the 87 infants approached were randomized to each study group, because it is unclear how many of the 30 infants who refused did so before randomization versus after randomization.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Pair matching was done by an investigator (K.M.H.) not involved in the clinical management of the children...The first member of a pair was randomly assigned to receive either the zinc supplement or the placebo." Comment: insufficient details available to make a judgement as to whether or not an allocation sequence was generated using a truly random method
Allocation concealment (selection bias)	Unclear risk	Quote: N/A Comment: insufficient details available to make a judgement
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "…double-blind, controlled study…The two syrups were indistinguishable in appearance...Test or control assignment was unknown to the families..." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "…double-blind, controlled study…The two syrups were indistinguishable in appearance...Test or control assignment was unknown to the...investigators involved in clinical care, anthropometry, or dietary analysis." Comment: sufficient blinding seems likely

Walravens 1989 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "…double-blind, controlled study…The two syrups were indistinguishable in appearance...Test or control assignment was unknown to the...investigators involved in clinical care, anthropometry, or dietary analysis." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	% Missing: N/A Reasons/details: "The families of 30 infants either refused participation after the introductory screening or refused to continue in the study after starting it." Comment: the following were not reported: number of participants randomized, number of participants randomized to each group, amount of missing data for each group
Selective reporting (reporting bias)	Unclear risk	Comment: no trial protocol referenced by the study
Other bias	Low risk	Comment: appears to be free of other bias

Wessells 2012

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Burkina Faso; setting: the catchment area of the governmental health clinic located in Toussiana; urbanicity: rural Inclusion criteria: currently breastfeeding; hemoglobin level ≥ 60 g/L; no fever or diarrhea (> 3 liquid or semi-liquid stools in a 24-h period) reported in the past week Exclusion criteria: currently consuming vitamin or mineral supplements or zinc-fortified infant formulas; demonstrated bipedal edema or other serious medical conditions; had a twin enrolled in the study **Baseline characteristics** Avg age (months): 13.7; min age (months): 6; max age (months): 23; % female: 49 Avg height-for-age z score: −1.5; stunting: unclear; avg height (cm): 72.5; avg zinc concentration (µg/dL): 62.9 Total N: 451; Group 1 N: 300; Group 2 N: 151
Interventions	**Group 1:** zinc Formulation: solution or dispersible tablets; compound: sulfate; frequency: daily; duration (months): 0.75; dose (mg): 5; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration (µg/dL)

Wessells 2012 *(Continued)*

- Prevalence of zinc deficiency
- Serum or plasma copper concentration (µg/dL)

Time point (week): 3

Notes	**Study dates:** September-December 2009 **Funding source(s):** Nutriset, SAS, Malauney, France **Comment(s):** 150 participants were randomized to receive dispersible zinc tablets, 150 participants were randomized to receive liquid zinc supplements, and 151 participants were randomized to receive liquid placebo supplements.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Eligible study participants were randomly assigned to 1 of 3 treatment groups by using an independently generated block randomization scheme, with a varied block length of 3 or 6...Tables of random permutation…" Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "Eligible study participants were randomly assigned to 1 of 3 treatment groups by using an independently generated block randomization scheme…" Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Unclear risk	Quote: "...partially-masked, placebo-controlled trial…Zn and placebo syrups were indistinguishable in appearance, flavor, and packaging...Treatment groups remained masked until all statistical analyses were completed." Comment: though the zinc and placebo syrups were indistinguishable, there was no placebo for the zinc tablets that some participants received. Thus, people involved in the study would not have been blind to the group assignment of the zinc tablet group
Blinding of personnel (performance bias) All outcomes	Unclear risk	Quote: "...partially-masked, placebo-controlled trial…Zn and placebo syrups were indistinguishable in appearance, flavor, and packaging...Treatment groups remained masked until all statistical analyses were completed." Comment: though the zinc and placebo syrups were indistinguishable, there was no placebo for the zinc tablets that some participants received. Thus, people involved in the study would not have been blind to the group assignment of the zinc tablet group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "...partially-masked, placebo-controlled trial…Zn and placebo syrups were indistinguishable in appearance, flavor, and packaging...Treatment groups remained masked until all statistical analyses were completed." Comment: though the zinc and placebo syrups were indistinguishable, there was no placebo for the zinc tablets that some participants received. Thus, people involved in the study would not have been blind to the group assignment of the zinc tablet group
Incomplete outcome data (attrition bias) All outcomes	Low risk	% Missing: 4 Reasons/details: in the zinc group (comprised of participants who received liquid zinc supplements and participants who received zinc tablets): 11 withdrew consent, 3 moved from the study area, and 2 withdrew due to illness. In the

Wessells 2012 *(Continued)*

		placebo group: 3 withdrew consent and 1 withdrew due to illness. In addition, there were 5 blood draw failures in the zinc group Comment: reasons for missing data were similar between study groups. Missing data seem too minimal to impact results
Selective reporting (reporting bias)	Unclear risk	Comment: prevalence of LRTI was measured, but is not reported. Prevalence of diarrhea was measured, but is not reported in a way that can be meta-analyzed. Neither LRTI nor diarrhea prevalence was pre-specified in the protocol for this study. However, based on email contact with an author of this study, it seems likely that there was probably not sufficient time to allow for detectable differences in morbidity and that morbidity outcomes were included in the measurements simply to control for any baseline differences or possible confounding Protocol identifier: NCT00944853
Other bias	Low risk	Comment: appears to be free of other bias

Wuehler 2008

Study characteristics	
Methods	IRCT; non-cross-over
Participants	Country: Ecuador; setting: El Carmen, a small town in the coastal plains, and the communities surrounding it, Latacunga, a medium-sized town in the Andean highlands, and several surrounding rural communities, and two shantytowns in the hills adjacent to the capital city of Quito, also in the Andean highlands; urbanicity: multiple Inclusion criteria: LAZ < −1.3 for children 12-20 months old and < −1.5 for children 21-29 months old, assessed by comparison with the WHO/NCHS international reference data; Hb ≥ 10.5 g/dL, adjusted for altitude; absence of chronic disease or congenital defects that restrict normal growth Exclusion criteria: N/A **Baseline characteristics** Avg age (months): 20.9; min age (months): 12; max age (months): 30; % female: 46.9 Avg height-for-age z score: −2.3; stunting: both - separate data not given; avg height (cm): 77.3; avg zinc concentration (µg/dL): 71.9 Total N: 503; Group 1 N: 376; Group 2 N: 127
Interventions	**Group 1:** zinc Formulation: solution; compound: sulfate; frequency: daily; duration (months): 6; dose (mg): 6.7 on average (among participants who received 3, 7, or 10 mg/d of zinc); co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary**

Wuehler 2008 *(Continued)*

- Incidence of all-cause diarrhea
- Height (cm)
- Weight (kg)
- Weight-to-height ratio
- Serum or plasma zinc concentration (µg/dL)
- Blood hemoglobin concentration (g/dL)
- Serum or plasma ferritin concentration (ng/mL)
- Serum or plasma copper concentration (µg/dL)

Time point (week): 24

Notes	**Study dates:** November 2001-April 2005 **Funding source(s):** United States Department of Agriculture; USAID Micronutrient Program; UNICEF; Bristol-Meyers/Squibb; Grupo Farma del Ecuador **Comment(s):** 127, 124, 126, 126, and 128 participants were randomized to receive placebo, 3 mg zinc/d, 7 mg zinc/d, 10 mg zinc/d, and 10 mg zinc/d + 0.5 mg copper/d, respectively. Baseline characteristics reported in this table are weighted averages of all groups except the zinc + copper group, since the zinc + copper group is not included in any meta-analyses in this review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization lists…were generated…by using a fixed block randomization procedure." "Participants were assigned a study number...The numbers were previously assigned to one of the five study groups by computer randomization by the study's statistician." Comment: N/A
Allocation concealment (selection bias)	Low risk	Quote: "The randomization lists…were generated independently…" Comment: indicates central randomization (i.e. randomization by someone not involved with enrolling patients) to conceal allocation
Blinding of participants (performance bias) All outcomes	Low risk	Quote: "...double-masked intervention trial...blinding of...participants to treatment group…" "There was no color or other method of distinguishing between supplements…The flavor of the zinc and copper were masked by the preservative that was added to all syrups." Comment: sufficient blinding seems likely
Blinding of personnel (performance bias) All outcomes	Low risk	Quote: "...double-masked intervention trial...blinding of investigators...to treatment group…" "There was no color or other method of distinguishing between supplements…The flavor of the zinc and copper were masked by the preservative that was added to all syrups." Comment: sufficient blinding seems likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "...double-masked intervention trial...blinding of investigators...to treatment group…" "There was no color or other method of distinguishing between supplements…The flavor of the zinc and copper were masked by the preservative that was added to all syrups." Comment: sufficient blinding seems likely
Incomplete outcome data (attrition bias)	Low risk	% Missing: 10.7

Wuehler 2008 *(Continued)*

All outcomes		Reasons/details: participants "moved out of the study area", "refused to continue supplement consumption", "refused blood draws", or "withdrew consent without a specified reason". "Moved out of the study area" was the most common reason for missing data. Comment: 10.7% of the randomized participants eligible for our review had data missing; this 10.7% missing figure includes all groups except the zinc + copper group, since the zinc + copper group is not included in any meta-analyses in this review. "There were no significant differences in rates of attrition by treatment group...nor any significant differences between the baseline characteristics of the children who left the study prematurely and those of children who completed the full 6-mo intervention." Migration was the most common reason for missing data and this reason is unlikely to bias results
Selective reporting (reporting bias)	High risk	Comment: diarrhea prevalence and LRTI prevalence were measured, but are not reported in a way that can be meta-analyzed
Other bias	Low risk	Comment: appears to be free of other bias

Avg: average; **CRCT:** cluster-randomized controlled trial; **Hb:** hemoglobin; **HIV:** human immunodeficiency virus; **ICDDR, B:** International Centre for Diarrheal Disease Research, Bangladesh; **IRCT:** individually randomized controlled trial; **IU:** international units; **LAZ:** length-for-age z-score; **LRTI:** lower respiratory tract infection; **mo:** month; **MM:** micronutrient mix/mixture; **MUAC:** mid-upper arm circumference; **min-**minimum, **max:** maximum, **n:** number, **N/A:** not available; **NCHS:** National Center for Health Statistics; **NIH:** National Institutes of Health;**RCT:** randomized controlled trial; **SD:** standard deviation; **SE:** standard error; **SQ-LNS:** small-quantity lipid-based nutrient supplements; **UNICEF:** The United Nations Children's Fund; **USAID:** United States Agency for International Development; **vs:** versus; **WAZ:** weight-for-age z-score; **WHO:** World Health Organization; **WLZ:** weight-for-length z-score; **Zn:** zinc

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abbeddou 2017	Ineligible population
Adhikari 2016	Ineligible population
Alves 2016	Ineligible study design
Bates 1993	Ineligible study design
Berger 2006	Ineligible population
Bobat 2005	Ineligible population
Brooks 2005	Ineligible population
Heinig 2006	Ineligible population
Hess 2011	Ineligible study design
Kartasurya 2020	Study did not assess any outcomes of interest
Khademain 2014	Study did not assess any outcomes of interest
Khera 2020	Ineligible intervention
Kordas 2005	Ineligible intervention

Study	Reason for exclusion
Lamberti 2014	Ineligible study design
Lauer 2019	Ineligible population
Lima 2013	Ineligible comparator
Locks 2016	Ineligible population
Martinez-Estevez 2016	Study did not assess any outcomes of interest
Nature 2013	Ineligible study design
NCT01472211	Ineligible intervention
Nuryanti 2020	Ineligible comparator
Osendarp 2002	Ineligible population
Payne-Robinson 1991	Ineligible population
Perrone 1999	Ineligible comparator
Priyadarshini 2013	Ineligible study design
Prodam 2013	Ineligible study design
Shaker 2018	Ineligible population
Shingwekar 1979	Ineligible study design
Surkan 2013	Study did not assess any outcomes of interest
Surkan 2015	Study did not assess any outcomes of interest
Vermeulen 2019	Ineligible comparator
Voss 2017	Ineligible intervention
Wasantwisut 2006	Ineligible population
Wastney 2018	Ineligible study design
Wulf 2013	Ineligible study design
Yanfeng 1997	Ineligible comparator
Yoshida 2020	Ineligible study design
Yuniritha 2020	Study did not assess any outcomes of interest
Zeba 2008	Ineligible comparator

Characteristics of studies awaiting classification *[ordered by study ID]*

Chicourel 2001

Methods	IRCT/CRCT: N/A; cross-over?: N/A
Participants	Country: Brazil; setting: municipality of Juiz de Fora; urbanicity: unclear Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 49; max age (months): 82; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 59; Group 1 N: 30; Group 2 N: 29
Interventions	**Group 1:** zinc Formulation: N/A; compound: N/A; frequency: N/A; duration (months): unclear; dose (mg): 10; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • N/A **Time point (week):** N/A
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • In addition to the study groups mentioned in this table, there was a group of 31 participants who received iron supplementation (30 mg). • A full-text trial report exists for this study, but could not be obtained • Article is in Portugeuse; translation is not available

Jimenez 2000

Methods	IRCT/CRCT: N/A; cross-over?: N/A
Participants	Country: N/A; setting: N/A; urbanicity: N/A Inclusion criteria: recently recovered from persistent diarrhea Exclusion criteria: N/A **Baseline characteristics**

Jimenez 2000 *(Continued)*

	Avg age (months): N/A; min age (months): N/A; max age (months): N/A; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: N/A; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: sulfate; frequency: N/A; duration (months): N/A; dose (mg): 10 mg/d; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • N/A **Time point (week):** N/A
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • Not enough information was available in the trial report to determine study eligibility (e.g. that participants met the age criteria for this review) • Study was available as an abstract only

Long 2013

Methods	IRCT/CRCT: N/A; cross-over?: N/A
Participants	Country: Mexico; setting: unclear; urbanicity: peri-urban Inclusion criteria: children 6-15 months of age; from peri-urban areas of Mexico City Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 15; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 707; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: N/A; frequency: daily; duration (months): N/A; dose (mg): N/A; co-intervention(s): N/A **Group 2:** no zinc

Long 2013 *(Continued)*

	Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • N/A **Time point (week):** N/A
Notes	**Study dates:** May 2001-September 2001 **Funding source(s):** N/A **Comment(s):** full-text paper could not be found

Mitter 2009

Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: a favela in northeast Brazil; urbanicity: urban Inclusion criteria: below median HAZ Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): N/A; max age (months): N/A; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: N/A; Group 1 N: N/A; Group 2 N: N/A; Group 3 N: N/A; Group 4 N: N/A; Group 5 N: N/A; Group 6 N: N/A; Group 7 N: N/A; Group 8 N: N/A
Interventions	**Group 1:** zinc Formulation: unclear; compound: unclear; frequency: 2 d/week; duration (months): 12; dose (mg): 40; co-intervention(s): N/A **Group 2:** no zinc Unclear whether or not placebo given; co-intervention(s): N/A **Group 3:** zinc Formulation: unclear; compound: unclear; frequency: 2 d/week; duration (months): 12; dose (mg): 40; co-intervention(s): 200,000 IU retinol every 4 months **Group 4:** no zinc Unclear whether or not placebo given; co-intervention(s): 200,000 IU retinol every 4 months **Group 5:** zinc Formulation: unclear; compound: unclear; frequency: 2 d/week; duration (months): 12; dose (mg): 40; co-intervention(s): 16 g of glutamine for 10 d **Group 6:** no zinc

Mitter 2009 *(Continued)*

	Unclear whether or not placebo given; co-intervention(s): 16 g of glutamine for 10 d **Group 7:** zinc Formulation: unclear; compound: unclear; frequency: 2 d/week; duration (months): 12; dose (mg): 40; co-intervention(s): 200,000 IU retinol every 4 months; 16 g of glutamine for 10 d **Group 8:** no zinc Unclear whether or not placebo given; co-intervention(s): 200,000 IU retinol every 4 months; 16 g of glutamine for 10 d
Outcomes	**Primary** • N/A **Secondary** • N/A **Time point (week):** N/A
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s)** • Not enough information was available in the trial report to determine study eligibility (e.g. that participants met the age criteria for this review) • Study was available as an abstract only

Sanchez 2014

Methods	IRCT/CRCT: N/A; cross-over?: N/A
Participants	Country: Colombia; setting: Medellin; urbanicity: unclear Inclusion criteria: children aged 2-5 years of age Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): N/A; max age (months): N/A; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: N/A; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: sulfate; frequency: N/A; duration (months): unclear; dose (mg): N/A; co-intervention(s): N/A **Group 2:** zinc Formulation: N/A; compound: amino acid chelate; frequency: N/A; duration (months): unclear; dose (mg): N/A; co-intervention(s): N/A **Group 3:** no zinc

Sanchez 2014 *(Continued)*

	Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of acute diarrhea • Incidence of LRTI **Time point (week):** N/A
Notes	**Study dates:** N/A **Funding source(s):** N/A **Comment(s):** study was written in Spanish; translation was not available

Smith 1985

Methods	IRCT; non-cross-over
Participants	Country: Australia; setting: 5 communities in the Kimberley region of Western Australia; urbanicity: unclear Inclusion criteria: N/A Exclusion criteria: N/A **Baseline characteristics** Avg age (months): N/A; min age (months): 60; max age (months): 180; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Sample size: N/A; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: unclear; compound: acetate; frequency: 5 d/week; duration (months): N/A; dose (mg): 20 mg to children aged 5-8 years, 40 mg to children aged 9-15 years; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Serum or plasma zinc concentration **Time point (week):** N/A
Notes	**Study dates:** N/A **Funding source(s):** N/A

Smith 1985 *(Continued)*

Comment(s)

- It was reported that, "Pairs of children…were randomized to receive oral zinc or placebo", and that "102 pairs…completed the trial." However, the number of children randomized was not reported.
- Not enough information was available in the trial report to determine study eligibility (e.g. that participants met the age criteria for this review)
- No abstract or full text was available

Surono 2014

Methods	IRCT/CRCT: N/A; cross-over?: N/A
Participants	Country: Indonesia; setting: N/A; urbanicity: unclear Inclusion criteria: apparently healthy children; between the ages of 12 and 24 months; agreement to conform to the trial guidelines or provide notification of non-compliance Exclusion criteria: congenital abnormality or disease; gastrointestinal disease; regular use of products with probiotic bacteria; receiving antibiotic therapy within 2 weeks prior to the intervention study; non-agreement to avoid potentially conflicting nutritional or trace element supplements during the 90 d of the trial **Baseline characteristics** Avg age (months): N/A; min age (months): 49; max age (months): 82; % female: N/A Avg height-for-age z score: N/A; stunting: unclear; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 48; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: sulfate monohydrate; frequency: N/A; duration (months): unclear; dose (mg): 8; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Plasma or serum zinc concentration **Time point (week):** N/A
Notes	**Study dates:** August 2009-March 2010 **Funding source(s):** N/A **Comment(s)** • Proper N values were not reported for the four study arms of placebo, probiotic, zinc and combination of probiotic and zinc groups • Study available as abstract only

Avg: average; **CRCT:** cluster-randomized controlled trial; **IRCT:** individually randomized controlled trial; **IU:** international units; **LRTI:** lower respiratory tract infection; **max:** maximum; **min:** minimum; **n:** number, **N/A:** not available; **NCHS:** National Center for Health Statistics

Characteristics of ongoing studies *[ordered by study ID]*

NCT00228254

Study name	**Public title:** Vitamin A and zinc: prevention of pneumonia (VAZPOP) study **Scientific title:** same as public title
Methods	CRCT; non-cross-over
Participants	Country: Ecuador; setting: Quito; urbanicity: urban Inclusion criteria: residence of 1 year or longer in the neighborhood Exclusion criteria: recent vitamin or micronutrient use; clinical evidence of zinc or vitamin A deficiency; severe malnutrition such as weight ≤ 60% of expected weight **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 36; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 2582; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: N/A; frequency: daily; duration (months): N/A; dose (mg): 12.5; co-intervention(s): 10,000 IU vitamin A per week **Group 2:** no zinc Placebo given; co-intervention(s): 10,000 IU vitamin A per week
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Height • Weight **Time point (week):** up to 50
Starting date	January 2000 **Study end date:** June 2004
Contact information	**Name:** Jeffrey K Griffiths **Email:** jeffrey.griffiths@tufts.edu. EMW emailed 20 January 2013
Notes	**Funding source(s):** Tufts University

NCT00374023

Study name	**Public title:** A study on immunological effect of vitamin A and zinc in a placebo controlled 4 cell trial **Scientific title:** not reported
Methods	CRCT; non-cross-over
Participants	Country: Bangladesh; setting: Dhaka city; urbanicity: N/A Inclusion criteria: children aged between 1 and 3 years having weight-for-age between 70% and 61% of NCHS standard; children who come to the outpatient department of ICDDR,B for treatment of acute watery diarrhea; no signs of vitamin A deficiency (non-invasive diarrhea and without systematic infection) and have not received vitamin A during last 4 months; children who have not received measles vaccine and did not have measles primarily identified for the study; children who did not reside in and around Dhaka city Exclusion criteria: children who need immediate vitamin A supplementation (clear sign of vitamin deficiency); children who received vitamin A within the last 4 months; children with other systematic infection; participants who develop any kind of sign and symptoms of vitamin A deficiency will be given vitamin A and will be analyzed separately **Baseline characteristics** Avg age (months): N/A; min age (months): 12; max age (months): 36; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 147; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: syrup; compound: acetate; frequency: twice daily; duration (months): 0.25 (7 d); dose (mg): 20; co-intervention(s): N/A (for 1 subset of participants); vitamin A (for another subset of participants) **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of LRTI • Height **Time point (week):** 24
Starting date	1 July 1993 **Study end date:** 30 November 1995
Contact information	**Name:** Swapan K Roy **Email:** not reported
Notes	**Funding source(s):** ICDDR, B

NCT01306097

Study name	**Public title:** Zinc supplementation and severe and recurrent diarrhea **Scientific title:** Evaluating the impact of 3 months daily zinc supplementation on incidence of severe and recurrent diarrhea in 6 to 36 months age children
Methods	IRCT; non-cross-over
Participants	Country: Iran; setting: Bandar Abbas, Hormozgan; urbanicity: N/A Inclusion criteria: all 6-36 months-old children without diarrhea at the time of study and without disease such as celiac inflammatory bowel disease and hypersensitivity to milk Exclusion criteria: diarrhea at the time of the study and background disease such as celiac, IBD or hypersensitivity to milk **Baseline characteristics** Avg age (months): N/A; min age (months): 6; max age (months): 36; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 100; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: N/A; compound: sulfate; frequency: N/A; duration (months): 3; dose (mg): 10 for children < 1 year, 20 for children > 1 year; co-intervention(s): N/A **Group 2:** no zinc Unclear whether or not placebo is given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Incidence of all-cause diarrhea • Incidence of severe diarrhea **Time point (week):** N/A
Starting date	January 2009 **Study end date:** May 2010
Contact information	**Name:** Marzie Barchinejad, Hormozgan University of Medical Sciences, Iran **Email:** not reported
Notes	**Funding source(s):** Hormozgan University of Medical Sciences

NCT01911260

Study name	**Public title:** Weekly zinc chelate supplementation on children's growth

NCT01911260 *(Continued)*

	Scientific title: Effect of weekly zinc chelate supplementation on schoolchildren's growth: a randomized double-blind controlled trial
Methods	IRCT; non-cross-over
Participants	Country: Brazil; setting: N/A; urbanicity: N/A Inclusion criteria: children with ≥ 1.5 SDs below the mean HAZ and gender of the reference population (Z-score < −1.6) were included in the Growth Deficit group (GD); for the Normal Stature group (NS), HAZ was set up as being between −1 and +1 SDs from the mean height reference for age and sex Exclusion criteria: any organic or genetic condition correlated with growth deficit **Baseline characteristics** Avg age (months): N/A; min age (months): 84; max age (months): 120; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 199; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: syrup; compound: amino acid chelate; frequency: daily; duration (months): 3; dose (mg): 30; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height **Time point (week):** 12
Starting date	September 2000 **Study end date:** March 2001
Contact information	**Name:** Ana Paula Poblacion, Federal University of São Paulo **Email:** not reported
Notes	**Funding source(s):** Federal University of São Paulo

NCT03098810

Study name	**Public title:** Effect of zinc supplementation on appetite and growth in primary malnourished children **Scientific title:** same as public title
Methods	IRCT; non-cross-over

NCT03098810 *(Continued)*

Participants	Country: N/A; setting: N/A; urbanicity: N/A Inclusion criteria: primary malnourished Exclusion criteria: zinc supplementation in the previous 3 months; children with chronic disease **Baseline characteristics** Avg age (months): N/A; min age (months): 24; max age (months): 120; % female: N/A Avg height-for-age z score: N/A; stunting: N/A; avg height (cm): N/A; avg zinc concentration (µg/dL): N/A Total N: 50; Group 1 N: N/A; Group 2 N: N/A
Interventions	**Group 1:** zinc Formulation: syrup; compound: sulfate; frequency: N/A; duration (months): 3; dose (mg): N/A; co-intervention(s): N/A **Group 2:** no zinc Placebo given; co-intervention(s): N/A
Outcomes	**Primary** • N/A **Secondary** • Height • Weight **Time point (week):** 12
Starting date	1 April 2017 (estimated) **Study end date:** 1 December 2017 (estimated)
Contact information	**Name:** Marian Girgis **Email:** mariangirgis2009@yahoo.com
Notes	**Funding source(s):** Ain Shams University

Avg: average; **CRCT:** cluster-randomized controlled trial;**HAZ:** height-for-age z-score; **ICDDR,B:** International Centre for Diarrheal Disease Research, Bangladesh; **IU:** international units; **LRTI:** lower respiratory tract infection; **Max:** Maximum; **Min:** Minimum; **N/A:** not available; **NCHS:** National Center for Health Statistics; **N:** Number; **SD:** standard deviation

DATA AND ANALYSES

Comparison 1. Zinc versus no zinc

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 All-cause mortality	17	143474	Risk Ratio (IV, Fixed, 95% CI)	0.93 [0.84, 1.03]

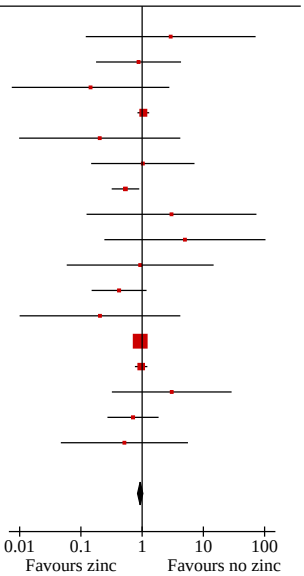
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Mortality due to all-cause diarrhea	4	132321	Risk Ratio (IV, Fixed, 95% CI)	0.95 [0.69, 1.31]
1.3 Mortality due to LRTI	3	132063	Risk Ratio (IV, Fixed, 95% CI)	0.86 [0.64, 1.15]
1.4 Mortality due to malaria	2	42818	Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.77, 1.06]
1.5 All-cause hospitalization	10	93817	Risk Ratio (IV, Fixed, 95% CI)	1.03 [0.96, 1.10]
1.6 Incidence of all-cause diarrhea	39	19468	Risk Ratio (IV, Fixed, 95% CI)	0.91 [0.90, 0.93]
1.7 Prevalence of all-cause diarrhea	15	8519	Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.86, 0.90]
1.8 Hospitalization due to all-cause diarrhea	5	74039	Risk Ratio (IV, Fixed, 95% CI)	1.03 [0.87, 1.22]
1.9 Incidence of severe diarrhea	10	8810	Risk Ratio (IV, Fixed, 95% CI)	0.91 [0.86, 0.96]
1.10 Incidence of persistent diarrhea	10	7161	Risk Ratio (IV, Fixed, 95% CI)	0.72 [0.62, 0.85]
1.11 Prevalence of persistent diarrhea	2	665	Risk Ratio (IV, Fixed, 95% CI)	0.70 [0.64, 0.76]
1.12 Incidence of LRTI	19	10555	Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.95, 1.08]
1.13 Prevalence of LRTI	4	1955	Risk Ratio (IV, Fixed, 95% CI)	1.20 [1.10, 1.30]
1.14 Hospitalization due to LRTI	4	74743	Risk Ratio (IV, Fixed, 95% CI)	1.10 [0.93, 1.30]
1.15 Incidence of malaria	8	5290	Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.94, 1.04]
1.16 Prevalence of malaria	1	661	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.47, 1.64]
1.17 Height	74	20720	Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [0.09, 0.14]
1.18 Weight	66	19891	Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [0.10, 0.15]
1.19 Weight-to-height ratio	33	12948	Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [0.10, 0.17]
1.20 Prevalence of stunting	13	8009	Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.94, 1.07]
1.21 Serum or plasma zinc concentration	64	12644	Std. Mean Difference (IV, Fixed, 95% CI)	0.60 [0.56, 0.63]
1.22 Prevalence of zinc deficiency	24	7518	Risk Ratio (IV, Fixed, 95% CI)	0.56 [0.52, 0.60]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.23 Study withdrawal	7	5226	Risk Ratio (M-H, Fixed, 95% CI)	1.81 [1.11, 2.95]
1.24 Participants with ≥ 1 side effect	3	850	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [1.00, 1.27]
1.25 Vomiting episodes	6	4095	Risk Ratio (IV, Fixed, 95% CI)	1.68 [1.61, 1.75]
1.26 Participants with ≥ 1 vomiting episode	5	35192	Risk Ratio (IV, Fixed, 95% CI)	1.29 [1.14, 1.46]
1.27 Blood hemoglobin concentration	40	12946	Std. Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.05, 0.02]
1.28 Prevalence of anemia	20	5762	Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.96, 1.06]
1.29 Serum or plasma ferritin concentration	27	5339	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [0.01, 0.12]
1.30 Prevalence of iron deficiency	15	3149	Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.89, 1.10]
1.31 Serum or plasma copper concentration	15	3317	Std. Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.27, -0.13]
1.32 Prevalence of copper deficiency	3	1337	Risk Ratio (IV, Fixed, 95% CI)	2.64 [1.28, 5.42]

Analysis 1.1. Comparison 1: Zinc versus no zinc, Outcome 1: All-cause mortality

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	1.07361099	1.62916074	161	157	0.1%	2.93 [0.12 , 71.29]
Becquey 2016	-0.1346	0.815	897	784	0.4%	0.87 [0.18 , 4.32]
Bhandari 2002	-1.93942189	1.51132135	1228	1236	0.1%	0.14 [0.01 , 2.78]
Bhandari 2007	0.04493755	0.11212408	36293	36145	20.3%	1.05 [0.84 , 1.30]
Chang 2010	-1.59447504	1.54597037	198	201	0.1%	0.20 [0.01 , 4.20]
Chhagan 2009	0.02643326	0.99114872	112	115	0.3%	1.03 [0.15 , 7.16]
Hess 2015	-0.6266	0.2642	1832	1387	3.7%	0.53 [0.32 , 0.90]
Larson 2010	1.10424611	1.6295395	176	177	0.1%	3.02 [0.12 , 73.56]
Lind 2003	1.60943791	1.54541389	170	170	0.1%	5.00 [0.24 , 103.38]
Malik 2014	-0.0736	1.409	141	131	0.1%	0.93 [0.06 , 14.70]
Müller 2001	-0.86670956	0.52677681	341	344	0.9%	0.42 [0.15 , 1.18]
Penny 2004	-1.58534036	1.54139551	81	83	0.1%	0.20 [0.01 , 4.20]
Sazawal 2006	-0.07257069	0.06862114	21274	21272	54.3%	0.93 [0.81 , 1.06]
Sazawal 2006 (2)	-0.03756725	0.11932628	8120	7950	18.0%	0.96 [0.76 , 1.22]
Shankar 2000	1.11321109	1.14836145	136	138	0.2%	3.04 [0.32 , 28.90]
Soofi 2013	-0.342704984498532	0.490437295227866	853	865	1.1%	0.71 [0.27 , 1.86]
Veenemans 2011	-0.6670019	1.2193957	151	155	0.2%	0.51 [0.05 , 5.60]
Total (95% CI)			**72164**	**71310**	**100.0%**	**0.93 [0.84 , 1.03]**

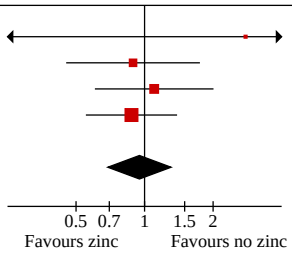
Heterogeneity: Chi² = 15.14, df = 16 (P = 0.51); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)
Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1: Zinc versus no zinc, Outcome 2: Mortality due to all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Malik 2014	1.02165124753198	1.62826879207926	134	124	1.0%	2.78 [0.11 , 67.56]
Sazawal 2006	-0.11653382	0.34500451	21274	21272	22.4%	0.89 [0.45 , 1.75]
Tielsch 2006 (2)	0.0973184	0.30604541	8951	8128	28.5%	1.10 [0.61 , 2.01]
Bhandari 2007	-0.13246169	0.2353465	36293	36145	48.1%	0.88 [0.55 , 1.39]
Total (95% CI)			**66652**	**65669**	**100.0%**	**0.95 [0.69 , 1.31]**

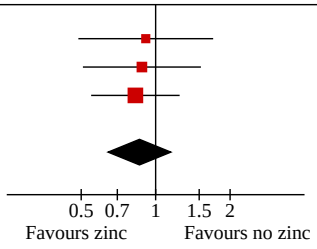
Heterogeneity: Chi² = 0.82, df = 3 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.32 (P = 0.75)
Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: Zinc versus no zinc, Outcome 3: Mortality due to LRTI

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Tielsch 2006	-0.0919236	0.32015621	8951	8128	21.6%	0.91 [0.49 , 1.71]
Sazawal 2006	-0.12783337	0.28026339	21274	21272	28.2%	0.88 [0.51 , 1.52]
Bhandari 2007	-0.18851085	0.21014892	36293	36145	50.2%	0.83 [0.55 , 1.25]
Total (95% CI)			**66518**	**65545**	**100.0%**	**0.86 [0.64 , 1.15]**

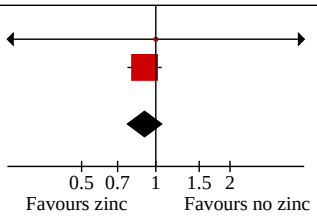
Heterogeneity: Chi² = 0.07, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 1.01 (P = 0.31)
Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1: Zinc versus no zinc, Outcome 4: Mortality due to malaria

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Shankar 2000	0	1.40900465	136	136	0.3%	1.00 [0.06 , 15.83]
Sazawal 2006	-0.10536052	0.0815407	21274	21272	99.7%	0.90 [0.77 , 1.06]
Total (95% CI)			**21410**	**21408**	**100.0%**	**0.90 [0.77 , 1.06]**

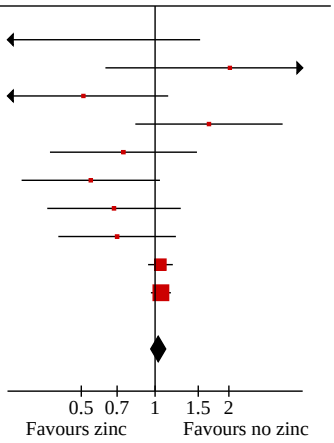
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 1.29 (P = 0.20)
Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1: Zinc versus no zinc, Outcome 5: All-cause hospitalization

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Meeks Gardner 1998	-2.42964397	1.45544155	31	30	0.1%	0.09 [0.01 , 1.53]
Chhagan 2009	0.70271663	0.5965407	104	105	0.4%	2.02 [0.63 , 6.50]
Islam 2022	-0.6733	0.4063	470	475	0.8%	0.51 [0.23 , 1.13]
Veenemans 2011 (2)	0.50620075	0.35290526	151	155	1.0%	1.66 [0.83 , 3.31]
Veenemans 2011	-0.29700703	0.35222173	153	153	1.0%	0.74 [0.37 , 1.48]
Chang 2010	-0.60400133	0.33149677	198	201	1.2%	0.55 [0.29 , 1.05]
Chang 2010 (2)	-0.38587877	0.31984651	400	201	1.3%	0.68 [0.36 , 1.27]
Bhandari 2002	-0.35667494	0.28167495	1241	1241	1.6%	0.70 [0.40 , 1.22]
Bhandari 2007	0.05040899	0.05921554	36293	36145	36.6%	1.05 [0.94 , 1.18]
Sazawal 2006 (2)	0.05454236	0.04780742	8120	7950	56.1%	1.06 [0.96 , 1.16]
Total (95% CI)			**47161**	**46656**	**100.0%**	**1.03 [0.96 , 1.10]**

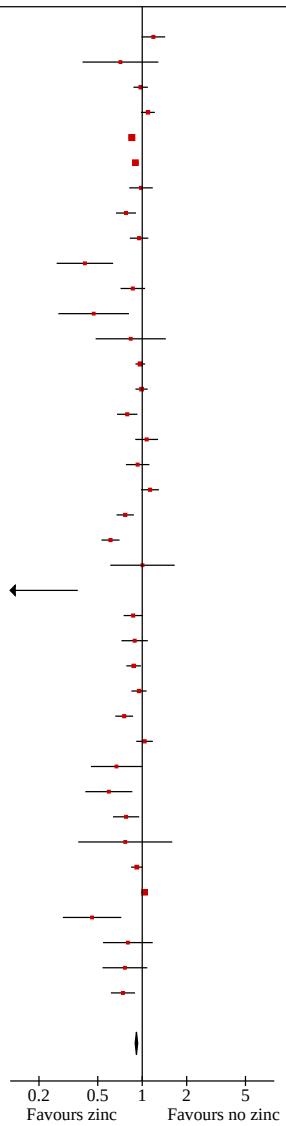
Heterogeneity: Chi² = 17.42, df = 9 (P = 0.04); I² = 48%
Test for overall effect: Z = 0.82 (P = 0.41)
Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1: Zinc versus no zinc, Outcome 6: Incidence of all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Abdollahi 2019	0.174	0.0939	272	308	1.1%	1.19 [0.99 , 1.43]
Alarcon 2004	-0.33963305	0.30181636	112	111	0.1%	0.71 [0.39 , 1.29]
Baqui 2003	-0.02439145	0.05739701	161	157	3.0%	0.98 [0.87 , 1.09]
Baqui 2003 (2)	0.08849308	0.05540904	162	165	3.2%	1.09 [0.98 , 1.22]
Becquey 2016	-0.1625	0.0246	1070	635	16.4%	0.85 [0.81 , 0.89]
Bhandari 2002	-0.10583655	0.02613411	1228	1236	14.5%	0.90 [0.85 , 0.95]
Chang 2010	-0.01868876	0.09337882	198	201	1.1%	0.98 [0.82 , 1.18]
Chang 2010 (2)	-0.25350318	0.0794688	201	201	1.6%	0.78 [0.66 , 0.91]
Chhagan 2009	-0.04913269	0.07335707	104	105	1.8%	0.95 [0.82 , 1.10]
Gupta 2003	-0.89381788	0.22473329	186	94	0.2%	0.41 [0.26 , 0.64]
Gupta 2007	-0.14660347	0.097381	854	858	1.0%	0.86 [0.71 , 1.05]
Han 2002	-0.756623021	0.280754333	33	22	0.1%	0.47 [0.27 , 0.81]
Han 2002 (2)	-0.179234677	0.279199046	24	26	0.1%	0.84 [0.48 , 1.44]
Hess 2015	-0.0305	0.0382	599	579	6.8%	0.97 [0.90 , 1.05]
Islam 2022	-0.0101	0.0486	482	481	4.2%	0.99 [0.90 , 1.09]
Larson 2010	-0.23381808	0.08123116	176	177	1.5%	0.79 [0.68 , 0.93]
Lind 2003	0.06899287	0.09065627	170	170	1.2%	1.07 [0.90 , 1.28]
Lind 2003 (2)	-0.07145896	0.09311961	170	170	1.1%	0.93 [0.78 , 1.12]
Long 2006	0.12218449	0.07061765	181	183	2.0%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	192	180	2.1%	0.77 [0.67 , 0.88]
Malik 2014	-0.4943	0.0717	134	124	1.9%	0.61 [0.53 , 0.70]
Meeks Gardner 1998	0.00421645	0.25610818	31	30	0.2%	1.00 [0.61 , 1.66]
Meeks Gardner 2005	-3.805154762	1.428808516	55	59	0.0%	0.02 [0.00 , 0.37]
Müller 2001	-0.14077255	0.07595902	342	344	1.7%	0.87 [0.75 , 1.01]
Penny 2004	-0.11778304	0.10486269	80	79	0.9%	0.89 [0.72 , 1.09]
Rahman 2001	-0.13353139	0.0579042	170	161	3.0%	0.88 [0.78 , 0.98]
Rahman 2001 (2)	-0.05001042	0.06042171	175	160	2.7%	0.95 [0.84 , 1.07]
Richard 2006	-0.28106642	0.07078211	209	215	2.0%	0.75 [0.66 , 0.87]
Richard 2006 (2)	0.03619935	0.06581383	210	208	2.3%	1.04 [0.91 , 1.18]
Rosado 1997	-0.40188729	0.20280294	54	56	0.2%	0.67 [0.45 , 1.00]
Rosado 1997 (2)	-0.52044108	0.18680745	55	54	0.3%	0.59 [0.41 , 0.86]
Ruel 1997	-0.25131443	0.10417938	55	53	0.9%	0.78 [0.63 , 0.95]
Sampaio 2013	-0.26503449302337	0.373888956972379	75	68	0.1%	0.77 [0.37 , 1.60]
Sazawal 1996	-0.08461665	0.04515217	286	293	4.9%	0.92 [0.84 , 1.00]
Soofi 2013	0.0377403279828471	0.0268956156251902	853	865	13.7%	1.04 [0.99 , 1.09]
Umeta 2000	-0.78170058	0.23234928	100	100	0.2%	0.46 [0.29 , 0.72]
Veenemans 2011	-0.22342699	0.19743482	153	153	0.3%	0.80 [0.54 , 1.18]
Veenemans 2011 (2)	-0.27010424	0.17803183	151	155	0.3%	0.76 [0.54 , 1.08]
Wuehler 2008	-0.30010459	0.09601332	353	116	1.1%	0.74 [0.61 , 0.89]
Total (95% CI)			**10116**	**9352**	**100.0%**	**0.91 [0.90 , 0.93]**

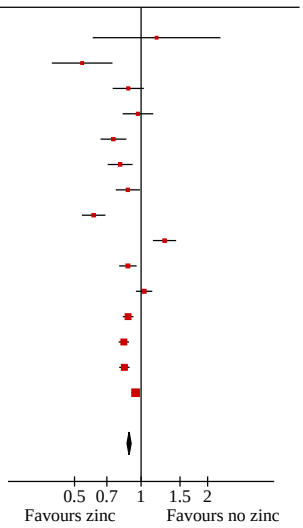
Heterogeneity: Chi² = 179.36, df = 38 (P < 0.00001); I² = 79%
Test for overall effect: Z = 9.06 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1: Zinc versus no zinc, Outcome 7: Prevalence of all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Shankar 2000	0.16121482	0.33931045	136	138	0.1%	1.17 [0.60 , 2.28]
Alarcon 2004	-0.61376215	0.1610153	112	111	0.5%	0.54 [0.39 , 0.74]
Chhagan 2009	-0.13353139	0.08272645	104	105	1.7%	0.88 [0.74 , 1.03]
Chang 2010	-0.03278982	0.08135338	198	201	1.8%	0.97 [0.83 , 1.14]
Chang 2010 (2)	-0.28768207	0.06864827	400	201	2.5%	0.75 [0.66 , 0.86]
Ruel 1997	-0.21813101	0.06585277	55	53	2.7%	0.80 [0.71 , 0.91]
Penny 2004	-0.13786979	0.06396739	80	79	2.9%	0.87 [0.77 , 0.99]
Malik 2014	-0.494296322	0.062532388	134	124	3.0%	0.61 [0.54 , 0.69]
Brown 2007	0.24419696	0.06163859	101	99	3.1%	1.28 [1.13 , 1.44]
Müller 2001	-0.13740764	0.04640859	332	329	5.5%	0.87 [0.80 , 0.95]
Soofi 2013	0.0312234804470357	0.0435336459823005	853	865	6.2%	1.03 [0.95 , 1.12]
Rahman 2001 (2)	-0.13550106	0.0280183	175	160	15.1%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	1228	1236	15.5%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	170	161	15.7%	0.84 [0.80 , 0.89]
Sazawal 1996	-0.05786738	0.02237039	286	293	23.6%	0.94 [0.90 , 0.99]
Total (95% CI)			**4364**	**4155**	**100.0%**	**0.88 [0.86 , 0.90]**

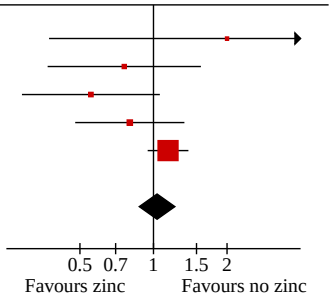
Heterogeneity: Chi² = 118.88, df = 14 (P < 0.00001); I² = 88%
Test for overall effect: Z = 11.49 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.8. Comparison 1: Zinc versus no zinc, Outcome 8: Hospitalization due to all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Chhagan 2009	0.69314718	0.85574581	113	113	1.0%	2.00 [0.37 , 10.70]
Chang 2010 (2)	-0.275374225	0.368438063	13	17	5.4%	0.76 [0.37 , 1.56]
Chang 2010	-0.58978851	0.331496772	14	26	6.7%	0.55 [0.29 , 1.06]
Soofi 2013	-0.22314355	0.262480512	659	646	10.6%	0.80 [0.48 , 1.34]
Bhandari 2007	0.13714331	0.09792914	36293	36145	76.3%	1.15 [0.95 , 1.39]
Total (95% CI)			**37092**	**36947**	**100.0%**	**1.03 [0.87 , 1.22]**

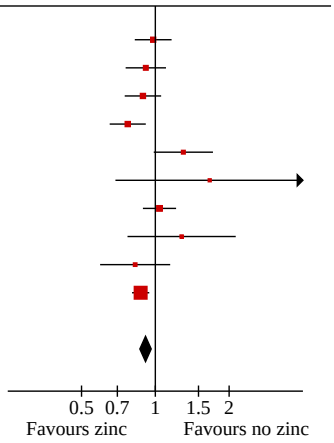
Heterogeneity: Chi² = 6.91, df = 4 (P = 0.14); I² = 42%
Test for overall effect: Z = 0.39 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 1.9. Comparison 1: Zinc versus no zinc, Outcome 9: Incidence of severe diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	-0.02014457	0.08816718	161	157	9.5%	0.98 [0.82 , 1.16]
Baqui 2003 (2)	-0.08940659	0.09665225	162	165	7.9%	0.91 [0.76 , 1.11]
Becquey 2016	-0.1165	0.0873	1070	635	9.7%	0.89 [0.75 , 1.06]
Bhandari 2002	-0.25917565	0.0864935	1228	1236	9.9%	0.77 [0.65 , 0.91]
Brown 2007	0.26323801	0.14186463	101	99	3.7%	1.30 [0.99 , 1.72]
Chhagan 2009	0.51082562	0.4518291	104	105	0.4%	1.67 [0.69 , 4.04]
Hess 2015	0.0392	0.0795	599	579	11.7%	1.04 [0.89 , 1.22]
Islam 2022	0.2469	0.2593	470	475	1.1%	1.28 [0.77 , 2.13]
Penny 2004	-0.18945353	0.16789406	80	79	2.6%	0.83 [0.60 , 1.15]
Soofi 2013	-0.13795944	0.041180476	659	646	43.6%	0.87 [0.80 , 0.94]
Total (95% CI)			**4634**	**4176**	**100.0%**	**0.91 [0.86 , 0.96]**

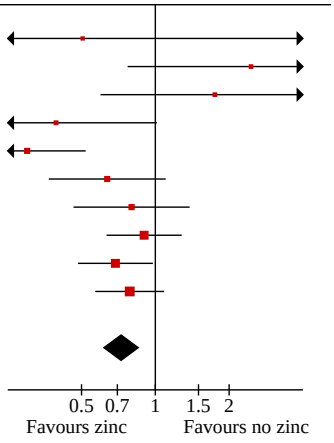
Heterogeneity: Chi² = 18.54, df = 9 (P = 0.03); I² = 51%
Test for overall effect: Z = 3.39 (P = 0.0007)
Test for subgroup differences: Not applicable



Analysis 1.10. Comparison 1: Zinc versus no zinc, Outcome 10: Incidence of persistent diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Islam 2022	-0.6826	1.223	470	475	0.5%	0.51 [0.05 , 5.55]
Long 2006	0.89929316	0.59160798	181	183	1.9%	2.46 [0.77 , 7.84]
Chhagan 2009	0.55961579	0.54838837	104	105	2.2%	1.75 [0.60 , 5.13]
Long 2006 (2)	-0.93249046	0.48304589	192	180	2.9%	0.39 [0.15 , 1.01]
Malik 2014	-1.203972804	0.280263387	134	124	8.6%	0.30 [0.17 , 0.52]
Rahman 2001 (2)	-0.45198512	0.28018595	175	160	8.6%	0.64 [0.37 , 1.10]
Rahman 2001	-0.22314355	0.27841345	170	161	8.7%	0.80 [0.46 , 1.38]
Soofi 2013	-0.10536052	0.179834478	659	646	20.9%	0.90 [0.63 , 1.28]
Bhandari 2002	-0.37475057	0.17949313	1228	1236	21.0%	0.69 [0.48 , 0.98]
Sazawal 1996	-0.24030015	0.16519497	286	292	24.7%	0.79 [0.57 , 1.09]
Total (95% CI)			**3599**	**3562**	**100.0%**	**0.72 [0.62 , 0.85]**

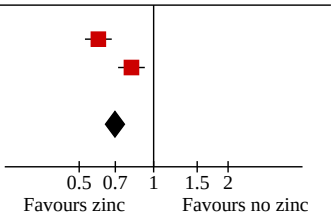
Heterogeneity: Chi² = 20.56, df = 9 (P = 0.01); I² = 56%
Test for overall effect: Z = 3.92 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 1.11. Comparison 1: Zinc versus no zinc, Outcome 11: Prevalence of persistent diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Rahman 2001 (2)	-0.5146644	0.06362023	175	159	49.8%	0.60 [0.53 , 0.68]
Rahman 2001	-0.20661425	0.0634239	170	161	50.2%	0.81 [0.72 , 0.92]
Total (95% CI)			**345**	**320**	**100.0%**	**0.70 [0.64 , 0.76]**

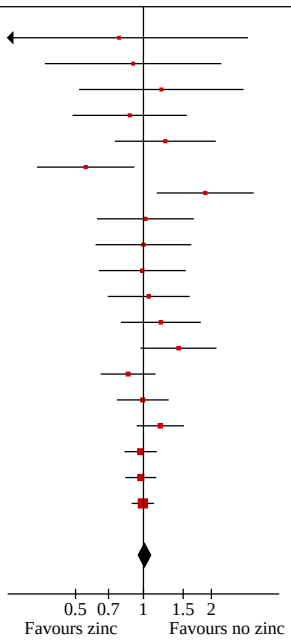
Heterogeneity: Chi² = 11.76, df = 1 (P = 0.0006); I² = 91%
Test for overall effect: Z = 8.02 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.12. Comparison 1: Zinc versus no zinc, Outcome 12: Incidence of LRTI

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Long 2006 (2)	-0.24816892	0.67082039	192	180	0.2%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	181	183	0.5%	0.90 [0.37 , 2.21]
Brown 2007	0.18232156	0.42839042	101	99	0.6%	1.20 [0.52 , 2.78]
Penny 2004	-0.14058195	0.29777877	80	79	1.2%	0.87 [0.48 , 1.56]
Soofi 2013	0.22314355131421	0.262771200970603	659	646	1.5%	1.25 [0.75 , 2.09]
Sazawal 1996	-0.59000642	0.25375961	297	306	1.6%	0.55 [0.34 , 0.91]
Rahman 2001	0.63062682	0.25241624	170	161	1.7%	1.88 [1.15 , 3.08]
Richard 2006 (2)	0.02032	0.25200806	210	208	1.7%	1.02 [0.62 , 1.67]
Rahman 2001 (2)	0	0.24928541	175	160	1.7%	1.00 [0.61 , 1.63]
Richard 2006	-0.01129956	0.22645541	209	209	2.1%	0.99 [0.63 , 1.54]
Veenemans 2011	0.05383699	0.2132558	153	153	2.3%	1.06 [0.69 , 1.60]
Veenemans 2011 (2)	0.17745056	0.20798032	151	155	2.4%	1.19 [0.79 , 1.80]
Islam 2022	0.3577	0.198	470	475	2.7%	1.43 [0.97 , 2.11]
Baqui 2003 (2)	-0.15645218	0.14256197	162	165	5.2%	0.86 [0.65 , 1.13]
Baqui 2003	-0.00673403	0.13486419	161	157	5.8%	0.99 [0.76 , 1.29]
Müller 2001	0.17162318	0.12304944	342	344	6.9%	1.19 [0.93 , 1.51]
Lind 2003 (2)	-0.02898754	0.08383997	170	170	15.0%	0.97 [0.82 , 1.14]
Lind 2003	-0.02739897	0.08077837	170	170	16.1%	0.97 [0.83 , 1.14]
Bhandari 2002	-0.00591199	0.05834957	1241	1241	30.9%	0.99 [0.89 , 1.11]
Total (95% CI)			**5294**	**5261**	**100.0%**	**1.01 [0.95 , 1.08]**

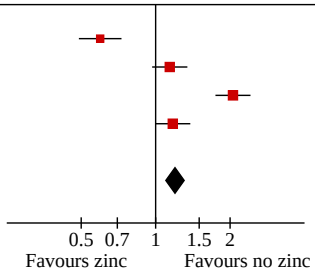
Heterogeneity: Chi² = 20.32, df = 18 (P = 0.32); I² = 11%
Test for overall effect: Z = 0.33 (P = 0.74)
Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1: Zinc versus no zinc, Outcome 13: Prevalence of LRTI

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Sazawal 1996	-0.5163946	0.10119037	297	306	18.4%	0.60 [0.49 , 0.73]
Müller 2001	0.13143132	0.08364305	342	344	27.0%	1.14 [0.97 , 1.34]
Rahman 2001	0.71999443	0.08321276	170	161	27.3%	2.05 [1.75 , 2.42]
Rahman 2001 (2)	0.15972172	0.08318405	175	160	27.3%	1.17 [1.00 , 1.38]
Total (95% CI)			**984**	**971**	**100.0%**	**1.20 [1.10 , 1.30]**

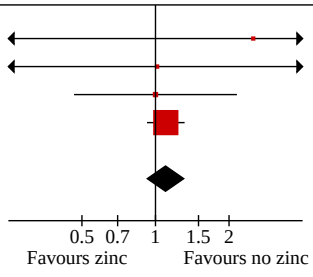
Heterogeneity: Chi² = 89.87, df = 3 (P < 0.00001); I² = 97%
Test for overall effect: Z = 4.15 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 1.14. Comparison 1: Zinc versus no zinc, Outcome 14: Hospitalization due to LRTI

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Chang 2010 (2)	0.92127827	1.54919334	400	201	0.3%	2.51 [0.12 , 52.33]
Chang 2010	0.01503788	1	198	201	0.8%	1.02 [0.14 , 7.21]
Soofi 2013	0	0.391499572	659	646	5.0%	1.00 [0.46 , 2.15]
Bhandari 2007	0.09729079	0.0903108	36293	36145	93.9%	1.10 [0.92 , 1.32]
Total (95% CI)			**37550**	**37193**	**100.0%**	**1.10 [0.93 , 1.30]**

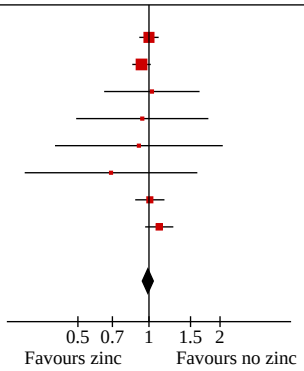
Heterogeneity: Chi² = 0.35, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 1.15. Comparison 1: Zinc versus no zinc, Outcome 15: Incidence of malaria

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Becquey 2016	0	0.0481	1070	635	32.3%	1.00 [0.91 , 1.10]
Hess 2015	-0.0726	0.0459	599	579	35.5%	0.93 [0.85 , 1.02]
Müller 2001	0.02817088	0.23737988	341	344	1.3%	1.03 [0.65 , 1.64]
Richard 2006	-0.06536678	0.32891813	209	209	0.7%	0.94 [0.49 , 1.78]
Richard 2006 (2)	-0.09844007	0.41742355	210	208	0.4%	0.91 [0.40 , 2.05]
Shankar 2000	-0.370185525332603	0.42956235	136	138	0.4%	0.69 [0.30 , 1.60]
Veenemans 2011	0.00837462	0.0727393	153	153	14.1%	1.01 [0.87 , 1.16]
Veenemans 2011 (2)	0.10019023	0.07006137	151	155	15.2%	1.11 [0.96 , 1.27]
Total (95% CI)			**2869**	**2421**	**100.0%**	**0.99 [0.94 , 1.04]**

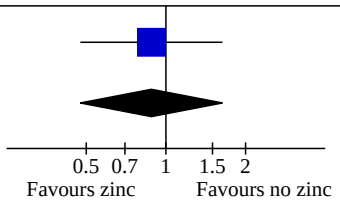
Heterogeneity: Chi² = 5.24, df = 7 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Not applicable



Analysis 1.16. Comparison 1: Zinc versus no zinc, Outcome 16: Prevalence of malaria

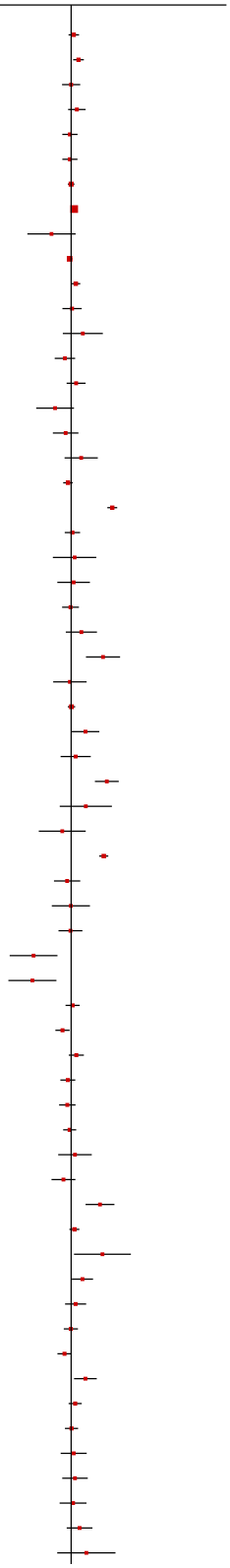
Study or Subgroup	Zinc Events	Zinc Total	No zinc Events	No zinc Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Müller 2001	18	334	20	327	100.0%	0.88 [0.47 , 1.64]
Total (95% CI)		**334**		**327**	**100.0%**	**0.88 [0.47 , 1.64]**
Total events:	18		20			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)
Test for subgroup differences: Not applicable



Analysis 1.17. Comparison 1: Zinc versus no zinc, Outcome 17: Height

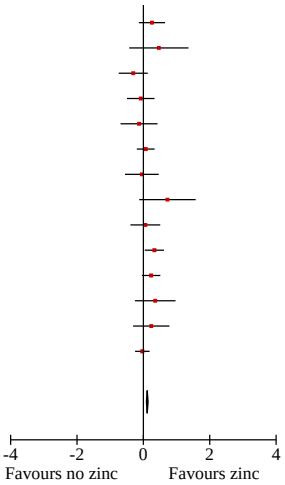
Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No Zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2014	0.081207	0.082178	291	302	2.5%	0.08 [-0.08 , 0.24]
Abdollahi 2019	0.2262	0.0835	272	308	2.5%	0.23 [0.06 , 0.39]
Akramuzzaman 1994	0	0.14216714	93	104	0.8%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.175624	0.13685249	109	104	0.9%	0.18 [-0.09 , 0.44]
Baqui 2003	-0.03691	0.11899992	141	140	1.2%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.03759	0.11833	135	150	1.2%	-0.04 [-0.27 , 0.19]
Barffour 2019	0	0.052	740	739	6.4%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	751	704	19.7%	0.09 [0.04 , 0.15]
Bertinato 2013	-0.60195	0.377514	27	10	0.1%	-0.60 [-1.34 , 0.14]
Bhandari 2002	-0.04597	0.04238854	1093	1133	9.6%	-0.05 [-0.13 , 0.04]
Bhandari 2007	0.142734	0.0697166	448	427	3.5%	0.14 [0.01 , 0.28]
Brown 2007	0.028317	0.15073647	83	92	0.8%	0.03 [-0.27 , 0.32]
Castillo-Durán 1994	0.35835	0.313	19	21	0.2%	0.36 [-0.26 , 0.97]
Cavan 1993	-0.19094	0.15976556	76	80	0.7%	-0.19 [-0.50 , 0.12]
Chen 2012	0.152273	0.148307705	88	93	0.8%	0.15 [-0.14 , 0.44]
Clark 1999	-0.49205	0.295419	25	21	0.2%	-0.49 [-1.07 , 0.09]
De Fonseca 2002	-0.16854	0.19990018	51	48	0.4%	-0.17 [-0.56 , 0.22]
Dehbozorgi 2007	0.308	0.2598	30	30	0.3%	0.31 [-0.20 , 0.82]
DiGirolamo 2010	-0.09681	0.07476273	360	355	3.1%	-0.10 [-0.24 , 0.05]
Ebrahimi 2006	1.261145	0.07721922	386	418	2.9%	1.26 [1.11 , 1.41]
Friis 1997	0.038991	0.12009587	141	135	1.2%	0.04 [-0.20 , 0.27]
Garcia 1998	0.105848	0.34006946	16	17	0.1%	0.11 [-0.56 , 0.77]
Gibson 1989	0.075924	0.25493989	30	30	0.3%	0.08 [-0.42 , 0.58]
Gracia 2005	-0.01896	0.13144479	115	115	1.0%	-0.02 [-0.28 , 0.24]
Hambidge 1978	0.313559	0.24369413	36	31	0.3%	0.31 [-0.16 , 0.79]
Han 2002	0.977632	0.26685037	34	28	0.2%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.03792	0.26134196	28	29	0.3%	-0.04 [-0.55 , 0.47]
Hess 2015	0.0098	0.0573	617	602	5.2%	0.01 [-0.10 , 0.12]
Hettiarachchi 2008	0.43865	0.21702312	99	40	0.4%	0.44 [0.01 , 0.86]
Hettiarachchi 2008 (2)	0.139306	0.23580261	113	30	0.3%	0.14 [-0.32 , 0.60]
Hong 1982	1.094003	0.18644996	64	67	0.5%	1.09 [0.73 , 1.46]
Ince 1995	0.450283	0.40793136	16	9	0.1%	0.45 [-0.35 , 1.25]
Isdiany 2021	-0.2724	0.3671	15	15	0.1%	-0.27 [-0.99 , 0.45]
Islam 2022	0.9992	0.071	441	453	3.4%	1.00 [0.86 , 1.14]
Kaseb 2013	-0.12359	0.205411	48	47	0.4%	-0.12 [-0.53 , 0.28]
Khodashenas 2015	-0.00828	0.298217	23	22	0.2%	-0.01 [-0.59 , 0.58]
Kikafunda 1998	-0.02126	0.18705861	59	54	0.5%	-0.02 [-0.39 , 0.35]
Kusumastuti 2018	-1.1518	0.3738	17	17	0.1%	-1.15 [-1.88 , -0.42]
Kusumastuti 2018 (2)	-1.1878	0.3757	17	17	0.1%	-1.19 [-1.92 , -0.45]
Lind 2003	0.044824	0.11052917	162	164	1.4%	0.04 [-0.17 , 0.26]
Lind 2003 (2)	-0.26456	0.11134035	161	163	1.4%	-0.26 [-0.48 , -0.05]
Long 2006	0.158402	0.11813857	144	142	1.2%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016	0.11663237	149	144	1.3%	-0.10 [-0.33 , 0.13]
Mandlik 2020	-0.1172	0.1284	124	119	1.0%	-0.12 [-0.37 , 0.13]
Mazariegos 2010	-0.04455	0.10189635	188	196	1.7%	-0.04 [-0.24 , 0.16]
Meeks Gardner 1998	0.117835	0.26252076	31	26	0.2%	0.12 [-0.40 , 0.63]
Meeks Gardner 2005	-0.23589	0.18682894	55	59	0.5%	-0.24 [-0.60 , 0.13]
Mozaffari-Khosravi 2009	0.884532	0.22577077	40	45	0.3%	0.88 [0.44 , 1.33]
Müller 2001	0.099886	0.07775177	332	329	2.8%	0.10 [-0.05 , 0.25]
Nakamura 1993	0.960095	0.44484717	10	11	0.1%	0.96 [0.09 , 1.83]
Ninh 1996	0.346345	0.16590035	73	73	0.6%	0.35 [0.02 , 0.67]
Penny 2004	0.137246	0.16491512	71	75	0.6%	0.14 [-0.19 , 0.46]
Rahman 2001	-0.00867	0.11069586	165	160	1.4%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.20323	0.11056287	171	157	1.4%	-0.20 [-0.42 , 0.01]
Rerksuppaphol 2018	0.437487	0.177583	66	64	0.5%	0.44 [0.09 , 0.79]
Richard 2006	0.124046	0.10262789	190	189	1.6%	0.12 [-0.08 , 0.33]
Richard 2006 (2)	0.011477	0.10286111	195	182	1.6%	0.01 [-0.19 , 0.21]
Rosado 1997	0.078132	0.20362659	31	47	0.4%	0.08 [-0.32 , 0.48]
Rosado 1997 (2)	0.118125	0.19963612	49	50	0.4%	0.12 [-0.27 , 0.51]
Ruel 1997	0.05884	0.21022626	45	44	0.4%	0.06 [-0.35 , 0.47]
Ruz 1997	0.258665	0.20129773	49	49	0.4%	0.26 [-0.14 , 0.65]
Sayeg Porto 2000	0.466375	0.45563575	9	9	0.1%	0.47 [-0.43 , 1.36]



Analysis 1.17. (Continued)

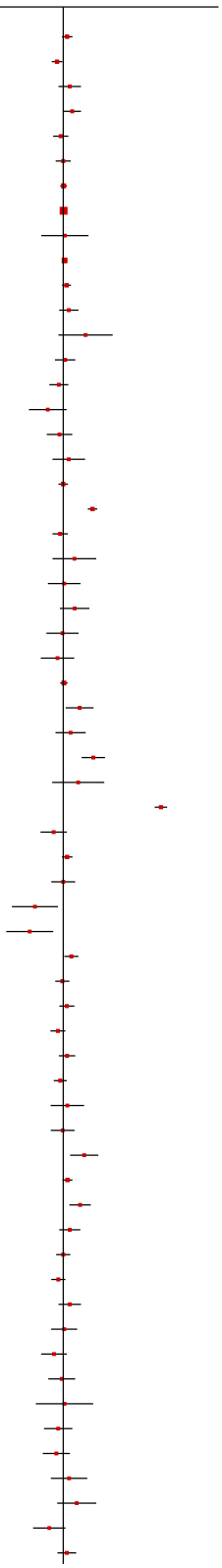
Ruz 1997	0.258665	0.20129773	49	49	0.4%	0.26 [-0.14 , 0.65]
Sayeg Porto 2000	0.466375	0.45563575	9	9	0.1%	0.47 [-0.43 , 1.36]
Sazawal 2006	-0.30538	0.22312277	44	58	0.3%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.07944	0.21183638	56	54	0.4%	-0.08 [-0.49 , 0.34]
Sempértegui 1996	-0.13048	0.28450141	23	25	0.2%	-0.13 [-0.69 , 0.43]
Shankar 2000	0.070551	0.13696712	103	109	0.9%	0.07 [-0.20 , 0.34]
Silva 2006	-0.04607	0.25926942	28	30	0.3%	-0.05 [-0.55 , 0.46]
Smith 1999	0.725292	0.43412761	10	11	0.1%	0.73 [-0.13 , 1.58]
Tupe 2009	0.058646	0.22908102	43	40	0.3%	0.06 [-0.39 , 0.51]
Umeta 2000	0.332226	0.14785133	92	92	0.8%	0.33 [0.04 , 0.62]
Vakili 2015	0.23296	0.14191	100	100	0.9%	0.23 [-0.05 , 0.51]
Walravens 1983	0.356412	0.31249613	20	20	0.2%	0.36 [-0.26 , 0.97]
Walravens 1989	0.237554	0.27941182	25	25	0.2%	0.24 [-0.31 , 0.79]
Wuehler 2008	-0.03193	0.11140371	313	108	1.4%	-0.03 [-0.25 , 0.19]
Total (95% CI)			**10514**	**10206**	**100.0%**	**0.12 [0.09 , 0.14]**

Heterogeneity: Chi² = 568.20, df = 73 (P < 0.00001); I² = 87%
Test for overall effect: Z = 8.85 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.18. Comparison 1: Zinc versus no zinc, Outcome 18: Weight

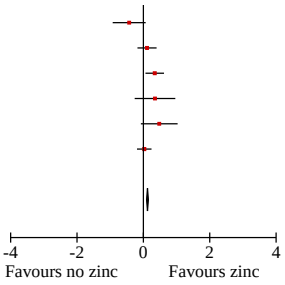
Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No Zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2014	0.121071	0.08222	291	302	2.7%	0.12 [-0.04 , 0.28]
Abdollahi 2019	-0.1898	0.0834	272	308	2.6%	-0.19 [-0.35 , -0.03]
Akramuzzaman 1994	0.200203	0.175885	93	104	0.6%	0.20 [-0.14 , 0.54]
Alarcon 2004	0.275987	0.13724067	109	104	1.0%	0.28 [0.01 , 0.54]
Baqui 2003	-0.07668	0.11903369	141	140	1.3%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	135	150	1.3%	0.00 [-0.23 , 0.23]
Barffour 2019	0.011229	0.052006	739	740	6.7%	0.01 [-0.09 , 0.11]
Becquey 2016	0.0113	0.0295	751	704	20.8%	0.01 [-0.05 , 0.07]
Bertinato 2013	0.048995	0.370234	27	10	0.1%	0.05 [-0.68 , 0.77]
Bhandari 2002	0.039993	0.04238717	1093	1133	10.1%	0.04 [-0.04 , 0.12]
Bhandari 2007	0.100931	0.06967226	448	427	3.7%	0.10 [-0.04 , 0.24]
Brown 2007	0.171493	0.15100736	83	92	0.8%	0.17 [-0.12 , 0.47]
Castillo-Durán 1994	0.684869	0.42465726	10	12	0.1%	0.68 [-0.15 , 1.52]
Cavan 1993	0.057204	0.15943234	76	80	0.7%	0.06 [-0.26 , 0.37]
Chen 2012	-0.13538	0.148262447	88	93	0.8%	-0.14 [-0.43 , 0.16]
Clark 1999	-0.4741	0.29509972	25	21	0.2%	-0.47 [-1.05 , 0.10]
De Fonseca 2002	-0.11383	0.19970491	51	48	0.5%	-0.11 [-0.51 , 0.28]
Dehbozorgi 2007	0.17052	0.25532062	30	30	0.3%	0.17 [-0.33 , 0.67]
DiGirolamo 2010	0	0.07471888	360	355	3.2%	0.00 [-0.15 , 0.15]
Ebrahimi 2006	0.898446	0.07399793	386	418	3.3%	0.90 [0.75 , 1.04]
Friis 1997	-0.09497	0.12015242	141	135	1.3%	-0.09 [-0.33 , 0.14]
Garcia 1998	0.342472	0.34242453	16	17	0.2%	0.34 [-0.33 , 1.01]
Gibson 1989	0.028831	0.25485925	30	30	0.3%	0.03 [-0.47 , 0.53]
Hambidge 1978	0.350582	0.23036496	38	37	0.3%	0.35 [-0.10 , 0.80]
Han 2002	-0.02302	0.25200321	34	28	0.3%	-0.02 [-0.52 , 0.47]
Han 2002 (2)	-0.17571	0.26183551	28	29	0.3%	-0.18 [-0.69 , 0.34]
Hess 2015	0.0213	0.0573	617	602	5.5%	0.02 [-0.09 , 0.13]
Hettiarachchi 2008	0.502657	0.21768626	99	40	0.4%	0.50 [0.08 , 0.93]
Hettiarachchi 2008 (2)	0.22531	0.23611165	113	30	0.3%	0.23 [-0.24 , 0.69]
Hong 1982	0.922806	0.18288181	64	67	0.5%	0.92 [0.56 , 1.28]
Ince 1995	0.45975	0.40814252	16	9	0.1%	0.46 [-0.34 , 1.26]
Islam 2022	2.9975	0.0976	441	453	1.9%	3.00 [2.81 , 3.19]
Kaseb 2013	-0.29308	0.206353	48	47	0.4%	-0.29 [-0.70 , 0.11]
Khodashenas 2015	0.121071	0.08222	291	302	2.7%	0.12 [-0.04 , 0.28]
Kikafunda 1998	0	0.18705326	59	54	0.5%	0.00 [-0.37 , 0.37]
Kusumastuti 2018	-0.8683	0.3608	17	17	0.1%	-0.87 [-1.58 , -0.16]
Kusumastuti 2018 (2)	-1.0274	0.3677	17	17	0.1%	-1.03 [-1.75 , -0.31]
Lind 2003	0.249296	0.11094564	162	164	1.5%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.02849	0.11085987	161	163	1.5%	-0.03 [-0.25 , 0.19]
Long 2006	0.111551	0.11804496	144	142	1.3%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.16372	0.11675288	149	144	1.3%	-0.16 [-0.39 , 0.07]
Mandlik 2020	0.117221	0.128439	119	124	1.1%	0.12 [-0.13 , 0.37]
Mazariegos 2010	-0.09075	0.10193628	188	196	1.7%	-0.09 [-0.29 , 0.11]
Meeks Gardner 1998	0.126756	0.26255721	31	26	0.3%	0.13 [-0.39 , 0.64]
Meeks Gardner 2005	-0.01741	0.18617821	55	59	0.5%	-0.02 [-0.38 , 0.35]
Mozaffari-Khosravi 2009	0.643554	0.22092161	40	45	0.4%	0.64 [0.21 , 1.08]
Müller 2001	0.129852	0.07778525	332	329	3.0%	0.13 [-0.02 , 0.28]
Ninh 1996	0.517435	0.16741874	73	73	0.6%	0.52 [0.19 , 0.85]
Penny 2004	0.200008	0.16513475	71	75	0.7%	0.20 [-0.12 , 0.52]
Rahman 2001	0	0.11069534	165	160	1.5%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.15092	0.11043509	171	157	1.5%	-0.15 [-0.37 , 0.07]
Rerksuppaphol 2018	0.200203	0.175885	66	64	0.6%	0.20 [-0.14 , 0.54]
Rosado 1997	0.028744	0.20355836	48	47	0.4%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2835	0.20047451	49	50	0.5%	-0.28 [-0.68 , 0.11]
Ruel 1997	-0.04608	0.21020838	45	44	0.4%	-0.05 [-0.46 , 0.37]
Sayeg Porto 2000	0.038555	0.44900267	9	9	0.1%	0.04 [-0.84 , 0.92]
Sazawal 2006	-0.15483	0.22216939	44	58	0.4%	-0.15 [-0.59 , 0.28]
Sazawal 2006 (2)	-0.21205	0.21235411	56	54	0.4%	-0.21 [-0.63 , 0.20]
Sempértegui 1996	0.178805	0.28477489	23	25	0.2%	0.18 [-0.38 , 0.74]
Smith 1999	0.413655	0.30646941	22	20	0.2%	0.41 [-0.19 , 1.01]
Tupe 2009	-0.42789	0.25358514	43	40	0.3%	-0.43 [-0.92 , 0.07]
Umeta 2000	0.109832	0.14694511	92	92	0.8%	0.11 [-0.18 , 0.40]



Analysis 1.18. (Continued)

Tupe 2009	-0.42789	0.25358514	43	40	0.3%	-0.43 [-0.92 , 0.07]
Umeta 2000	0.109832	0.14694511	92	92	0.8%	0.11 [-0.18 , 0.40]
Vakili 2015	0.342569	0.142476	100	100	0.9%	0.34 [0.06 , 0.62]
Walravens 1983	0.350119	0.31240719	20	20	0.2%	0.35 [-0.26 , 0.96]
Walravens 1989	0.478085	0.28247531	25	25	0.2%	0.48 [-0.08 , 1.03]
Wuehler 2008	0.026577	0.11140204	313	108	1.5%	0.03 [-0.19 , 0.24]
Total (95% CI)			**10093**	**9798**	**100.0%**	**0.12 [0.10 , 0.15]**

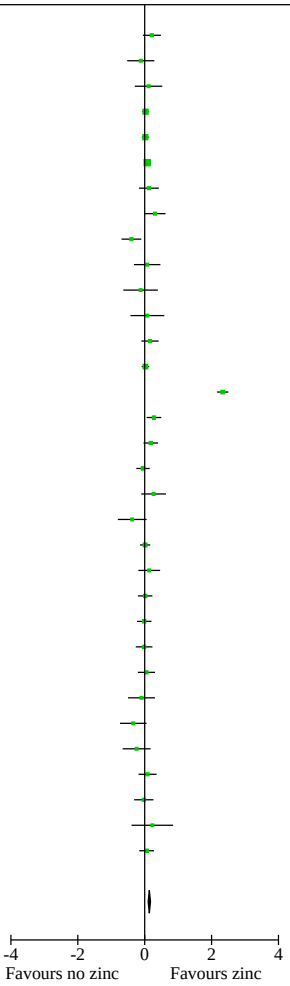
Heterogeneity: Chi² = 1140.37, df = 65 (P < 0.00001); I² = 94%
Test for overall effect: Z = 9.19 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.19. Comparison 1: Zinc versus no zinc, Outcome 19: Weight-to-height ratio

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No Zinc Mean	No Zinc SD	No Zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	1.7%	0.22 [-0.05 , 0.48]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	0.8%	-0.12 [-0.52 , 0.29]
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	0.7%	0.12 [-0.29 , 0.53]
Barffour 2019	-0.72	0.79	739	-0.74	0.82	740	11.9%	0.02 [-0.08 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	11.7%	0.02 [-0.08 , 0.12]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	17.8%	0.08 [-0.01 , 0.16]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	1.4%	0.13 [-0.17 , 0.42]
Cavan 1993	0.49	1	76	0.23	0.66	80	1.2%	0.31 [-0.01 , 0.62]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	1.4%	-0.40 [-0.69 , -0.10]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	0.8%	0.07 [-0.32 , 0.47]
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	0.5%	-0.12 [-0.64 , 0.39]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	0.5%	0.08 [-0.43 , 0.59]
Gracia 2005	0.12	1.1	115	-0.04	0.9	115	1.8%	0.16 [-0.10 , 0.42]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	9.8%	0.02 [-0.09 , 0.13]
Islam 2022	-0.64	0.03	441	-0.71	0.03	453	4.3%	2.33 [2.16 , 2.50]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	2.6%	0.28 [0.06 , 0.50]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	2.6%	0.18 [-0.04 , 0.40]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	3.1%	-0.05 [-0.25 , 0.15]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	0.9%	0.27 [-0.10 , 0.64]
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	0.7%	-0.37 [-0.80 , 0.06]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	5.3%	0.01 [-0.14 , 0.17]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	1.2%	0.14 [-0.19 , 0.46]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	2.6%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	2.6%	-0.01 [-0.23 , 0.20]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	2.0%	-0.02 [-0.27 , 0.23]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	1.9%	0.05 [-0.20 , 0.31]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	0.8%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	0.8%	-0.34 [-0.74 , 0.06]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	0.7%	-0.24 [-0.66 , 0.18]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	1.7%	0.09 [-0.18 , 0.35]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	1.5%	-0.03 [-0.31 , 0.26]
Walravens 1983	0.29	0.49	20	0.19	0.36	20	0.3%	0.23 [-0.39 , 0.85]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	2.6%	0.06 [-0.16 , 0.28]
Total (95% CI)			**6576**			**6372**	**100.0%**	**0.14 [0.10 , 0.17]**

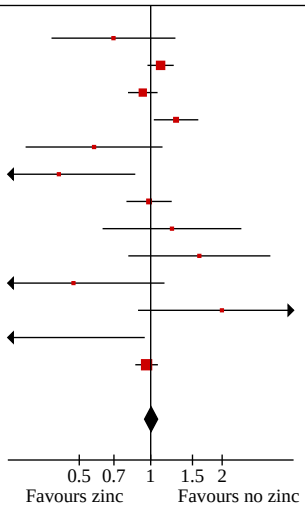
Heterogeneity: Chi² = 702.69, df = 32 (P < 0.00001); I² = 95%
Test for overall effect: Z = 7.73 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.20. Comparison 1: Zinc versus no zinc, Outcome 20: Prevalence of stunting

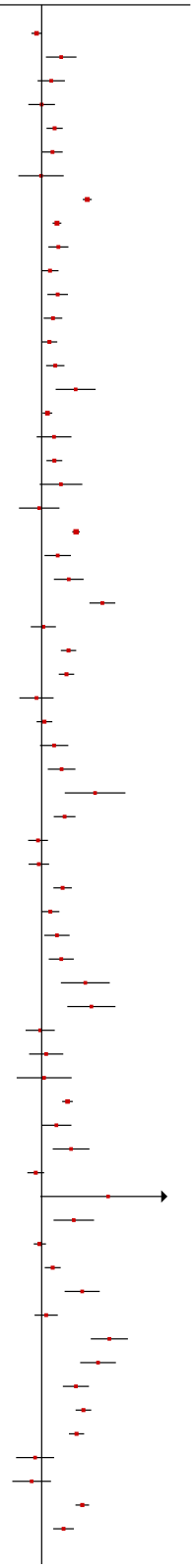
Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Abdollahi 2019	-0.3612	0.3067	272	308	1.1%	0.70 [0.38 , 1.27]
Barffour 2019	0.096038	0.06494	738	740	24.7%	1.10 [0.97 , 1.25]
Bhandari 2007	-0.07685737	0.0731752	448	427	19.4%	0.93 [0.80 , 1.07]
Hess 2015	0.246	0.1101	602	617	8.6%	1.28 [1.03 , 1.59]
Hettiarachchi 2008	-0.54956545	0.33886193	99	40	0.9%	0.58 [0.30 , 1.12]
Hettiarachchi 2008 (2)	-0.89087237	0.37822715	113	30	0.7%	0.41 [0.20 , 0.86]
Islam 2022	-0.0157	0.112	441	453	8.3%	0.98 [0.79 , 1.23]
Lind 2003	0.20642611	0.34348464	162	164	0.9%	1.23 [0.63 , 2.41]
Lind 2003 (2)	0.47187817	0.3515946	161	163	0.8%	1.60 [0.80 , 3.19]
Long 2006	-0.74934174	0.45060058	183	173	0.5%	0.47 [0.20 , 1.14]
Long 2006 (2)	0.69107321	0.41523044	181	170	0.6%	2.00 [0.88 , 4.50]
Mozaffari-Khosravi 2009	-2.07944154	1.0314499	40	45	0.1%	0.13 [0.02 , 0.94]
Soofi 2013	-0.039819767	0.055877937	622	617	33.3%	0.96 [0.86 , 1.07]
Total (95% CI)			**4062**	**3947**	**100.0%**	**1.00 [0.94 , 1.07]**

Heterogeneity: Chi² = 30.12, df = 12 (P = 0.003); I² = 60%
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Analysis 1.21. Comparison 1: Zinc versus no zinc, Outcome 21: Serum or plasma zinc concentration

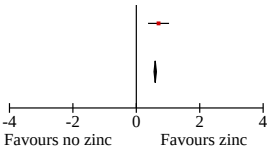
Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2019	-0.1642	0.0833	272	308	5.1%	-0.16 [-0.33 , -0.00]
Ba Lo 2011	0.6254259	0.24941159	34	32	0.6%	0.63 [0.14 , 1.11]
Baqui 2003	0.3070635	0.22305208	42	38	0.7%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	41	42	0.7%	0.00 [-0.43 , 0.43]
Becquey 2016	0.414934	0.132252	109	195	2.0%	0.41 [0.16 , 0.67]
Berger 2015	0.3469	0.1663	75	72	1.3%	0.35 [0.02 , 0.67]
Bertinato 2013	-0.019684	0.370193	27	10	0.3%	-0.02 [-0.75 , 0.71]
Bhandari 2002	1.460237	0.07309568	450	499	6.6%	1.46 [1.32 , 1.60]
Bhandari 2007	0.4903102	0.0714016	438	419	6.9%	0.49 [0.35 , 0.63]
Brown 2007	0.5352062	0.16389707	70	84	1.3%	0.54 [0.21 , 0.86]
Caulfield 2013	0.266939	0.139047	101	108	1.8%	0.27 [-0.01 , 0.54]
Cavan 1993	0.5124513	0.1679712	71	74	1.3%	0.51 [0.18 , 0.84]
Chang 2010	0.3620484	0.15223956	85	89	1.5%	0.36 [0.06 , 0.66]
Chang 2010 (2)	0.2481705	0.12815887	177	93	2.1%	0.25 [-0.00 , 0.50]
Chen 2012	0.4358568	0.149852942732796	88	93	1.6%	0.44 [0.14 , 0.73]
Clark 1999	1.0885729	0.32653377	23	19	0.3%	1.09 [0.45 , 1.73]
DiGirolamo 2010	0.1853881	0.07877571	328	318	5.7%	0.19 [0.03 , 0.34]
Fallahi 2007	0.3962728	0.28402418	24	25	0.4%	0.40 [-0.16 , 0.95]
Friis 1997	0.4064713	0.1292236	122	121	2.1%	0.41 [0.15 , 0.66]
Garcia 1998	0.6189534	0.34825576	16	17	0.3%	0.62 [-0.06 , 1.30]
Gibson 1989	-0.0788767	0.33058919	17	18	0.3%	-0.08 [-0.73 , 0.57]
Hess 2015	1.101	0.0615	617	602	9.3%	1.10 [0.98 , 1.22]
Hettiarachchi 2008	0.5136992	0.21562749	100	41	0.8%	0.51 [0.09 , 0.94]
Hettiarachchi 2008 (2)	0.8673939	0.24267158	114	30	0.6%	0.87 [0.39 , 1.34]
Hong 1982	1.9442131	0.21124116	64	67	0.8%	1.94 [1.53 , 2.36]
Kaseb 2013	0.053227	0.205245	48	47	0.8%	0.05 [-0.35 , 0.46]
Lind 2003	0.8602713	0.12535047	134	143	2.2%	0.86 [0.61 , 1.11]
Lind 2003 (2)	0.7946871	0.12563884	136	136	2.2%	0.79 [0.55 , 1.04]
Mahloudji 1975	-0.165458	0.2788914	25	25	0.5%	-0.17 [-0.71 , 0.38]
Mandlik 2020	0.0895	0.1284	119	124	2.1%	0.09 [-0.16 , 0.34]
Mazariegos 2010	0.3998476	0.23138369	35	40	0.7%	0.40 [-0.05 , 0.85]
Müller 2001	0.6383069	0.22576313	41	40	0.7%	0.64 [0.20 , 1.08]
Nakamura 1993	1.7108436	0.49561271	10	11	0.1%	1.71 [0.74 , 2.68]
Penny 2004	0.7347106	0.17762983	65	69	1.1%	0.73 [0.39 , 1.08]
Rahman 2001	-0.1159815	0.16210648	74	77	1.3%	-0.12 [-0.43 , 0.20]
Rahman 2001 (2)	-0.089988	0.16760985	71	70	1.3%	-0.09 [-0.42 , 0.24]
Richard 2006	0.6706337	0.15053466	93	92	1.6%	0.67 [0.38 , 0.97]
Richard 2006 (2)	0.2776981	0.14757993	94	90	1.6%	0.28 [-0.01 , 0.57]
Rosado 1997	0.4900139	0.20662869	48	47	0.8%	0.49 [0.09 , 0.89]
Rosado 1997 (2)	0.6277488	0.20438775	49	50	0.8%	0.63 [0.23 , 1.03]
Rosales 2004	1.397723	0.39918356	16	14	0.2%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.5917843	0.393349	18	15	0.2%	1.59 [0.82 , 2.36]
Ruz 1997	-0.0479478	0.23832669	36	33	0.6%	-0.05 [-0.52 , 0.42]
Sandstead 2008	0.1449293	0.27877714	25	25	0.5%	0.14 [-0.40 , 0.69]
Sayeg Porto 2000	0.0792674	0.44915102	9	9	0.2%	0.08 [-0.80 , 0.96]
Sazawal 1996	0.8263088	0.08664303	285	292	4.7%	0.83 [0.66 , 1.00]
Schultink 1997	0.4714449	0.24494512	33	34	0.6%	0.47 [-0.01 , 0.95]
Sempértegui 1996	0.9419596	0.30001048	23	25	0.4%	0.94 [0.35 , 1.53]
Shankar 2000	-0.1895463	0.13723333	103	109	1.9%	-0.19 [-0.46 , 0.08]
Silva 2006	2.1275749	1.10761519	28	30	0.0%	2.13 [-0.04 , 4.30]
Smith 1999	1.028717	0.33059672	20	20	0.3%	1.03 [0.38 , 1.68]
Soofi 2013	-0.0581411	0.099716268	198	203	3.6%	-0.06 [-0.25 , 0.14]
Tielsch 2006	0.3533933	0.13023913	152	146	2.1%	0.35 [0.10 , 0.61]
Tupe 2009	1.2972891	0.28675374	43	40	0.4%	1.30 [0.74 , 1.86]
Uçkardeş 2009	0.1443531	0.18964639	56	54	1.0%	0.14 [-0.23 , 0.52]
Udomkesmalee 1992	2.1672463	0.30343932	33	35	0.4%	2.17 [1.57 , 2.76]
Udomkesmalee 1992 (2)	1.8051936	0.29181765	32	33	0.4%	1.81 [1.23 , 2.38]
Umeta 2000	1.0964071	0.21307062	50	50	0.8%	1.10 [0.68 , 1.51]
Veenemans 2011	1.3365769	0.1276632	149	150	2.2%	1.34 [1.09 , 1.59]
Veenemans 2011 (2)	1.1162615	0.12407823	148	151	2.3%	1.12 [0.87 , 1.36]
Walravens 1983	-0.2100284	0.31083333	20	20	0.4%	-0.21 [-0.82 , 0.40]
Walravens 1989	-0.3204417	0.3159476	16	25	0.4%	-0.32 [-0.94 , 0.30]
Wessells 2012	1.3007638	0.11129748	279	146	2.9%	1.30 [1.08 , 1.52]
Wuehler 2008	0.7012294	0.16887846	142	49	1.2%	0.70 [0.37 , 1.03]



Analysis 1.21. (Continued)

Wuehler 2008	0.7012294	0.16887846	142	49	1.2%	0.70 [0.37 , 1.03]
Total (95% CI)			**6461**	**6183**	**100.0%**	**0.60 [0.56 , 0.63]**

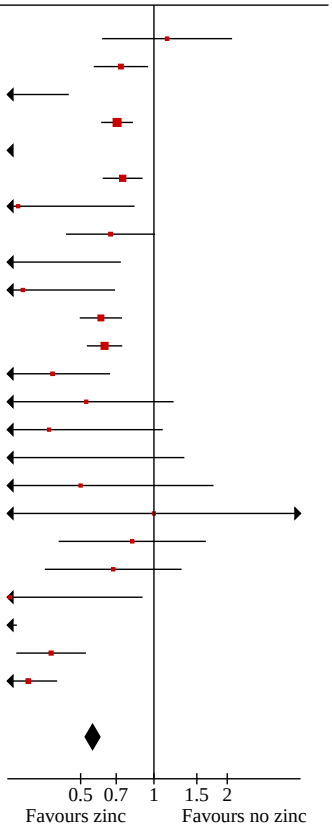
Heterogeneity: Chi² = 769.87, df = 63 (P < 0.00001); I² = 92%
Test for overall effect: Z = 31.72 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.22. Comparison 1: Zinc versus no zinc, Outcome 22: Prevalence of zinc deficiency

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Abdollahi 2019	0.1243	0.3136	272	308	1.3%	1.13 [0.61 , 2.09]
Albert 2003	-0.311863	0.131122	63	63	7.4%	0.73 [0.57 , 0.95]
Albert 2003 (2)	-1.96217067	0.59027952	62	61	0.4%	0.14 [0.04 , 0.45]
Barffour 2019	-0.348307	0.076539	145	140	21.7%	0.71 [0.61 , 0.82]
Bhandari 2002	-2.39729649	0.21748349	450	499	2.7%	0.09 [0.06 , 0.14]
Bhandari 2007	-0.29566242	0.09609274	438	419	13.8%	0.74 [0.62 , 0.90]
DiGirolamo 2010	-1.28372519	0.56145805	328	318	0.4%	0.28 [0.09 , 0.83]
Hess 2015	-0.4103	0.2148	617	602	2.8%	0.66 [0.44 , 1.01]
Hettiarachchi 2008	-1.40242374	0.55584104	100	41	0.4%	0.25 [0.08 , 0.73]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	114	30	0.6%	0.29 [0.12 , 0.69]
Lind 2003	-0.50139064	0.10210941	134	143	12.2%	0.61 [0.50 , 0.74]
Lind 2003 (2)	-0.46661953	0.08533585	136	136	17.4%	0.63 [0.53 , 0.74]
Müller 2001	-0.95900185	0.2779085	41	40	1.6%	0.38 [0.22 , 0.66]
Rosado 1997	-0.64009262	0.42150954	48	47	0.7%	0.53 [0.23 , 1.20]
Rosado 1997 (2)	-0.9913982	0.54817965	49	50	0.4%	0.37 [0.13 , 1.09]
Rosales 2004	-2.52305842	1.43399023	16	14	0.1%	0.08 [0.00 , 1.33]
Rosales 2004 (2)	-0.69314718	0.64117947	18	15	0.3%	0.50 [0.14 , 1.76]
Sayeg Porto 2000	0	0.8819171	9	9	0.2%	1.00 [0.18 , 5.63]
Shankar 2000	-0.20479441	0.35491126	54	56	1.0%	0.81 [0.41 , 1.63]
Tielsch 2006	-0.38511439	0.32989001	152	146	1.2%	0.68 [0.36 , 1.30]
Tupe 2009	-1.3600085	0.63908093	59	53	0.3%	0.26 [0.07 , 0.90]
Veenemans 2011	-1.77459918	0.24422989	149	150	2.1%	0.17 [0.11 , 0.27]
Veenemans 2011 (2)	-0.97206125	0.16780856	148	151	4.5%	0.38 [0.27 , 0.53]
Wessells 2012	-1.18817275	0.13936783	279	146	6.5%	0.30 [0.23 , 0.40]
Total (95% CI)			**3881**	**3637**	**100.0%**	**0.56 [0.52 , 0.60]**

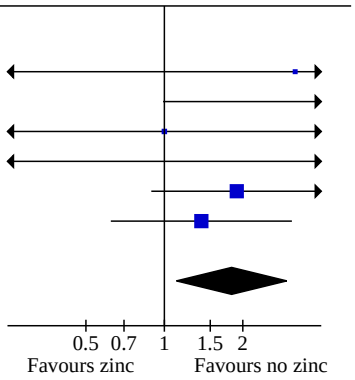
Heterogeneity: Chi² = 167.52, df = 23 (P < 0.00001); I² = 86%
Test for overall effect: Z = 16.28 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.23. Comparison 1: Zinc versus no zinc, Outcome 23: Study withdrawal

Study or Subgroup	Zinc Events	Zinc Total	No zinc Events	No zinc Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Mazariegos 2010	0	204	0	208		Not estimable
Meeks Gardner 2005	1	67	0	71	2.0%	3.18 [0.13 , 76.64]
Bhandari 2002	8	1228	0	1236	2.0%	17.11 [0.99 , 296.12]
Kurugöl 2006	1	100	1	100	4.1%	1.00 [0.06 , 15.77]
Alarcon 2004	0	112	2	111	10.2%	0.20 [0.01 , 4.08]
Islam 2022	19	482	10	481	40.8%	1.90 [0.89 , 4.04]
Kartasurya 2012	14	415	10	411	40.9%	1.39 [0.62 , 3.09]
Total (95% CI)		**2608**		**2618**	**100.0%**	**1.81 [1.11 , 2.95]**
Total events:	43		23			

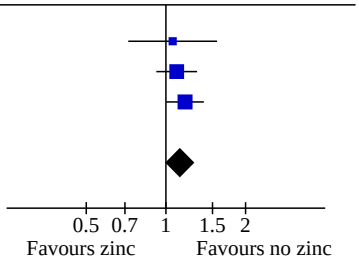
Heterogeneity: Chi² = 5.18, df = 5 (P = 0.39); I² = 3%
Test for overall effect: Z = 2.39 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.24. Comparison 1: Zinc versus no zinc, Outcome 24: Participants with ≥ 1 side effect

Study or Subgroup	Zinc Events	Zinc Total	No zinc Events	No zinc Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Kurugöl 2006	35	100	33	100	14.9%	1.06 [0.72 , 1.56]
Lind 2003	102	162	94	164	42.1%	1.10 [0.92 , 1.31]
Lind 2003 (2)	112	161	96	163	43.0%	1.18 [1.00 , 1.39]
Total (95% CI)		**423**		**427**	**100.0%**	**1.13 [1.00 , 1.27]**
Total events:	249		223			

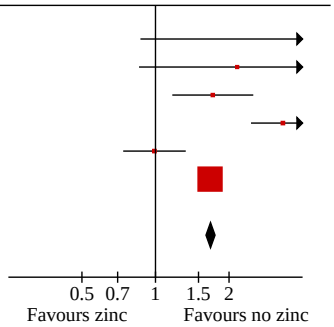
Heterogeneity: Chi² = 0.49, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 2.02 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 1.25. Comparison 1: Zinc versus no zinc, Outcome 25: Vomiting episodes

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Chhagan 2009	1.95357302	1.06904497	104	105	0.0%	7.05 [0.87 , 57.33]
Malik 2014	0.769739626	0.471771168	134	124	0.2%	2.16 [0.86 , 5.44]
Chang 2010	0.54004814	0.19466389	198	201	1.2%	1.72 [1.17 , 2.51]
Chang 2010 (2)	1.20076358	0.15327943	400	201	2.0%	3.32 [2.46 , 4.49]
Penny 2004	-0.0095101	0.1503508	81	83	2.1%	0.99 [0.74 , 1.33]
Bhandari 2002	0.51422096	0.02237259	1228	1236	94.4%	1.67 [1.60 , 1.75]
Total (95% CI)			**2145**	**1950**	**100.0%**	**1.68 [1.61 , 1.75]**

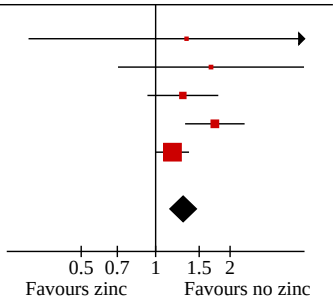
Heterogeneity: Chi² = 34.28, df = 5 (P < 0.00001); I² = 85%
Test for overall effect: Z = 23.86 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.26. Comparison 1: Zinc versus no zinc, Outcome 26: Participants with ≥ 1 vomiting episode

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Kurugöl 2006	0.28768207	0.75055535	100	100	0.7%	1.33 [0.31 , 5.81]
Gupta 2007	0.51549853	0.44177764	854	858	2.0%	1.67 [0.70 , 3.98]
Lind 2003	0.25343215	0.16826769	162	164	13.9%	1.29 [0.93 , 1.79]
Lind 2003 (2)	0.55134234	0.14130384	161	163	19.7%	1.74 [1.32 , 2.29]
Bhandari 2007	0.15688142	0.0785542	16289	16341	63.7%	1.17 [1.00 , 1.36]
Total (95% CI)			**17566**	**17626**	**100.0%**	**1.29 [1.14 , 1.46]**

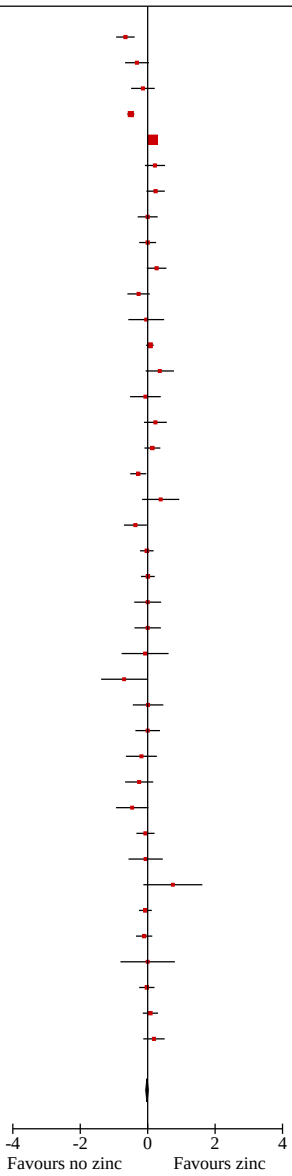
Heterogeneity: Chi² = 6.31, df = 4 (P = 0.18); I² = 37%
Test for overall effect: Z = 4.08 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 1.27. Comparison 1: Zinc versus no zinc, Outcome 27: Blood hemoglobin concentration

Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Alarcon 2004	-0.65988	0.14027963	109	104	1.6%	-0.66 [-0.93 , -0.38]
Baqui 2003	-0.31819	0.17973118	64	60	1.0%	-0.32 [-0.67 , 0.03]
Baqui 2003 (2)	-0.1408	0.1787069	57	68	1.0%	-0.14 [-0.49 , 0.21]
Barffour 2019	-0.49974	0.053375	722	726	11.3%	-0.50 [-0.60 , -0.40]
Becquey 2016	0.150661	0.031845	1720	2326	31.8%	0.15 [0.09 , 0.21]
Brown 2007	0.215756	0.15252629	81	91	1.4%	0.22 [-0.08 , 0.51]
Caulfield 2013	0.2349	0.1389	101	108	1.7%	0.23 [-0.04 , 0.51]
Chang 2010	0	0.15099742	85	89	1.4%	0.00 [-0.30 , 0.30]
Chang 2010 (2)	0	0.12771313	177	93	2.0%	0.00 [-0.25 , 0.25]
Chen 2012	0.26447	0.148742524	88	93	1.5%	0.26 [-0.03 , 0.56]
Chhagan 2009	-0.26859	0.1695139	71	68	1.1%	-0.27 [-0.60 , 0.06]
Fallahi 2007	-0.04319	0.27074191	26	27	0.4%	-0.04 [-0.57 , 0.49]
Hess 2015	0.0666	0.0573	617	602	9.8%	0.07 [-0.05 , 0.18]
Hettiarachchi 2008	0.359586	0.21415043	100	41	0.7%	0.36 [-0.06 , 0.78]
Hettiarachchi 2008 (2)	-0.06685	0.23201837	116	31	0.6%	-0.07 [-0.52 , 0.39]
Larson 2010	0.229456	0.17236099	67	67	1.1%	0.23 [-0.11 , 0.57]
Lind 2003	0.140477	0.12005207	134	143	2.2%	0.14 [-0.09 , 0.38]
Lind 2003 (2)	-0.27972	0.12152387	136	136	2.2%	-0.28 [-0.52 , -0.04]
Mahloudji 1975	0.386072	0.28106433	25	25	0.4%	0.39 [-0.16 , 0.94]
Penny 2004	-0.36438	0.17330205	65	69	1.1%	-0.36 [-0.70 , -0.02]
Richard 2006	-0.02458	0.10239943	191	189	3.1%	-0.02 [-0.23 , 0.18]
Richard 2006 (2)	0.006531	0.10404523	185	183	3.0%	0.01 [-0.20 , 0.21]
Rosado 1997	0	0.20354768	48	47	0.8%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	49	50	0.8%	0.00 [-0.39 , 0.39]
Rosales 2004	-0.07679	0.3554178	15	15	0.3%	-0.08 [-0.77 , 0.62]
Rosales 2004 (2)	-0.69864	0.34771623	19	15	0.3%	-0.70 [-1.38 , -0.02]
Ruz 1997	0.011349	0.23082689	40	34	0.6%	0.01 [-0.44 , 0.46]
Sazawal 1996	0	0.18560454	61	54	0.9%	0.00 [-0.36 , 0.36]
Sazawal 2006	-0.1856	0.2338561	54	61	0.6%	-0.19 [-0.64 , 0.27]
Sazawal 2006 (2)	-0.25258	0.21260589	56	54	0.7%	-0.25 [-0.67 , 0.16]
Schultink 1997	-0.45927	0.24477245	33	34	0.5%	-0.46 [-0.94 , 0.02]
Shankar 2000	-0.0656	0.13696131	103	109	1.7%	-0.07 [-0.33 , 0.20]
Silva 2006	-0.06048	0.259294937	28	30	0.5%	-0.06 [-0.57 , 0.45]
Smith 1999	0.746471	0.44636222	11	9	0.2%	0.75 [-0.13 , 1.62]
Soofi 2013	-0.06694	0.096656017	217	210	3.4%	-0.07 [-0.26 , 0.12]
Tielsch 2006 (2)	-0.10462	0.12265454	182	152	2.1%	-0.10 [-0.35 , 0.14]
Tupe 2009	0	0.41177862	43	40	0.2%	0.00 [-0.81 , 0.81]
Veenemans 2011	-0.02525	0.11537593	149	150	2.4%	-0.03 [-0.25 , 0.20]
Veenemans 2011 (2)	0.081227	0.11542427	148	151	2.4%	0.08 [-0.15 , 0.31]
Wuehler 2008	0.186979	0.16202415	148	51	1.2%	0.19 [-0.13 , 0.50]
Total (95% CI)			**6341**	**6605**	**100.0%**	**-0.02 [-0.05 , 0.02]**

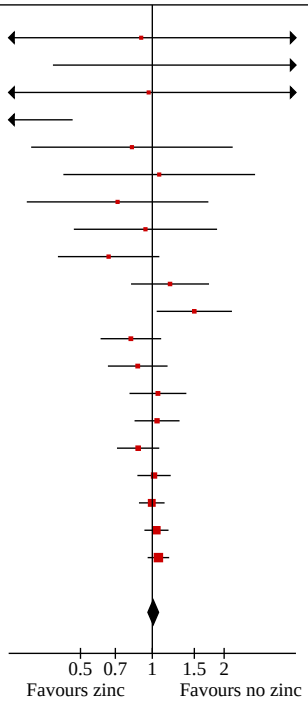
Heterogeneity: Chi² = 180.16, df = 39 (P < 0.00001); I² = 78%
Test for overall effect: Z = 1.10 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 1.28. Comparison 1: Zinc versus no zinc, Outcome 28: Prevalence of anemia

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Tupe 2009	-0.10724553	2.6517494	59	53	0.0%	0.90 [0.00 , 162.40]
Tielsch 2006 (2)	1.42931175	1.21856809	182	152	0.0%	4.18 [0.38 , 45.50]
Sazawal 2006 (2)	-0.03509132	0.78550816	319	308	0.1%	0.97 [0.21 , 4.50]
Alarcon 2004	-1.79615684	0.5241074	109	104	0.2%	0.17 [0.06 , 0.46]
Rosado 1997	-0.19671029	0.49610282	42	46	0.3%	0.82 [0.31 , 2.17]
Hettiarachchi 2008 (2)	0.06669137	0.47195062	116	31	0.3%	1.07 [0.42 , 2.70]
Rosado 1997 (2)	-0.33516874	0.44703626	46	47	0.3%	0.72 [0.30 , 1.72]
Shankar 2000	-0.0661398	0.35260528	100	108	0.6%	0.94 [0.47 , 1.87]
Hettiarachchi 2008	-0.42159449	0.24965948	100	41	1.1%	0.66 [0.40 , 1.07]
Soofi 2013	0.170994927	0.191953448	162	166	1.9%	1.19 [0.81 , 1.73]
Lind 2003 (2)	0.40546511	0.18523964	136	136	2.0%	1.50 [1.04 , 2.16]
Lind 2003	-0.20692889	0.14916654	134	143	3.1%	0.81 [0.61 , 1.09]
Sazawal 2006	-0.14064043	0.14680505	44	58	3.2%	0.87 [0.65 , 1.16]
Chhagan 2009	0.05427392	0.13991047	67	64	3.5%	1.06 [0.80 , 1.39]
Veenemans 2011 (2)	0.04570999	0.11075183	148	151	5.6%	1.05 [0.84 , 1.30]
Brown 2007	-0.13703855	0.10402621	81	91	6.3%	0.87 [0.71 , 1.07]
Veenemans 2011	0.01673932	0.0819935	149	150	10.2%	1.02 [0.87 , 1.19]
Chang 2010 (2)	-0.0052113	0.06303318	177	120	17.3%	0.99 [0.88 , 1.13]
Barffour 2019	0.040065	0.05932	722	726	19.5%	1.04 [0.93 , 1.17]
Chang 2010	0.05888852	0.05297985	85	89	24.4%	1.06 [0.96 , 1.18]
Total (95% CI)			**2978**	**2784**	**100.0%**	**1.01 [0.96 , 1.06]**

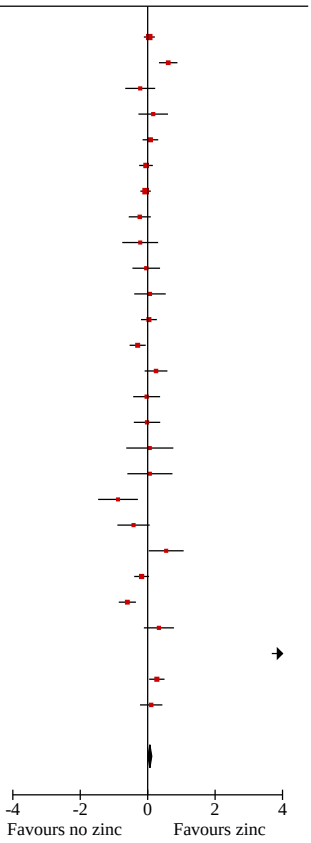
Heterogeneity: Chi² = 28.86, df = 19 (P = 0.07); I² = 34%
Test for overall effect: Z = 0.34 (P = 0.74)
Test for subgroup differences: Not applicable



Analysis 1.29. Comparison 1: Zinc versus no zinc, Outcome 29: Serum or plasma ferritin concentration

Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2019	0.0499	0.0832	272	308	11.8%	0.05 [-0.11 , 0.21]
Alarcon 2004	0.609097	0.13973937	109	104	4.2%	0.61 [0.34 , 0.88]
Baqui 2003	-0.22141	0.22650955	40	37	1.6%	-0.22 [-0.67 , 0.22]
Baqui 2003 (2)	0.164061	0.22336122	41	38	1.6%	0.16 [-0.27 , 0.60]
Becquey 2016	0.08108	0.118537	145	140	5.8%	0.08 [-0.15 , 0.31]
Bhandari 2002	-0.04944	0.1033257	172	204	7.7%	-0.05 [-0.25 , 0.15]
Bhandari 2007	-0.06163	0.07921676	354	323	13.1%	-0.06 [-0.22 , 0.09]
Brown 2007	-0.23437	0.16675888	67	77	2.9%	-0.23 [-0.56 , 0.09]
Fallahi 2007	-0.22115	0.27156027	26	27	1.1%	-0.22 [-0.75 , 0.31]
Hettiarachchi 2008	-0.04255	0.20891616	101	43	1.9%	-0.04 [-0.45 , 0.37]
Hettiarachchi 2008 (2)	0.068376	0.23842946	115	29	1.4%	0.07 [-0.40 , 0.54]
Lind 2003	0.036753	0.1199138	134	143	5.7%	0.04 [-0.20 , 0.27]
Lind 2003 (2)	-0.29683	0.12159844	136	136	5.5%	-0.30 [-0.54 , -0.06]
Penny 2004	0.247714	0.17253156	65	69	2.8%	0.25 [-0.09 , 0.59]
Rosado 1997	-0.03062	0.20355981	48	47	2.0%	-0.03 [-0.43 , 0.37]
Rosado 1997 (2)	-0.01974	0.19946448	49	50	2.1%	-0.02 [-0.41 , 0.37]
Rosales 2004	0.063304	0.35616542	16	14	0.6%	0.06 [-0.63 , 0.76]
Rosales 2004 (2)	0.066212	0.34117341	18	15	0.7%	0.07 [-0.60 , 0.73]
Sandstead 2008	-0.87998	0.30091972	24	23	0.9%	-0.88 [-1.47 , -0.29]
Schultink 1997	-0.41923	0.24423569	33	34	1.4%	-0.42 [-0.90 , 0.06]
Silva 2006	0.548783	0.264194167	28	30	1.2%	0.55 [0.03 , 1.07]
Soofi 2013	-0.17988	0.11229157	159	158	6.5%	-0.18 [-0.40 , 0.04]
Tielsch 2006 (2)	-0.60298	0.12976071	164	146	4.9%	-0.60 [-0.86 , -0.35]
Tupe 2009	0.333026	0.22748483	43	40	1.6%	0.33 [-0.11 , 0.78]
Veenemans 2011	4.078946	0.202812589	150	149	2.0%	4.08 [3.68 , 4.48]
Veenemans 2011 (2)	0.271917	0.11591106	151	148	6.1%	0.27 [0.04 , 0.50]
Wuehler 2008	0.103987	0.16907035	91	56	2.9%	0.10 [-0.23 , 0.44]
Total (95% CI)			**2751**	**2588**	**100.0%**	**0.06 [0.01 , 0.12]**

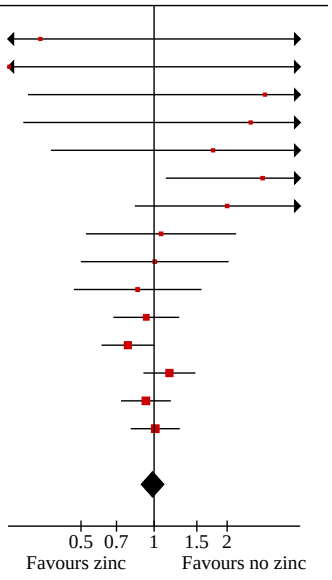
Heterogeneity: Chi² = 480.55, df = 26 (P < 0.00001); I² = 95%
Test for overall effect: Z = 2.25 (P = 0.02)
Test for subgroup differences: Not applicable



Analysis 1.30. Comparison 1: Zinc versus no zinc, Outcome 30: Prevalence of iron deficiency

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Veenemans 2011 (2)	-1.07867807	1.62891875	148	151	0.1%	0.34 [0.01 , 8.28]
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	115	29	0.1%	0.25 [0.01 , 5.96]
Alarcon 2004	1.05165531	1.14653549	109	104	0.2%	2.86 [0.30 , 27.08]
Rosales 2004 (2)	0.91629073	1.10050493	18	15	0.2%	2.50 [0.29 , 21.61]
Rosales 2004	0.55961579	0.78490218	16	14	0.5%	1.75 [0.38 , 8.15]
Tielsch 2006 (2)	1.0288725	0.46819442	164	146	1.3%	2.80 [1.12 , 7.00]
Lind 2003 (2)	0.69314718	0.44674359	136	136	1.5%	2.00 [0.83 , 4.80]
Rosado 1997	0.06595797	0.36350034	48	47	2.2%	1.07 [0.52 , 2.18]
Hettiarachchi 2008	0.00628086	0.35773941	101	43	2.3%	1.01 [0.50 , 2.03]
Veenemans 2011	-0.15582994	0.30894248	149	150	3.0%	0.86 [0.47 , 1.57]
Lind 2003	-0.07383161	0.15918361	134	143	11.5%	0.93 [0.68 , 1.27]
Brown 2007	-0.24865273	0.12751685	67	77	17.9%	0.78 [0.61 , 1.00]
Bhandari 2007	0.145356	0.12569767	354	323	18.4%	1.16 [0.90 , 1.48]
Sazawal 2006	-0.07738666	0.12047289	44	58	20.1%	0.93 [0.73 , 1.17]
Sazawal 2006 (2)	0.0112604	0.11869286	56	54	20.7%	1.01 [0.80 , 1.28]
Total (95% CI)			**1659**	**1490**	**100.0%**	**0.99 [0.89 , 1.10]**

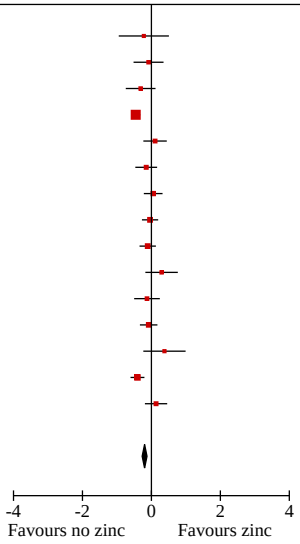
Heterogeneity: Chi² = 16.44, df = 14 (P = 0.29); I² = 15%
Test for overall effect: Z = 0.27 (P = 0.79)
Test for subgroup differences: Not applicable



Analysis 1.31. Comparison 1: Zinc versus no zinc, Outcome 31: Serum or plasma copper concentration

Study or Subgroup	Std. Mean Difference	SE	Zinc Total	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Abdollahi 2014	-0.21991	0.371172	27	10	0.9%	-0.22 [-0.95 , 0.51]
Baqui 2003	-0.08319	0.22182466	42	38	2.6%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.31239	0.22014163	41	41	2.6%	-0.31 [-0.74 , 0.12]
Bhandari 2002	-0.45543	0.0664687	440	490	28.9%	-0.46 [-0.59 , -0.33]
Bhandari 2007	0.10597	0.1732339	79	63	4.3%	0.11 [-0.23 , 0.45]
Brown 2007	-0.15036	0.16126262	70	84	4.9%	-0.15 [-0.47 , 0.17]
Caulfield 2013	0.051391	0.138444	101	108	6.7%	0.05 [-0.22 , 0.32]
Lind 2003	-0.03911	0.11991514	134	143	8.9%	-0.04 [-0.27 , 0.20]
Lind 2003 (2)	-0.10717	0.12101791	136	136	8.7%	-0.11 [-0.34 , 0.13]
Ruz 1997	0.295163	0.24001271	37	32	2.2%	0.30 [-0.18 , 0.77]
Sazawal 1996	-0.12808	0.189844	58	52	3.5%	-0.13 [-0.50 , 0.24]
Tielsch 2006	-0.07976	0.12950733	152	145	7.6%	-0.08 [-0.33 , 0.17]
Walravens 1983	0.378517	0.31282088	20	20	1.3%	0.38 [-0.23 , 0.99]
Wessells 2012	-0.4044	0.10290265	279	146	12.1%	-0.40 [-0.61 , -0.20]
Wuehler 2008	0.134643	0.16487845	144	49	4.7%	0.13 [-0.19 , 0.46]
Total (95% CI)			**1760**	**1557**	**100.0%**	**-0.20 [-0.27 , -0.13]**

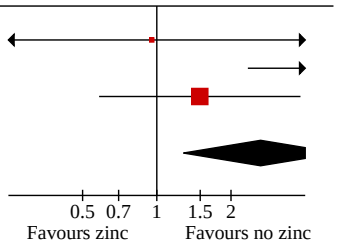
Heterogeneity: Chi² = 40.95, df = 14 (P = 0.0002); I² = 66%
Test for overall effect: Z = 5.54 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.32. Comparison 1: Zinc versus no zinc, Outcome 32: Prevalence of copper deficiency

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	No zinc Total	Weight	Risk Ratio IV, Fixed, 95% CI
Tielsch 2006	-0.04714678	1.57580317	152	145	5.4%	0.95 [0.04 , 20.93]
Bhandari 2002	2.05354081	0.61370908	440	490	35.9%	7.80 [2.34 , 25.96]
Sazawal 1996	0.40162633	0.47978591	58	52	58.7%	1.49 [0.58 , 3.83]
Total (95% CI)			**650**	**687**	**100.0%**	**2.64 [1.28 , 5.42]**

Heterogeneity: Chi² = 4.94, df = 2 (P = 0.08); I² = 59%
Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: Not applicable



Comparison 2. Zinc versus no zinc: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 All-cause mortality: age subgroup analysis	18		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.1.1 6 months to < 1 year	8		Risk Ratio (IV, Fixed, 95% CI)	0.98 [0.82, 1.17]
2.1.2 1 to < 5 years	11		Risk Ratio (IV, Fixed, 95% CI)	0.89 [0.80, 0.99]
2.2 All-cause mortality: dose subgroup analysis	20		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.2.1 0 to < 5 mg	2		Risk Ratio (IV, Fixed, 95% CI)	0.72 [0.08, 6.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2.2 5 to < 10 mg	3		Risk Ratio (IV, Fixed, 95% CI)	0.61 [0.37, 0.98]
2.2.3 10 to < 15 mg	11		Risk Ratio (IV, Fixed, 95% CI)	0.93 [0.84, 1.02]
2.2.4 20 mg or more	4		Risk Ratio (IV, Fixed, 95% CI)	0.39 [0.05, 2.94]
2.3 All-cause mortality: duration subgroup analysis	18		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.3.1 0 to < 6 months	4		Risk Ratio (IV, Fixed, 95% CI)	0.55 [0.33, 0.90]
2.3.2 6 to < 12 months	8		Risk Ratio (IV, Fixed, 95% CI)	0.70 [0.39, 1.24]
2.3.3 12 months or more	6		Risk Ratio (IV, Fixed, 95% CI)	0.93 [0.85, 1.03]
2.4 All-cause mortality: iron co-interventions subgroup analysis	17		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.4.1 Iron co-intervention	4		Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.86, 1.15]
2.4.2 No iron co-intervention	13		Risk Ratio (IV, Fixed, 95% CI)	0.87 [0.78, 0.97]
2.5 All-cause mortality: formulation subgroup analysis	18		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.5.1 Solution	6		Risk Ratio (IV, Fixed, 95% CI)	0.98 [0.29, 3.35]
2.5.2 Pill/tablet	10		Risk Ratio (IV, Fixed, 95% CI)	0.91 [0.83, 1.00]
2.5.3 Capsule	1		Risk Ratio (IV, Fixed, 95% CI)	0.51 [0.05, 5.60]
2.5.4 Powder	1		Risk Ratio (IV, Fixed, 95% CI)	0.71 [0.27, 1.86]
2.6 Incidence of all-cause diarrhea: age subgroup analysis	38		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.6.1 6 months to < 1 year	16		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.87, 0.92]
2.6.2 1 to < 5 years	21		Risk Ratio (IV, Fixed, 95% CI)	0.87 [0.85, 0.89]
2.6.3 5 to < 13 years	2		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.81, 0.98]
2.7 Incidence of all-cause diarrhea: dose subgroup analysis	39		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.7.1 0 to < 5 mg	7		Risk Ratio (IV, Fixed, 95% CI)	0.95 [0.89, 1.01]
2.7.2 5 to < 10 mg	9		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.85, 0.91]
2.7.3 10 to < 15 mg	14		Risk Ratio (IV, Fixed, 95% CI)	0.96 [0.93, 1.00]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.7.4 15 to < 20 mg	3		Risk Ratio (IV, Fixed, 95% CI)	0.61 [0.58, 0.65]
2.7.5 20 mg or more	8		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.87, 0.94]
2.8 Incidence of all-cause diarrhea: duration subgroup analysis	38		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.8.1 0 to < 6 months	8		Risk Ratio (IV, Fixed, 95% CI)	0.89 [0.85, 0.93]
2.8.2 6 to < 12 months	21		Risk Ratio (IV, Fixed, 95% CI)	0.87 [0.85, 0.89]
2.8.3 12 months or more	9		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.82, 0.95]
2.9 Incidence of all-cause diarrhea: iron co-interventions subgroup analysis	39		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.9.1 Iron co-intervention	10		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.96, 1.05]
2.9.2 No iron co-intervention	30		Risk Ratio (IV, Fixed, 95% CI)	0.85 [0.83, 0.87]
2.10 Incidence of all-cause diarrhea: formulation subgroup analysis	37		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.10.1 Solution	26		Risk Ratio (IV, Fixed, 95% CI)	0.85 [0.82, 0.87]
2.10.2 Pill/tablet	7		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.87, 0.93]
2.10.3 Capsule	2		Risk Ratio (IV, Fixed, 95% CI)	0.78 [0.60, 1.01]
2.10.4 Powder	2		Risk Ratio (IV, Fixed, 95% CI)	1.04 [0.98, 1.09]
2.11 Prevalence of all-cause diarrhea: age subgroup analysis	15		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.11.1 6 months to < 1 year	8		Risk Ratio (IV, Fixed, 95% CI)	0.96 [0.93, 1.00]
2.11.2 1 to < 5 years	8		Risk Ratio (IV, Fixed, 95% CI)	0.85 [0.83, 0.87]
2.12 Prevalence of all-cause diarrhea: dose subgroup analysis	15		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.12.1 0 to < 5 mg	3		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.92, 1.08]
2.12.2 5 to < 10 mg	1		Risk Ratio (IV, Fixed, 95% CI)	1.17 [0.60, 2.28]
2.12.3 10 to < 15 mg	6		Risk Ratio (IV, Fixed, 95% CI)	0.93 [0.90, 0.96]
2.12.4 15 to < 20 mg	1		Risk Ratio (IV, Fixed, 95% CI)	0.61 [0.54, 0.69]
2.12.5 20 mg or more	4		Risk Ratio (IV, Fixed, 95% CI)	0.85 [0.82, 0.87]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.13 Prevalence of all-cause diarrhea: duration subgroup analysis	15		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.13.1 0 to < 6 months	4		Risk Ratio (IV, Fixed, 95% CI)	0.85 [0.82, 0.87]
2.13.2 6 to < 12 months	10		Risk Ratio (IV, Fixed, 95% CI)	0.92 [0.89, 0.95]
2.13.3 12 months or more	1		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.74, 1.03]
2.14 Prevalence of all-cause diarrhea: iron co-interventions subgroup analysis	15		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.14.1 Iron co-intervention	3		Risk Ratio (IV, Fixed, 95% CI)	0.96 [0.88, 1.05]
2.14.2 No iron co-intervention	12		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.86, 0.90]
2.15 Prevalence of all-cause diarrhea: formulation subgroup analysis	15		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.15.1 Solution	9		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.85, 0.90]
2.15.2 Pill/tablet	5		Risk Ratio (IV, Fixed, 95% CI)	0.86 [0.81, 0.92]
2.15.3 Powder	1		Risk Ratio (IV, Fixed, 95% CI)	1.03 [0.95, 1.12]
2.16 Incidence of LRTI: age subgroup analysis	22		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.16.1 6 months to < 1 year	9		Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.90, 1.09]
2.16.2 1 to < 5 years	11		Risk Ratio (IV, Fixed, 95% CI)	1.05 [0.96, 1.16]
2.16.3 5 to < 13 years	2		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.72, 1.40]
2.17 Incidence of LRTI: dose subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.17.1 0 to < 5 mg	3		Risk Ratio (IV, Fixed, 95% CI)	0.94 [0.78, 1.13]
2.17.2 10 to < 15 mg	9		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.93, 1.12]
2.17.3 20 mg or more	7		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.92, 1.13]
2.18 Incidence of LRTI: duration subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.18.1 0 to < 6 months	3		Risk Ratio (IV, Fixed, 95% CI)	1.03 [0.92, 1.14]
2.18.2 6 to < 12 months	12		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.92, 1.08]
2.18.3 12 months or more	4		Risk Ratio (IV, Fixed, 95% CI)	1.08 [0.83, 1.42]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.19 Incidence of LRTI: iron co-interventions subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.19.1 Iron co-intervention	6		Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.87, 1.12]
2.19.2 No iron co-intervention	13		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.95, 1.10]
2.20 Incidence of LRTI: formulation subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.20.1 Solution	14		Risk Ratio (IV, Fixed, 95% CI)	0.98 [0.91, 1.05]
2.20.2 Pill/tablet	2		Risk Ratio (IV, Fixed, 95% CI)	1.25 [1.02, 1.53]
2.20.3 Capsule	2		Risk Ratio (IV, Fixed, 95% CI)	1.12 [0.84, 1.51]
2.20.4 Powder	1		Risk Ratio (IV, Fixed, 95% CI)	1.25 [0.75, 2.09]
2.21 Height: country income level subgroup analysis	75		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.21.1 Low- or middle-income	67		Std. Mean Difference (IV, Fixed, 95% CI)	0.11 [0.09, 0.14]
2.21.2 High-income	8		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.11, 0.25]
2.22 Height: age subgroup analysis	72		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.22.1 6 months to < 1 year	15		Std. Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.07, 0.03]
2.22.2 1 to < 5 years	33		Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [0.05, 0.11]
2.22.3 5 to < 13 years	25		Std. Mean Difference (IV, Fixed, 95% CI)	0.20 [0.14, 0.26]
2.23 Height: stunting subgroup analysis	20		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.23.1 Stunted	11		Std. Mean Difference (IV, Fixed, 95% CI)	0.23 [0.08, 0.37]
2.23.2 Non-stunted	10		Std. Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.02, 0.24]
2.24 Height: dose subgroup analysis	70		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.24.1 0 to < 5 mg	7		Std. Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.10, 0.13]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.24.2 5 to < 10 mg	17		Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [0.10, 0.18]
2.24.3 10 to < 15 mg	31		Std. Mean Difference (IV, Fixed, 95% CI)	0.18 [0.13, 0.23]
2.24.4 15 to < 20 mg	5		Std. Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.07, 0.32]
2.24.5 20 mg or more	12		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.07, 0.04]
2.25 Height: duration subgroup analysis	75		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.25.1 0 to < 6 months	20		Std. Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.08, 0.03]
2.25.2 6 to < 12 months	39		Std. Mean Difference (IV, Fixed, 95% CI)	0.16 [0.13, 0.19]
2.25.3 12 months or more	16		Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [0.02, 0.17]
2.26 Height: iron co-interventions subgroup analysis	65		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.26.1 Iron co-intervention	13		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.08, 0.07]
2.26.2 No iron co-intervention	52		Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [0.12, 0.17]
2.27 Height: formulation subgroup analysis	65		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.27.1 Solution	42		Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [0.08, 0.16]
2.27.2 Pill/tablet	20		Std. Mean Difference (IV, Fixed, 95% CI)	0.11 [0.07, 0.14]
2.27.3 Capsule	3		Std. Mean Difference (IV, Fixed, 95% CI)	0.31 [0.03, 0.59]
2.28 Weight: country income level subgroup analysis	67		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.28.1 Low- or middle-income	60		Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.02, 0.04]
2.28.2 High-income	7		Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.28, 0.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.29 Weight: age subgroup analysis	64		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.29.1 6 months to < 1 year	15		Std. Mean Difference (IV, Fixed, 95% CI)	-0.45 [-0.51, -0.40]
2.29.2 1 to < 5 years	30		Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.00, 0.07]
2.29.3 5 to < 13 years	21		Std. Mean Difference (IV, Fixed, 95% CI)	0.22 [0.15, 0.28]
2.30 Weight: stunting subgroup analysis	17		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.30.1 Stunted	8		Std. Mean Difference (IV, Fixed, 95% CI)	0.25 [0.09, 0.40]
2.30.2 Non-stunted	10		Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.01, 0.20]
2.31 Weight: dose subgroup analysis	63		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.31.1 0 to < 5 mg	7		Std. Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.11, 0.12]
2.31.2 5 to < 10 mg	16		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [0.03, 0.10]
2.31.3 10 to < 15 mg	28		Std. Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.21, -0.09]
2.31.4 15 to < 20 mg	4		Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.26, 0.15]
2.31.5 20 mg or more	10		Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.03, 0.09]
2.32 Weight: duration subgroup analysis	67		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.32.1 0 to < 6 months	18		Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [0.01, 0.12]
2.32.2 6 to < 12 months	34		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.04, 0.03]
2.32.3 12 months or more	15		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.09, 0.07]
2.33 Weight: iron co-interventions subgroup analysis	58		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.33.1 Iron co-intervention	11		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.01, 0.15]
2.33.2 No iron co-intervention	47		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
2.34 Weight: formulation subgroup analysis	60		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.34.1 Solution	37		Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [0.08, 0.16]
2.34.2 Pill/tablet	20		Std. Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.12, -0.05]
2.34.3 Capsule	3		Std. Mean Difference (IV, Fixed, 95% CI)	0.41 [0.12, 0.71]
2.35 Weight-to-height ratio: country income level subgroup analysis	32		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.35.1 Low- or middle-income	30	11954	Std. Mean Difference (IV, Fixed, 95% CI)	0.04 [0.00, 0.08]
2.35.2 High-income	2	100	Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [-0.25, 0.53]
2.36 Weight-to-height ratio: age subgroup analysis	30	13612	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [0.01, 0.08]
2.36.1 6 months to < 1 year	10	3778	Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.03, 0.09]
2.36.2 1 to < 5 years	16	8977	Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [0.01, 0.09]
2.36.3 5 to < 13 years	6	857	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.06, 0.20]
2.37 Weight-to-height ratio: dose subgroup analysis	31		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.37.1 0 to < 5 mg	5	671	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.08, 0.22]
2.37.2 5 to < 10 mg	9	5382	Std. Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.03, 0.07]
2.37.3 10 to < 15 mg	11	2389	Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [-0.01, 0.16]
2.37.4 15 to < 20 mg	2	194	Std. Mean Difference (IV, Fixed, 95% CI)	-0.22 [-0.50, 0.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.37.5 20 mg or more	6	3576	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.00, 0.13]
2.38 Weight-to-height ratio: duration subgroup analysis	32		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.38.1 0 to < 6 months	6	3337	Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [0.00, 0.14]
2.38.2 6 to < 12 months	21	8365	Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.01, 0.08]
2.38.3 12 months or more	5	352	Std. Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.31, 0.11]
2.39 Weight-to-height ratio: iron co-interventions subgroup analysis	30		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.39.1 Iron co-intervention	8	1409	Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [0.03, 0.24]
2.39.2 No iron co-intervention	22	8936	Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.02, 0.07]
2.40 Weight-to-height ratio: formulation subgroup analysis	31		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.40.1 Solution	22	6019	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [0.01, 0.12]
2.40.2 Pill/tablet	9	5805	Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.04, 0.06]
2.41 Serum or plasma zinc concentration: country income level subgroup analysis	64		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.41.1 Low- or middle-income	56		Std. Mean Difference (IV, Fixed, 95% CI)	0.61 [0.57, 0.65]
2.41.2 High-income	8		Std. Mean Difference (IV, Fixed, 95% CI)	0.27 [0.07, 0.46]
2.42 Serum or plasma zinc concentration: age subgroup analysis	57		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.42.1 6 months to < 1 year	13		Std. Mean Difference (IV, Fixed, 95% CI)	0.66 [0.59, 0.73]
2.42.2 1 to < 5 years	24		Std. Mean Difference (IV, Fixed, 95% CI)	0.63 [0.57, 0.68]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.42.3 5 to < 13 years	22		Std. Mean Difference (IV, Fixed, 95% CI)	0.46 [0.38, 0.54]
2.43 Serum or plasma zinc concentration: dose subgroup analysis	59		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.43.1 0 to < 5 mg	6		Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [0.21, 0.49]
2.43.2 5 to < 10 mg	12		Std. Mean Difference (IV, Fixed, 95% CI)	0.55 [0.48, 0.62]
2.43.3 10 to < 15 mg	26		Std. Mean Difference (IV, Fixed, 95% CI)	0.57 [0.51, 0.63]
2.43.4 15 to < 20 mg	8		Std. Mean Difference (IV, Fixed, 95% CI)	0.76 [0.58, 0.94]
2.43.5 20 mg or more	9		Std. Mean Difference (IV, Fixed, 95% CI)	0.88 [0.78, 0.98]
2.44 Serum or plasma zinc concentration: duration subgroup analysis	63		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.44.1 0 to < 6 months	20		Std. Mean Difference (IV, Fixed, 95% CI)	0.75 [0.68, 0.82]
2.44.2 6 to < 12 months	32		Std. Mean Difference (IV, Fixed, 95% CI)	0.54 [0.49, 0.59]
2.44.3 12 months or more	11		Std. Mean Difference (IV, Fixed, 95% CI)	0.59 [0.50, 0.67]
2.45 Serum or plasma zinc concentration: iron co-interventions subgroup analysis	59		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.45.1 Iron co-intervention	17		Std. Mean Difference (IV, Fixed, 95% CI)	0.47 [0.39, 0.54]
2.45.2 No iron co-intervention	42		Std. Mean Difference (IV, Fixed, 95% CI)	0.68 [0.64, 0.73]
2.46 Serum or plasma zinc concentration: formulation subgroup analysis	60		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.46.1 Solution	33		Std. Mean Difference (IV, Fixed, 95% CI)	0.65 [0.60, 0.71]
2.46.2 Pill/tablet	19		Std. Mean Difference (IV, Fixed, 95% CI)	0.54 [0.48, 0.59]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.46.3 Capsule	8		Std. Mean Difference (IV, Fixed, 95% CI)	1.07 [0.94, 1.21]
2.46.4 Powder	1		Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.25, 0.14]
2.47 Prevalence of zinc deficiency: age subgroup analysis	25		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.47.1 6 months to < 1 year	3		Risk Ratio (IV, Fixed, 95% CI)	0.62 [0.55, 0.70]
2.47.2 1 to < 5 years	14		Risk Ratio (IV, Fixed, 95% CI)	0.52 [0.47, 0.56]
2.47.3 5 to < 13 years	8		Risk Ratio (IV, Fixed, 95% CI)	0.31 [0.20, 0.49]
2.48 Prevalence of zinc deficiency: dose subgroup analysis	24		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.48.1 5 to < 10 mg	5		Risk Ratio (IV, Fixed, 95% CI)	0.45 [0.37, 0.56]
2.48.2 10 to < 15 mg	11		Risk Ratio (IV, Fixed, 95% CI)	0.57 [0.52, 0.63]
2.48.3 15 to < 20 mg	2		Risk Ratio (IV, Fixed, 95% CI)	0.46 [0.24, 0.89]
2.48.4 20 mg or more	6		Risk Ratio (IV, Fixed, 95% CI)	0.14 [0.10, 0.19]
2.49 Prevalence of zinc deficiency: duration subgroup analysis	25		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.49.1 0 to < 6 months	10		Risk Ratio (IV, Fixed, 95% CI)	0.27 [0.22, 0.33]
2.49.2 6 to < 12 months	9		Risk Ratio (IV, Fixed, 95% CI)	0.64 [0.59, 0.71]
2.49.3 12 months or more	6		Risk Ratio (IV, Fixed, 95% CI)	0.55 [0.48, 0.64]
2.50 Prevalence of zinc deficiency: iron co-interventions subgroup analysis	24		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.50.1 Iron co-intervention	6		Risk Ratio (IV, Fixed, 95% CI)	0.62 [0.55, 0.69]
2.50.2 No iron co-intervention	18		Risk Ratio (IV, Fixed, 95% CI)	0.40 [0.36, 0.45]
2.51 Prevalence of zinc deficiency: formulation subgroup analysis	25		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.51.1 Solution	13		Risk Ratio (IV, Fixed, 95% CI)	0.50 [0.45, 0.56]
2.51.2 Pill/tablet	9		Risk Ratio (IV, Fixed, 95% CI)	0.64 [0.58, 0.71]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.51.3 Capsule	4		Risk Ratio (IV, Fixed, 95% CI)	0.29 [0.23, 0.37]
2.52 Blood hemoglobin concentration: age subgroup analysis	38		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.52.1 6 months to < 1 year	13		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.08, 0.05]
2.52.2 1 to < 5 years	16		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.05, 0.04]
2.52.3 5 to < 13 years	9		Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.11, 0.13]
2.53 Blood hemoglobin concentration: dose subgroup analysis	40		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.53.1 0 to < 5 mg	6		Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.12, 0.14]
2.53.2 5 to < 10 mg	5		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.05, 0.04]
2.53.3 10 to < 15 mg	21		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.08, 0.06]
2.53.4 15 to < 20 mg	5		Std. Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.24, 0.17]
2.53.5 20 mg or more	5		Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.02, 0.22]
2.54 Blood hemoglobin concentration: duration subgroup analysis	38		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.54.1 0 to < 6 months	9		Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [0.01, 0.19]
2.54.2 6 to < 12 months	19		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [0.03, 0.12]
2.54.3 12 months or more	10		Std. Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.09, 0.11]
2.55 Blood hemoglobin concentration: iron co-interventions subgroup analysis	38		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.55.1 Iron co-intervention	17		Std. Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.08, 0.07]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.55.2 No iron co-intervention	21		Std. Mean Difference (IV, Fixed, 95% CI)	0.10 [0.05, 0.14]
2.56 Blood hemoglobin concentration: formulation subgroup analysis	40		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.56.1 Solution	21		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.07, 0.07]
2.56.2 Pill/tablet	12		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.05, 0.04]
2.56.3 Capsule	6		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.06, 0.20]
2.56.4 Powder	1		Std. Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.26, 0.12]
2.57 Prevalence of anemia: age subgroup analysis	20		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.57.1 6 months to < 1 year	8		Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.95, 1.08]
2.57.2 1 to < 5 years	9		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.93, 1.11]
2.57.3 5 to < 13 years	3		Risk Ratio (IV, Fixed, 95% CI)	0.73 [0.47, 1.12]
2.58 Prevalence of anemia: dose subgroup analysis	20		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.58.1 0 to < 5 mg	3		Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.94, 1.09]
2.58.2 5 to < 10 mg	2		Risk Ratio (IV, Fixed, 95% CI)	1.04 [0.93, 1.16]
2.58.3 10 to < 15 mg	12		Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.92, 1.11]
2.58.4 15 to < 20 mg	2		Risk Ratio (IV, Fixed, 95% CI)	0.76 [0.40, 1.46]
2.58.5 20 mg or more	1		Risk Ratio (IV, Fixed, 95% CI)	0.17 [0.06, 0.46]
2.59 Prevalence of anemia: duration subgroup analysis	20		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.59.1 0 to < 6 months	2		Risk Ratio (IV, Fixed, 95% CI)	0.18 [0.06, 0.48]
2.59.2 6 to < 12 months	10		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.96, 1.08]
2.59.3 12 months or more	8		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.90, 1.12]
2.60 Prevalence of anemia: iron co-interventions subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.60.1 Iron co-intervention	10		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.91, 1.09]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.60.2 No iron co-intervention	9		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.93, 1.08]
2.61 Prevalence of anemia: formulation subgroup analysis	19		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.61.1 Solution	6		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.78, 1.04]
2.61.2 Pill/tablet	8		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.95, 1.10]
2.61.3 Capsule	4		Risk Ratio (IV, Fixed, 95% CI)	1.00 [0.88, 1.13]
2.61.4 Powder	1		Risk Ratio (IV, Fixed, 95% CI)	1.19 [0.81, 1.73]
2.62 Serum or plasma ferritin concentration: country income level subgroup analysis	27		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.62.1 Low- or middle-income	26		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [0.02, 0.13]
2.62.2 High-income	1		Std. Mean Difference (IV, Fixed, 95% CI)	-0.88 [-1.47, -0.29]
2.63 Serum or plasma ferritin concentration: age subgroup analysis	27		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.63.1 6 months to < 1 year	6		Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [0.03, 0.26]
2.63.2 1 to < 5 years	14		Std. Mean Difference (IV, Fixed, 95% CI)	0.08 [0.03, 0.14]
2.63.3 5 to < 13 years	7		Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.15, 0.24]
2.64 Serum or plasma ferritin concentration: dose subgroup analysis	28		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.64.1 0 to < 5 mg	4		Std. Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.14, 0.28]
2.64.2 5 to < 10 mg	4		Std. Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.17, 0.08]
2.64.3 10 to < 15 mg	14		Std. Mean Difference (IV, Fixed, 95% CI)	0.20 [0.13, 0.28]
2.64.4 15 to < 20 mg	4		Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [-0.08, 0.36]

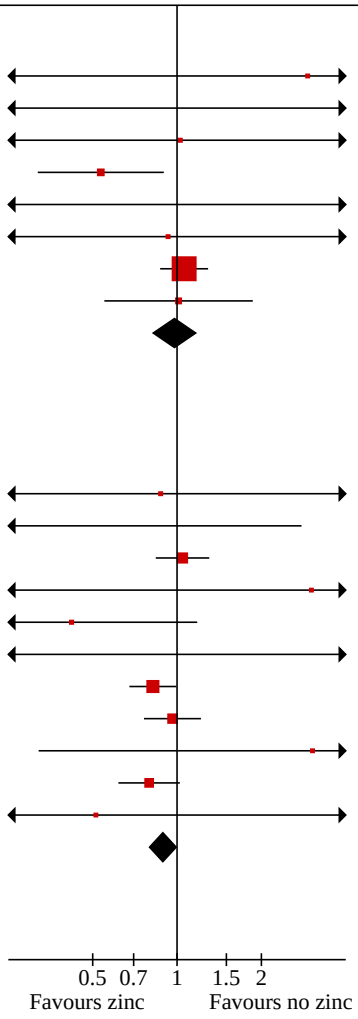
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.64.5 20 mg or more	4		Std. Mean Difference (IV, Fixed, 95% CI)	-0.17 [-0.33, -0.02]
2.65 Serum or plasma ferritin concentration: duration subgroup analysis	27		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.65.1 0 to < 6 months	9		Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.20, 0.07]
2.65.2 6 to < 12 months	12		Std. Mean Difference (IV, Fixed, 95% CI)	0.03 [-0.05, 0.10]
2.65.3 12 months or more	6		Std. Mean Difference (IV, Fixed, 95% CI)	0.34 [0.24, 0.45]
2.66 Serum or plasma ferritin concentration: iron co-interventions subgroup analysis	27		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.66.1 Iron co-intervention	14		Std. Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.02, 0.13]
2.66.2 No iron co-intervention	13		Std. Mean Difference (IV, Fixed, 95% CI)	0.15 [0.07, 0.23]
2.67 Serum or plasma ferritin concentration: formulation subgroup analysis	25		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.67.1 Solution	15		Std. Mean Difference (IV, Fixed, 95% CI)	0.00 [-0.07, 0.08]
2.67.2 Pill/tablet	4		Std. Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.00, 0.22]
2.67.3 Capsule	5		Std. Mean Difference (IV, Fixed, 95% CI)	0.54 [0.38, 0.69]
2.67.4 Powder	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.18 [-0.04, 0.40]
2.68 Prevalence of iron deficiency: age subgroup analysis	16		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.68.1 6 months to < 1 year	5		Risk Ratio (IV, Fixed, 95% CI)	0.92 [0.82, 1.05]
2.68.2 1 to < 5 years	7		Risk Ratio (IV, Fixed, 95% CI)	1.16 [0.94, 1.44]
2.68.3 5 to < 13 years	4		Risk Ratio (IV, Fixed, 95% CI)	1.12 [0.61, 2.04]
2.69 Prevalence of iron deficiency: dose subgroup analysis	16		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.69.1 0 to < 5 mg	1		Risk Ratio (IV, Fixed, 95% CI)	0.78 [0.61, 1.00]
2.69.2 10 to < 15 mg	10		Risk Ratio (IV, Fixed, 95% CI)	1.03 [0.91, 1.16]
2.69.3 15 to < 20 mg	2		Risk Ratio (IV, Fixed, 95% CI)	1.07 [0.52, 2.18]
2.69.4 20 mg or more	3		Risk Ratio (IV, Fixed, 95% CI)	2.16 [0.72, 6.44]
2.70 Prevalence of iron deficiency: duration subgroup analysis	16		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.70.1 0 to < 6 months	3		Risk Ratio (IV, Fixed, 95% CI)	2.16 [0.72, 6.44]
2.70.2 6 to < 12 months	5		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.73, 1.05]
2.70.3 12 months or more	8		Risk Ratio (IV, Fixed, 95% CI)	1.04 [0.91, 1.18]
2.71 Prevalence of iron deficiency: Iron co-interventions subgroup analysis	16		Risk Ratio (IV, Fixed, 95% CI)	0.99 [0.89, 1.10]
2.71.1 Iron co-intervention	10		Risk Ratio (IV, Fixed, 95% CI)	1.02 [0.89, 1.17]
2.71.2 No iron co-intervention	6		Risk Ratio (IV, Fixed, 95% CI)	0.94 [0.79, 1.11]
2.72 Prevalence of iron deficiency: formulation subgroup analysis	16		Risk Ratio (IV, Fixed, 95% CI)	Subtotals only
2.72.1 Solution	8		Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.75, 1.08]
2.72.2 Pill/tablet	4		Risk Ratio (IV, Fixed, 95% CI)	1.05 [0.91, 1.20]
2.72.3 Capsule	4		Risk Ratio (IV, Fixed, 95% CI)	0.88 [0.56, 1.37]
2.73 Serum or plasma copper concentration: country income level subgroup analysis	15		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.73.1 Low- or middle-income	14		Std. Mean Difference (IV, Fixed, 95% CI)	-0.21 [-0.28, -0.14]
2.73.2 High-income	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.38 [-0.23, 0.99]
2.74 Serum or plasma copper concentration: age subgroup analysis	15		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.74.1 6 months to < 1 year	6		Std. Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.20, 0.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.74.2 1 to < 5 years	9		Std. Mean Difference (IV, Fixed, 95% CI)	-0.26 [-0.35, -0.17]
2.75 Serum or plasma copper concentration: dose subgroup analysis	15		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.75.1 0 to < 5 mg	4		Std. Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.27, 0.12]
2.75.2 5 to < 10 mg	3		Std. Mean Difference (IV, Fixed, 95% CI)	-0.31 [-0.48, -0.13]
2.75.3 10 to < 15 mg	9		Std. Mean Difference (IV, Fixed, 95% CI)	-0.00 [-0.10, 0.10]
2.75.4 20 mg or more	1		Std. Mean Difference (IV, Fixed, 95% CI)	-0.46 [-0.59, -0.33]
2.76 Serum or plasma copper concentration: duration subgroup analysis	15		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.76.1 0 to < 6 months	3		Std. Mean Difference (IV, Fixed, 95% CI)	-0.44 [-0.54, -0.33]
2.76.2 6 to < 12 months	8		Std. Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.17, 0.05]
2.76.3 12 months or more	4		Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.11, 0.24]
2.77 Serum or plasma copper concentration: iron co-interventions subgroup analysis	13		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.77.1 Iron co-intervention	4		Std. Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.25, 0.05]
2.77.2 No iron co-intervention	9		Std. Mean Difference (IV, Fixed, 95% CI)	-0.25 [-0.33, -0.17]
2.78 Serum or plasma copper concentration: formulation subgroup analysis	15		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.78.1 Solution	13		Std. Mean Difference (IV, Fixed, 95% CI)	-0.34 [-0.42, -0.26]
2.78.2 Pill/Tablet	3		Std. Mean Difference (IV, Fixed, 95% CI)	-0.83 [-1.01, -0.65]

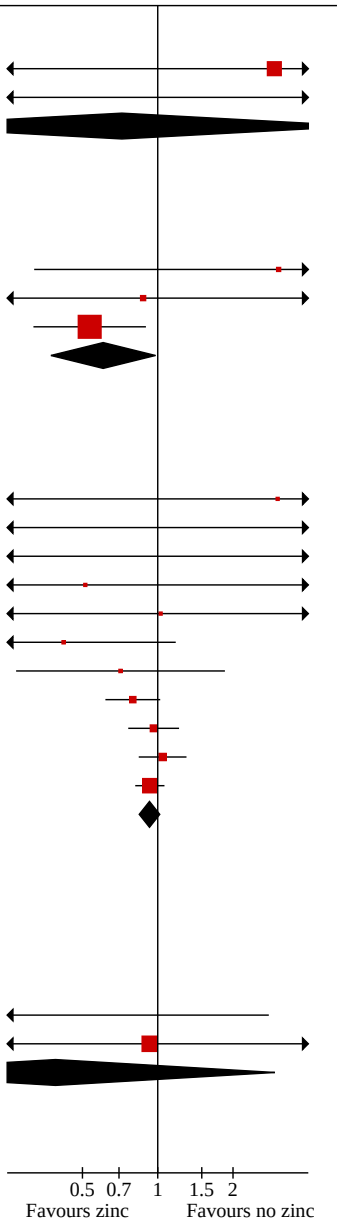
Analysis 2.1. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 1: All-cause mortality: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.1.1 6 months to < 1 year				
Baqui 2003	1.07361099	1.62916074	0.3%	2.93 [0.12 , 71.29]
Chang 2010	-1.59447504	1.54597037	0.3%	0.20 [0.01 , 4.20]
Chhagan 2009	0.02643326	0.99114872	0.8%	1.03 [0.15 , 7.16]
Hess 2015	-0.6266	0.2642	11.3%	0.53 [0.32 , 0.90]
Lind 2003	1.60943791	1.54541389	0.3%	5.00 [0.24 , 103.38]
Malik 2014	-0.0736	1.409	0.4%	0.93 [0.06 , 14.70]
Sazawal 2006	0.05826891	0.10048763	78.3%	1.06 [0.87 , 1.29]
Tielsch 2006 (2)	0.01267064	0.31113591	8.2%	1.01 [0.55 , 1.86]
Subtotal (95% CI)			**100.0%**	**0.98 [0.82 , 1.17]**
Heterogeneity: Chi² = 8.49, df = 7 (P = 0.29); I² = 18%				
Test for overall effect: Z = 0.24 (P = 0.81)				
2.1.2 1 to < 5 years				
Becquey 2016	-0.1346	0.815	0.5%	0.87 [0.18 , 4.32]
Bhandari 2002	-1.93942189	1.51132135	0.1%	0.14 [0.01 , 2.78]
Bhandari 2007	0.04493755	0.11212408	24.8%	1.05 [0.84 , 1.30]
Larson 2010	1.10424611	1.6295395	0.1%	3.02 [0.12 , 73.56]
Müller 2001	-0.86670956	0.52677681	1.1%	0.42 [0.15 , 1.18]
Penny 2004	-1.58534036	1.54139551	0.1%	0.20 [0.01 , 4.20]
Sazawal 2006	-0.19845094	0.09838509	32.2%	0.82 [0.68 , 0.99]
Sazawal 2006 (2)	-0.03756725	0.11932628	21.9%	0.96 [0.76 , 1.22]
Shankar 2000	1.11321109	1.14836145	0.2%	3.04 [0.32 , 28.90]
Tielsch 2006	-0.22948879	0.12870764	18.8%	0.79 [0.62 , 1.02]
Veenemans 2011 (2)	-0.6670019	1.2193957	0.2%	0.51 [0.05 , 5.60]
Subtotal (95% CI)			**100.0%**	**0.89 [0.80 , 0.99]**
Heterogeneity: Chi² = 10.28, df = 10 (P = 0.42); I² = 3%				
Test for overall effect: Z = 2.09 (P = 0.04)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



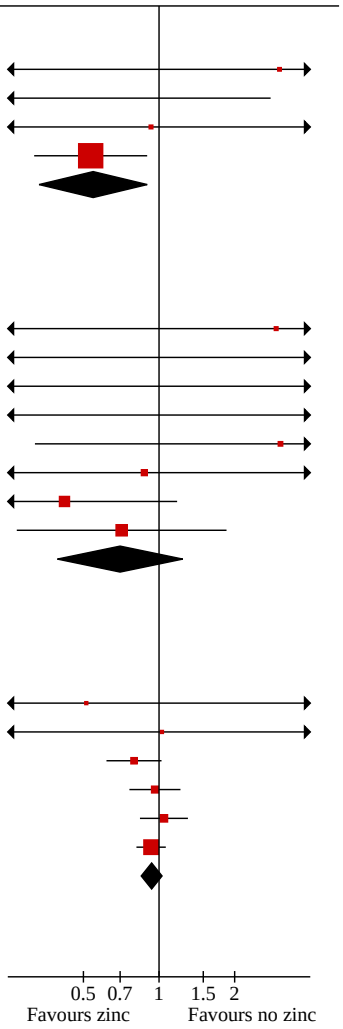
Analysis 2.2. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 2: All-cause mortality: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.2.1 0 to < 5 mg				
Baqui 2003	1.07361099	1.62916074	47.4%	2.93 [0.12 , 71.29]
Chang 2010	-1.59447504	1.54597037	52.6%	0.20 [0.01 , 4.20]
Subtotal (95% CI)			**100.0%**	**0.72 [0.08 , 6.47]**
Heterogeneity: Chi² = 1.41, df = 1 (P = 0.23); I² = 29%				
Test for overall effect: Z = 0.29 (P = 0.77)				
2.2.2 5 to < 10 mg				
Shankar 2000	1.11321109	1.14836145	4.6%	3.04 [0.32 , 28.90]
Becquey 2016	-0.1346	0.815	9.1%	0.87 [0.18 , 4.32]
Hess 2015	-0.6266	0.2642	86.4%	0.53 [0.32 , 0.90]
Subtotal (95% CI)			**100.0%**	**0.61 [0.37 , 0.98]**
Heterogeneity: Chi² = 2.40, df = 2 (P = 0.30); I² = 17%				
Test for overall effect: Z = 2.05 (P = 0.04)				
2.2.3 10 to < 15 mg				
Larson 2010	1.10424611	1.6295395	0.1%	3.02 [0.12 , 73.56]
Lind 2003	1.60943791	1.54541389	0.1%	5.00 [0.24 , 103.38]
Penny 2004	-1.58534036	1.54139551	0.1%	0.20 [0.01 , 4.20]
Veenemans 2011 (2)	-0.6670019	1.2193957	0.2%	0.51 [0.05 , 5.60]
Chhagan 2009	0.02643326	0.99114872	0.2%	1.03 [0.15 , 7.16]
Müller 2001	-0.86670956	0.52677681	0.8%	0.42 [0.15 , 1.18]
Soofi 2013	-0.342704984498532	0.490437295227866	1.0%	0.71 [0.27 , 1.86]
Tielsch 2006	-0.22948879	0.12870764	13.9%	0.79 [0.62 , 1.02]
Sazawal 2006 (2)	-0.03756725	0.11932628	16.2%	0.96 [0.76 , 1.22]
Bhandari 2007	0.04493755	0.11212408	18.4%	1.05 [0.84 , 1.30]
Sazawal 2006	-0.07257069	0.06862114	49.0%	0.93 [0.81 , 1.06]
Subtotal (95% CI)			**100.0%**	**0.93 [0.84 , 1.02]**
Heterogeneity: Chi² = 8.16, df = 10 (P = 0.61); I² = 0%				
Test for overall effect: Z = 1.58 (P = 0.11)				
2.2.4 20 mg or more				
Richard 2006	0	0		Not estimable
Richard 2006 (2)	0	0		Not estimable
Bhandari 2002	-1.93942189	1.51132135	46.5%	0.14 [0.01 , 2.78]
Malik 2014	-0.0736	1.409	53.5%	0.93 [0.06 , 14.70]
Subtotal (95% CI)			**100.0%**	**0.39 [0.05 , 2.94]**
Heterogeneity: Chi² = 0.82, df = 1 (P = 0.37); I² = 0%				
Test for overall effect: Z = 0.91 (P = 0.36)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



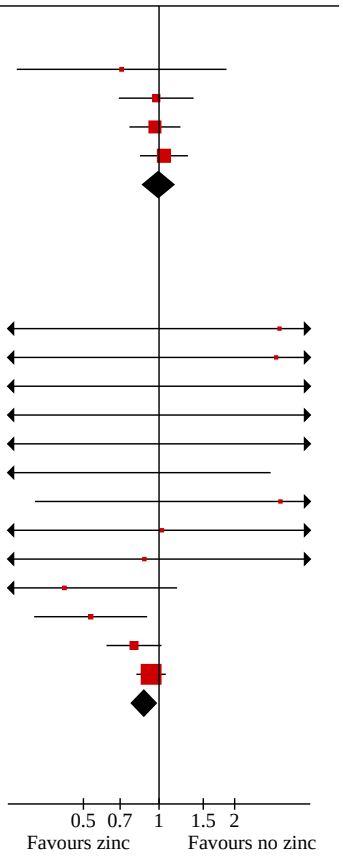
Analysis 2.3. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 3: All-cause mortality: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.3.1 0 to < 6 months				
Larson 2010	1.10424611	1.6295395	2.4%	3.02 [0.12 , 73.56]
Bhandari 2002	-1.93942189	1.51132135	2.8%	0.14 [0.01 , 2.78]
Malik 2014	-0.0736	1.409	3.2%	0.93 [0.06 , 14.70]
Hess 2015	-0.6266	0.2642	91.6%	0.53 [0.32 , 0.90]
Subtotal (95% CI)			**100.0%**	**0.55 [0.33 , 0.90]**
Heterogeneity: Chi² = 2.03, df = 3 (P = 0.57); I² = 0%				
Test for overall effect: Z = 2.39 (P = 0.02)				
2.3.2 6 to < 12 months				
Baqui 2003	1.07361099	1.62916074	3.2%	2.93 [0.12 , 71.29]
Chang 2010	-1.59447504	1.54597037	3.6%	0.20 [0.01 , 4.20]
Lind 2003	1.60943791	1.54541389	3.6%	5.00 [0.24 , 103.38]
Penny 2004	-1.58534036	1.54139551	3.6%	0.20 [0.01 , 4.20]
Shankar 2000	1.11321109	1.14836145	6.5%	3.04 [0.32 , 28.90]
Becquey 2016	-0.1346	0.815	12.9%	0.87 [0.18 , 4.32]
Müller 2001	-0.86670956	0.52677681	30.9%	0.42 [0.15 , 1.18]
Soofi 2013	-0.342704984498532	0.490437295227866	35.7%	0.71 [0.27 , 1.86]
Subtotal (95% CI)			**100.0%**	**0.70 [0.39 , 1.24]**
Heterogeneity: Chi² = 6.32, df = 7 (P = 0.50); I² = 0%				
Test for overall effect: Z = 1.22 (P = 0.22)				
2.3.3 12 months or more				
Veenemans 2011	-0.6670019	1.2193957	0.2%	0.51 [0.05 , 5.60]
Chhagan 2009	0.02643326	0.99114872	0.2%	1.03 [0.15 , 7.16]
Tielsch 2006	-0.22948879	0.12870764	14.2%	0.79 [0.62 , 1.02]
Sazawal 2006 (2)	-0.03756725	0.11932628	16.6%	0.96 [0.76 , 1.22]
Bhandari 2007	0.04493755	0.11212408	18.8%	1.05 [0.84 , 1.30]
Sazawal 2006	-0.07257069	0.06862114	50.1%	0.93 [0.81 , 1.06]
Subtotal (95% CI)			**100.0%**	**0.93 [0.85 , 1.03]**
Heterogeneity: Chi² = 2.91, df = 5 (P = 0.71); I² = 0%				
Test for overall effect: Z = 1.40 (P = 0.16)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



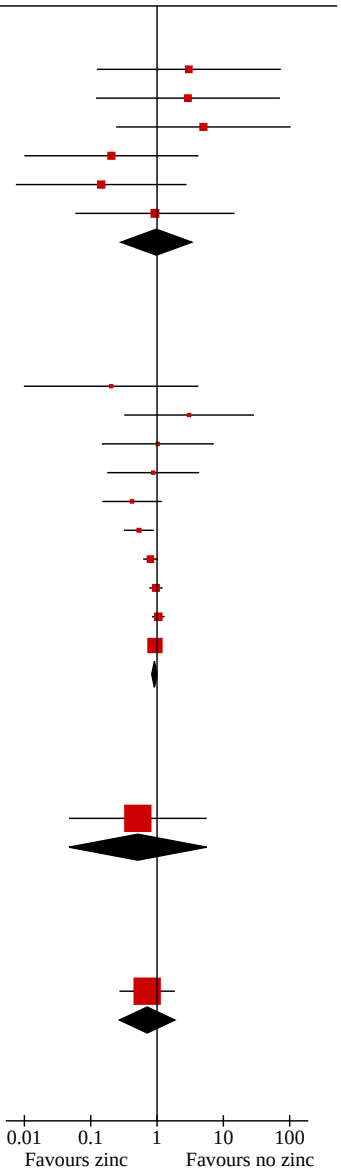
Analysis 2.4. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 4: All-cause mortality: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.4.1 Iron co-intervention				
Soofi 2013	-0.342704984498532	0.490437295227866	2.2%	0.71 [0.27 , 1.86]
Tielsch 2006 (2)	-0.02581357	0.17489571	17.5%	0.97 [0.69 , 1.37]
Sazawal 2006 (2)	-0.03756725	0.11932628	37.6%	0.96 [0.76 , 1.22]
Bhandari 2007	0.04493755	0.11212408	42.6%	1.05 [0.84 , 1.30]
Subtotal (95% CI)			**100.0%**	**0.99 [0.86 , 1.15]**
Heterogeneity: Chi² = 0.76, df = 3 (P = 0.86); I² = 0%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2.4.2 No iron co-intervention				
Larson 2010	1.10424611	1.6295395	0.1%	3.02 [0.12 , 73.56]
Baqui 2003	1.07361099	1.62916074	0.1%	2.93 [0.12 , 71.29]
Chang 2010	-1.59447504	1.54597037	0.1%	0.20 [0.01 , 4.20]
Lind 2003	1.60943791	1.54541389	0.1%	5.00 [0.24 , 103.38]
Penny 2004	-1.58534036	1.54139551	0.1%	0.20 [0.01 , 4.20]
Bhandari 2002	-1.93942189	1.51132135	0.1%	0.14 [0.01 , 2.78]
Shankar 2000	1.11321109	1.14836145	0.3%	3.04 [0.32 , 28.90]
Chhagan 2009	0.02643326	0.99114872	0.3%	1.03 [0.15 , 7.16]
Becquey 2016	-0.1346	0.815	0.5%	0.87 [0.18 , 4.32]
Müller 2001	-0.86670956	0.52677681	1.2%	0.42 [0.15 , 1.18]
Hess 2015	-0.6266	0.2642	4.8%	0.53 [0.32 , 0.90]
Tielsch 2006	-0.22948879	0.12870764	20.4%	0.79 [0.62 , 1.02]
Sazawal 2006	-0.07257069	0.06862114	71.7%	0.93 [0.81 , 1.06]
Subtotal (95% CI)			**100.0%**	**0.87 [0.78 , 0.97]**
Heterogeneity: Chi² = 13.56, df = 12 (P = 0.33); I² = 12%				
Test for overall effect: Z = 2.40 (P = 0.02)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



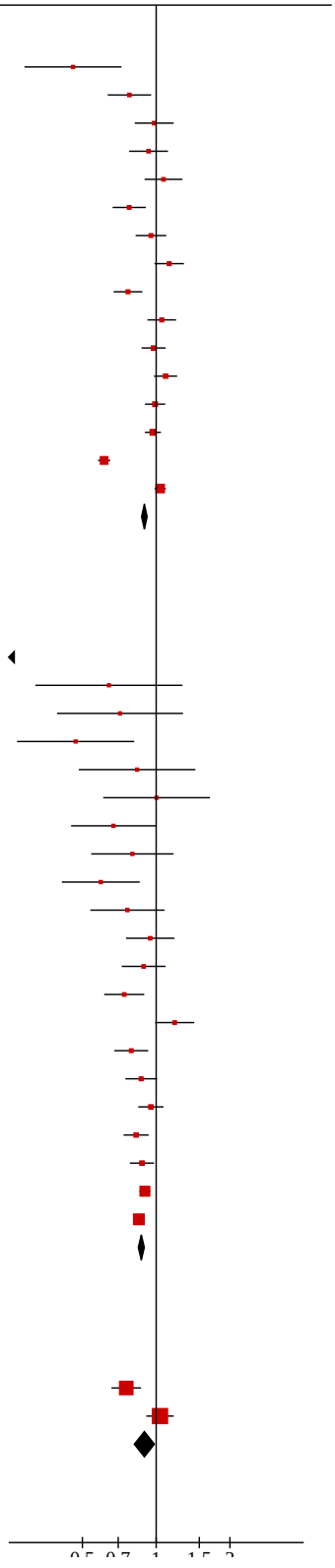
Analysis 2.5. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 5: All-cause mortality: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.5.1 Solution				
Larson 2010	1.10424611	1.6295395	14.9%	3.02 [0.12 , 73.56]
Baqui 2003	1.07361099	1.62916074	14.9%	2.93 [0.12 , 71.29]
Lind 2003	1.60943791	1.54541389	16.5%	5.00 [0.24 , 103.38]
Penny 2004	-1.58534036	1.54139551	16.6%	0.20 [0.01 , 4.20]
Bhandari 2002	-1.93942189	1.51132135	17.3%	0.14 [0.01 , 2.78]
Malik 2014	-0.0736	1.409	19.9%	0.93 [0.06 , 14.70]
Subtotal (95% CI)			**100.0%**	**0.98 [0.29 , 3.35]**
Heterogeneity: Chi² = 4.68, df = 5 (P = 0.46); I² = 0%				
Test for overall effect: Z = 0.04 (P = 0.97)				
2.5.2 Pill/tablet				
Chang 2010	-1.59447504	1.54597037	0.1%	0.20 [0.01 , 4.20]
Shankar 2000	1.11321109	1.14836145	0.2%	3.04 [0.32 , 28.90]
Chhagan 2009	0.02643326	0.99114872	0.2%	1.03 [0.15 , 7.16]
Becquey 2016	-0.1346	0.815	0.3%	0.87 [0.18 , 4.32]
Müller 2001	-0.86670956	0.52677681	0.8%	0.42 [0.15 , 1.18]
Hess 2015	-0.6266	0.2642	3.2%	0.53 [0.32 , 0.90]
Tielsch 2006	-0.22948879	0.12870764	13.6%	0.79 [0.62 , 1.02]
Sazawal 2006 (2)	-0.03756725	0.11932628	15.8%	0.96 [0.76 , 1.22]
Bhandari 2007	0.04493755	0.11212408	17.9%	1.05 [0.84 , 1.30]
Sazawal 2006	-0.07257069	0.06862114	47.8%	0.93 [0.81 , 1.06]
Subtotal (95% CI)			**100.0%**	**0.91 [0.83 , 1.00]**
Heterogeneity: Chi² = 11.24, df = 9 (P = 0.26); I² = 20%				
Test for overall effect: Z = 1.92 (P = 0.06)				
2.5.3 Capsule				
Veenemans 2011	-0.6670019	1.2193957	100.0%	0.51 [0.05 , 5.60]
Subtotal (95% CI)			**100.0%**	**0.51 [0.05 , 5.60]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.55 (P = 0.58)				
2.5.4 Powder				
Soofi 2013	-0.342704984498532	0.490437295227866	100.0%	0.71 [0.27 , 1.86]
Subtotal (95% CI)			**100.0%**	**0.71 [0.27 , 1.86]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.70 (P = 0.48)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



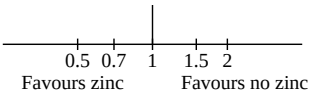
Analysis 2.6. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 6: Incidence of all-cause diarrhea: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.6.1 6 months to < 1 year				
Umeta 2000	-0.78170058	0.23234928	0.3%	0.46 [0.29 , 0.72]
Ruel 1997	-0.25131443	0.10417938	1.6%	0.78 [0.63 , 0.95]
Chang 2010	-0.01868876	0.09337882	2.0%	0.98 [0.82 , 1.18]
Lind 2003 (2)	-0.07145896	0.09311961	2.0%	0.93 [0.78 , 1.12]
Lind 2003	0.06899287	0.09065627	2.1%	1.07 [0.90 , 1.28]
Chang 2010 (2)	-0.25350318	0.0794688	2.8%	0.78 [0.66 , 0.91]
Chhagan 2009	-0.04913269	0.07335707	3.2%	0.95 [0.82 , 1.10]
Long 2006	0.12218449	0.07061765	3.5%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	3.7%	0.77 [0.67 , 0.88]
Sazawal 1996	0.05253358	0.06856712	3.7%	1.05 [0.92 , 1.21]
Baqui 2003	-0.02439145	0.05739701	5.3%	0.98 [0.87 , 1.09]
Baqui 2003 (2)	0.08849308	0.05540904	5.7%	1.09 [0.98 , 1.22]
Islam 2022	-0.0101	0.0486	7.4%	0.99 [0.90 , 1.09]
Hess 2015	-0.0305	0.0382	12.0%	0.97 [0.90 , 1.05]
Malik 2014	-0.489176152	0.029183580172245	20.5%	0.61 [0.58 , 0.65]
Soofi 2013	0.0377403279828471	0.0268956156251902	24.1%	1.04 [0.99 , 1.09]
Subtotal (95% CI)			**100.0%**	**0.90 [0.87 , 0.92]**
Heterogeneity: Chi² = 263.27, df = 15 (P < 0.00001); I² = 94%				
Test for overall effect: Z = 8.39 (P < 0.00001)				
2.6.2 1 to < 5 years				
Meeks Gardner 2005	-4.48367263	1.42163731	0.0%	0.01 [0.00 , 0.18]
Gupta 2003	-0.44425113	0.35257821	0.2%	0.64 [0.32 , 1.28]
Alarcon 2004	-0.33963305	0.30181636	0.2%	0.71 [0.39 , 1.29]
Han 2002	-0.756623021	0.280754333	0.3%	0.47 [0.27 , 0.81]
Han 2002 (2)	-0.179234677	0.279199046	0.3%	0.84 [0.48 , 1.44]
Meeks Gardner 1998	0.00421645	0.25610818	0.3%	1.00 [0.61 , 1.66]
Rosado 1997	-0.40188729	0.20280294	0.5%	0.67 [0.45 , 1.00]
Veenemans 2011	-0.22342699	0.19743482	0.5%	0.80 [0.54 , 1.18]
Rosado 1997 (2)	-0.52044108	0.18680745	0.6%	0.59 [0.41 , 0.86]
Veenemans 2011 (2)	-0.27010424	0.17803183	0.7%	0.76 [0.54 , 1.08]
Gupta 2007	-0.05588046	0.1160778	1.5%	0.95 [0.75 , 1.19]
Penny 2004	-0.11778304	0.10486269	1.9%	0.89 [0.72 , 1.09]
Wuehler 2008	-0.30010459	0.09601332	2.2%	0.74 [0.61 , 0.89]
Abdollahi 2019	0.174	0.0939	2.3%	1.19 [0.99 , 1.43]
Larson 2010	-0.23381808	0.08123116	3.1%	0.79 [0.68 , 0.93]
Müller 2001	-0.14077255	0.07595902	3.6%	0.87 [0.75 , 1.01]
Rahman 2001 (2)	-0.05001042	0.06042171	5.7%	0.95 [0.84 , 1.07]
Sazawal 1996	-0.18865578	0.06017222	5.7%	0.83 [0.74 , 0.93]
Rahman 2001	-0.13353139	0.0579042	6.2%	0.88 [0.78 , 0.98]
Bhandari 2002	-0.10583655	0.02613411	30.2%	0.90 [0.85 , 0.95]
Becquey 2016	-0.1625	0.0246	34.1%	0.85 [0.81 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.87 [0.85 , 0.89]**
Heterogeneity: Chi² = 43.50, df = 20 (P = 0.002); I² = 54%				
Test for overall effect: Z = 9.72 (P < 0.00001)				
2.6.3 5 to < 13 years				
Richard 2006	-0.28106642	0.07078211	46.4%	0.75 [0.66 , 0.87]
Richard 2006 (2)	0.03619935	0.06581383	53.6%	1.04 [0.91 , 1.18]
Subtotal (95% CI)			**100.0%**	**0.90 [0.81 , 0.98]**
Heterogeneity: Chi² = 10.78, df = 1 (P = 0.001); I² = 91%				
Test for overall effect: Z = 2.30 (P = 0.02)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.6. (Continued)

Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%



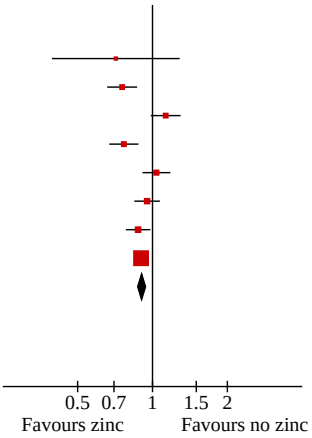
Analysis 2.7. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 7: Incidence of all-cause diarrhea: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.7.1 0 to < 5 mg				
Han 2002	-0.756623021	0.280754333	1.3%	0.47 [0.27 , 0.81]
Han 2002 (2)	-0.179234677	0.279199046	1.3%	0.84 [0.48 , 1.44]
Wuehler 2008	-0.25131443	0.12052263	6.9%	0.78 [0.61 , 0.99]
Chang 2010	-0.01868876	0.09337882	11.5%	0.98 [0.82 , 1.18]
Chang 2010 (2)	-0.25350318	0.0794688	15.9%	0.78 [0.66 , 0.91]
Baqui 2003	-0.02439145	0.05739701	30.5%	0.98 [0.87 , 1.09]
Baqui 2003 (2)	0.08849308	0.05540904	32.7%	1.09 [0.98 , 1.22]
Subtotal (95% CI)			**100.0%**	**0.95 [0.89 , 1.01]**
Heterogeneity: Chi² = 22.46, df = 6 (P = 0.001); I² = 73%				
Test for overall effect: Z = 1.59 (P = 0.11)				
2.7.2 5 to < 10 mg				
Sampaio 2013	-0.26503449302337	0.373888956972379	0.3%	0.77 [0.37 , 1.60]
Meeks Gardner 1998	0.00421645	0.25610818	0.6%	1.00 [0.61 , 1.66]
Umeta 2000	-0.78170058	0.23234928	0.7%	0.46 [0.29 , 0.72]
Gupta 2003	-0.89381788	0.22473329	0.7%	0.41 [0.26 , 0.64]
Wuehler 2008	-0.35139789	0.12371864	2.4%	0.70 [0.55 , 0.90]
Gupta 2007	-0.14660347	0.097381	3.9%	0.86 [0.71 , 1.05]
Abdollahi 2019	0.174	0.0939	4.2%	1.19 [0.99 , 1.43]
Hess 2015	-0.0305	0.0382	25.5%	0.97 [0.90 , 1.05]
Becquey 2016	-0.1625	0.0246	61.6%	0.85 [0.81 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.88 [0.85 , 0.91]**
Heterogeneity: Chi² = 42.05, df = 8 (P < 0.00001); I² = 81%				
Test for overall effect: Z = 6.61 (P < 0.00001)				
2.7.3 10 to < 15 mg				
Meeks Gardner 2005	-4.48367263	1.42163731	0.0%	0.01 [0.00 , 0.18]
Veenemans 2011	-0.22342699	0.19743482	0.8%	0.80 [0.54 , 1.18]
Veenemans 2011 (2)	-0.27010424	0.17803183	0.9%	0.76 [0.54 , 1.08]
Wuehler 2008	-0.25131443	0.12023611	2.1%	0.78 [0.61 , 0.98]
Penny 2004	-0.11778304	0.10486269	2.7%	0.89 [0.72 , 1.09]
Ruel 1997	-0.25131443	0.10417938	2.7%	0.78 [0.63 , 0.95]
Lind 2003 (2)	-0.07145896	0.09311961	3.4%	0.93 [0.78 , 1.12]
Lind 2003	0.06899287	0.09065627	3.6%	1.07 [0.90 , 1.28]
Larson 2010	-0.23381808	0.08123116	4.5%	0.79 [0.68 , 0.93]
Müller 2001	-0.14077255	0.07595902	5.2%	0.87 [0.75 , 1.01]
Chhagan 2009	-0.04913269	0.07335707	5.5%	0.95 [0.82 , 1.10]
Islam 2022	-0.0101	0.0486	12.6%	0.99 [0.90 , 1.09]
Sazawal 1996	-0.08461665	0.04515217	14.6%	0.92 [0.84 , 1.00]
Soofi 2013	0.0377403279828471	0.0268956156251902	41.2%	1.04 [0.99 , 1.09]
Subtotal (95% CI)			**100.0%**	**0.96 [0.93 , 1.00]**
Heterogeneity: Chi² = 38.79, df = 13 (P = 0.0002); I² = 66%				
Test for overall effect: Z = 2.25 (P = 0.02)				
2.7.4 15 to < 20 mg				
Rosado 1997	-0.40188729	0.20280294	2.0%	0.67 [0.45 , 1.00]
Rosado 1997 (2)	-0.52044108	0.18680745	2.3%	0.59 [0.41 , 0.86]
Malik 2014	-0.489176152	0.029183580172245	95.7%	0.61 [0.58 , 0.65]
Subtotal (95% CI)			**100.0%**	**0.61 [0.58 , 0.65]**
Heterogeneity: Chi² = 0.21, df = 2 (P = 0.90); I² = 0%				
Test for overall effect: Z = 17.10 (P < 0.00001)				
2.7.5 20 mg or more				
Alarcon 2004	-0.33963305	0.30181636	0.4%	0.71 [0.39 , 1.29]

Analysis 2.7. (Continued)

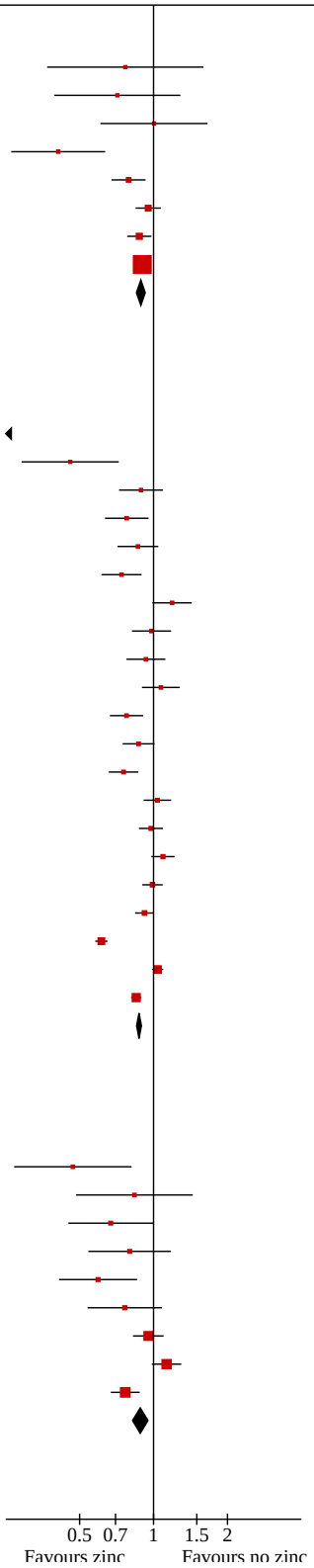
2.7.5 20 mg or more				
Alarcon 2004	-0.33963305	0.30181636	0.4%	0.71 [0.39 , 1.29]
Richard 2006	-0.28106642	0.07078211	6.9%	0.75 [0.66 , 0.87]
Long 2006	0.12218449	0.07061765	6.9%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	7.3%	0.77 [0.67 , 0.88]
Richard 2006 (2)	0.03619935	0.06581383	8.0%	1.04 [0.91 , 1.18]
Rahman 2001 (2)	-0.05001042	0.06042171	9.5%	0.95 [0.84 , 1.07]
Rahman 2001	-0.13353139	0.0579042	10.3%	0.88 [0.78 , 0.98]
Bhandari 2002	-0.10583655	0.02613411	50.7%	0.90 [0.85 , 0.95]
Subtotal (95% CI)			**100.0%**	**0.90 [0.87 , 0.94]**
Heterogeneity: Chi² = 28.17, df = 7 (P = 0.0002); I² = 75%				
Test for overall effect: Z = 5.42 (P < 0.00001)				

Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%



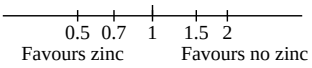
Analysis 2.8. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 8: Incidence of all-cause diarrhea: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.8.1 0 to < 6 months				
Sampaio 2013	-0.26503449302337	0.373888956972379	0.3%	0.77 [0.37 , 1.60]
Alarcon 2004	-0.33963305	0.30181636	0.5%	0.71 [0.39 , 1.29]
Meeks Gardner 1998	0.00421645	0.25610818	0.7%	1.00 [0.61 , 1.66]
Gupta 2003	-0.89381788	0.22473329	0.9%	0.41 [0.26 , 0.64]
Larson 2010	-0.23381808	0.08123116	6.8%	0.79 [0.68 , 0.93]
Rahman 2001 (2)	-0.05001042	0.06042171	12.2%	0.95 [0.84 , 1.07]
Rahman 2001	-0.13353139	0.0579042	13.3%	0.88 [0.78 , 0.98]
Bhandari 2002	-0.10583655	0.02613411	65.3%	0.90 [0.85 , 0.95]
Subtotal (95% CI)			**100.0%**	**0.89 [0.85 , 0.93]**
Heterogeneity: Chi² = 16.42, df = 7 (P = 0.02); I² = 57%				
Test for overall effect: Z = 5.64 (P < 0.00001)				
2.8.2 6 to < 12 months				
Meeks Gardner 2005	-4.48367263	1.42163731	0.0%	0.01 [0.00 , 0.18]
Umeta 2000	-0.78170058	0.23234928	0.3%	0.46 [0.29 , 0.72]
Penny 2004	-0.11778304	0.10486269	1.2%	0.89 [0.72 , 1.09]
Ruel 1997	-0.25131443	0.10417938	1.2%	0.78 [0.63 , 0.95]
Gupta 2007	-0.14660347	0.097381	1.4%	0.86 [0.71 , 1.05]
Wuehler 2008	-0.30010459	0.09601332	1.5%	0.74 [0.61 , 0.89]
Abdollahi 2019	0.174	0.0939	1.5%	1.19 [0.99 , 1.43]
Chang 2010	-0.01868876	0.09337882	1.6%	0.98 [0.82 , 1.18]
Lind 2003 (2)	-0.07145896	0.09311961	1.6%	0.93 [0.78 , 1.12]
Lind 2003	0.06899287	0.09065627	1.6%	1.07 [0.90 , 1.28]
Chang 2010 (2)	-0.25350318	0.0794688	2.1%	0.78 [0.66 , 0.91]
Müller 2001	-0.14077255	0.07595902	2.3%	0.87 [0.75 , 1.01]
Richard 2006	-0.28106642	0.07078211	2.7%	0.75 [0.66 , 0.87]
Richard 2006 (2)	0.03619935	0.06581383	3.1%	1.04 [0.91 , 1.18]
Baqui 2003	-0.02439145	0.05739701	4.1%	0.98 [0.87 , 1.09]
Baqui 2003 (2)	0.08849308	0.05540904	4.4%	1.09 [0.98 , 1.22]
Islam 2022	-0.0101	0.0486	5.7%	0.99 [0.90 , 1.09]
Sazawal 1996	-0.08461665	0.04515217	6.6%	0.92 [0.84 , 1.00]
Malik 2014	-0.489176152	0.029183580172245	15.9%	0.61 [0.58 , 0.65]
Soofi 2013	0.0377403279828471	0.0268956156251902	18.7%	1.04 [0.99 , 1.09]
Becquey 2016	-0.1625	0.0246	22.3%	0.85 [0.81 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.87 [0.85 , 0.89]**
Heterogeneity: Chi² = 270.12, df = 20 (P < 0.00001); I² = 93%				
Test for overall effect: Z = 11.72 (P < 0.00001)				
2.8.3 12 months or more				
Han 2002	-0.756623021	0.280754333	1.7%	0.47 [0.27 , 0.81]
Han 2002 (2)	-0.179234677	0.279199046	1.8%	0.84 [0.48 , 1.44]
Rosado 1997	-0.40188729	0.20280294	3.3%	0.67 [0.45 , 1.00]
Veenemans 2011	-0.22342699	0.19743482	3.5%	0.80 [0.54 , 1.18]
Rosado 1997 (2)	-0.52044108	0.18680745	3.9%	0.59 [0.41 , 0.86]
Veenemans 2011 (2)	-0.27010424	0.17803183	4.3%	0.76 [0.54 , 1.08]
Chhagan 2009	-0.04913269	0.07335707	25.4%	0.95 [0.82 , 1.10]
Long 2006	0.12218449	0.07061765	27.4%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	28.8%	0.77 [0.67 , 0.88]
Subtotal (95% CI)			**100.0%**	**0.88 [0.82 , 0.95]**
Heterogeneity: Chi² = 29.82, df = 8 (P = 0.0002); I² = 73%				
Test for overall effect: Z = 3.37 (P = 0.0007)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



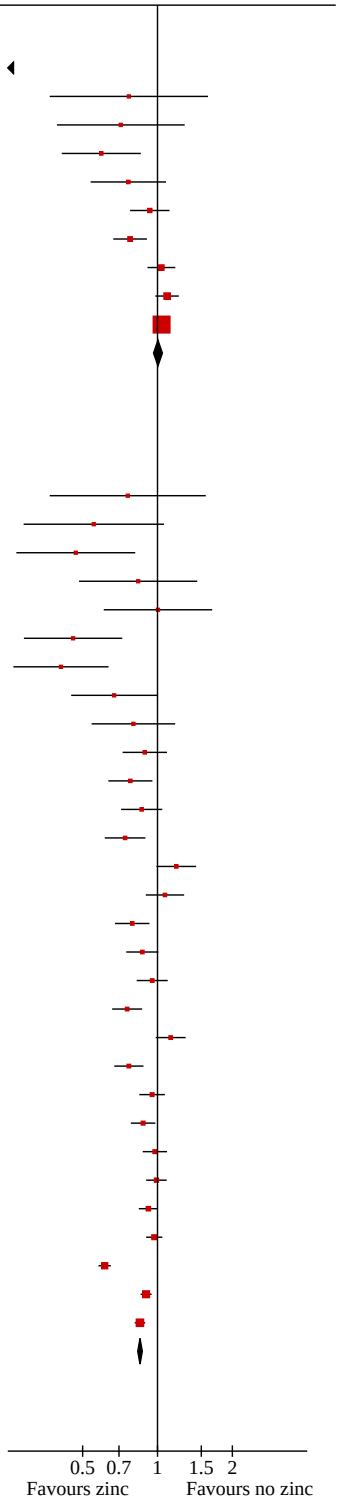
Analysis 2.8. (Continued)

Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%

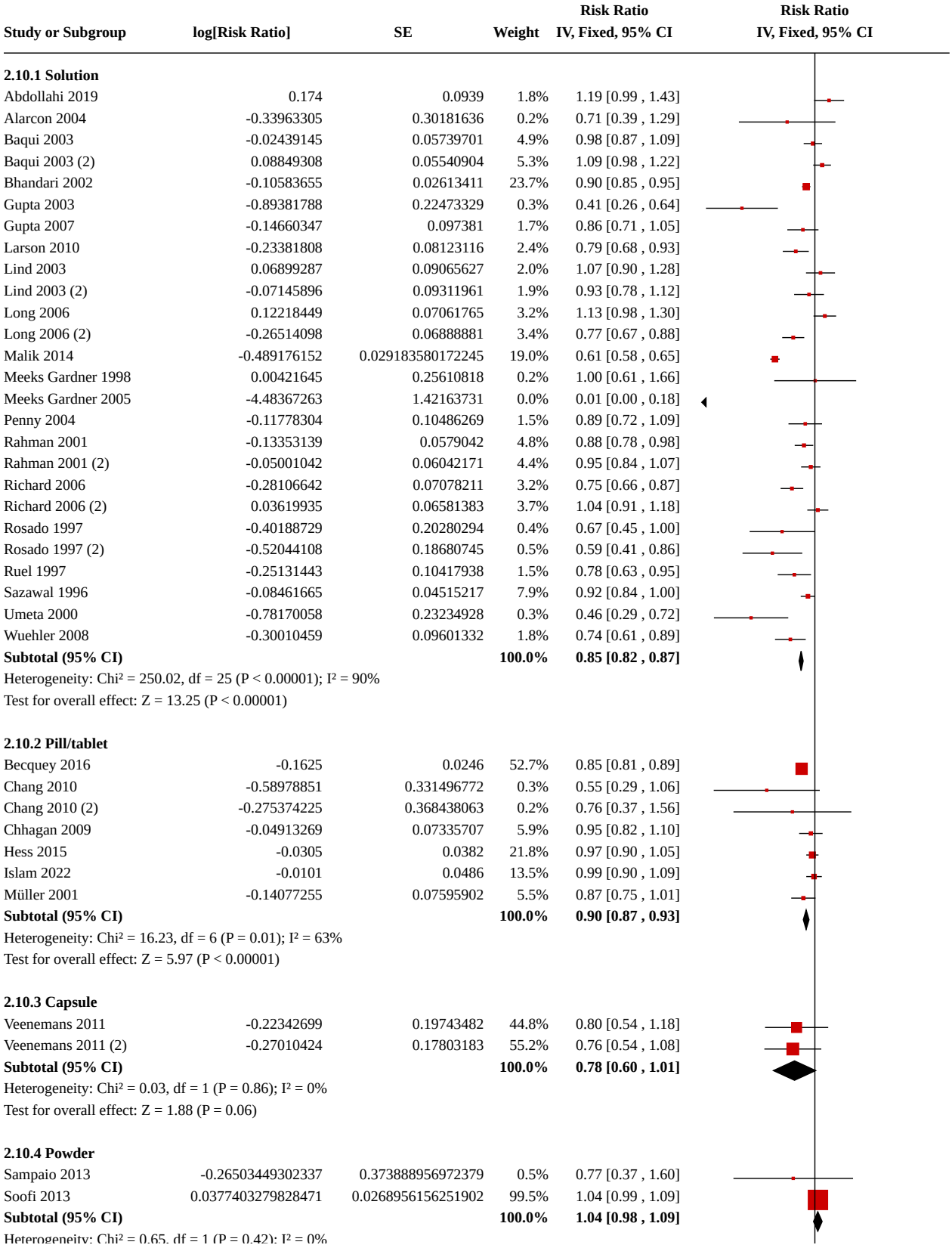


Analysis 2.9. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 9: Incidence of all-cause diarrhea: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.9.1 Iron co-intervention				
Meeks Gardner 2005	-4.48367263	1.42163731	0.0%	0.01 [0.00 , 0.18]
Sampaio 2013	-0.26503449302337	0.373888956972379	0.3%	0.77 [0.37 , 1.60]
Alarcon 2004	-0.33963305	0.30181636	0.5%	0.71 [0.39 , 1.29]
Rosado 1997 (2)	-0.52044108	0.18680745	1.3%	0.59 [0.41 , 0.86]
Veenemans 2011 (2)	-0.27010424	0.17803183	1.4%	0.76 [0.54 , 1.08]
Lind 2003 (2)	-0.07145896	0.09311961	5.0%	0.93 [0.78 , 1.12]
Chang 2010 (2)	-0.25350318	0.0794688	6.9%	0.78 [0.66 , 0.91]
Richard 2006 (2)	0.03619935	0.06581383	10.1%	1.04 [0.91 , 1.18]
Baqui 2003 (2)	0.08849308	0.05540904	14.2%	1.09 [0.98 , 1.22]
Soofi 2013	0.0377403279828471	0.0268956156251902	60.3%	1.04 [0.99 , 1.09]
Subtotal (95% CI)			**100.0%**	**1.00 [0.96 , 1.05]**
Heterogeneity: Chi² = 37.33, df = 9 (P < 0.0001); I² = 76%				
Test for overall effect: Z = 0.20 (P = 0.84)				
2.9.2 No iron co-intervention				
Chang 2010 (2)	-0.275374225	0.368438063	0.1%	0.76 [0.37 , 1.56]
Chang 2010	-0.58978851	0.331496772	0.1%	0.55 [0.29 , 1.06]
Han 2002	-0.756623021	0.280754333	0.1%	0.47 [0.27 , 0.81]
Han 2002 (2)	-0.179234677	0.279199046	0.1%	0.84 [0.48 , 1.44]
Meeks Gardner 1998	0.00421645	0.25610818	0.2%	1.00 [0.61 , 1.66]
Umeta 2000	-0.78170058	0.23234928	0.2%	0.46 [0.29 , 0.72]
Gupta 2003	-0.89381788	0.22473329	0.2%	0.41 [0.26 , 0.64]
Rosado 1997	-0.40188729	0.20280294	0.3%	0.67 [0.45 , 1.00]
Veenemans 2011	-0.22342699	0.19743482	0.3%	0.80 [0.54 , 1.18]
Penny 2004	-0.11778304	0.10486269	1.0%	0.89 [0.72 , 1.09]
Ruel 1997	-0.25131443	0.10417938	1.1%	0.78 [0.63 , 0.95]
Gupta 2007	-0.14660347	0.097381	1.2%	0.86 [0.71 , 1.05]
Wuehler 2008	-0.30010459	0.09601332	1.3%	0.74 [0.61 , 0.89]
Abdollahi 2019	0.174	0.0939	1.3%	1.19 [0.99 , 1.43]
Lind 2003	0.06899287	0.09065627	1.4%	1.07 [0.90 , 1.28]
Larson 2010	-0.23381808	0.08123116	1.7%	0.79 [0.68 , 0.93]
Müller 2001	-0.14077255	0.07595902	2.0%	0.87 [0.75 , 1.01]
Chhagan 2009	-0.04913269	0.07335707	2.1%	0.95 [0.82 , 1.10]
Richard 2006	-0.28106642	0.07078211	2.3%	0.75 [0.66 , 0.87]
Long 2006	0.12218449	0.07061765	2.3%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	2.4%	0.77 [0.67 , 0.88]
Rahman 2001 (2)	-0.05001042	0.06042171	3.2%	0.95 [0.84 , 1.07]
Rahman 2001	-0.13353139	0.0579042	3.4%	0.88 [0.78 , 0.98]
Baqui 2003	-0.02439145	0.05739701	3.5%	0.98 [0.87 , 1.09]
Islam 2022	-0.0101	0.0486	4.9%	0.99 [0.90 , 1.09]
Sazawal 1996	-0.08461665	0.04515217	5.7%	0.92 [0.84 , 1.00]
Hess 2015	-0.0305	0.0382	7.9%	0.97 [0.90 , 1.05]
Malik 2014	-0.489176152	0.029183580172245	13.6%	0.61 [0.58 , 0.65]
Bhandari 2002	-0.10583655	0.02613411	16.9%	0.90 [0.85 , 0.95]
Becquey 2016	-0.1625	0.0246	19.1%	0.85 [0.81 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.85 [0.83 , 0.87]**
Heterogeneity: Chi² = 236.97, df = 29 (P < 0.00001); I² = 88%				
Test for overall effect: Z = 15.07 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



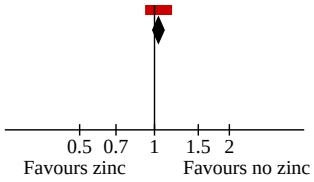
Analysis 2.10. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 10: Incidence of all-cause diarrhea: formulation subgroup analysis



Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.10.1 Solution				
Abdollahi 2019	0.174	0.0939	1.8%	1.19 [0.99 , 1.43]
Alarcon 2004	-0.33963305	0.30181636	0.2%	0.71 [0.39 , 1.29]
Baqui 2003	-0.02439145	0.05739701	4.9%	0.98 [0.87 , 1.09]
Baqui 2003 (2)	0.08849308	0.05540904	5.3%	1.09 [0.98 , 1.22]
Bhandari 2002	-0.10583655	0.02613411	23.7%	0.90 [0.85 , 0.95]
Gupta 2003	-0.89381788	0.22473329	0.3%	0.41 [0.26 , 0.64]
Gupta 2007	-0.14660347	0.097381	1.7%	0.86 [0.71 , 1.05]
Larson 2010	-0.23381808	0.08123116	2.4%	0.79 [0.68 , 0.93]
Lind 2003	0.06899287	0.09065627	2.0%	1.07 [0.90 , 1.28]
Lind 2003 (2)	-0.07145896	0.09311961	1.9%	0.93 [0.78 , 1.12]
Long 2006	0.12218449	0.07061765	3.2%	1.13 [0.98 , 1.30]
Long 2006 (2)	-0.26514098	0.06888881	3.4%	0.77 [0.67 , 0.88]
Malik 2014	-0.489176152	0.029183580172245	19.0%	0.61 [0.58 , 0.65]
Meeks Gardner 1998	0.00421645	0.25610818	0.2%	1.00 [0.61 , 1.66]
Meeks Gardner 2005	-4.48367263	1.42163731	0.0%	0.01 [0.00 , 0.18]
Penny 2004	-0.11778304	0.10486269	1.5%	0.89 [0.72 , 1.09]
Rahman 2001	-0.13353139	0.0579042	4.8%	0.88 [0.78 , 0.98]
Rahman 2001 (2)	-0.05001042	0.06042171	4.4%	0.95 [0.84 , 1.07]
Richard 2006	-0.28106642	0.07078211	3.2%	0.75 [0.66 , 0.87]
Richard 2006 (2)	0.03619935	0.06581383	3.7%	1.04 [0.91 , 1.18]
Rosado 1997	-0.40188729	0.20280294	0.4%	0.67 [0.45 , 1.00]
Rosado 1997 (2)	-0.52044108	0.18680745	0.5%	0.59 [0.41 , 0.86]
Ruel 1997	-0.25131443	0.10417938	1.5%	0.78 [0.63 , 0.95]
Sazawal 1996	-0.08461665	0.04515217	7.9%	0.92 [0.84 , 1.00]
Umeta 2000	-0.78170058	0.23234928	0.3%	0.46 [0.29 , 0.72]
Wuehler 2008	-0.30010459	0.09601332	1.8%	0.74 [0.61 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.85 [0.82 , 0.87]**
Heterogeneity: Chi² = 250.02, df = 25 (P < 0.00001); I² = 90%				
Test for overall effect: Z = 13.25 (P < 0.00001)				
2.10.2 Pill/tablet				
Becquey 2016	-0.1625	0.0246	52.7%	0.85 [0.81 , 0.89]
Chang 2010	-0.58978851	0.331496772	0.3%	0.55 [0.29 , 1.06]
Chang 2010 (2)	-0.275374225	0.368438063	0.2%	0.76 [0.37 , 1.56]
Chhagan 2009	-0.04913269	0.07335707	5.9%	0.95 [0.82 , 1.10]
Hess 2015	-0.0305	0.0382	21.8%	0.97 [0.90 , 1.05]
Islam 2022	-0.0101	0.0486	13.5%	0.99 [0.90 , 1.09]
Müller 2001	-0.14077255	0.07595902	5.5%	0.87 [0.75 , 1.01]
Subtotal (95% CI)			**100.0%**	**0.90 [0.87 , 0.93]**
Heterogeneity: Chi² = 16.23, df = 6 (P = 0.01); I² = 63%				
Test for overall effect: Z = 5.97 (P < 0.00001)				
2.10.3 Capsule				
Veenemans 2011	-0.22342699	0.19743482	44.8%	0.80 [0.54 , 1.18]
Veenemans 2011 (2)	-0.27010424	0.17803183	55.2%	0.76 [0.54 , 1.08]
Subtotal (95% CI)			**100.0%**	**0.78 [0.60 , 1.01]**
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%				
Test for overall effect: Z = 1.88 (P = 0.06)				
2.10.4 Powder				
Sampaio 2013	-0.26503449302337	0.373888956972379	0.5%	0.77 [0.37 , 1.60]
Soofi 2013	0.0377403279828471	0.0268956156251902	99.5%	1.04 [0.99 , 1.09]
Subtotal (95% CI)			**100.0%**	**1.04 [0.98 , 1.09]**
Heterogeneity: Chi² = 0.65, df = 1 (P = 0.42); I² = 0%				

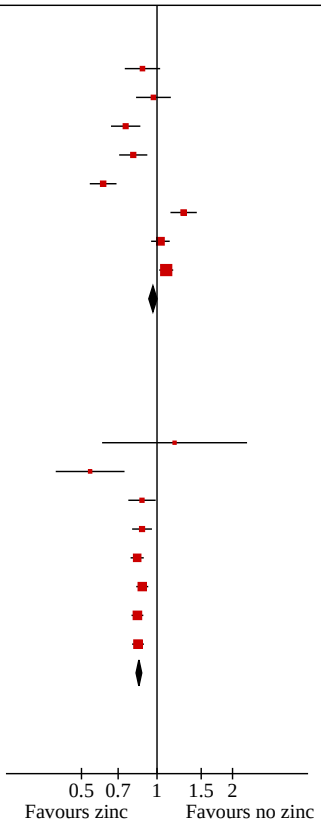
Analysis 2.10. (Continued)

Subtotal (95% CI)			**100.0%**	**1.04 [0.98 , 1.09]**
Heterogeneity: Chi² = 0.65, df = 1 (P = 0.42); I² = 0%				
Test for overall effect: Z = 1.35 (P = 0.18)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



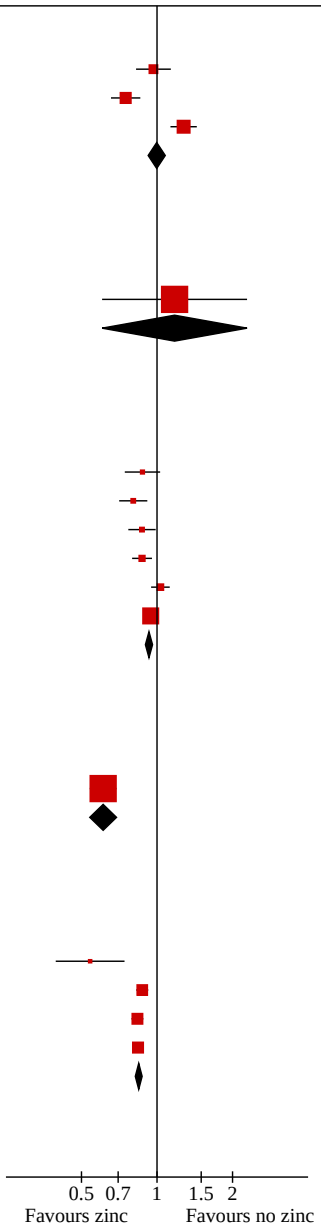
Analysis 2.11. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 11: Prevalence of all-cause diarrhea: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.11.1 6 months to < 1 year				
Chhagan 2009	-0.13353139	0.08272645	5.4%	0.88 [0.74 , 1.03]
Chang 2010	-0.03278982	0.08135338	5.5%	0.97 [0.83 , 1.14]
Chang 2010 (2)	-0.28768207	0.06864827	7.8%	0.75 [0.66 , 0.86]
Ruel 1997	-0.21813101	0.06585277	8.5%	0.80 [0.71 , 0.91]
Malik 2014	-0.494296322	0.062532388	9.4%	0.61 [0.54 , 0.69]
Brown 2007	0.24419696	0.06163859	9.7%	1.28 [1.13 , 1.44]
Soofi 2013	0.0312234804470357	0.0435336459823005	19.4%	1.03 [0.95 , 1.12]
Sazawal 1996	0.08441583	0.03268014	34.4%	1.09 [1.02 , 1.16]
Subtotal (95% CI)			**100.0%**	**0.96 [0.93 , 1.00]**
Heterogeneity: Chi² = 112.81, df = 7 (P < 0.00001); I² = 94%				
Test for overall effect: Z = 1.96 (P = 0.05)				
2.11.2 1 to < 5 years				
Shankar 2000	0.16121482	0.33931045	0.2%	1.17 [0.60 , 2.28]
Alarcon 2004	-0.61376215	0.1610153	0.7%	0.54 [0.39 , 0.74]
Penny 2004	-0.13786979	0.06396739	4.3%	0.87 [0.77 , 0.99]
Müller 2001	-0.13740764	0.04640859	8.1%	0.87 [0.80 , 0.95]
Sazawal 1996	-0.18199862	0.03080603	18.4%	0.83 [0.78 , 0.89]
Rahman 2001 (2)	-0.13550106	0.0280183	22.3%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	22.9%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	23.2%	0.84 [0.80 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.85 [0.83 , 0.87]**
Heterogeneity: Chi² = 11.03, df = 7 (P = 0.14); I² = 37%				
Test for overall effect: Z = 12.58 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



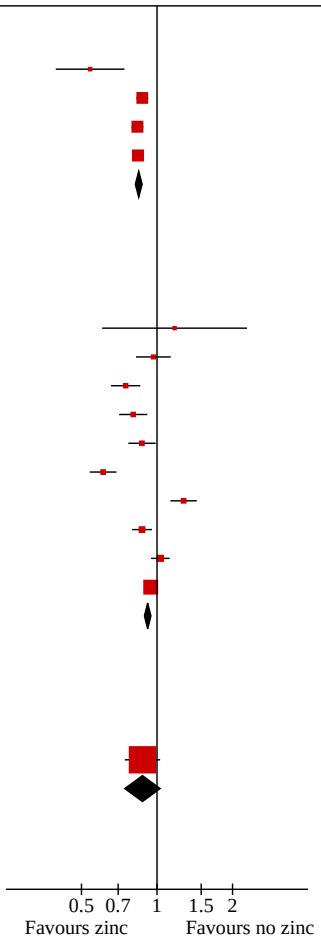
Analysis 2.12. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 12: Prevalence of all-cause diarrhea: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.12.1 0 to < 5 mg				
Chang 2010	-0.03278982	0.08135338	24.1%	0.97 [0.83 , 1.14]
Chang 2010 (2)	-0.28768207	0.06864827	33.9%	0.75 [0.66 , 0.86]
Brown 2007	0.24419696	0.06163859	42.0%	1.28 [1.13 , 1.44]
Subtotal (95% CI)			**100.0%**	**1.00 [0.92 , 1.08]**
Heterogeneity: Chi² = 33.41, df = 2 (P < 0.00001); I² = 94%				
Test for overall effect: Z = 0.07 (P = 0.95)				
2.12.2 5 to < 10 mg				
Shankar 2000	0.16121482	0.33931045	100.0%	1.17 [0.60 , 2.28]
Subtotal (95% CI)			**100.0%**	**1.17 [0.60 , 2.28]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.48 (P = 0.63)				
2.12.3 10 to < 15 mg				
Chhagan 2009	-0.13353139	0.08272645	4.0%	0.88 [0.74 , 1.03]
Ruel 1997	-0.21813101	0.06585277	6.4%	0.80 [0.71 , 0.91]
Penny 2004	-0.13786979	0.06396739	6.8%	0.87 [0.77 , 0.99]
Müller 2001	-0.13740764	0.04640859	12.9%	0.87 [0.80 , 0.95]
Soofi 2013	0.0312234804470357	0.0435336459823005	14.6%	1.03 [0.95 , 1.12]
Sazawal 1996	-0.05786738	0.02237039	55.3%	0.94 [0.90 , 0.99]
Subtotal (95% CI)			**100.0%**	**0.93 [0.90 , 0.96]**
Heterogeneity: Chi² = 14.53, df = 5 (P = 0.01); I² = 66%				
Test for overall effect: Z = 4.43 (P < 0.00001)				
2.12.4 15 to < 20 mg				
Malik 2014	-0.494296322	0.062532388	100.0%	0.61 [0.54 , 0.69]
Subtotal (95% CI)			**100.0%**	**0.61 [0.54 , 0.69]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 7.90 (P < 0.00001)				
2.12.5 20 mg or more				
Alarcon 2004	-0.61376215	0.1610153	1.0%	0.54 [0.39 , 0.74]
Rahman 2001 (2)	-0.13550106	0.0280183	32.2%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	33.2%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	33.6%	0.84 [0.80 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.85 [0.82 , 0.87]**
Heterogeneity: Chi² = 9.24, df = 3 (P = 0.03); I² = 68%				
Test for overall effect: Z = 10.55 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				



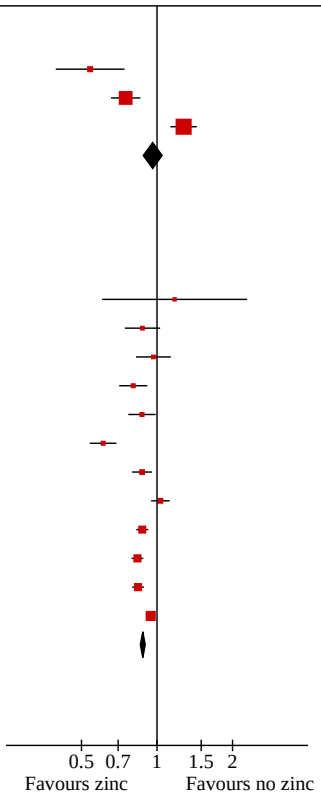
Analysis 2.13. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 13: Prevalence of all-cause diarrhea: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.13.1 0 to < 6 months				
Alarcon 2004	-0.61376215	0.1610153	1.0%	0.54 [0.39 , 0.74]
Rahman 2001 (2)	-0.13550106	0.0280183	32.2%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	33.2%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	33.6%	0.84 [0.80 , 0.89]
Subtotal (95% CI)			**100.0%**	**0.85 [0.82 , 0.87]**
Heterogeneity: Chi² = 9.24, df = 3 (P = 0.03); I² = 68%				
Test for overall effect: Z = 10.55 (P < 0.00001)				
2.13.2 6 to < 12 months				
Shankar 2000	0.16121482	0.33931045	0.2%	1.17 [0.60 , 2.28]
Chang 2010	-0.03278982	0.08135338	3.5%	0.97 [0.83 , 1.14]
Chang 2010 (2)	-0.28768207	0.06864827	4.9%	0.75 [0.66 , 0.86]
Ruel 1997	-0.21813101	0.06585277	5.3%	0.80 [0.71 , 0.91]
Penny 2004	-0.13786979	0.06396739	5.6%	0.87 [0.77 , 0.99]
Malik 2014	-0.494296322	0.062532388	5.9%	0.61 [0.54 , 0.69]
Brown 2007	0.24419696	0.06163859	6.0%	1.28 [1.13 , 1.44]
Müller 2001	-0.13740764	0.04640859	10.7%	0.87 [0.80 , 0.95]
Soofi 2013	0.0312234804470357	0.0435336459823005	12.1%	1.03 [0.95 , 1.12]
Sazawal 1996	-0.05786738	0.02237039	45.9%	0.94 [0.90 , 0.99]
Subtotal (95% CI)			**100.0%**	**0.92 [0.89 , 0.95]**
Heterogeneity: Chi² = 95.66, df = 9 (P < 0.00001); I² = 91%				
Test for overall effect: Z = 5.66 (P < 0.00001)				
2.13.3 12 months or more				
Chhagan 2009	-0.13353139	0.08272645	100.0%	0.88 [0.74 , 1.03]
Subtotal (95% CI)			**100.0%**	**0.88 [0.74 , 1.03]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.61 (P = 0.11)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



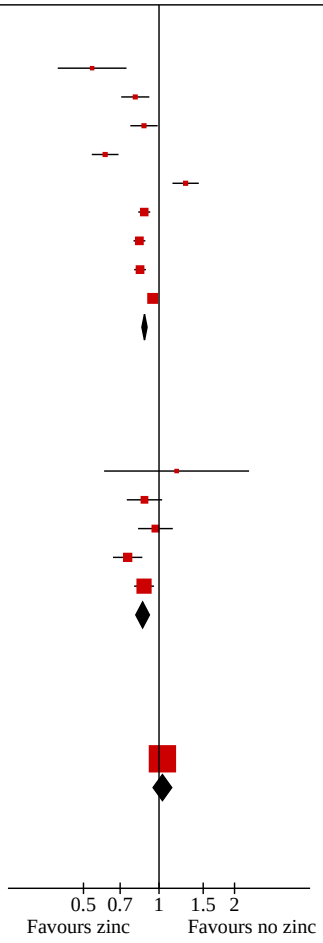
Analysis 2.14. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 14: Prevalence of all-cause diarrhea: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.14.1 Iron co-intervention				
Alarcon 2004	-0.61376215	0.1610153	7.5%	0.54 [0.39 , 0.74]
Chang 2010 (2)	-0.28768207	0.06864827	41.3%	0.75 [0.66 , 0.86]
Brown 2007	0.24419696	0.06163859	51.2%	1.28 [1.13 , 1.44]
Subtotal (95% CI)			**100.0%**	**0.96 [0.88 , 1.05]**
Heterogeneity: Chi² = 46.97, df = 2 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 0.90 (P = 0.37)				
2.14.2 No iron co-intervention				
Shankar 2000	0.16121482	0.33931045	0.1%	1.17 [0.60 , 2.28]
Chhagan 2009	-0.13353139	0.08272645	1.8%	0.88 [0.74 , 1.03]
Chang 2010	-0.03278982	0.08135338	1.9%	0.97 [0.83 , 1.14]
Ruel 1997	-0.21813101	0.06585277	2.9%	0.80 [0.71 , 0.91]
Penny 2004	-0.13786979	0.06396739	3.1%	0.87 [0.77 , 0.99]
Malik 2014	-0.494296322	0.062532388	3.2%	0.61 [0.54 , 0.69]
Müller 2001	-0.13740764	0.04640859	5.8%	0.87 [0.80 , 0.95]
Soofi 2013	0.0312234804470357	0.0435336459823005	6.6%	1.03 [0.95 , 1.12]
Rahman 2001 (2)	-0.13550106	0.0280183	16.0%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	16.5%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	16.7%	0.84 [0.80 , 0.89]
Sazawal 1996	-0.05786738	0.02237039	25.2%	0.94 [0.90 , 0.99]
Subtotal (95% CI)			**100.0%**	**0.88 [0.86 , 0.90]**
Heterogeneity: Chi² = 67.94, df = 11 (P < 0.00001); I² = 84%				
Test for overall effect: Z = 11.63 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



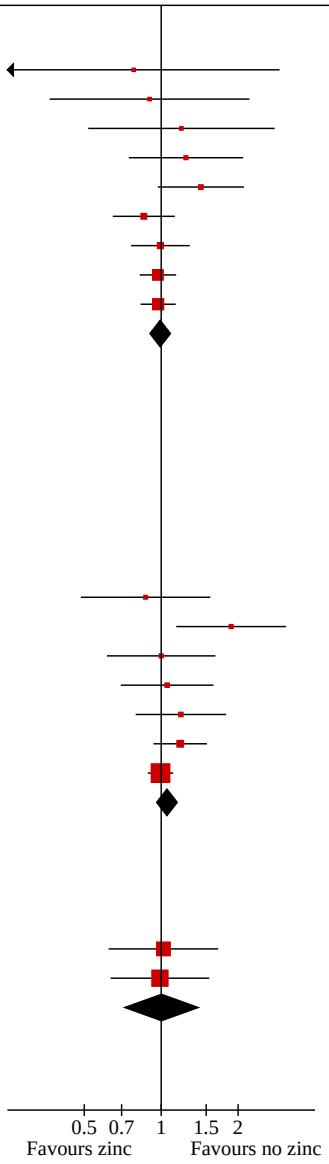
Analysis 2.15. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 15: Prevalence of all-cause diarrhea: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.15.1 Solution				
Alarcon 2004	-0.61376215	0.1610153	0.6%	0.54 [0.39 , 0.74]
Ruel 1997	-0.21813101	0.06585277	3.3%	0.80 [0.71 , 0.91]
Penny 2004	-0.13786979	0.06396739	3.5%	0.87 [0.77 , 0.99]
Malik 2014	-0.494296322	0.062532388	3.7%	0.61 [0.54 , 0.69]
Brown 2007	0.24419696	0.06163859	3.8%	1.28 [1.13 , 1.44]
Rahman 2001 (2)	-0.13550106	0.0280183	18.3%	0.87 [0.83 , 0.92]
Bhandari 2002	-0.17979311	0.02761673	18.9%	0.84 [0.79 , 0.88]
Rahman 2001	-0.17423253	0.02743331	19.1%	0.84 [0.80 , 0.89]
Sazawal 1996	-0.05786738	0.02237039	28.8%	0.94 [0.90 , 0.99]
Subtotal (95% CI)			**100.0%**	**0.88 [0.85 , 0.90]**
Heterogeneity: Chi² = 97.84, df = 8 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 11.10 (P < 0.00001)				
2.15.2 Pill/tablet				
Shankar 2000	0.16121482	0.33931045	0.9%	1.17 [0.60 , 2.28]
Chhagan 2009	-0.13353139	0.08272645	14.9%	0.88 [0.74 , 1.03]
Chang 2010	-0.03278982	0.08135338	15.4%	0.97 [0.83 , 1.14]
Chang 2010 (2)	-0.28768207	0.06864827	21.6%	0.75 [0.66 , 0.86]
Müller 2001	-0.13740764	0.04640859	47.3%	0.87 [0.80 , 0.95]
Subtotal (95% CI)			**100.0%**	**0.86 [0.81 , 0.92]**
Heterogeneity: Chi² = 7.05, df = 4 (P = 0.13); I² = 43%				
Test for overall effect: Z = 4.72 (P < 0.00001)				
2.15.3 Powder				
Soofi 2013	0.0312234804470357	0.0435336459823005	100.0%	1.03 [0.95 , 1.12]
Subtotal (95% CI)			**100.0%**	**1.03 [0.95 , 1.12]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.72 (P = 0.47)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



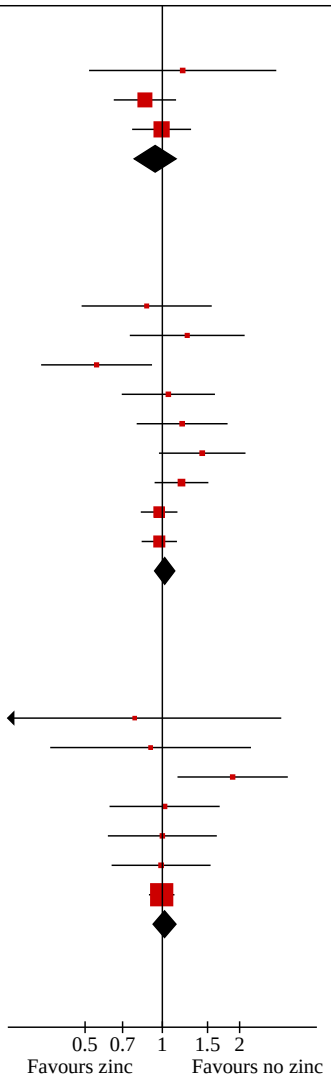
Analysis 2.16. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 16: Incidence of LRTI: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.16.1 6 months to < 1 year				
Long 2006 (2)	-0.24816892	0.67082039	0.5%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	1.0%	0.90 [0.37 , 2.21]
Brown 2007	0.18232156	0.42839042	1.2%	1.20 [0.52 , 2.78]
Soofi 2013	0.22314355131421	0.262771200970603	3.2%	1.25 [0.75 , 2.09]
Islam 2022	0.3577	0.198	5.6%	1.43 [0.97 , 2.11]
Baqui 2003 (2)	-0.15645218	0.14256197	10.9%	0.86 [0.65 , 1.13]
Baqui 2003	-0.00673403	0.13486419	12.2%	0.99 [0.76 , 1.29]
Lind 2003 (2)	-0.02898754	0.08383997	31.5%	0.97 [0.82 , 1.14]
Lind 2003	-0.02739897	0.08077837	33.9%	0.97 [0.83 , 1.14]
Subtotal (95% CI)			**100.0%**	**0.99 [0.90 , 1.09]**
Heterogeneity: Chi² = 5.76, df = 8 (P = 0.67); I² = 0%				
Test for overall effect: Z = 0.19 (P = 0.85)				
2.16.2 1 to < 5 years				
Meeks Gardner 1998	0	0		Not estimable
Meeks Gardner 2005	0	0		Not estimable
Sazawal 1996	0	0		Not estimable
Sempértegui 1996	0	0		Not estimable
Penny 2004	-0.14058195	0.29777877	2.5%	0.87 [0.48 , 1.56]
Rahman 2001	0.63062682	0.25241624	3.5%	1.88 [1.15 , 3.08]
Rahman 2001 (2)	0	0.24928541	3.6%	1.00 [0.61 , 1.63]
Veenemans 2011	0.05383699	0.2132558	4.9%	1.06 [0.69 , 1.60]
Veenemans 2011 (2)	0.17745056	0.20798032	5.2%	1.19 [0.79 , 1.80]
Müller 2001	0.17162318	0.12304944	14.7%	1.19 [0.93 , 1.51]
Bhandari 2002	-0.00591199	0.05834957	65.6%	0.99 [0.89 , 1.11]
Subtotal (95% CI)			**100.0%**	**1.05 [0.96 , 1.16]**
Heterogeneity: Chi² = 8.01, df = 6 (P = 0.24); I² = 25%				
Test for overall effect: Z = 1.10 (P = 0.27)				
2.16.3 5 to < 13 years				
Richard 2006 (2)	0.02032	0.25200806	44.7%	1.02 [0.62 , 1.67]
Richard 2006	-0.01129956	0.22645541	55.3%	0.99 [0.63 , 1.54]
Subtotal (95% CI)			**100.0%**	**1.00 [0.72 , 1.40]**
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%				
Test for overall effect: Z = 0.02 (P = 0.99)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



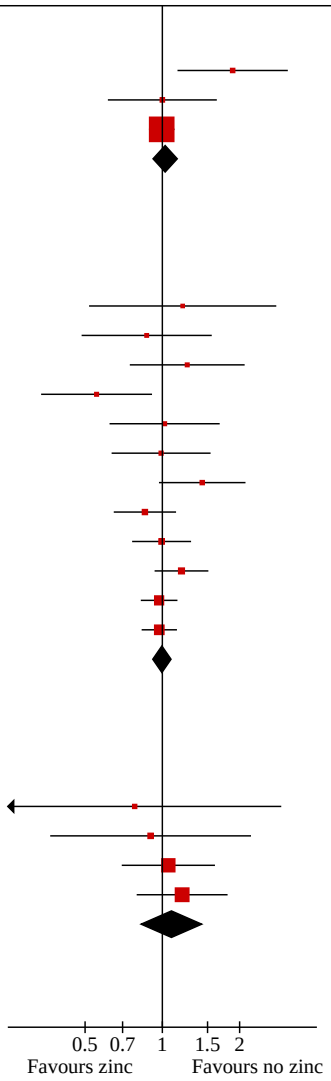
Analysis 2.17. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 17: Incidence of LRTI: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.17.1 0 to < 5 mg				
Brown 2007	0.18232156	0.42839042	5.0%	1.20 [0.52 , 2.78]
Baqui 2003 (2)	-0.15645218	0.14256197	44.9%	0.86 [0.65 , 1.13]
Baqui 2003	-0.00673403	0.13486419	50.1%	0.99 [0.76 , 1.29]
Subtotal (95% CI)			**100.0%**	**0.94 [0.78 , 1.13]**
Heterogeneity: Chi² = 0.93, df = 2 (P = 0.63); I² = 0%				
Test for overall effect: Z = 0.68 (P = 0.50)				
2.17.2 10 to < 15 mg				
Penny 2004	-0.14058195	0.29777877	2.4%	0.87 [0.48 , 1.56]
Soofi 2013	0.22314355131421	0.262771200970603	3.1%	1.25 [0.75 , 2.09]
Sazawal 1996	-0.59000642	0.25375961	3.3%	0.55 [0.34 , 0.91]
Veenemans 2011	0.05383699	0.2132558	4.6%	1.06 [0.69 , 1.60]
Veenemans 2011 (2)	0.17745056	0.20798032	4.9%	1.19 [0.79 , 1.80]
Islam 2022	0.3577	0.198	5.4%	1.43 [0.97 , 2.11]
Müller 2001	0.17162318	0.12304944	13.9%	1.19 [0.93 , 1.51]
Lind 2003 (2)	-0.02898754	0.08383997	30.0%	0.97 [0.82 , 1.14]
Lind 2003	-0.02739897	0.08077837	32.4%	0.97 [0.83 , 1.14]
Subtotal (95% CI)			**100.0%**	**1.02 [0.93 , 1.12]**
Heterogeneity: Chi² = 12.38, df = 8 (P = 0.14); I² = 35%				
Test for overall effect: Z = 0.46 (P = 0.65)				
2.17.3 20 mg or more				
Long 2006 (2)	-0.24816892	0.67082039	0.6%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	1.3%	0.90 [0.37 , 2.21]
Rahman 2001	0.63062682	0.25241624	4.3%	1.88 [1.15 , 3.08]
Richard 2006 (2)	0.02032	0.25200806	4.3%	1.02 [0.62 , 1.67]
Rahman 2001 (2)	0	0.24928541	4.4%	1.00 [0.61 , 1.63]
Richard 2006	-0.01129956	0.22645541	5.3%	0.99 [0.63 , 1.54]
Bhandari 2002	-0.00591199	0.05834957	79.9%	0.99 [0.89 , 1.11]
Subtotal (95% CI)			**100.0%**	**1.02 [0.92 , 1.13]**
Heterogeneity: Chi² = 6.31, df = 6 (P = 0.39); I² = 5%				
Test for overall effect: Z = 0.38 (P = 0.71)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



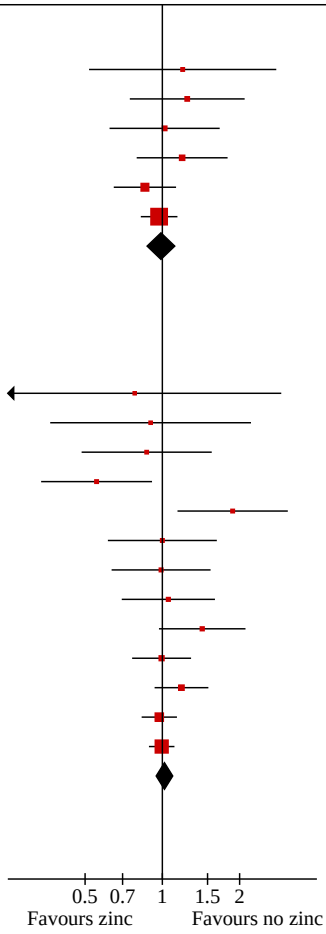
Analysis 2.18. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 18: Incidence of LRTI: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.18.1 0 to < 6 months				
Rahman 2001	0.63062682	0.25241624	4.8%	1.88 [1.15 , 3.08]
Rahman 2001 (2)	0	0.24928541	4.9%	1.00 [0.61 , 1.63]
Bhandari 2002	-0.00591199	0.05834957	90.2%	0.99 [0.89 , 1.11]
Subtotal (95% CI)			**100.0%**	**1.03 [0.92 , 1.14]**
Heterogeneity: Chi² = 6.05, df = 2 (P = 0.05); I² = 67%				
Test for overall effect: Z = 0.45 (P = 0.65)				
2.18.2 6 to < 12 months				
Brown 2007	0.18232156	0.42839042	1.0%	1.20 [0.52 , 2.78]
Penny 2004	-0.14058195	0.29777877	2.0%	0.87 [0.48 , 1.56]
Soofi 2013	0.22314355131421	0.262771200970603	2.5%	1.25 [0.75 , 2.09]
Sazawal 1996	-0.59000642	0.25375961	2.7%	0.55 [0.34 , 0.91]
Richard 2006 (2)	0.02032	0.25200806	2.7%	1.02 [0.62 , 1.67]
Richard 2006	-0.01129956	0.22645541	3.4%	0.99 [0.63 , 1.54]
Islam 2022	0.3577	0.198	4.4%	1.43 [0.97 , 2.11]
Baqui 2003 (2)	-0.15645218	0.14256197	8.6%	0.86 [0.65 , 1.13]
Baqui 2003	-0.00673403	0.13486419	9.6%	0.99 [0.76 , 1.29]
Müller 2001	0.17162318	0.12304944	11.5%	1.19 [0.93 , 1.51]
Lind 2003 (2)	-0.02898754	0.08383997	24.8%	0.97 [0.82 , 1.14]
Lind 2003	-0.02739897	0.08077837	26.7%	0.97 [0.83 , 1.14]
Subtotal (95% CI)			**100.0%**	**1.00 [0.92 , 1.08]**
Heterogeneity: Chi² = 13.18, df = 11 (P = 0.28); I² = 17%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2.18.3 12 months or more				
Long 2006 (2)	-0.24816892	0.67082039	4.3%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	9.1%	0.90 [0.37 , 2.21]
Veenemans 2011	0.05383699	0.2132558	42.2%	1.06 [0.69 , 1.60]
Veenemans 2011 (2)	0.17745056	0.20798032	44.4%	1.19 [0.79 , 1.80]
Subtotal (95% CI)			**100.0%**	**1.08 [0.83 , 1.42]**
Heterogeneity: Chi² = 0.64, df = 3 (P = 0.89); I² = 0%				
Test for overall effect: Z = 0.59 (P = 0.56)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



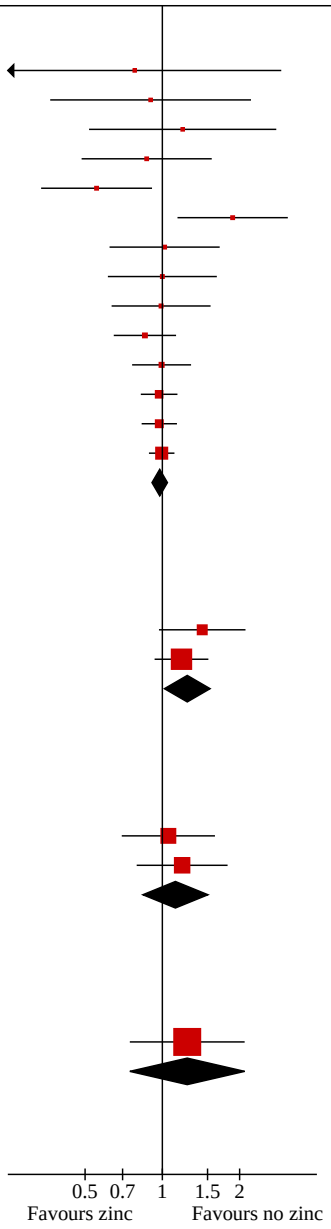
Analysis 2.19. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 19: Incidence of LRTI: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.19.1 Iron co-intervention				
Brown 2007	0.18232156	0.42839042	2.2%	1.20 [0.52 , 2.78]
Soofi 2013	0.22314355131421	0.262771200970603	5.8%	1.25 [0.75 , 2.09]
Richard 2006 (2)	0.02032	0.25200806	6.3%	1.02 [0.62 , 1.67]
Veenemans 2011 (2)	0.17745056	0.20798032	9.2%	1.19 [0.79 , 1.80]
Baqui 2003 (2)	-0.15645218	0.14256197	19.7%	0.86 [0.65 , 1.13]
Lind 2003 (2)	-0.02898754	0.08383997	56.8%	0.97 [0.82 , 1.14]
Subtotal (95% CI)			**100.0%**	**0.99 [0.87 , 1.12]**
Heterogeneity: Chi² = 2.92, df = 5 (P = 0.71); I² = 0%				
Test for overall effect: Z = 0.20 (P = 0.84)				
2.19.2 No iron co-intervention				
Long 2006 (2)	-0.24816892	0.67082039	0.3%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	0.7%	0.90 [0.37 , 2.21]
Penny 2004	-0.14058195	0.29777877	1.6%	0.87 [0.48 , 1.56]
Sazawal 1996	-0.59000642	0.25375961	2.2%	0.55 [0.34 , 0.91]
Rahman 2001	0.63062682	0.25241624	2.2%	1.88 [1.15 , 3.08]
Rahman 2001 (2)	0	0.24928541	2.3%	1.00 [0.61 , 1.63]
Richard 2006	-0.01129956	0.22645541	2.8%	0.99 [0.63 , 1.54]
Veenemans 2011	0.05383699	0.2132558	3.1%	1.06 [0.69 , 1.60]
Islam 2022	0.3577	0.198	3.6%	1.43 [0.97 , 2.11]
Baqui 2003	-0.00673403	0.13486419	7.8%	0.99 [0.76 , 1.29]
Müller 2001	0.17162318	0.12304944	9.4%	1.19 [0.93 , 1.51]
Lind 2003	-0.02739897	0.08077837	21.9%	0.97 [0.83 , 1.14]
Bhandari 2002	-0.00591199	0.05834957	41.9%	0.99 [0.89 , 1.11]
Subtotal (95% CI)			**100.0%**	**1.02 [0.95 , 1.10]**
Heterogeneity: Chi² = 17.21, df = 12 (P = 0.14); I² = 30%				
Test for overall effect: Z = 0.50 (P = 0.62)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Analysis 2.20. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 20: Incidence of LRTI: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.20.1 Solution				
Long 2006 (2)	-0.24816892	0.67082039	0.3%	0.78 [0.21 , 2.91]
Long 2006	-0.10536052	0.45946829	0.6%	0.90 [0.37 , 2.21]
Brown 2007	0.18232156	0.42839042	0.7%	1.20 [0.52 , 2.78]
Penny 2004	-0.14058195	0.29777877	1.4%	0.87 [0.48 , 1.56]
Sazawal 1996	-0.59000642	0.25375961	1.9%	0.55 [0.34 , 0.91]
Rahman 2001	0.63062682	0.25241624	2.0%	1.88 [1.15 , 3.08]
Richard 2006 (2)	0.02032	0.25200806	2.0%	1.02 [0.62 , 1.67]
Rahman 2001 (2)	0	0.24928541	2.0%	1.00 [0.61 , 1.63]
Richard 2006	-0.01129956	0.22645541	2.4%	0.99 [0.63 , 1.54]
Baqui 2003 (2)	-0.15645218	0.14256197	6.2%	0.86 [0.65 , 1.13]
Baqui 2003	-0.00673403	0.13486419	6.9%	0.99 [0.76 , 1.29]
Lind 2003 (2)	-0.02898754	0.08383997	17.8%	0.97 [0.82 , 1.14]
Lind 2003	-0.02739897	0.08077837	19.2%	0.97 [0.83 , 1.14]
Bhandari 2002	-0.00591199	0.05834957	36.7%	0.99 [0.89 , 1.11]
Subtotal (95% CI)			**100.0%**	**0.98 [0.91 , 1.05]**
Heterogeneity: Chi² = 13.25, df = 13 (P = 0.43); I² = 2%				
Test for overall effect: Z = 0.67 (P = 0.50)				
2.20.2 Pill/tablet				
Islam 2022	0.3577	0.198	27.9%	1.43 [0.97 , 2.11]
Müller 2001	0.17162318	0.12304944	72.1%	1.19 [0.93 , 1.51]
Subtotal (95% CI)			**100.0%**	**1.25 [1.02 , 1.53]**
Heterogeneity: Chi² = 0.64, df = 1 (P = 0.42); I² = 0%				
Test for overall effect: Z = 2.14 (P = 0.03)				
2.20.3 Capsule				
Veenemans 2011	0.05383699	0.2132558	48.7%	1.06 [0.69 , 1.60]
Veenemans 2011 (2)	0.17745056	0.20798032	51.3%	1.19 [0.79 , 1.80]
Subtotal (95% CI)			**100.0%**	**1.12 [0.84 , 1.51]**
Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² = 0%				
Test for overall effect: Z = 0.79 (P = 0.43)				
2.20.4 Powder				
Soofi 2013	0.22314355131421	0.262771200970603	100.0%	1.25 [0.75 , 2.09]
Subtotal (95% CI)			**100.0%**	**1.25 [0.75 , 2.09]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.85 (P = 0.40)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				

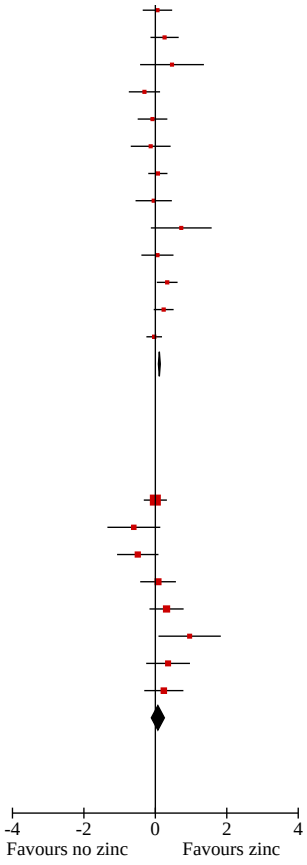


Analysis 2.21. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 21: Height: country income level subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.21.1 Low- or middle-income				
Abdollahi 2014	0.081207	0.082178	2.6%	0.08 [-0.08 , 0.24]
Abdollahi 2019	0.2262	0.0835	2.5%	0.23 [0.06 , 0.39]
Akramuzzaman 1994	0	0.14216714	0.9%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.17562403	0.13685249	0.9%	0.18 [-0.09 , 0.44]
Baqui 2003	-0.0369072	0.11899992	1.2%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.0375915	0.11833	1.2%	-0.04 [-0.27 , 0.19]
Barffour 2019	0	0.052	6.4%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	20.0%	0.09 [0.04 , 0.15]
Bhandari 2002	-0.045968	0.04238854	9.7%	-0.05 [-0.13 , 0.04]
Bhandari 2007	0.14273438	0.0697166	3.6%	0.14 [0.01 , 0.28]
Brown 2007	0.02831727	0.15073647	0.8%	0.03 [-0.27 , 0.32]
Castillo-Durán 1994	0.35835025	0.313	0.2%	0.36 [-0.26 , 0.97]
Cavan 1993	-0.1909372	0.15976556	0.7%	-0.19 [-0.50 , 0.12]
Chen 2012	0.1524128	0.148308100564911	0.8%	0.15 [-0.14 , 0.44]
De Fonseca 2002	-0.1685443	0.19990018	0.4%	-0.17 [-0.56 , 0.22]
Dehbozorgi 2007	-1.9734985	0.31209312	0.2%	-1.97 [-2.59 , -1.36]
DiGirolamo 2010	-0.0968094	0.07476273	3.1%	-0.10 [-0.24 , 0.05]
Ebrahimi 2006	1.2611452	0.07721922	2.9%	1.26 [1.11 , 1.41]
Friis 1997	0.03899074	0.12009587	1.2%	0.04 [-0.20 , 0.27]
Garcia 1998	0.10584806	0.34006946	0.2%	0.11 [-0.56 , 0.77]
Gracia 2005	-0.0189634	0.13144479	1.0%	-0.02 [-0.28 , 0.24]
Han 2002	0.97763178	0.26685037	0.2%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.0379151	0.26134196	0.3%	-0.04 [-0.55 , 0.47]
Hess 2015	0.0098	0.0573	5.3%	0.01 [-0.10 , 0.12]
Hettiarachchi 2008	0.43865049	0.21702312	0.4%	0.44 [0.01 , 0.86]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	0.3%	0.14 [-0.32 , 0.60]
Hong 1982	1.09400346	0.18644996	0.5%	1.09 [0.73 , 1.46]
Ince 1995	0.45028253	0.40793136	0.1%	0.45 [-0.35 , 1.25]
Isdiany 2021	-0.2724	0.3671	0.1%	-0.27 [-0.99 , 0.45]
Islam 2022	0.9992	0.071	3.5%	1.00 [0.86 , 1.14]
Kaseb 2013	-0.123585	0.205411	0.4%	-0.12 [-0.53 , 0.28]
Khodashenas 2015	-0.008279	0.298217	0.2%	-0.01 [-0.59 , 0.58]
Kikafunda 1998	-0.0212582	0.18705861	0.5%	-0.02 [-0.39 , 0.35]
Kusumastuti 2018	-1.1518	0.3738	0.1%	-1.15 [-1.88 , -0.42]
Kusumastuti 2018 (2)	-1.1878	0.3757	0.1%	-1.19 [-1.92 , -0.45]
Lind 2003	0.04482357	0.11052917	1.4%	0.04 [-0.17 , 0.26]
Lind 2003 (2)	-0.2645621	0.11134035	1.4%	-0.26 [-0.48 , -0.05]
Long 2006	0.1584015	0.11813857	1.2%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	1.3%	-0.10 [-0.33 , 0.13]
Mandlik 2020	-0.1172	0.1284	1.1%	-0.12 [-0.37 , 0.13]
Mazariegos 2010	-0.0445451	0.10189635	1.7%	-0.04 [-0.24 , 0.16]
Meeks Gardner 1998	0.11783456	0.26252076	0.3%	0.12 [-0.40 , 0.63]
Meeks Gardner 2005	-0.2358912	0.18682894	0.5%	-0.24 [-0.60 , 0.13]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.3%	0.88 [0.44 , 1.33]
Müller 2001	0.09988615	0.07775177	2.9%	0.10 [-0.05 , 0.25]
Ninh 1996	0.34634509	0.16590035	0.6%	0.35 [0.02 , 0.67]
Penny 2004	0.13724615	0.16491512	0.6%	0.14 [-0.19 , 0.46]
Rahman 2001	-0.0086731	0.11069586	1.4%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	1.4%	-0.20 [-0.42 , 0.01]
Rerksuppaphol 2018	0.437487	0.177583	0.6%	0.44 [0.09 , 0.79]
Richard 2006	0.12404623	0.10262789	1.7%	0.12 [-0.08 , 0.33]
Richard 2006 (2)	0.01147736	0.10286111	1.6%	0.01 [-0.19 , 0.21]
Rosado 1997	0.07813202	0.20362659	0.4%	0.08 [-0.32 , 0.48]
Rosado 1997 (2)	0.11812477	0.19963612	0.4%	0.12 [-0.27 , 0.51]
Ruel 1997	0.05883983	0.21022626	0.4%	0.06 [-0.35 , 0.47]
Ruz 1997	0.25866462	0.20129773	0.4%	0.26 [-0.14 , 0.65]
Sazawal Porto 2000	0.46627519	0.45563575	0.1%	0.47 [-0.42 , 1.36]

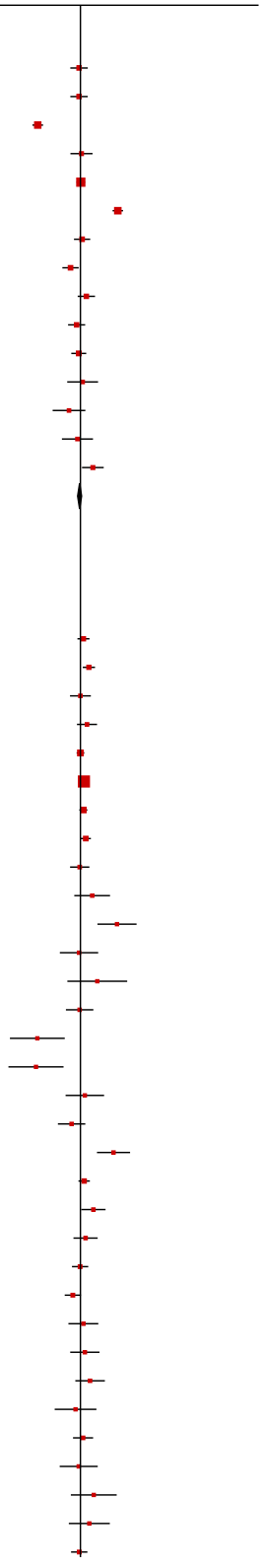
Analysis 2.21. (Continued)

Ruz 1997	0.25866462	0.20129773	0.4%	0.26 [-0.14 , 0.65]
Sayeg Porto 2000	0.46637519	0.45563575	0.1%	0.47 [-0.43 , 1.36]
Sazawal 2006	-0.3053788	0.22312277	0.3%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.0794432	0.21183638	0.4%	-0.08 [-0.49 , 0.34]
Sempértegui 1996	-0.1304811	0.28450141	0.2%	-0.13 [-0.69 , 0.43]
Shankar 2000	0.07055089	0.13696712	0.9%	0.07 [-0.20 , 0.34]
Silva 2006	-0.0460732	0.25926942	0.3%	-0.05 [-0.55 , 0.46]
Smith 1999	0.725292	0.43412761	0.1%	0.73 [-0.13 , 1.58]
Tupe 2009	0.05864615	0.22908102	0.3%	0.06 [-0.39 , 0.51]
Umeta 2000	0.33222629	0.14785133	0.8%	0.33 [0.04 , 0.62]
Vakili 2015	0.23296	0.14191	0.9%	0.23 [-0.05 , 0.51]
Wuehler 2008	-0.0319341	0.11140371	1.4%	-0.03 [-0.25 , 0.19]
Subtotal (95% CI)			**100.0%**	**0.11 [0.09 , 0.14]**
Heterogeneity: Chi² = 599.46, df = 66 (P < 0.00001); I² = 89%				
Test for overall effect: Z = 8.48 (P < 0.00001)				
2.21.2 High-income				
Berger 2015	0	0.164992	31.8%	0.00 [-0.32 , 0.32]
Bertinato 2013	-0.601946	0.377514	6.1%	-0.60 [-1.34 , 0.14]
Clark 1999	-0.4920502	0.295419	9.9%	-0.49 [-1.07 , 0.09]
Gibson 1989	0.07592408	0.25493989	13.3%	0.08 [-0.42 , 0.58]
Hambidge 1978	0.31355858	0.24369413	14.6%	0.31 [-0.16 , 0.79]
Nakamura 1993	0.96009475	0.44484717	4.4%	0.96 [0.09 , 1.83]
Walravens 1983	0.3564118	0.31249613	8.9%	0.36 [-0.26 , 0.97]
Walravens 1989	0.2375538	0.27941182	11.1%	0.24 [-0.31 , 0.79]
Subtotal (95% CI)			**100.0%**	**0.07 [-0.11 , 0.25]**
Heterogeneity: Chi² = 13.17, df = 7 (P = 0.07); I² = 47%				
Test for overall effect: Z = 0.76 (P = 0.45)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



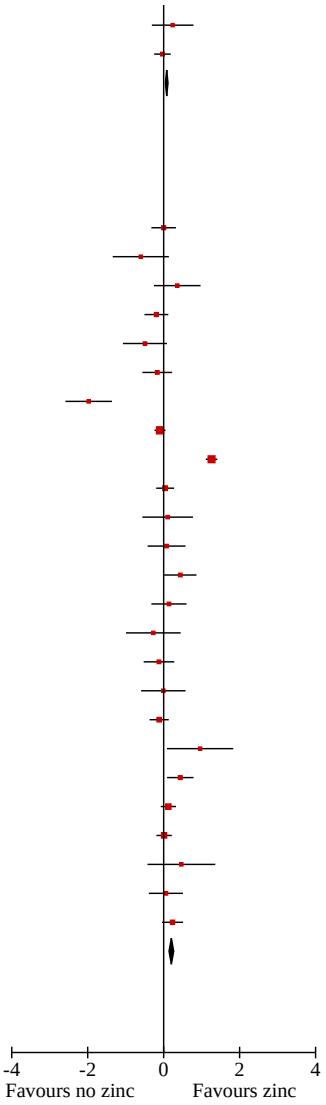
Analysis 2.22. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 22: Height: age subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.22.1 6 months to < 1 year				
Baqui 2003	-0.0369072	0.11899992	5.1%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.0375915	0.11833	5.1%	-0.04 [-0.27 , 0.19]
Bhandari 2002	-1.1409712	0.07231489	13.7%	-1.14 [-1.28 , -1.00]
Brown 2007	0.02831727	0.15073647	3.2%	0.03 [-0.27 , 0.32]
Hess 2015	0.0098	0.0573	21.8%	0.01 [-0.10 , 0.12]
Islam 2022	0.9992	0.071	14.2%	1.00 [0.86 , 1.14]
Lind 2003	0.04482357	0.11052917	5.9%	0.04 [-0.17 , 0.26]
Lind 2003 (2)	-0.2645621	0.11134035	5.8%	-0.26 [-0.48 , -0.05]
Long 2006	0.1584015	0.11813857	5.1%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	5.3%	-0.10 [-0.33 , 0.13]
Mazariegos 2010	-0.0445451	0.10189635	6.9%	-0.04 [-0.24 , 0.16]
Ruel 1997	0.05883983	0.21022626	1.6%	0.06 [-0.35 , 0.47]
Sazawal 2006	-0.3053788	0.22312277	1.4%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.0794432	0.21183638	1.6%	-0.08 [-0.49 , 0.34]
Umeta 2000	0.33222629	0.14785133	3.3%	0.33 [0.04 , 0.62]
Subtotal (95% CI)			**100.0%**	**-0.02 [-0.07 , 0.03]**
Heterogeneity: Chi^2 = 462.29, df = 14 (P < 0.00001); I^2 = 97%				
Test for overall effect: Z = 0.82 (P = 0.41)				
2.22.2 1 to < 5 years				
Abdollahi 2014	0.081207	0.082178	4.5%	0.08 [-0.08 , 0.24]
Abdollahi 2019	0.2262	0.0835	4.3%	0.23 [0.06 , 0.39]
Akramuzzaman 1994	0	0.14216714	1.5%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.17562403	0.13685249	1.6%	0.18 [-0.09 , 0.44]
Barffour 2019	0	0.052	11.1%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	34.5%	0.09 [0.04 , 0.15]
Bhandari 2002	0.07809866	0.05477259	10.0%	0.08 [-0.03 , 0.19]
Bhandari 2007	0.14273438	0.0697166	6.2%	0.14 [0.01 , 0.28]
Gracia 2005	-0.0189634	0.13144479	1.7%	-0.02 [-0.28 , 0.24]
Hambidge 1978	0.31355858	0.24369413	0.5%	0.31 [-0.16 , 0.79]
Han 2002	0.97763178	0.26685037	0.4%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.0379151	0.26134196	0.4%	-0.04 [-0.55 , 0.47]
Ince 1995	0.45028253	0.40793136	0.2%	0.45 [-0.35 , 1.25]
Kikafunda 1998	-0.0212582	0.18705861	0.9%	-0.02 [-0.39 , 0.35]
Kusumastuti 2018	-1.1518	0.3738	0.2%	-1.15 [-1.88 , -0.42]
Kusumastuti 2018 (2)	-1.1878	0.3757	0.2%	-1.19 [-1.92 , -0.45]
Meeks Gardner 1998	0.11783456	0.26252076	0.4%	0.12 [-0.40 , 0.63]
Meeks Gardner 2005	-0.2358912	0.18682894	0.9%	-0.24 [-0.60 , 0.13]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.6%	0.88 [0.44 , 1.33]
Müller 2001	0.09988615	0.07775177	5.0%	0.10 [-0.05 , 0.25]
Ninh 1996	0.34634509	0.16590035	1.1%	0.35 [0.02 , 0.67]
Penny 2004	0.13724615	0.16491512	1.1%	0.14 [-0.19 , 0.46]
Rahman 2001	-0.0086731	0.11069586	2.5%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	2.5%	-0.20 [-0.42 , 0.01]
Rosado 1997	0.07813202	0.20362659	0.7%	0.08 [-0.32 , 0.48]
Rosado 1997 (2)	0.11812477	0.19963612	0.8%	0.12 [-0.27 , 0.51]
Ruz 1997	0.25866462	0.20129773	0.7%	0.26 [-0.14 , 0.65]
Sempértegui 1996	-0.1304811	0.28450141	0.4%	-0.13 [-0.69 , 0.43]
Shankar 2000	0.07055089	0.13696712	1.6%	0.07 [-0.20 , 0.34]
Silva 2006	-0.0460732	0.25926942	0.4%	-0.05 [-0.55 , 0.46]
Walravens 1983	0.3564118	0.31249613	0.3%	0.36 [-0.26 , 0.97]
Walravens 1989	0.2375538	0.27941182	0.4%	0.24 [-0.31 , 0.79]
Wuehler 2008	-0.0319341	0.11140371	2.4%	-0.03 [-0.25 , 0.19]



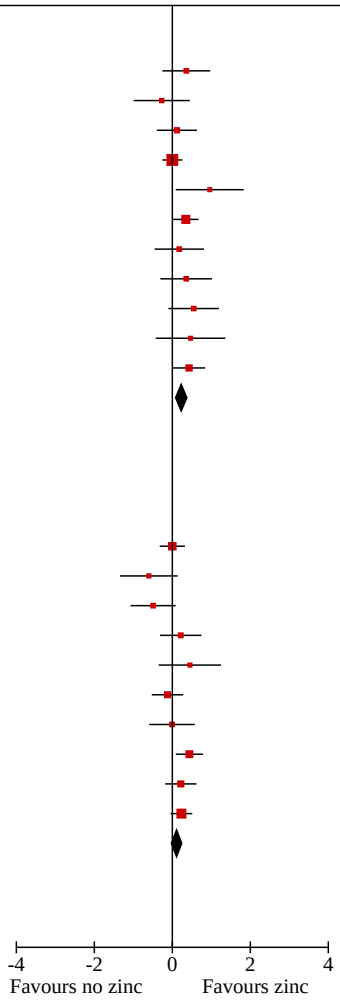
Analysis 2.22. (Continued)

Walravens 1989	0.2375538	0.27941182	0.4%	0.24 [-0.31 , 0.79]
Wuehler 2008	-0.0319341	0.11140371	2.4%	-0.03 [-0.25 , 0.19]
Subtotal (95% CI)			**100.0%**	**0.08 [0.05 , 0.11]**
Heterogeneity: Chi² = 72.89, df = 32 (P < 0.0001); I² = 56%				
Test for overall effect: Z = 4.60 (P < 0.00001)				
2.22.3 5 to < 13 years				
Berger 2015	0	0.164992	3.6%	0.00 [-0.32 , 0.32]
Bertinato 2013	-0.601946	0.377514	0.7%	-0.60 [-1.34 , 0.14]
Castillo-Durán 1994	0.35835025	0.313	1.0%	0.36 [-0.26 , 0.97]
Cavan 1993	-0.1909372	0.15976556	3.8%	-0.19 [-0.50 , 0.12]
Clark 1999	-0.4920502	0.295419	1.1%	-0.49 [-1.07 , 0.09]
De Fonseca 2002	-0.1685443	0.19990018	2.4%	-0.17 [-0.56 , 0.22]
Dehbozorgi 2007	-1.9734985	0.31209312	1.0%	-1.97 [-2.59 , -1.36]
DiGirolamo 2010	-0.0968094	0.07476273	17.5%	-0.10 [-0.24 , 0.05]
Ebrahimi 2006	1.2611452	0.07721922	16.4%	1.26 [1.11 , 1.41]
Friis 1997	0.03899074	0.12009587	6.8%	0.04 [-0.20 , 0.27]
Garcia 1998	0.10584806	0.34006946	0.8%	0.11 [-0.56 , 0.77]
Gibson 1989	0.07592408	0.25493989	1.5%	0.08 [-0.42 , 0.58]
Hettiarachchi 2008	0.43865049	0.21702312	2.1%	0.44 [0.01 , 0.86]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	1.8%	0.14 [-0.32 , 0.60]
Isdiany 2021	-0.2724	0.3671	0.7%	-0.27 [-0.99 , 0.45]
Kaseb 2013	-0.123585	0.205411	2.3%	-0.12 [-0.53 , 0.28]
Khodashenas 2015	-0.008279	0.298217	1.1%	-0.01 [-0.59 , 0.58]
Mandlik 2020	-0.1172	0.1284	5.9%	-0.12 [-0.37 , 0.13]
Nakamura 1993	0.96009475	0.44484717	0.5%	0.96 [0.09 , 1.83]
Rerksuppaphol 2018	0.437487	0.177583	3.1%	0.44 [0.09 , 0.79]
Richard 2006	0.12404623	0.10262789	9.3%	0.12 [-0.08 , 0.33]
Richard 2006 (2)	0.01147736	0.10286111	9.2%	0.01 [-0.19 , 0.21]
Sayeg Porto 2000	0.46637519	0.45563575	0.5%	0.47 [-0.43 , 1.36]
Tupe 2009	0.05864615	0.22908102	1.9%	0.06 [-0.39 , 0.51]
Vakili 2015	0.23296	0.14191	4.9%	0.23 [-0.05 , 0.51]
Subtotal (95% CI)			**100.0%**	**0.20 [0.14 , 0.26]**
Heterogeneity: Chi² = 297.72, df = 24 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 6.48 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.23. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 23: Height: stunting subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.23.1 Stunted				
Castillo-Durán 1994	0.35835025	0.313	5.5%	0.36 [-0.26 , 0.97]
Isdiany 2021	-0.2724	0.3671	4.0%	-0.27 [-0.99 , 0.45]
Meeks Gardner 1998	0.11783456	0.26252076	7.8%	0.12 [-0.40 , 0.63]
Müller 2001	0	0.13121916	31.2%	0.00 [-0.26 , 0.26]
Nakamura 1993	0.96009475	0.44484717	2.7%	0.96 [0.09 , 1.83]
Ninh 1996	0.34634509	0.16590035	19.5%	0.35 [0.02 , 0.67]
Rosado 1997	0.17781309	0.32248232	5.2%	0.18 [-0.45 , 0.81]
Rosado 1997 (2)	0.35504653	0.33765126	4.7%	0.36 [-0.31 , 1.02]
Ruel 1997	0.54855892	0.33095524	4.9%	0.55 [-0.10 , 1.20]
Sayeg Porto 2000	0.46637519	0.45563575	2.6%	0.47 [-0.43 , 1.36]
Umeta 2000	0.42869384	0.21144491	12.0%	0.43 [0.01 , 0.84]
Subtotal (95% CI)			**100.0%**	**0.23 [0.08 , 0.37]**
Heterogeneity: Chi² = 10.72, df = 10 (P = 0.38); I² = 7%				
Test for overall effect: Z = 3.11 (P = 0.002)				
2.23.2 Non-stunted				
Berger 2015	0	0.164992	17.1%	0.00 [-0.32 , 0.32]
Bertinato 2013	-0.601946	0.377514	3.3%	-0.60 [-1.34 , 0.14]
Clark 1999	-0.4920502	0.295419	5.3%	-0.49 [-1.07 , 0.09]
De Fonseca 2002	0.21562858	0.27068867	6.4%	0.22 [-0.31 , 0.75]
Ince 1995	0.45028253	0.40793136	2.8%	0.45 [-0.35 , 1.25]
Kaseb 2013	-0.123585	0.205411	11.0%	-0.12 [-0.53 , 0.28]
Khodashenas 2015	-0.008279	0.298217	5.2%	-0.01 [-0.59 , 0.58]
Rerksuppaphol 2018	0.437487	0.177583	14.8%	0.44 [0.09 , 0.79]
Umeta 2000	0.2171002	0.20520976	11.0%	0.22 [-0.19 , 0.62]
Vakili 2015	0.23296	0.14191	23.1%	0.23 [-0.05 , 0.51]
Subtotal (95% CI)			**100.0%**	**0.11 [-0.02 , 0.24]**
Heterogeneity: Chi² = 14.88, df = 9 (P = 0.09); I² = 40%				
Test for overall effect: Z = 1.59 (P = 0.11)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				

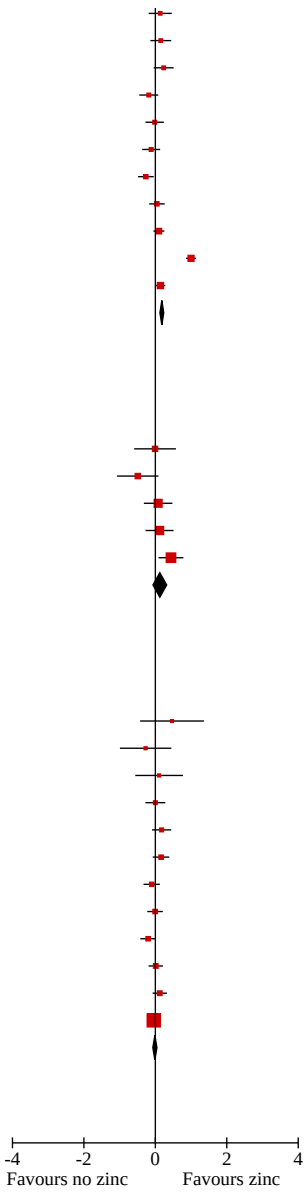


Analysis 2.24. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 24: Height: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.24.1 0 to < 5 mg				
Han 2002	0.97763178	0.26685037	4.8%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.0379151	0.26134196	5.0%	-0.04 [-0.55 , 0.47]
De Fonseca 2002	-0.1685443	0.19990018	8.5%	-0.17 [-0.56 , 0.22]
Brown 2007	0.02831727	0.15073647	15.0%	0.03 [-0.27 , 0.32]
Wuehler 2008	0	0.13722953	18.1%	0.00 [-0.27 , 0.27]
Baqui 2003	-0.0369072	0.11899992	24.1%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.0375915	0.11833	24.4%	-0.04 [-0.27 , 0.19]
Subtotal (95% CI)			**100.0%**	**0.02 [-0.10 , 0.13]**
Heterogeneity: Chi² = 14.30, df = 6 (P = 0.03); I² = 58%				
Test for overall effect: Z = 0.29 (P = 0.77)				
2.24.2 5 to < 10 mg				
Dehbozorgi 2007	-1.9734985	0.31209312	0.4%	-1.97 [-2.59 , -1.36]
Meeks Gardner 1998	0.11783456	0.26252076	0.6%	0.12 [-0.40 , 0.63]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.8%	0.88 [0.44 , 1.33]
Kaseb 2013	-0.123585	0.205411	0.9%	-0.12 [-0.53 , 0.28]
Kikafunda 1998	-0.0212582	0.18705861	1.1%	-0.02 [-0.39 , 0.35]
Berger 2015	0	0.164992	1.5%	0.00 [-0.32 , 0.32]
Cavan 1993	-0.1909372	0.15976556	1.6%	-0.19 [-0.50 , 0.12]
Umeta 2000	0.33222629	0.14785133	1.8%	0.33 [0.04 , 0.62]
Wuehler 2008	0.13026379	0.13841928	2.1%	0.13 [-0.14 , 0.40]
Shankar 2000	0.07055089	0.13696712	2.1%	0.07 [-0.20 , 0.34]
Mazariegos 2010	-0.0445451	0.10189635	3.8%	-0.04 [-0.24 , 0.16]
Abdollahi 2019	0.2262	0.0835	5.7%	0.23 [0.06 , 0.39]
Abdollahi 2014	0.081207	0.082178	5.9%	0.08 [-0.08 , 0.24]
Ebrahimi 2006	1.2611452	0.07721922	6.7%	1.26 [1.11 , 1.41]
DiGirolamo 2010	-0.0968094	0.07476273	7.1%	-0.10 [-0.24 , 0.05]
Hess 2015	0.0098	0.0573	12.1%	0.01 [-0.10 , 0.12]
Becquey 2016	0.0935	0.0295	45.7%	0.09 [0.04 , 0.15]
Subtotal (95% CI)			**100.0%**	**0.14 [0.10 , 0.18]**
Heterogeneity: Chi² = 299.42, df = 16 (P < 0.00001); I² = 95%				
Test for overall effect: Z = 7.15 (P < 0.00001)				
2.24.3 10 to < 15 mg				
Smith 1999	0.725292	0.43412761	0.4%	0.73 [-0.13 , 1.58]
Ince 1995	0.45028253	0.40793136	0.4%	0.45 [-0.35 , 1.25]
Bertinato 2013	-0.601946	0.377514	0.5%	-0.60 [-1.34 , 0.14]
Kusumastuti 2018 (2)	-1.1878	0.3757	0.5%	-1.19 [-1.92 , -0.45]
Kusumastuti 2018	-1.1518	0.3738	0.5%	-1.15 [-1.88 , -0.42]
Castillo-Durán 1994	0.35835025	0.313	0.7%	0.36 [-0.26 , 0.97]
Walravens 1983	0.3564118	0.31249613	0.8%	0.36 [-0.26 , 0.97]
Sempértegui 1996	-0.1304811	0.28450141	0.9%	-0.13 [-0.69 , 0.43]
Silva 2006	-0.0460732	0.25926942	1.1%	-0.05 [-0.55 , 0.46]
Gibson 1989	0.07592408	0.25493989	1.1%	0.08 [-0.42 , 0.58]
Hambidge 1978	0.31355858	0.24369413	1.2%	0.31 [-0.16 , 0.79]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	1.3%	0.14 [-0.32 , 0.60]
Tupe 2009	0.05864615	0.22908102	1.4%	0.06 [-0.39 , 0.51]
Sazawal 2006	-0.3053788	0.22312277	1.5%	-0.31 [-0.74 , 0.13]
Hettiarachchi 2008	0.43865049	0.21702312	1.6%	0.44 [0.01 , 0.86]
Sazawal 2006 (2)	-0.0794432	0.21183638	1.6%	-0.08 [-0.49 , 0.34]
Ruel 1997	0.05883983	0.21022626	1.7%	0.06 [-0.35 , 0.47]
Ruz 1997	0.25866462	0.20129773	1.8%	0.26 [-0.14 , 0.65]
Meeks Gardner 2005	-0.2358912	0.18682894	2.1%	-0.24 [-0.60 , 0.13]
Ninh 1996	0.34634509	0.16590035	2.7%	0.35 [0.02 , 0.67]
Penny 2004	0.13724615	0.16491512	2.7%	0.14 [-0.19 , 0.46]
Chen 2012	0.1524128	0.148308100564911	3.3%	0.15 [-0.14 , 0.44]
Vakili 2015	0.22296	0.14191	3.6%	0.22 [-0.05 , 0.51]

Analysis 2.24. (Continued)

Penny 2004	0.13724615	0.16491512	2.7%	0.14 [-0.19 , 0.46]
Chen 2012	0.1524128	0.148308100564911	3.3%	0.15 [-0.14 , 0.44]
Vakili 2015	0.23296	0.14191	3.6%	0.23 [-0.05 , 0.51]
Wuehler 2008	-0.1839257	0.13527897	4.0%	-0.18 [-0.45 , 0.08]
Gracia 2005	-0.0189634	0.13144479	4.2%	-0.02 [-0.28 , 0.24]
Mandlik 2020	-0.1172	0.1284	4.5%	-0.12 [-0.37 , 0.13]
Lind 2003 (2)	-0.2645621	0.11134035	5.9%	-0.26 [-0.48 , -0.05]
Lind 2003	0.04482357	0.11052917	6.0%	0.04 [-0.17 , 0.26]
Müller 2001	0.09988615	0.07775177	12.1%	0.10 [-0.05 , 0.25]
Islam 2022	0.9992	0.071	14.6%	1.00 [0.86 , 1.14]
Bhandari 2007	0.14273438	0.0697166	15.1%	0.14 [0.01 , 0.28]
Subtotal (95% CI)			**100.0%**	**0.18 [0.13 , 0.23]**
Heterogeneity: Chi² = 216.76, df = 30 (P < 0.00001); I² = 86%				
Test for overall effect: Z = 6.70 (P < 0.00001)				
2.24.4 15 to < 20 mg				
Khodashenas 2015	-0.008279	0.298217	10.9%	-0.01 [-0.59 , 0.58]
Clark 1999	-0.4920502	0.295419	11.1%	-0.49 [-1.07 , 0.09]
Rosado 1997	0.07813202	0.20362659	23.3%	0.08 [-0.32 , 0.48]
Rosado 1997 (2)	0.11812477	0.19963612	24.2%	0.12 [-0.27 , 0.51]
Rerksuppaphol 2018	0.437487	0.177583	30.6%	0.44 [0.09 , 0.79]
Subtotal (95% CI)			**100.0%**	**0.13 [-0.07 , 0.32]**
Heterogeneity: Chi² = 7.71, df = 4 (P = 0.10); I² = 48%				
Test for overall effect: Z = 1.28 (P = 0.20)				
2.24.5 20 mg or more				
Sayeg Porto 2000	0.46637519	0.45563575	0.4%	0.47 [-0.43 , 1.36]
Isdiany 2021	-0.2724	0.3671	0.6%	-0.27 [-0.99 , 0.45]
Garcia 1998	0.10584806	0.34006946	0.7%	0.11 [-0.56 , 0.77]
Akramuzzaman 1994	0	0.14216714	4.2%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.17562403	0.13685249	4.5%	0.18 [-0.09 , 0.44]
Long 2006	0.1584015	0.11813857	6.1%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	6.2%	-0.10 [-0.33 , 0.13]
Rahman 2001	-0.0086731	0.11069586	6.9%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	6.9%	-0.20 [-0.42 , 0.01]
Richard 2006 (2)	0.01147736	0.10286111	8.0%	0.01 [-0.19 , 0.21]
Richard 2006	0.12404623	0.10262789	8.1%	0.12 [-0.08 , 0.33]
Bhandari 2002	-0.045968	0.04238854	47.2%	-0.05 [-0.13 , 0.04]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.07 , 0.04]**
Heterogeneity: Chi² = 11.73, df = 11 (P = 0.38); I² = 6%				
Test for overall effect: Z = 0.46 (P = 0.65)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				

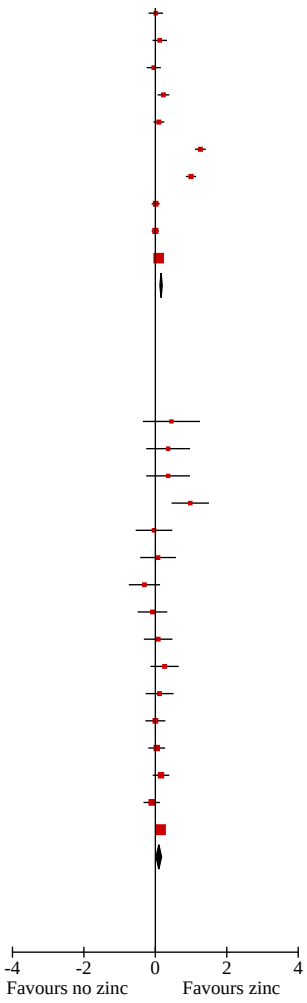


Analysis 2.25. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 25: Height: duration subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.25.1 0 to < 6 months				
Bertinato 2013	-0.601946	0.377514	0.5%	-0.60 [-1.34 , 0.14]
Kusumastuti 2018 (2)	-1.1878	0.3757	0.5%	-1.19 [-1.92 , -0.45]
Kusumastuti 2018	-1.1518	0.3738	0.5%	-1.15 [-1.88 , -0.42]
Isdiany 2021	-0.2724	0.3671	0.5%	-0.27 [-0.99 , 0.45]
Clark 1999	-0.4920502	0.295419	0.8%	-0.49 [-1.07 , 0.09]
Sempértegui 1996	-0.1304811	0.28450141	0.9%	-0.13 [-0.69 , 0.43]
Meeks Gardner 1998	0.11783456	0.26252076	1.1%	0.12 [-0.40 , 0.63]
Silva 2006	-0.0460732	0.25926942	1.1%	-0.05 [-0.55 , 0.46]
Tupe 2009	0.05864615	0.22908102	1.4%	0.06 [-0.39 , 0.51]
Kaseb 2013	-0.123585	0.205411	1.8%	-0.12 [-0.53 , 0.28]
De Fonseca 2002	-0.1685443	0.19990018	1.9%	-0.17 [-0.56 , 0.22]
Hong 1982	1.09400346	0.18644996	2.1%	1.09 [0.73 , 1.46]
Ninh 1996	0.34634509	0.16590035	2.7%	0.35 [0.02 , 0.67]
Berger 2015	0	0.164992	2.7%	0.00 [-0.32 , 0.32]
Alarcon 2004	0.17562403	0.13685249	3.9%	0.18 [-0.09 , 0.44]
Rahman 2001	-0.0086731	0.11069586	6.0%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	6.1%	-0.20 [-0.42 , 0.01]
Abdollahi 2014	0.081207	0.082178	11.0%	0.08 [-0.08 , 0.24]
DiGirolamo 2010	-0.0968094	0.07476273	13.2%	-0.10 [-0.24 , 0.05]
Bhandari 2002	-0.045968	0.04238854	41.2%	-0.05 [-0.13 , 0.04]
Subtotal (95% CI)			**100.0%**	**-0.02 [-0.08 , 0.03]**
Heterogeneity: Chi² = 73.92, df = 19 (P < 0.00001); I² = 74%				
Test for overall effect: Z = 0.81 (P = 0.42)				
2.25.2 6 to < 12 months				
Sayeg Porto 2000	0.46637519	0.45563575	0.1%	0.47 [-0.43 , 1.36]
Nakamura 1993	0.96009475	0.44484717	0.1%	0.96 [0.09 , 1.83]
Smith 1999	0.725292	0.43412761	0.1%	0.73 [-0.13 , 1.58]
Garcia 1998	0.10584806	0.34006946	0.2%	0.11 [-0.56 , 0.77]
Dehbozorgi 2007	-1.9734985	0.31209312	0.3%	-1.97 [-2.59 , -1.36]
Khodashenas 2015	-0.008279	0.298217	0.3%	-0.01 [-0.59 , 0.58]
Walravens 1989	0.2375538	0.27941182	0.3%	0.24 [-0.31 , 0.79]
Hambidge 1978	0.31355858	0.24369413	0.4%	0.31 [-0.16 , 0.79]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	0.5%	0.14 [-0.32 , 0.60]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.5%	0.88 [0.44 , 1.33]
Hettiarachchi 2008	0.43865049	0.21702312	0.6%	0.44 [0.01 , 0.86]
Ruel 1997	0.05883983	0.21022626	0.6%	0.06 [-0.35 , 0.47]
Kikafunda 1998	-0.0212582	0.18705861	0.7%	-0.02 [-0.39 , 0.35]
Meeks Gardner 2005	-0.2358912	0.18682894	0.7%	-0.24 [-0.60 , 0.13]
Rerksuppaphol 2018	0.437487	0.177583	0.8%	0.44 [0.09 , 0.79]
Penny 2004	0.13724615	0.16491512	1.0%	0.14 [-0.19 , 0.46]
Cavan 1993	-0.1909372	0.15976556	1.0%	-0.19 [-0.50 , 0.12]
Brown 2007	0.02831727	0.15073647	1.1%	0.03 [-0.27 , 0.32]
Chen 2012	0.1524128	0.148308100564911	1.2%	0.15 [-0.14 , 0.44]
Umeta 2000	0.33222629	0.14785133	1.2%	0.33 [0.04 , 0.62]
Vakili 2015	0.23296	0.14191	1.3%	0.23 [-0.05 , 0.51]
Shankar 2000	0.07055089	0.13696712	1.4%	0.07 [-0.20 , 0.34]
Gracia 2005	-0.0189634	0.13144479	1.5%	-0.02 [-0.28 , 0.24]
Mandlik 2020	-0.1172	0.1284	1.6%	-0.12 [-0.37 , 0.13]
Baqui 2003	-0.0369072	0.11899992	1.8%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.0375915	0.11833	1.9%	-0.04 [-0.27 , 0.19]
Wuehler 2008	-0.0319341	0.11140371	2.1%	-0.03 [-0.25 , 0.19]
Lind 2003 (2)	-0.2645621	0.11134035	2.1%	-0.26 [-0.48 , -0.05]
Lind 2003	0.04482357	0.11052917	2.1%	0.04 [-0.17 , 0.26]
Richard 2006 (2)	0.01147736	0.10286111	2.5%	0.01 [-0.19 , 0.21]
Richard 2006	0.12404623	0.10262789	2.5%	0.12 [-0.08 , 0.33]
Mazariegos 2010	0.0445451	0.10189625	2.5%	0.04 [-0.24 , 0.16]

Analysis 2.25. (Continued)

Richard 2006 (2)	0.01147736	0.10286111	2.5%	0.01 [-0.19 , 0.21]
Richard 2006	0.12404623	0.10262789	2.5%	0.12 [-0.08 , 0.33]
Mazariegos 2010	-0.0445451	0.10189635	2.5%	-0.04 [-0.24 , 0.16]
Abdollahi 2019	0.2262	0.0835	3.7%	0.23 [0.06 , 0.39]
Müller 2001	0.09988615	0.07775177	4.3%	0.10 [-0.05 , 0.25]
Ebrahimi 2006	1.2611452	0.07721922	4.4%	1.26 [1.11 , 1.41]
Islam 2022	0.9992	0.071	5.2%	1.00 [0.86 , 1.14]
Hess 2015	0.0098	0.0573	7.9%	0.01 [-0.10 , 0.12]
Barffour 2019	0	0.052	9.6%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	29.9%	0.09 [0.04 , 0.15]
Subtotal (95% CI)			**100.0%**	**0.16 [0.13 , 0.19]**
Heterogeneity: Chi² = 483.22, df = 38 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 9.95 (P < 0.00001)				
2.25.3 12 months or more				
Ince 1995	0.45028253	0.40793136	0.9%	0.45 [-0.35 , 1.25]
Castillo-Durán 1994	0.35835025	0.313	1.6%	0.36 [-0.26 , 0.97]
Walravens 1983	0.3564118	0.31249613	1.6%	0.36 [-0.26 , 0.97]
Han 2002	0.97763178	0.26685037	2.1%	0.98 [0.45 , 1.50]
Han 2002 (2)	-0.0379151	0.26134196	2.2%	-0.04 [-0.55 , 0.47]
Gibson 1989	0.07592408	0.25493989	2.3%	0.08 [-0.42 , 0.58]
Sazawal 2006	-0.3053788	0.22312277	3.1%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.0794432	0.21183638	3.4%	-0.08 [-0.49 , 0.34]
Rosado 1997	0.07813202	0.20362659	3.7%	0.08 [-0.32 , 0.48]
Ruz 1997	0.25866462	0.20129773	3.8%	0.26 [-0.14 , 0.65]
Rosado 1997 (2)	0.11812477	0.19963612	3.8%	0.12 [-0.27 , 0.51]
Akramuzzaman 1994	0	0.14216714	7.5%	0.00 [-0.28 , 0.28]
Friis 1997	0.03899074	0.12009587	10.6%	0.04 [-0.20 , 0.27]
Long 2006	0.1584015	0.11813857	10.9%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	11.2%	-0.10 [-0.33 , 0.13]
Bhandari 2007	0.14273438	0.0697166	31.3%	0.14 [0.01 , 0.28]
Subtotal (95% CI)			**100.0%**	**0.10 [0.02 , 0.17]**
Heterogeneity: Chi² = 22.21, df = 15 (P = 0.10); I² = 32%				
Test for overall effect: Z = 2.48 (P = 0.01)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.26. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 26: Height: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.26.1 Iron co-intervention				
Kusumastuti 2018 (2)	-1.1878	0.3757	1.0%	-1.19 [-1.92 , -0.45]
Silva 2006	-0.0460732	0.25926942	2.1%	-0.05 [-0.55 , 0.46]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	2.6%	0.14 [-0.32 , 0.60]
Sazawal 2006 (2)	-0.0794432	0.21183638	3.2%	-0.08 [-0.49 , 0.34]
Rosado 1997 (2)	0.11812477	0.19963612	3.6%	0.12 [-0.27 , 0.51]
Meeks Gardner 2005	-0.2358912	0.18682894	4.1%	-0.24 [-0.60 , 0.13]
Cavan 1993	-0.1909372	0.15976556	5.6%	-0.19 [-0.50 , 0.12]
Brown 2007	0.02831727	0.15073647	6.2%	0.03 [-0.27 , 0.32]
Alarcon 2004	0.17562403	0.13685249	7.6%	0.18 [-0.09 , 0.44]
Baqui 2003 (2)	-0.0375915	0.11833	10.1%	-0.04 [-0.27 , 0.19]
Lind 2003 (2)	-0.2645621	0.11134035	11.4%	-0.26 [-0.48 , -0.05]
Richard 2006 (2)	0.01147736	0.10286111	13.4%	0.01 [-0.19 , 0.21]
Bhandari 2007	0.14273438	0.0697166	29.2%	0.14 [0.01 , 0.28]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.08 , 0.07]**
Heterogeneity: Chi² = 25.51, df = 12 (P = 0.01); I² = 53%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2.26.2 No iron co-intervention				
Sayeg Porto 2000	0.46637519	0.45563575	0.1%	0.47 [-0.43 , 1.36]
Nakamura 1993	0.96009475	0.44484717	0.1%	0.96 [0.09 , 1.83]
Smith 1999	0.725292	0.43412761	0.1%	0.73 [-0.13 , 1.58]
Ince 1995	0.45028253	0.40793136	0.1%	0.45 [-0.35 , 1.25]
Kusumastuti 2018	-1.1518	0.3738	0.2%	-1.15 [-1.88 , -0.42]
Isdiany 2021	-0.2724	0.3671	0.2%	-0.27 [-0.99 , 0.45]
Garcia 1998	0.10584806	0.34006946	0.2%	0.11 [-0.56 , 0.77]
Castillo-Durán 1994	0.35835025	0.313	0.2%	0.36 [-0.26 , 0.97]
Walravens 1983	0.3564118	0.31249613	0.2%	0.36 [-0.26 , 0.97]
Dehbozorgi 2007	-1.9734985	0.31209312	0.2%	-1.97 [-2.59 , -1.36]
Clark 1999	-0.4920502	0.295419	0.3%	-0.49 [-1.07 , 0.09]
Sempértegui 1996	-0.1304811	0.28450141	0.3%	-0.13 [-0.69 , 0.43]
Walravens 1989	0.2375538	0.27941182	0.3%	0.24 [-0.31 , 0.79]
Han 2002	0.97763178	0.26685037	0.3%	0.98 [0.45 , 1.50]
Meeks Gardner 1998	0.11783456	0.26252076	0.3%	0.12 [-0.40 , 0.63]
Han 2002 (2)	-0.0379151	0.26134196	0.3%	-0.04 [-0.55 , 0.47]
Gibson 1989	0.07592408	0.25493989	0.4%	0.08 [-0.42 , 0.58]
Hambidge 1978	0.31355858	0.24369413	0.4%	0.31 [-0.16 , 0.79]
Tupe 2009	0.05864615	0.22908102	0.4%	0.06 [-0.39 , 0.51]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.5%	0.88 [0.44 , 1.33]
Sazawal 2006	-0.3053788	0.22312277	0.5%	-0.31 [-0.74 , 0.13]
Hettiarachchi 2008	0.43865049	0.21702312	0.5%	0.44 [0.01 , 0.86]
Ruel 1997	0.05883983	0.21022626	0.5%	0.06 [-0.35 , 0.47]
Rosado 1997	0.07813202	0.20362659	0.6%	0.08 [-0.32 , 0.48]
Ruz 1997	0.25866462	0.20129773	0.6%	0.26 [-0.14 , 0.65]
De Fonseca 2002	-0.1685443	0.19990018	0.6%	-0.17 [-0.56 , 0.22]
Kikafunda 1998	-0.0212582	0.18705861	0.7%	-0.02 [-0.39 , 0.35]
Hong 1982	1.09400346	0.18644996	0.7%	1.09 [0.73 , 1.46]
Ninh 1996	0.34634509	0.16590035	0.8%	0.35 [0.02 , 0.67]
Penny 2004	0.13724615	0.16491512	0.8%	0.14 [-0.19 , 0.46]
Chen 2012	0.1524128	0.148308100564911	1.0%	0.15 [-0.14 , 0.44]
Umeta 2000	0.33222629	0.14785133	1.1%	0.33 [0.04 , 0.62]
Akramuzzaman 1994	0	0.14216714	1.1%	0.00 [-0.28 , 0.28]
Shankar 2000	0.07055089	0.13696712	1.2%	0.07 [-0.20 , 0.34]
Friis 1997	0.03899074	0.12009587	1.6%	0.04 [-0.20 , 0.27]
Baqui 2003	-0.0369072	0.11899992	1.6%	-0.04 [-0.27 , 0.20]
Long 2006	0.1584015	0.11813857	1.6%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	1.7%	-0.10 [-0.33 , 0.13]
Wuehler 2008	0.0219241	0.11140271	1.9%	0.02 [-0.25 , 0.19]

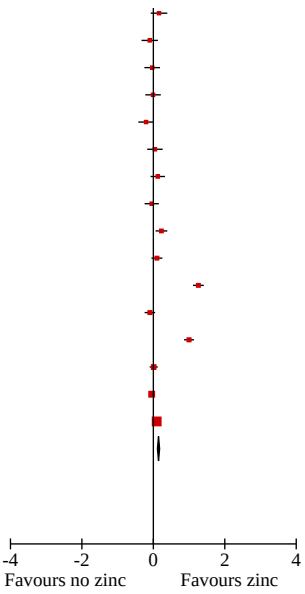
Analysis 2.26. (Continued)

Long 2006	0.1584015	0.11813857	1.6%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	1.7%	-0.10 [-0.33 , 0.13]
Wuehler 2008	-0.0319341	0.11140371	1.9%	-0.03 [-0.25 , 0.19]
Rahman 2001	-0.0086731	0.11069586	1.9%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	1.9%	-0.20 [-0.42 , 0.01]
Lind 2003	0.04482357	0.11052917	1.9%	0.04 [-0.17 , 0.26]
Richard 2006	0.12404623	0.10262789	2.2%	0.12 [-0.08 , 0.33]
Mazariegos 2010	-0.0445451	0.10189635	2.2%	-0.04 [-0.24 , 0.16]
Abdollahi 2019	0.2262	0.0835	3.3%	0.23 [0.06 , 0.39]
Müller 2001	0.09988615	0.07775177	3.8%	0.10 [-0.05 , 0.25]
Ebrahimi 2006	1.2611452	0.07721922	3.9%	1.26 [1.11 , 1.41]
DiGirolamo 2010	-0.0968094	0.07476273	4.1%	-0.10 [-0.24 , 0.05]
Islam 2022	0.9992	0.071	4.6%	1.00 [0.86 , 1.14]
Hess 2015	0.0098	0.0573	7.0%	0.01 [-0.10 , 0.12]
Bhandari 2002	-0.045968	0.04238854	12.8%	-0.05 [-0.13 , 0.04]
Becquey 2016	0.0935	0.0295	26.4%	0.09 [0.04 , 0.15]
Subtotal (95% CI)			**100.0%**	**0.14 [0.12 , 0.17]**

Heterogeneity: Chi² = 554.59, df = 51 (P < 0.00001); I² = 91%

Test for overall effect: Z = 9.57 (P < 0.00001)

Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%

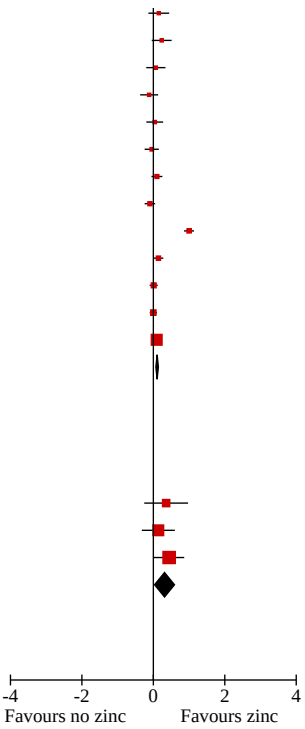


Analysis 2.27. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 27: Height: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.27.1 Solution				
Sayeg Porto 2000	0.46637519	0.45563575	0.2%	0.47 [-0.43 , 1.36]
Smith 1999	0.725292	0.43412761	0.2%	0.73 [-0.13 , 1.58]
Ince 1995	0.45028253	0.40793136	0.2%	0.45 [-0.35 , 1.25]
Isdiany 2021	-0.2724	0.3671	0.3%	-0.27 [-0.99 , 0.45]
Walravens 1983	0.3564118	0.31249613	0.4%	0.36 [-0.26 , 0.97]
Dehbozorgi 2007	-1.9734985	0.31209312	0.4%	-1.97 [-2.59 , -1.36]
Khodashenas 2015	-0.008279	0.298217	0.4%	-0.01 [-0.59 , 0.58]
Sempértegui 1996	-0.1304811	0.28450141	0.5%	-0.13 [-0.69 , 0.43]
Walravens 1989	0.2375538	0.27941182	0.5%	0.24 [-0.31 , 0.79]
Meeks Gardner 1998	0.11783456	0.26252076	0.6%	0.12 [-0.40 , 0.63]
Silva 2006	-0.0460732	0.25926942	0.6%	-0.05 [-0.55 , 0.46]
Gibson 1989	0.07592408	0.25493989	0.6%	0.08 [-0.42 , 0.58]
Hambidge 1978	0.31355858	0.24369413	0.7%	0.31 [-0.16 , 0.79]
Mozaffari-Khosravi 2009	0.88453187	0.22577077	0.8%	0.88 [0.44 , 1.33]
Ruel 1997	0.05883983	0.21022626	0.9%	0.06 [-0.35 , 0.47]
Rosado 1997	0.07813202	0.20362659	1.0%	0.08 [-0.32 , 0.48]
Ruz 1997	0.25866462	0.20129773	1.0%	0.26 [-0.14 , 0.65]
De Fonseca 2002	-0.1685443	0.19990018	1.0%	-0.17 [-0.56 , 0.22]
Rosado 1997 (2)	0.11812477	0.19963612	1.0%	0.12 [-0.27 , 0.51]
Meeks Gardner 2005	-0.2358912	0.18682894	1.1%	-0.24 [-0.60 , 0.13]
Hong 1982	1.09400346	0.18644996	1.1%	1.09 [0.73 , 1.46]
Ninh 1996	0.34634509	0.16590035	1.5%	0.35 [0.02 , 0.67]
Penny 2004	0.13724615	0.16491512	1.5%	0.14 [-0.19 , 0.46]
Brown 2007	0.02831727	0.15073647	1.8%	0.03 [-0.27 , 0.32]
Umeta 2000	0.33222629	0.14785133	1.8%	0.33 [0.04 , 0.62]
Akramuzzaman 1994	0	0.14216714	2.0%	0.00 [-0.28 , 0.28]
Alarcon 2004	0.17562403	0.13685249	2.1%	0.18 [-0.09 , 0.44]
Baqui 2003	-0.0369072	0.11899992	2.8%	-0.04 [-0.27 , 0.20]
Baqui 2003 (2)	-0.0375915	0.11833	2.9%	-0.04 [-0.27 , 0.19]
Long 2006	0.1584015	0.11813857	2.9%	0.16 [-0.07 , 0.39]
Long 2006 (2)	-0.1016009	0.11663237	2.9%	-0.10 [-0.33 , 0.13]
Wuehler 2008	-0.0319341	0.11140371	3.2%	-0.03 [-0.25 , 0.19]
Lind 2003 (2)	-0.2645621	0.11134035	3.2%	-0.26 [-0.48 , -0.05]
Rahman 2001	-0.0086731	0.11069586	3.3%	-0.01 [-0.23 , 0.21]
Rahman 2001 (2)	-0.2032314	0.11056287	3.3%	-0.20 [-0.42 , 0.01]
Lind 2003	0.04482357	0.11052917	3.3%	0.04 [-0.17 , 0.26]
Richard 2006 (2)	0.01147736	0.10286111	3.8%	0.01 [-0.19 , 0.21]
Richard 2006	0.12404623	0.10262789	3.8%	0.12 [-0.08 , 0.33]
Abdollahi 2019	0.2262	0.0835	5.7%	0.23 [0.06 , 0.39]
Abdollahi 2014	0.081207	0.082178	5.9%	0.08 [-0.08 , 0.24]
Ebrahimi 2006	1.2611452	0.07721922	6.7%	1.26 [1.11 , 1.41]
Bhandari 2002	-0.045968	0.04238854	22.2%	-0.05 [-0.13 , 0.04]
Subtotal (95% CI)			**100.0%**	**0.12 [0.08 , 0.16]**
Heterogeneity: Chi² = 370.40, df = 41 (P < 0.00001); I² = 89%				
Test for overall effect: Z = 5.94 (P < 0.00001)				
2.27.2 Pill/tablet				
Bertinato 2013	-0.601946	0.377514	0.2%	-0.60 [-1.34 , 0.14]
Tupe 2009	0.05864615	0.22908102	0.6%	0.06 [-0.39 , 0.51]
Sazawal 2006	-0.3053788	0.22312277	0.6%	-0.31 [-0.74 , 0.13]
Sazawal 2006 (2)	-0.0794432	0.21183638	0.7%	-0.08 [-0.49 , 0.34]
Kaseb 2013	-0.123585	0.205411	0.8%	-0.12 [-0.53 , 0.28]
Kikafunda 1998	-0.0212582	0.18705861	0.9%	-0.02 [-0.39 , 0.35]
Cavan 1993	-0.1909372	0.15976556	1.3%	-0.19 [-0.50 , 0.12]
Chen 2012	0.1524128	0.148308100564911	1.5%	0.15 [-0.14 , 0.44]
Vakili 2015	0.23296	0.14191	1.6%	0.23 [-0.05 , 0.51]
Shankar 2000	0.07055089	0.12696712	1.7%	0.07 [-0.20 , 0.34]

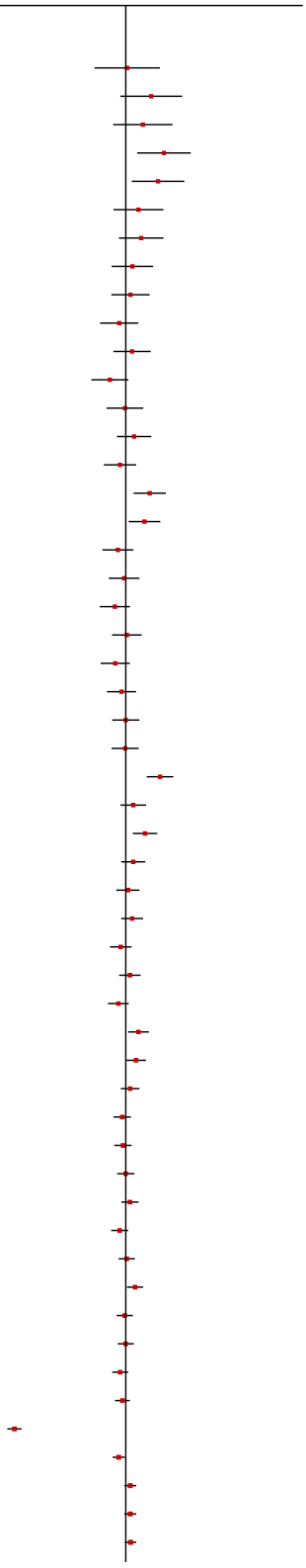
Analysis 2.27. (Continued)

Chen 2012	0.1524128	0.14630610056491	1.5%	0.15 [-0.14 , 0.44]
Vakili 2015	0.23296	0.14191	1.6%	0.23 [-0.05 , 0.51]
Shankar 2000	0.07055089	0.13696712	1.7%	0.07 [-0.20 , 0.34]
Mandlik 2020	-0.1172	0.1284	2.0%	-0.12 [-0.37 , 0.13]
Friis 1997	0.03899074	0.12009587	2.2%	0.04 [-0.20 , 0.27]
Mazariegos 2010	-0.0445451	0.10189635	3.1%	-0.04 [-0.24 , 0.16]
Müller 2001	0.09988615	0.07775177	5.3%	0.10 [-0.05 , 0.25]
DiGirolamo 2010	-0.0968094	0.07476273	5.8%	-0.10 [-0.24 , 0.05]
Islam 2022	0.9992	0.071	6.4%	1.00 [0.86 , 1.14]
Bhandari 2007	0.14273438	0.0697166	6.6%	0.14 [0.01 , 0.28]
Hess 2015	0.0098	0.0573	9.8%	0.01 [-0.10 , 0.12]
Barffour 2019	0	0.052	11.9%	0.00 [-0.10 , 0.10]
Becquey 2016	0.0935	0.0295	37.0%	0.09 [0.04 , 0.15]
Subtotal (95% CI)			**100.0%**	**0.11 [0.07 , 0.14]**
Heterogeneity: Chi² = 192.43, df = 19 (P < 0.00001); I² = 90%				
Test for overall effect: Z = 5.90 (P < 0.00001)				
2.27.3 Capsule				
Castillo-Durán 1994	0.35835025	0.313	20.7%	0.36 [-0.26 , 0.97]
Hettiarachchi 2008 (2)	0.13930582	0.23580261	36.4%	0.14 [-0.32 , 0.60]
Hettiarachchi 2008	0.43865049	0.21702312	43.0%	0.44 [0.01 , 0.86]
Subtotal (95% CI)			**100.0%**	**0.31 [0.03 , 0.59]**
Heterogeneity: Chi² = 0.90, df = 2 (P = 0.64); I² = 0%				
Test for overall effect: Z = 2.20 (P = 0.03)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



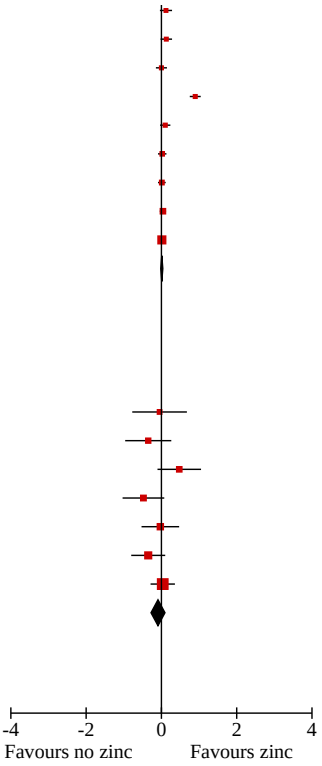
Analysis 2.28. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 28: Weight: country income level subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.28.1 Low- or middle-income				
Sayeg Porto 2000	0.03855533	0.44900267	0.1%	0.04 [-0.84 , 0.92]
Castillo-Durán 1994	0.68486898	0.42465726	0.1%	0.68 [-0.15 , 1.52]
Ince 1995	0.45975026	0.40814252	0.1%	0.46 [-0.34 , 1.26]
Kusumastuti 2018 (2)	1.0274	0.3677	0.1%	1.03 [0.31 , 1.75]
Kusumastuti 2018	0.8683	0.3608	0.1%	0.87 [0.16 , 1.58]
Garcia 1998	0.34247211	0.34242453	0.2%	0.34 [-0.33 , 1.01]
Smith 1999	0.41365482	0.30646941	0.2%	0.41 [-0.19 , 1.01]
Sempértegui 1996	0.17880543	0.28477489	0.2%	0.18 [-0.38 , 0.74]
Meeks Gardner 1998	0.1267561	0.26255721	0.3%	0.13 [-0.39 , 0.64]
Han 2002 (2)	-0.1757106	0.26183551	0.3%	-0.18 [-0.69 , 0.34]
Dehbozorgi 2007	0.17051953	0.25532062	0.3%	0.17 [-0.33 , 0.67]
Tupe 2009	-0.4278935	0.25358514	0.3%	-0.43 [-0.92 , 0.07]
Han 2002	-0.0230153	0.25200321	0.3%	-0.02 [-0.52 , 0.47]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	0.3%	0.23 [-0.24 , 0.69]
Sazawal 2006	-0.1548301	0.22216939	0.4%	-0.15 [-0.59 , 0.28]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.4%	0.64 [0.21 , 1.08]
Hettiarachchi 2008	0.50265662	0.21768626	0.4%	0.50 [0.08 , 0.93]
Sazawal 2006 (2)	-0.2120463	0.21235411	0.4%	-0.21 [-0.63 , 0.20]
Ruel 1997	-0.0460843	0.21020838	0.4%	-0.05 [-0.46 , 0.37]
Kaseb 2013	-0.29308	0.206353	0.4%	-0.29 [-0.70 , 0.11]
Rosado 1997	0.02874363	0.20355836	0.4%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2834995	0.20047451	0.5%	-0.28 [-0.68 , 0.11]
De Fonseca 2002	-0.1138287	0.19970491	0.5%	-0.11 [-0.51 , 0.28]
Kikafunda 1998	0	0.18705326	0.5%	0.00 [-0.37 , 0.37]
Meeks Gardner 2005	-0.0174125	0.18617821	0.5%	-0.02 [-0.38 , 0.35]
Hong 1982	0.92280618	0.18288181	0.5%	0.92 [0.56 , 1.28]
Rerksuppaphol 2018	0.200203	0.175885	0.6%	0.20 [-0.14 , 0.54]
Ninh 1996	0.51743485	0.16741874	0.7%	0.52 [0.19 , 0.85]
Penny 2004	0.20000822	0.16513475	0.7%	0.20 [-0.12 , 0.52]
Cavan 1993	0.05720422	0.15943234	0.7%	0.06 [-0.26 , 0.37]
Brown 2007	0.1714931	0.15100736	0.8%	0.17 [-0.12 , 0.47]
Chen 2012	-0.1353824	0.148262447	0.8%	-0.14 [-0.43 , 0.16]
Umeta 2000	0.1098315	0.14694511	0.8%	0.11 [-0.18 , 0.40]
Akramuzzaman 1994	-0.1992298	0.14252101	0.9%	-0.20 [-0.48 , 0.08]
Vakili 2015	0.342569	0.142476	0.9%	0.34 [0.06 , 0.62]
Alarcon 2004	0.27598738	0.13724067	1.0%	0.28 [0.01 , 0.54]
Mandlik 2020	0.117221	0.128439	1.1%	0.12 [-0.13 , 0.37]
Friis 1997	-0.0949685	0.12015242	1.3%	-0.09 [-0.33 , 0.14]
Baqui 2003	-0.0766763	0.11903369	1.3%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	1.3%	0.00 [-0.23 , 0.23]
Long 2006	0.11155133	0.11804496	1.3%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	1.3%	-0.16 [-0.39 , 0.07]
Wuehler 2008	0.02657707	0.11140204	1.5%	0.03 [-0.19 , 0.24]
Lind 2003	0.24929568	0.11094564	1.5%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.0284882	0.11085987	1.5%	-0.03 [-0.25 , 0.19]
Rahman 2001	0	0.11069534	1.5%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	1.5%	-0.15 [-0.37 , 0.07]
Mazariegos 2010	-0.09075	0.10193628	1.8%	-0.09 [-0.29 , 0.11]
Islam 2022	-2.9975	0.0976	1.9%	-3.00 [-3.19 , -2.81]
Abdollahi 2019	-0.1898	0.0834	2.6%	-0.19 [-0.35 , -0.03]
Abdollahi 2014	0.121071	0.08222	2.7%	0.12 [-0.04 , 0.28]
Khodashenas 2015	0.121071	0.08222	2.7%	0.12 [-0.04 , 0.28]
Müller 2001	0.12985199	0.07778525	3.0%	0.13 [-0.02 , 0.28]



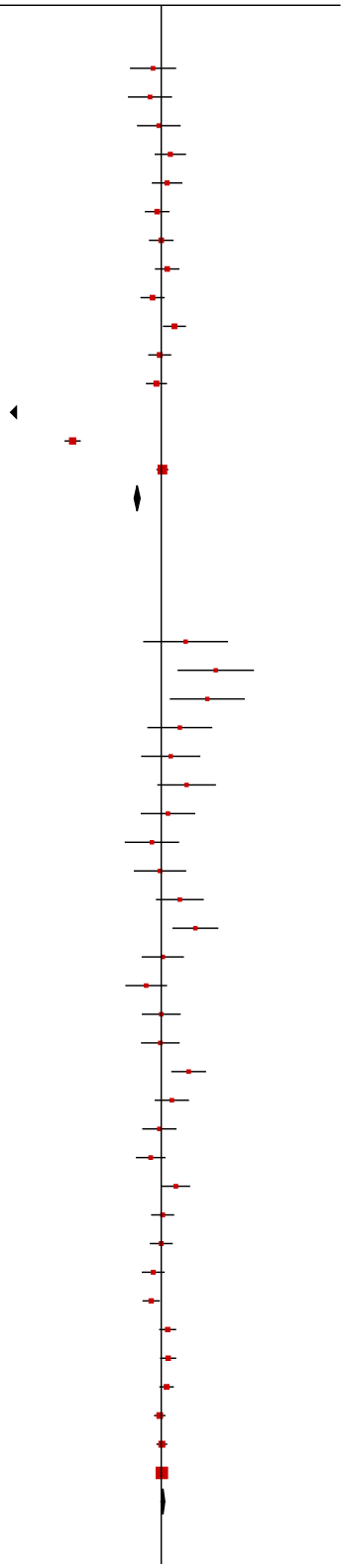
Analysis 2.28. (Continued)

Khodasheras 2015	0.121071	0.06222	2.7%	0.12 [-0.04 , 0.28]
Müller 2001	0.12985199	0.07778525	3.0%	0.13 [-0.02 , 0.28]
DiGirolamo 2010	0	0.07471888	3.3%	0.00 [-0.15 , 0.15]
Ebrahimi 2006	0.89844604	0.07399793	3.3%	0.90 [0.75 , 1.04]
Bhandari 2007	0.1009309	0.06967226	3.8%	0.10 [-0.04 , 0.24]
Hess 2015	0.0213	0.0573	5.6%	0.02 [-0.09 , 0.13]
Barffour 2019	0.011229	0.052006	6.8%	0.01 [-0.09 , 0.11]
Bhandari 2002	0.0399929	0.04238717	10.2%	0.04 [-0.04 , 0.12]
Becquey 2016	0.0113	0.0295	21.1%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**0.01 [-0.02 , 0.04]**
Heterogeneity: Chi² = 1215.97, df = 59 (P < 0.00001); I² = 95%				
Test for overall effect: Z = 0.73 (P = 0.46)				
2.28.2 High-income				
Bertinato 2013	-0.048995	0.370234	6.5%	-0.05 [-0.77 , 0.68]
Walravens 1983	-0.35011864	0.31240719	9.1%	-0.35 [-0.96 , 0.26]
Clark 1999	0.47409697	0.29509972	10.2%	0.47 [-0.10 , 1.05]
Walravens 1989	-0.47808527	0.28247531	11.1%	-0.48 [-1.03 , 0.08]
Gibson 1989	-0.02883096	0.25485925	13.7%	-0.03 [-0.53 , 0.47]
Hambidge 1978	-0.3505815	0.23036496	16.7%	-0.35 [-0.80 , 0.10]
Berger 2015	0.035004	0.165005	32.6%	0.04 [-0.29 , 0.36]
Subtotal (95% CI)			**100.0%**	**-0.09 [-0.28 , 0.09]**
Heterogeneity: Chi² = 8.16, df = 6 (P = 0.23); I² = 26%				
Test for overall effect: Z = 0.97 (P = 0.33)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Analysis 2.29. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 29: Weight: age subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.29.1 6 months to < 1 year				
Sazawal 2006	-0.1548301	0.22216939	1.6%	-0.15 [-0.59 , 0.28]
Sazawal 2006 (2)	-0.2120463	0.21235411	1.7%	-0.21 [-0.63 , 0.20]
Ruel 1997	-0.0460843	0.21020838	1.8%	-0.05 [-0.46 , 0.37]
Brown 2007	0.1714931	0.15100736	3.4%	0.17 [-0.12 , 0.47]
Umeta 2000	0.1098315	0.14694511	3.6%	0.11 [-0.18 , 0.40]
Baqui 2003	-0.0766763	0.11903369	5.5%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	5.6%	0.00 [-0.23 , 0.23]
Long 2006	0.11155133	0.11804496	5.6%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	5.8%	-0.16 [-0.39 , 0.07]
Lind 2003	0.24929568	0.11094564	6.4%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.0284882	0.11085987	6.4%	-0.03 [-0.25 , 0.19]
Mazariegos 2010	-0.09075	0.10193628	7.5%	-0.09 [-0.29 , 0.11]
Islam 2022	-2.9975	0.0976	8.2%	-3.00 [-3.19 , -2.81]
Bhandari 2002	-1.6710025	0.07788341	12.9%	-1.67 [-1.82 , -1.52]
Hess 2015	0.0213	0.0573	23.9%	0.02 [-0.09 , 0.13]
Subtotal (95% CI)			**100.0%**	**-0.45 [-0.51 , -0.40]**
Heterogeneity: Chi² = 1152.40, df = 14 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 16.24 (P < 0.00001)				
2.29.2 1 to < 5 years				
Ince 1995	0.45975026	0.40814252	0.2%	0.46 [-0.34 , 1.26]
Kusumastuti 2018 (2)	1.0274	0.3677	0.2%	1.03 [0.31 , 1.75]
Kusumastuti 2018	0.8683	0.3608	0.2%	0.87 [0.16 , 1.58]
Walravens 1983	0.35011864	0.31240719	0.3%	0.35 [-0.26 , 0.96]
Sempértegui 1996	0.17880543	0.28477489	0.4%	0.18 [-0.38 , 0.74]
Walravens 1989	0.47808527	0.28247531	0.4%	0.48 [-0.08 , 1.03]
Meeks Gardner 1998	0.1267561	0.26255721	0.5%	0.13 [-0.39 , 0.64]
Han 2002 (2)	-0.1757106	0.26183551	0.5%	-0.18 [-0.69 , 0.34]
Han 2002	-0.0230153	0.25200321	0.5%	-0.02 [-0.52 , 0.47]
Hambidge 1978	0.3505815	0.23036496	0.6%	0.35 [-0.10 , 0.80]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.6%	0.64 [0.21 , 1.08]
Rosado 1997	0.02874363	0.20355836	0.8%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2834995	0.20047451	0.8%	-0.28 [-0.68 , 0.11]
Kikafunda 1998	0	0.18705326	0.9%	0.00 [-0.37 , 0.37]
Meeks Gardner 2005	-0.0174125	0.18617821	0.9%	-0.02 [-0.38 , 0.35]
Ninh 1996	0.51743485	0.16741874	1.1%	0.52 [0.19 , 0.85]
Penny 2004	0.20000822	0.16513475	1.1%	0.20 [-0.12 , 0.52]
Berger 2015	-0.035004	0.165005	1.1%	-0.04 [-0.36 , 0.29]
Akramuzzaman 1994	-0.1992298	0.14252101	1.5%	-0.20 [-0.48 , 0.08]
Alarcon 2004	0.27598738	0.13724067	1.6%	0.28 [0.01 , 0.54]
Wuehler 2008	0.02657707	0.11140204	2.5%	0.03 [-0.19 , 0.24]
Rahman 2001	0	0.11069534	2.5%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	2.5%	-0.15 [-0.37 , 0.07]
Abdollahi 2019	-0.1898	0.0834	4.5%	-0.19 [-0.35 , -0.03]
Abdollahi 2014	0.121071	0.08222	4.6%	0.12 [-0.04 , 0.28]
Müller 2001	0.12985199	0.07778525	5.1%	0.13 [-0.02 , 0.28]
Bhandari 2007	0.1009309	0.06967226	6.4%	0.10 [-0.04 , 0.24]
Bhandari 2002	-0.0281548	0.05475441	10.4%	-0.03 [-0.14 , 0.08]
Barffour 2019	0.011229	0.052006	11.5%	0.01 [-0.09 , 0.11]
Becquey 2016	0.0113	0.0295	35.7%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**0.03 [-0.00 , 0.07]**
Heterogeneity: Chi² = 61.45, df = 29 (P = 0.0004); I² = 53%				
Test for overall effect: Z = 1.77 (P = 0.08)				



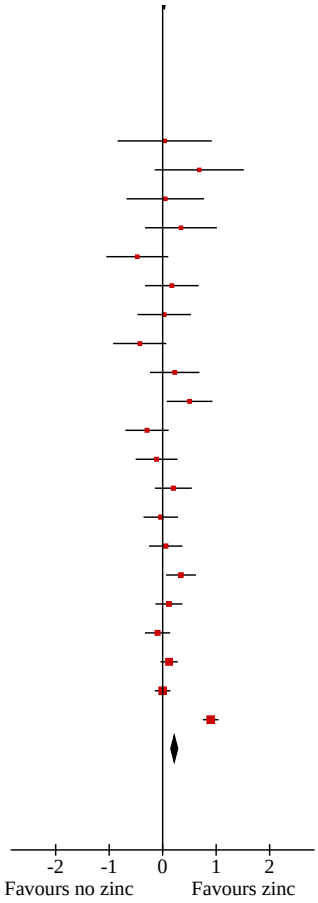
Analysis 2.29. (Continued)

Heterogeneity: Chi² = 61.45, df = 29 (P = 0.0004); I² = 53%
Test for overall effect: Z = 1.77 (P = 0.08)

2.29.3 5 to < 13 years				
Sayeg Porto 2000	0.03855533	0.44900267	0.5%	0.04 [-0.84 , 0.92]
Castillo-Durán 1994	0.68486898	0.42465726	0.6%	0.68 [-0.15 , 1.52]
Bertinato 2013	0.048995	0.370234	0.8%	0.05 [-0.68 , 0.77]
Garcia 1998	0.34247211	0.34242453	0.9%	0.34 [-0.33 , 1.01]
Clark 1999	-0.474097	0.29509972	1.2%	-0.47 [-1.05 , 0.10]
Dehbozorgi 2007	0.17051953	0.25532062	1.6%	0.17 [-0.33 , 0.67]
Gibson 1989	0.02883096	0.25485925	1.6%	0.03 [-0.47 , 0.53]
Tupe 2009	-0.4278935	0.25358514	1.6%	-0.43 [-0.92 , 0.07]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	1.9%	0.23 [-0.24 , 0.69]
Hettiarachchi 2008	0.50265662	0.21768626	2.2%	0.50 [0.08 , 0.93]
Kaseb 2013	-0.29308	0.206353	2.4%	-0.29 [-0.70 , 0.11]
De Fonseca 2002	-0.1138287	0.19970491	2.6%	-0.11 [-0.51 , 0.28]
Rerksuppaphol 2018	0.200203	0.175885	3.3%	0.20 [-0.14 , 0.54]
Berger 2015	-0.035004	0.165005	3.8%	-0.04 [-0.36 , 0.29]
Cavan 1993	0.05720422	0.15943234	4.1%	0.06 [-0.26 , 0.37]
Vakili 2015	0.342569	0.142476	5.1%	0.34 [0.06 , 0.62]
Mandlik 2020	0.117221	0.128439	6.3%	0.12 [-0.13 , 0.37]
Friis 1997	-0.0949685	0.12015242	7.1%	-0.09 [-0.33 , 0.14]
Khodashenas 2015	0.121071	0.08222	15.3%	0.12 [-0.04 , 0.28]
DiGirolamo 2010	0	0.07471888	18.5%	0.00 [-0.15 , 0.15]
Ebrahimi 2006	0.89844604	0.07399793	18.8%	0.90 [0.75 , 1.04]
Subtotal (95% CI)			**100.0%**	**0.22 [0.15 , 0.28]**

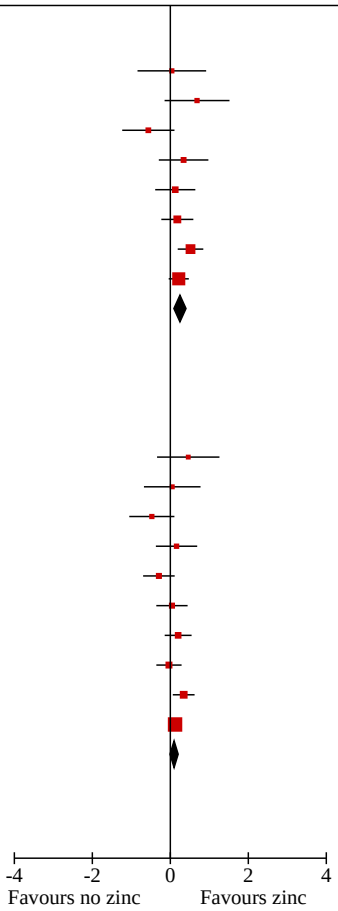
Heterogeneity: Chi² = 130.89, df = 20 (P < 0.00001); I² = 85%
Test for overall effect: Z = 6.75 (P < 0.00001)

Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%



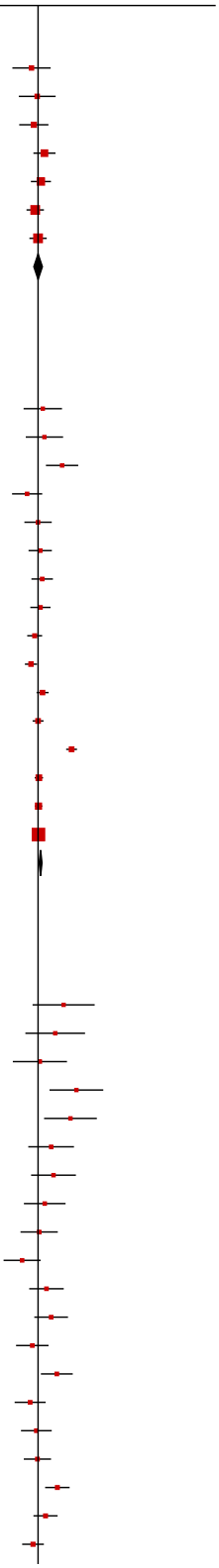
Analysis 2.30. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 30: Weight: stunting subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.30.1 Stunted				
Sayeg Porto 2000	0.03855533	0.44900267	3.1%	0.04 [-0.84 , 0.92]
Castillo-Durán 1994	0.68486898	0.42465726	3.5%	0.68 [-0.15 , 1.52]
Rosado 1997 (2)	-0.5637679	0.34180201	5.4%	-0.56 [-1.23 , 0.11]
Rosado 1997	0.34014253	0.32423919	6.0%	0.34 [-0.30 , 0.98]
Meeks Gardner 1998	0.1267561	0.26255721	9.1%	0.13 [-0.39 , 0.64]
Umeta 2000	0.1796098	0.20944493	14.3%	0.18 [-0.23 , 0.59]
Ninh 1996	0.51743485	0.16741874	22.4%	0.52 [0.19 , 0.85]
Müller 2001	0.21595628	0.13160324	36.2%	0.22 [-0.04 , 0.47]
Subtotal (95% CI)			**100.0%**	**0.25 [0.09 , 0.40]**
Heterogeneity: Chi² = 9.97, df = 7 (P = 0.19); I² = 30%				
Test for overall effect: Z = 3.11 (P = 0.002)				
2.30.2 Non-stunted				
Ince 1995	0.45975026	0.40814252	1.7%	0.46 [-0.34 , 1.26]
Bertinato 2013	0.048995	0.370234	2.1%	0.05 [-0.68 , 0.77]
Clark 1999	-0.474097	0.29509972	3.3%	-0.47 [-1.05 , 0.10]
De Fonseca 2002	0.15913169	0.27032631	3.9%	0.16 [-0.37 , 0.69]
Kaseb 2013	-0.29308	0.206353	6.7%	-0.29 [-0.70 , 0.11]
Umeta 2000	0.04166297	0.20462056	6.8%	0.04 [-0.36 , 0.44]
Rerksuppaphol 2018	0.200203	0.175885	9.2%	0.20 [-0.14 , 0.54]
Berger 2015	-0.035004	0.165005	10.4%	-0.04 [-0.36 , 0.29]
Vakili 2015	0.342569	0.142476	14.0%	0.34 [0.06 , 0.62]
Khodashenas 2015	0.121071	0.08222	42.0%	0.12 [-0.04 , 0.28]
Subtotal (95% CI)			**100.0%**	**0.10 [-0.01 , 0.20]**
Heterogeneity: Chi² = 12.29, df = 9 (P = 0.20); I² = 27%				
Test for overall effect: Z = 1.81 (P = 0.07)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



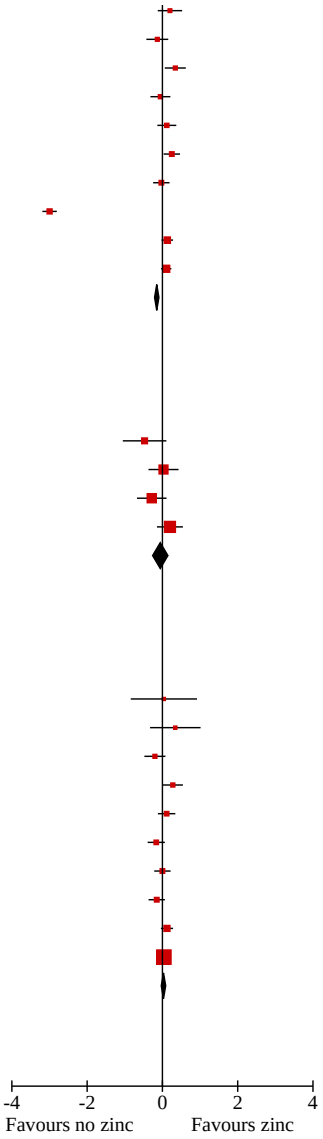
Analysis 2.31. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 31: Weight: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.31.1 0 to < 5 mg				
Han 2002 (2)	-0.1757106	0.26183551	5.0%	-0.18 [-0.69 , 0.34]
Han 2002	-0.0230153	0.25200321	5.3%	-0.02 [-0.52 , 0.47]
De Fonseca 2002	-0.1138287	0.19970491	8.5%	-0.11 [-0.51 , 0.28]
Brown 2007	0.1714931	0.15100736	14.9%	0.17 [-0.12 , 0.47]
Wuehler 2008	0.07602929	0.13727943	18.0%	0.08 [-0.19 , 0.35]
Baqui 2003	-0.0766763	0.11903369	24.0%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	24.3%	0.00 [-0.23 , 0.23]
Subtotal (95% CI)			**100.0%**	**0.00 [-0.11 , 0.12]**
Heterogeneity: Chi² = 2.79, df = 6 (P = 0.83); I² = 0%				
Test for overall effect: Z = 0.02 (P = 0.98)				
2.31.2 5 to < 10 mg				
Meeks Gardner 1998	0.1267561	0.26255721	0.5%	0.13 [-0.39 , 0.64]
Dehbozorgi 2007	0.17051953	0.25532062	0.5%	0.17 [-0.33 , 0.67]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.7%	0.64 [0.21 , 1.08]
Kaseb 2013	-0.29308	0.206353	0.8%	-0.29 [-0.70 , 0.11]
Kikafunda 1998	0	0.18705326	1.0%	0.00 [-0.37 , 0.37]
Cavan 1993	0.05720422	0.15943234	1.4%	0.06 [-0.26 , 0.37]
Umeta 2000	0.1098315	0.14694511	1.6%	0.11 [-0.18 , 0.40]
Wuehler 2008	0.06307275	0.13830644	1.9%	0.06 [-0.21 , 0.33]
Mazariegos 2010	-0.09075	0.10193628	3.4%	-0.09 [-0.29 , 0.11]
Abdollahi 2019	-0.1898	0.0834	5.1%	-0.19 [-0.35 , -0.03]
Abdollahi 2014	0.121071	0.08222	5.3%	0.12 [-0.04 , 0.28]
DiGirolamo 2010	0	0.07471888	6.4%	0.00 [-0.15 , 0.15]
Ebrahimi 2006	0.89844604	0.07399793	6.5%	0.90 [0.75 , 1.04]
Hess 2015	0.0213	0.0573	10.8%	0.02 [-0.09 , 0.13]
Barffour 2019	0.011229	0.052006	13.1%	0.01 [-0.09 , 0.11]
Becquey 2016	0.0113	0.0295	40.8%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**0.07 [0.03 , 0.10]**
Heterogeneity: Chi² = 155.00, df = 15 (P < 0.00001); I² = 90%				
Test for overall effect: Z = 3.60 (P = 0.0003)				
2.31.3 10 to < 15 mg				
Castillo-Durán 1994	0.68486898	0.42465726	0.5%	0.68 [-0.15 , 1.52]
Ince 1995	0.45975026	0.40814252	0.5%	0.46 [-0.34 , 1.26]
Bertinato 2013	0.048995	0.370234	0.6%	0.05 [-0.68 , 0.77]
Kusumastuti 2018 (2)	1.0274	0.3677	0.6%	1.03 [0.31 , 1.75]
Kusumastuti 2018	0.8683	0.3608	0.7%	0.87 [0.16 , 1.58]
Walravens 1983	0.35011864	0.31240719	0.9%	0.35 [-0.26 , 0.96]
Smith 1999	0.41365482	0.30646941	0.9%	0.41 [-0.19 , 1.01]
Sempértegui 1996	0.17880543	0.28477489	1.1%	0.18 [-0.38 , 0.74]
Gibson 1989	0.02883096	0.25485925	1.3%	0.03 [-0.47 , 0.53]
Tupe 2009	-0.4278935	0.25358514	1.3%	-0.43 [-0.92 , 0.07]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	1.5%	0.23 [-0.24 , 0.69]
Hambidge 1978	0.3505815	0.23036496	1.6%	0.35 [-0.10 , 0.80]
Sazawal 2006	-0.1548301	0.22216939	1.7%	-0.15 [-0.59 , 0.28]
Hettiarachchi 2008	0.50265662	0.21768626	1.8%	0.50 [0.08 , 0.93]
Sazawal 2006 (2)	-0.2120463	0.21235411	1.9%	-0.21 [-0.63 , 0.20]
Ruel 1997	-0.0460843	0.21020838	1.9%	-0.05 [-0.46 , 0.37]
Meeks Gardner 2005	-0.0174125	0.18617821	2.5%	-0.02 [-0.38 , 0.35]
Ninh 1996	0.51743485	0.16741874	3.0%	0.52 [0.19 , 0.85]
Penny 2004	0.20000822	0.16513475	3.1%	0.20 [-0.12 , 0.52]
Chen 2012	-0.1353824	0.148262447	3.9%	-0.14 [-0.43 , 0.16]



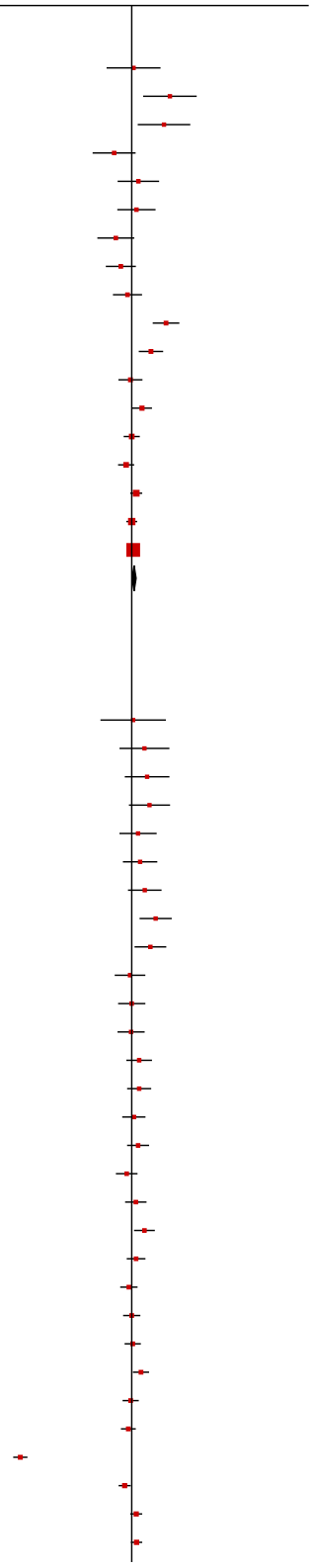
Analysis 2.31. (Continued)

Penny 2004	0.20000822	0.16513473	3.1%	0.20 [-0.12 , 0.52]
Chen 2012	-0.1353824	0.148262447	3.9%	-0.14 [-0.43 , 0.16]
Vakili 2015	0.342569	0.142476	4.2%	0.34 [0.06 , 0.62]
Wuehler 2008	-0.0535012	0.13501621	4.7%	-0.05 [-0.32 , 0.21]
Mandlik 2020	0.117221	0.128439	5.2%	0.12 [-0.13 , 0.37]
Lind 2003	0.24929568	0.11094564	6.9%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.0284882	0.11085987	6.9%	-0.03 [-0.25 , 0.19]
Islam 2022	-2.9975	0.0976	9.0%	-3.00 [-3.19 , -2.81]
Müller 2001	0.12985199	0.07778525	14.1%	0.13 [-0.02 , 0.28]
Bhandari 2007	0.1009309	0.06967226	17.6%	0.10 [-0.04 , 0.24]
Subtotal (95% CI)			**100.0%**	**-0.15 [-0.21 , -0.09]**
Heterogeneity: Chi² = 979.10, df = 27 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 5.16 (P < 0.00001)				
2.31.4 15 to < 20 mg				
Clark 1999	-0.474097	0.29509972	12.4%	-0.47 [-1.05 , 0.10]
Rosado 1997	0.02874363	0.20355836	26.0%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2834995	0.20047451	26.8%	-0.28 [-0.68 , 0.11]
Rerksuppaphol 2018	0.200203	0.175885	34.8%	0.20 [-0.14 , 0.54]
Subtotal (95% CI)			**100.0%**	**-0.06 [-0.26 , 0.15]**
Heterogeneity: Chi² = 5.59, df = 3 (P = 0.13); I² = 46%				
Test for overall effect: Z = 0.55 (P = 0.58)				
2.31.5 20 mg or more				
Sayeg Porto 2000	0.03855533	0.44900267	0.4%	0.04 [-0.84 , 0.92]
Garcia 1998	0.34247211	0.34242453	0.8%	0.34 [-0.33 , 1.01]
Akramuzzaman 1994	-0.1992298	0.14252101	4.4%	-0.20 [-0.48 , 0.08]
Alarcon 2004	0.27598738	0.13724067	4.7%	0.28 [0.01 , 0.54]
Long 2006	0.11155133	0.11804496	6.4%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	6.5%	-0.16 [-0.39 , 0.07]
Rahman 2001	0	0.11069534	7.2%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	7.3%	-0.15 [-0.37 , 0.07]
Khodashenas 2015	0.121071	0.08222	13.1%	0.12 [-0.04 , 0.28]
Bhandari 2002	0.0399929	0.04238717	49.3%	0.04 [-0.04 , 0.12]
Subtotal (95% CI)			**100.0%**	**0.03 [-0.03 , 0.09]**
Heterogeneity: Chi² = 13.90, df = 9 (P = 0.13); I² = 35%				
Test for overall effect: Z = 0.94 (P = 0.34)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				



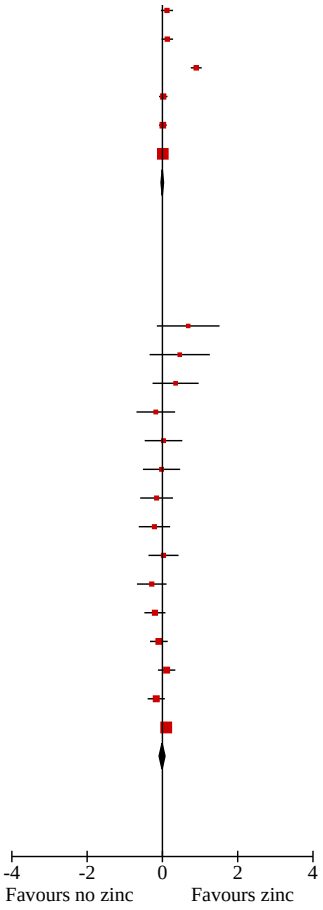
Analysis 2.32. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 32: Weight: duration subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.32.1 0 to < 6 months				
Bertinato 2013	0.048995	0.370234	0.5%	0.05 [-0.68 , 0.77]
Kusumastuti 2018 (2)	1.0274	0.3677	0.6%	1.03 [0.31 , 1.75]
Kusumastuti 2018	0.8683	0.3608	0.6%	0.87 [0.16 , 1.58]
Clark 1999	-0.474097	0.29509972	0.9%	-0.47 [-1.05 , 0.10]
Sempértegui 1996	0.17880543	0.28477489	0.9%	0.18 [-0.38 , 0.74]
Meeks Gardner 1998	0.1267561	0.26255721	1.1%	0.13 [-0.39 , 0.64]
Tupe 2009	-0.4278935	0.25358514	1.2%	-0.43 [-0.92 , 0.07]
Kaseb 2013	-0.29308	0.206353	1.8%	-0.29 [-0.70 , 0.11]
De Fonseca 2002	-0.1138287	0.19970491	1.9%	-0.11 [-0.51 , 0.28]
Hong 1982	0.92280618	0.18288181	2.3%	0.92 [0.56 , 1.28]
Ninh 1996	0.51743485	0.16741874	2.7%	0.52 [0.19 , 0.85]
Berger 2015	-0.035004	0.165005	2.8%	-0.04 [-0.36 , 0.29]
Alarcon 2004	0.27598738	0.13724067	4.0%	0.28 [0.01 , 0.54]
Rahman 2001	0	0.11069534	6.1%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	6.2%	-0.15 [-0.37 , 0.07]
Abdollahi 2014	0.121071	0.08222	11.1%	0.12 [-0.04 , 0.28]
DiGirolamo 2010	0	0.07471888	13.5%	0.00 [-0.15 , 0.15]
Bhandari 2002	0.0399929	0.04238717	41.9%	0.04 [-0.04 , 0.12]
Subtotal (95% CI)			**100.0%**	**0.06 [0.01 , 0.12]**
Heterogeneity: Chi² = 60.72, df = 17 (P < 0.00001); I² = 72%				
Test for overall effect: Z = 2.31 (P = 0.02)				
2.32.2 6 to < 12 months				
Sayeg Porto 2000	0.03855533	0.44900267	0.1%	0.04 [-0.84 , 0.92]
Garcia 1998	0.34247211	0.34242453	0.2%	0.34 [-0.33 , 1.01]
Smith 1999	0.41365482	0.30646941	0.3%	0.41 [-0.19 , 1.01]
Walravens 1989	0.47808527	0.28247531	0.3%	0.48 [-0.08 , 1.03]
Dehbozorgi 2007	0.17051953	0.25532062	0.4%	0.17 [-0.33 , 0.67]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	0.5%	0.23 [-0.24 , 0.69]
Hambidge 1978	0.3505815	0.23036496	0.5%	0.35 [-0.10 , 0.80]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.6%	0.64 [0.21 , 1.08]
Hettiarachchi 2008	0.50265662	0.21768626	0.6%	0.50 [0.08 , 0.93]
Ruel 1997	-0.0460843	0.21020838	0.6%	-0.05 [-0.46 , 0.37]
Kikafunda 1998	0	0.18705326	0.8%	0.00 [-0.37 , 0.37]
Meeks Gardner 2005	-0.0174125	0.18617821	0.8%	-0.02 [-0.38 , 0.35]
Rerksuppaphol 2018	0.200203	0.175885	0.9%	0.20 [-0.14 , 0.54]
Penny 2004	0.20000822	0.16513475	1.0%	0.20 [-0.12 , 0.52]
Cavan 1993	0.05720422	0.15943234	1.1%	0.06 [-0.26 , 0.37]
Brown 2007	0.1714931	0.15100736	1.2%	0.17 [-0.12 , 0.47]
Chen 2012	-0.1353824	0.148262447	1.3%	-0.14 [-0.43 , 0.16]
Umeta 2000	0.1098315	0.14694511	1.3%	0.11 [-0.18 , 0.40]
Vakili 2015	0.342569	0.142476	1.4%	0.34 [0.06 , 0.62]
Mandlik 2020	0.117221	0.128439	1.7%	0.12 [-0.13 , 0.37]
Baqui 2003	-0.0766763	0.11903369	2.0%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	2.0%	0.00 [-0.23 , 0.23]
Wuehler 2008	0.02657707	0.11140204	2.2%	0.03 [-0.19 , 0.24]
Lind 2003	0.24929568	0.11094564	2.2%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.0284882	0.11085987	2.3%	-0.03 [-0.25 , 0.19]
Mazariegos 2010	-0.09075	0.10193628	2.7%	-0.09 [-0.29 , 0.11]
Islam 2022	-2.9975	0.0976	2.9%	-3.00 [-3.19 , -2.81]
Abdollahi 2019	-0.1898	0.0834	4.0%	-0.19 [-0.35 , -0.03]
Khodashenas 2015	0.121071	0.08222	4.1%	0.12 [-0.04 , 0.28]
Müller 2001	0.12985199	0.07778525	4.6%	0.13 [-0.02 , 0.28]



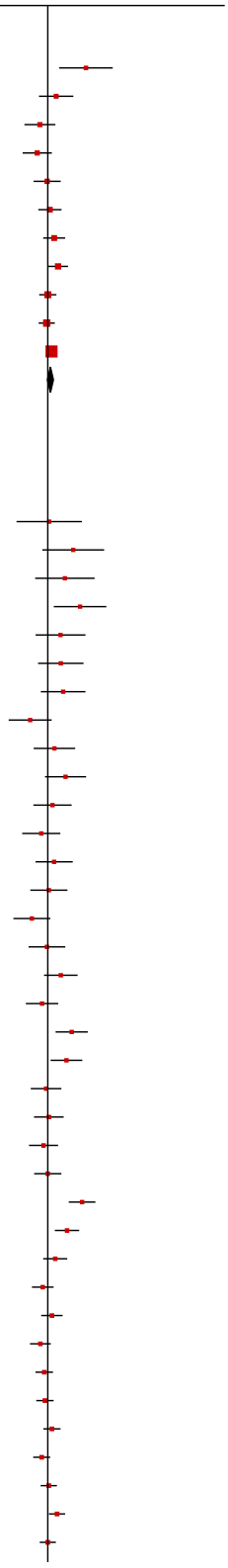
Analysis 2.32. (Continued)

Khodasheras 2015	0.121071	0.06222	4.1%	0.12 [-0.04 , 0.28]
Müller 2001	0.12985199	0.07778525	4.6%	0.13 [-0.02 , 0.28]
Ebrahimi 2006	0.89844604	0.07399793	5.1%	0.90 [0.75 , 1.04]
Hess 2015	0.0213	0.0573	8.4%	0.02 [-0.09 , 0.13]
Barffour 2019	0.011229	0.052006	10.2%	0.01 [-0.09 , 0.11]
Becquey 2016	0.0113	0.0295	31.8%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.04 , 0.03]**
Heterogeneity: Chi² = 1142.87, df = 33 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 0.22 (P = 0.82)				
2.32.3 12 months or more				
Castillo-Durán 1994	0.68486898	0.42465726	0.9%	0.68 [-0.15 , 1.52]
Ince 1995	0.45975026	0.40814252	1.0%	0.46 [-0.34 , 1.26]
Walravens 1983	0.35011864	0.31240719	1.6%	0.35 [-0.26 , 0.96]
Han 2002 (2)	-0.1757106	0.26183551	2.3%	-0.18 [-0.69 , 0.34]
Gibson 1989	0.02883096	0.25485925	2.4%	0.03 [-0.47 , 0.53]
Han 2002	-0.0230153	0.25200321	2.5%	-0.02 [-0.52 , 0.47]
Sazawal 2006	-0.1548301	0.22216939	3.2%	-0.15 [-0.59 , 0.28]
Sazawal 2006 (2)	-0.2120463	0.21235411	3.5%	-0.21 [-0.63 , 0.20]
Rosado 1997	0.02874363	0.20355836	3.8%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2834995	0.20047451	4.0%	-0.28 [-0.68 , 0.11]
Akramuzzaman 1994	-0.1992298	0.14252101	7.8%	-0.20 [-0.48 , 0.08]
Friis 1997	-0.0949685	0.12015242	11.0%	-0.09 [-0.33 , 0.14]
Long 2006	0.11155133	0.11804496	11.4%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	11.7%	-0.16 [-0.39 , 0.07]
Bhandari 2007	0.1009309	0.06967226	32.8%	0.10 [-0.04 , 0.24]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.09 , 0.07]**
Heterogeneity: Chi² = 16.58, df = 14 (P = 0.28); I² = 16%				
Test for overall effect: Z = 0.24 (P = 0.81)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.33. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 33: Weight: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.33.1 Iron co-intervention				
Kusumastuti 2018 (2)	1.0274	0.3677	1.2%	1.03 [0.31 , 1.75]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	3.0%	0.23 [-0.24 , 0.69]
Sazawal 2006 (2)	-0.2120463	0.21235411	3.7%	-0.21 [-0.63 , 0.20]
Rosado 1997 (2)	-0.2834995	0.20047451	4.2%	-0.28 [-0.68 , 0.11]
Meeks Gardner 2005	-0.0174125	0.18617821	4.8%	-0.02 [-0.38 , 0.35]
Cavan 1993	0.05720422	0.15943234	6.6%	0.06 [-0.26 , 0.37]
Brown 2007	0.1714931	0.15100736	7.4%	0.17 [-0.12 , 0.47]
Alarcon 2004	0.27598738	0.13724067	8.9%	0.28 [0.01 , 0.54]
Baqui 2003 (2)	0	0.11831952	12.0%	0.00 [-0.23 , 0.23]
Lind 2003 (2)	-0.0284882	0.11085987	13.6%	-0.03 [-0.25 , 0.19]
Bhandari 2007	0.1009309	0.06967226	34.5%	0.10 [-0.04 , 0.24]
Subtotal (95% CI)			**100.0%**	**0.07 [-0.01 , 0.15]**
Heterogeneity: Chi² = 16.35, df = 10 (P = 0.09); I² = 39%				
Test for overall effect: Z = 1.73 (P = 0.08)				
2.33.2 No iron co-intervention				
Sayeg Porto 2000	0.03855533	0.44900267	0.1%	0.04 [-0.84 , 0.92]
Castillo-Durán 1994	0.68486898	0.42465726	0.1%	0.68 [-0.15 , 1.52]
Ince 1995	0.45975026	0.40814252	0.1%	0.46 [-0.34 , 1.26]
Kusumastuti 2018	0.8683	0.3608	0.2%	0.87 [0.16 , 1.58]
Garcia 1998	0.34247211	0.34242453	0.2%	0.34 [-0.33 , 1.01]
Walravens 1983	0.35011864	0.31240719	0.3%	0.35 [-0.26 , 0.96]
Smith 1999	0.41365482	0.30646941	0.3%	0.41 [-0.19 , 1.01]
Clark 1999	-0.474097	0.29509972	0.3%	-0.47 [-1.05 , 0.10]
Sempértegui 1996	0.17880543	0.28477489	0.3%	0.18 [-0.38 , 0.74]
Walravens 1989	0.47808527	0.28247531	0.3%	0.48 [-0.08 , 1.03]
Meeks Gardner 1998	0.1267561	0.26255721	0.4%	0.13 [-0.39 , 0.64]
Han 2002 (2)	-0.1757106	0.26183551	0.4%	-0.18 [-0.69 , 0.34]
Dehbozorgi 2007	0.17051953	0.25532062	0.4%	0.17 [-0.33 , 0.67]
Gibson 1989	0.02883096	0.25485925	0.4%	0.03 [-0.47 , 0.53]
Tupe 2009	-0.4278935	0.25358514	0.4%	-0.43 [-0.92 , 0.07]
Han 2002	-0.0230153	0.25200321	0.4%	-0.02 [-0.52 , 0.47]
Hambidge 1978	0.3505815	0.23036496	0.5%	0.35 [-0.10 , 0.80]
Sazawal 2006	-0.1548301	0.22216939	0.5%	-0.15 [-0.59 , 0.28]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.5%	0.64 [0.21 , 1.08]
Hettiarachchi 2008	0.50265662	0.21768626	0.5%	0.50 [0.08 , 0.93]
Ruel 1997	-0.0460843	0.21020838	0.6%	-0.05 [-0.46 , 0.37]
Rosado 1997	0.02874363	0.20355836	0.6%	0.03 [-0.37 , 0.43]
De Fonseca 2002	-0.1138287	0.19970491	0.6%	-0.11 [-0.51 , 0.28]
Kikafunda 1998	0	0.18705326	0.7%	0.00 [-0.37 , 0.37]
Hong 1982	0.92280618	0.18288181	0.7%	0.92 [0.56 , 1.28]
Ninh 1996	0.51743485	0.16741874	0.9%	0.52 [0.19 , 0.85]
Penny 2004	0.20000822	0.16513475	0.9%	0.20 [-0.12 , 0.52]
Chen 2012	-0.1353824	0.148262447	1.1%	-0.14 [-0.43 , 0.16]
Umeta 2000	0.1098315	0.14694511	1.1%	0.11 [-0.18 , 0.40]
Akramuzzaman 1994	-0.1992298	0.14252101	1.2%	-0.20 [-0.48 , 0.08]
Friis 1997	-0.0949685	0.12015242	1.7%	-0.09 [-0.33 , 0.14]
Baqui 2003	-0.0766763	0.11903369	1.7%	-0.08 [-0.31 , 0.16]
Long 2006	0.11155133	0.11804496	1.8%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	1.8%	-0.16 [-0.39 , 0.07]
Wuehler 2008	0.02657707	0.11140204	2.0%	0.03 [-0.19 , 0.24]
Lind 2003	0.24929568	0.11094564	2.0%	0.25 [0.03 , 0.47]
Rahman 2001	0	0.11069534	2.0%	0.00 [-0.22 , 0.22]



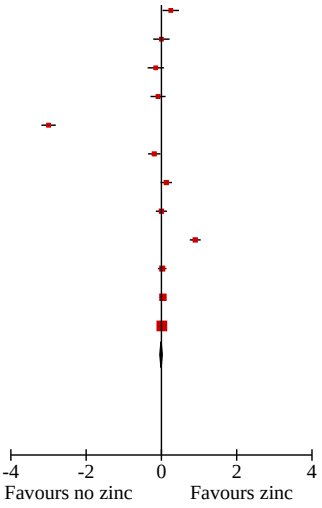
Analysis 2.33. (Continued)

Lind 2003	0.24929568	0.11094564	2.0%	0.25 [0.03 , 0.47]
Rahman 2001	0	0.11069534	2.0%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	2.0%	-0.15 [-0.37 , 0.07]
Mazariegos 2010	-0.09075	0.10193628	2.3%	-0.09 [-0.29 , 0.11]
Islam 2022	-2.9975	0.0976	2.6%	-3.00 [-3.19 , -2.81]
Abdollahi 2019	-0.1898	0.0834	3.5%	-0.19 [-0.35 , -0.03]
Müller 2001	0.12985199	0.07778525	4.0%	0.13 [-0.02 , 0.28]
DiGirolamo 2010	0	0.07471888	4.4%	0.00 [-0.15 , 0.15]
Ebrahimi 2006	0.89844604	0.07399793	4.5%	0.90 [0.75 , 1.04]
Hess 2015	0.0213	0.0573	7.4%	0.02 [-0.09 , 0.13]
Bhandari 2002	0.0399929	0.04238717	13.6%	0.04 [-0.04 , 0.12]
Becquey 2016	0.0113	0.0295	28.0%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.04 , 0.02]**

Heterogeneity: Chi² = 1191.48, df = 46 (P < 0.00001); I² = 96%

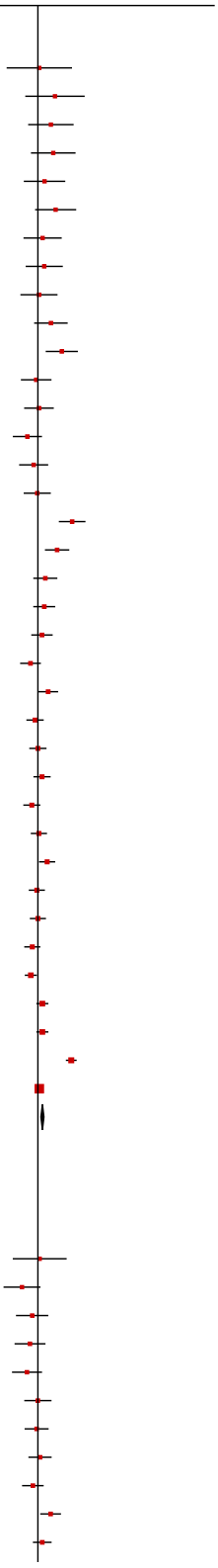
Test for overall effect: Z = 0.63 (P = 0.53)

Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%



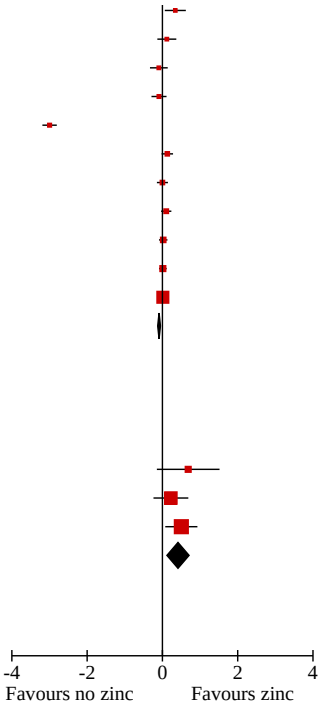
Analysis 2.34. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 34: Weight: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.34.1 Solution				
Sayeg Porto 2000	0.03855533	0.44900267	0.2%	0.04 [-0.84 , 0.92]
Ince 1995	0.45975026	0.40814252	0.2%	0.46 [-0.34 , 1.26]
Walravens 1983	0.35011864	0.31240719	0.4%	0.35 [-0.26 , 0.96]
Smith 1999	0.41365482	0.30646941	0.4%	0.41 [-0.19 , 1.01]
Sempértegui 1996	0.17880543	0.28477489	0.5%	0.18 [-0.38 , 0.74]
Walravens 1989	0.47808527	0.28247531	0.5%	0.48 [-0.08 , 1.03]
Meeks Gardner 1998	0.1267561	0.26255721	0.6%	0.13 [-0.39 , 0.64]
Dehbozorgi 2007	0.17051953	0.25532062	0.6%	0.17 [-0.33 , 0.67]
Gibson 1989	0.02883096	0.25485925	0.6%	0.03 [-0.47 , 0.53]
Hambidge 1978	0.3505815	0.23036496	0.8%	0.35 [-0.10 , 0.80]
Mozaffari-Khosravi 2009	0.64355443	0.22092161	0.8%	0.64 [0.21 , 1.08]
Ruel 1997	-0.0460843	0.21020838	0.9%	-0.05 [-0.46 , 0.37]
Rosado 1997	0.02874363	0.20355836	1.0%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	-0.2834995	0.20047451	1.0%	-0.28 [-0.68 , 0.11]
De Fonseca 2002	-0.1138287	0.19970491	1.0%	-0.11 [-0.51 , 0.28]
Meeks Gardner 2005	-0.0174125	0.18617821	1.2%	-0.02 [-0.38 , 0.35]
Hong 1982	0.92280618	0.18288181	1.2%	0.92 [0.56 , 1.28]
Ninh 1996	0.51743485	0.16741874	1.5%	0.52 [0.19 , 0.85]
Penny 2004	0.20000822	0.16513475	1.5%	0.20 [-0.12 , 0.52]
Brown 2007	0.1714931	0.15100736	1.8%	0.17 [-0.12 , 0.47]
Umeta 2000	0.1098315	0.14694511	1.9%	0.11 [-0.18 , 0.40]
Akramuzzaman 1994	-0.1992298	0.14252101	2.0%	-0.20 [-0.48 , 0.08]
Alarcon 2004	0.27598738	0.13724067	2.2%	0.28 [0.01 , 0.54]
Baqui 2003	-0.0766763	0.11903369	2.9%	-0.08 [-0.31 , 0.16]
Baqui 2003 (2)	0	0.11831952	2.9%	0.00 [-0.23 , 0.23]
Long 2006	0.11155133	0.11804496	2.9%	0.11 [-0.12 , 0.34]
Long 2006 (2)	-0.1637194	0.11675288	3.0%	-0.16 [-0.39 , 0.07]
Wuehler 2008	0.02657707	0.11140204	3.3%	0.03 [-0.19 , 0.24]
Lind 2003	0.24929568	0.11094564	3.3%	0.25 [0.03 , 0.47]
Lind 2003 (2)	-0.0284882	0.11085987	3.3%	-0.03 [-0.25 , 0.19]
Rahman 2001	0	0.11069534	3.4%	0.00 [-0.22 , 0.22]
Rahman 2001 (2)	-0.1509247	0.11043509	3.4%	-0.15 [-0.37 , 0.07]
Abdollahi 2019	-0.1898	0.0834	5.9%	-0.19 [-0.35 , -0.03]
Abdollahi 2014	0.121071	0.08222	6.1%	0.12 [-0.04 , 0.28]
Khodashenas 2015	0.121071	0.08222	6.1%	0.12 [-0.04 , 0.28]
Ebrahimi 2006	0.89844604	0.07399793	7.5%	0.90 [0.75 , 1.04]
Bhandari 2002	0.0399929	0.04238717	22.9%	0.04 [-0.04 , 0.12]
Subtotal (95% CI)			**100.0%**	**0.12 [0.08 , 0.16]**
Heterogeneity: Chi² = 197.72, df = 36 (P < 0.00001); I² = 82%				
Test for overall effect: Z = 6.02 (P < 0.00001)				
2.34.2 Pill/tablet				
Bertinato 2013	0.048995	0.370234	0.2%	0.05 [-0.68 , 0.77]
Tupe 2009	-0.4278935	0.25358514	0.5%	-0.43 [-0.92 , 0.07]
Sazawal 2006	-0.1548301	0.22216939	0.7%	-0.15 [-0.59 , 0.28]
Sazawal 2006 (2)	-0.2120463	0.21235411	0.7%	-0.21 [-0.63 , 0.20]
Kaseb 2013	-0.29308	0.206353	0.8%	-0.29 [-0.70 , 0.11]
Kikafunda 1998	0	0.18705326	1.0%	0.00 [-0.37 , 0.37]
Berger 2015	-0.035004	0.165005	1.2%	-0.04 [-0.36 , 0.29]
Cavan 1993	0.05720422	0.15943234	1.3%	0.06 [-0.26 , 0.37]
Chen 2012	-0.1353824	0.148262447	1.5%	-0.14 [-0.43 , 0.16]
Vakili 2015	0.342569	0.142476	1.6%	0.34 [0.06 , 0.62]
Mandlik 2020	0.117221	0.128439	2.0%	0.12 [-0.13 , 0.37]



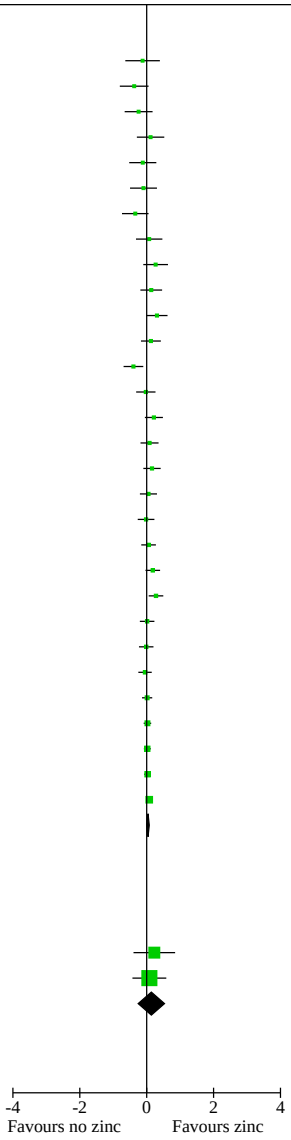
Analysis 2.34. (Continued)

Vakili 2015	0.342369	0.142476	1.6%	0.34 [0.06 , 0.62]
Mandlik 2020	0.117221	0.128439	2.0%	0.12 [-0.13 , 0.37]
Friis 1997	-0.0949685	0.12015242	2.3%	-0.09 [-0.33 , 0.14]
Mazariegos 2010	-0.09075	0.10193628	3.2%	-0.09 [-0.29 , 0.11]
Islam 2022	-2.9975	0.0976	3.5%	-3.00 [-3.19 , -2.81]
Müller 2001	0.12985199	0.07778525	5.5%	0.13 [-0.02 , 0.28]
DiGirolamo 2010	0	0.07471888	6.0%	0.00 [-0.15 , 0.15]
Bhandari 2007	0.1009309	0.06967226	6.9%	0.10 [-0.04 , 0.24]
Hess 2015	0.0213	0.0573	10.2%	0.02 [-0.09 , 0.13]
Barffour 2019	0.011229	0.052006	12.4%	0.01 [-0.09 , 0.11]
Becquey 2016	0.0113	0.0295	38.4%	0.01 [-0.05 , 0.07]
Subtotal (95% CI)			**100.0%**	**-0.09 [-0.12 , -0.05]**
Heterogeneity: Chi² = 940.15, df = 19 (P < 0.00001); I² = 98%				
Test for overall effect: Z = 4.87 (P < 0.00001)				
2.34.3 Capsule				
Castillo-Durán 1994	0.68486898	0.42465726	12.4%	0.68 [-0.15 , 1.52]
Hettiarachchi 2008 (2)	0.22531019	0.23611165	40.2%	0.23 [-0.24 , 0.69]
Hettiarachchi 2008	0.50265662	0.21768626	47.3%	0.50 [0.08 , 0.93]
Subtotal (95% CI)			**100.0%**	**0.41 [0.12 , 0.71]**
Heterogeneity: Chi² = 1.21, df = 2 (P = 0.55); I² = 0%				
Test for overall effect: Z = 2.76 (P = 0.006)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



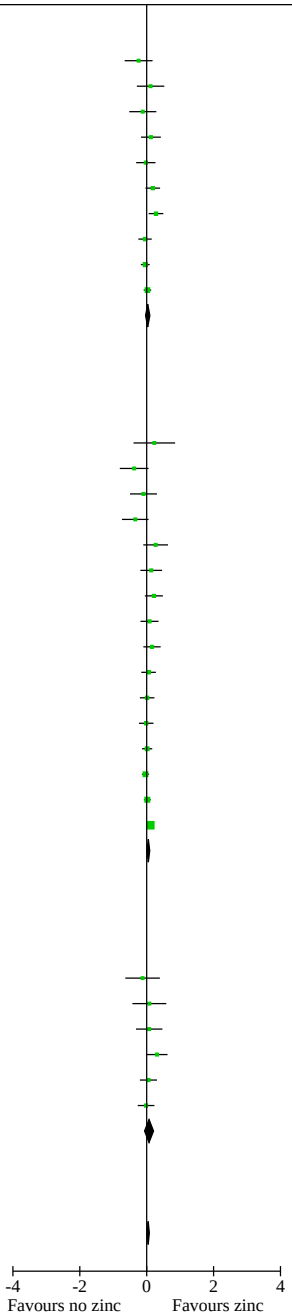
Analysis 2.35. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 35: Weight-to-height ratio: country income level subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.35.1 Low- or middle-income								
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	0.5%	-0.12 [-0.64 , 0.39]
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	0.7%	-0.37 [-0.80 , 0.06]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	0.7%	-0.24 [-0.66 , 0.18]
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	0.8%	0.12 [-0.29 , 0.53]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	0.8%	-0.12 [-0.52 , 0.29]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	0.8%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	0.8%	-0.34 [-0.74 , 0.06]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	0.8%	0.07 [-0.32 , 0.47]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	1.0%	0.27 [-0.10 , 0.64]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	1.2%	0.14 [-0.19 , 0.46]
Cavan 1993	0.49	1	76	0.23	0.66	80	1.3%	0.31 [-0.01 , 0.62]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	1.5%	0.13 [-0.17 , 0.42]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	1.5%	-0.40 [-0.69 , -0.10]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	1.6%	-0.03 [-0.31 , 0.26]
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	1.8%	0.22 [-0.05 , 0.48]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	1.8%	0.09 [-0.18 , 0.35]
Gracia 2005	0.12	1.1	115	-0.04	0.9	115	1.9%	0.16 [-0.10 , 0.42]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	2.0%	0.05 [-0.20 , 0.31]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	2.1%	-0.02 [-0.27 , 0.23]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	2.7%	0.06 [-0.16 , 0.28]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	2.7%	0.18 [-0.04 , 0.40]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	2.7%	0.28 [0.06 , 0.50]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	2.7%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	2.8%	-0.01 [-0.23 , 0.20]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	3.2%	-0.05 [-0.25 , 0.15]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	5.6%	0.01 [-0.14 , 0.17]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	10.3%	0.02 [-0.09 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	12.3%	0.02 [-0.08 , 0.12]
Barffour 2019	-0.72	0.79	739	-0.74	0.82	740	12.5%	0.02 [-0.08 , 0.13]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	18.8%	0.08 [-0.01 , 0.16]
Subtotal (95% CI)			**6085**			**5869**	**100.0%**	**0.04 [0.00 , 0.08]**
Heterogeneity: Chi² = 35.17, df = 29 (P = 0.20); I² = 18%								
Test for overall effect: Z = 2.18 (P = 0.03)								
2.35.2 High-income								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	39.8%	0.23 [-0.39 , 0.85]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	60.2%	0.08 [-0.43 , 0.59]
Subtotal (95% CI)			**50**			**50**	**100.0%**	**0.14 [-0.25 , 0.53]**
Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 0.69 (P = 0.49)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%								



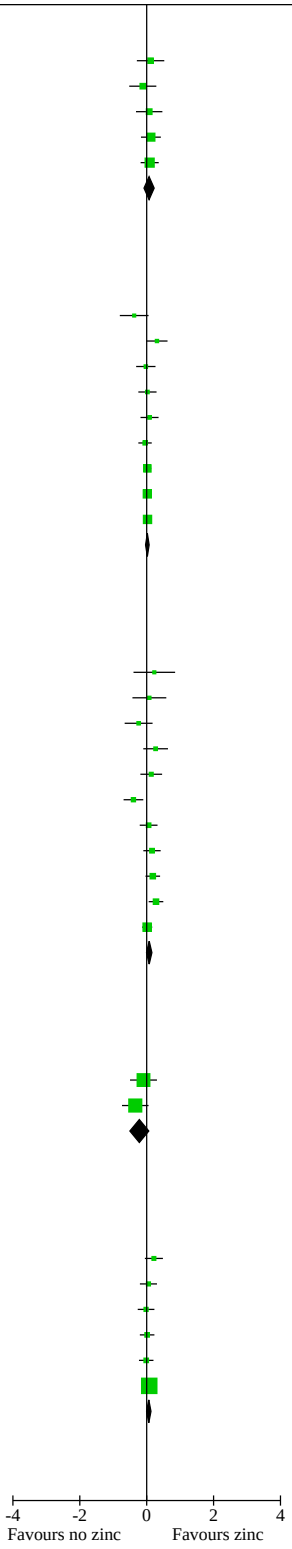
Analysis 2.36. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 36: Weight-to-height ratio: age subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.36.1 6 months to < 1 year								
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	0.7%	-0.24 [-0.66 , 0.18]
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	0.7%	0.12 [-0.29 , 0.53]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	0.7%	-0.12 [-0.52 , 0.29]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	1.3%	0.13 [-0.17 , 0.42]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	1.4%	-0.03 [-0.31 , 0.26]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	2.4%	0.18 [-0.04 , 0.40]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	2.4%	0.28 [0.06 , 0.50]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	2.9%	-0.05 [-0.25 , 0.15]
Bhandari 2002	-0.49	0.67	473	-0.46	0.75	418	6.6%	-0.04 [-0.17 , 0.09]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	9.1%	0.02 [-0.09 , 0.13]
Subtotal (95% CI)			**1913**			**1865**	**28.1%**	**0.03 [-0.03 , 0.09]**
Heterogeneity: Chi² = 11.48, df = 9 (P = 0.24); I² = 22%								
Test for overall effect: Z = 0.94 (P = 0.35)								
2.36.2 1 to < 5 years								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	0.3%	0.23 [-0.39 , 0.85]
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	0.6%	-0.37 [-0.80 , 0.06]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	0.7%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	0.7%	-0.34 [-0.74 , 0.06]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	0.8%	0.27 [-0.10 , 0.64]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	1.1%	0.14 [-0.19 , 0.46]
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	1.6%	0.22 [-0.05 , 0.48]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	1.6%	0.09 [-0.18 , 0.35]
Gracia 2005	0.12	1.1	115	-0.04	0.9	115	1.7%	0.16 [-0.10 , 0.42]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	2.4%	0.06 [-0.16 , 0.28]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	2.4%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	2.4%	-0.01 [-0.23 , 0.20]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	4.9%	0.01 [-0.14 , 0.17]
Bhandari 2002	-0.01	0.6	659	0.01	0.51	674	9.9%	-0.04 [-0.14 , 0.07]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	10.8%	0.02 [-0.08 , 0.12]
Hess 2015	-0.7364	0.9439	1833	-0.8389	0.9654	1387	23.5%	0.11 [0.04 , 0.18]
Subtotal (95% CI)			**4836**			**4141**	**65.6%**	**0.05 [0.01 , 0.09]**
Heterogeneity: Chi² = 18.17, df = 15 (P = 0.25); I² = 17%								
Test for overall effect: Z = 2.29 (P = 0.02)								
2.36.3 5 to < 13 years								
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	0.4%	-0.12 [-0.64 , 0.39]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	0.4%	0.08 [-0.43 , 0.59]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	0.7%	0.07 [-0.32 , 0.47]
Cavan 1993	0.49	1	76	0.23	0.66	80	1.1%	0.31 [-0.01 , 0.62]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	1.8%	0.05 [-0.20 , 0.31]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	1.8%	-0.02 [-0.27 , 0.23]
Subtotal (95% CI)			**426**			**431**	**6.4%**	**0.07 [-0.06 , 0.20]**
Heterogeneity: Chi² = 3.20, df = 5 (P = 0.67); I² = 0%								
Test for overall effect: Z = 1.03 (P = 0.30)								
Total (95% CI)			**7175**			**6437**	**100.0%**	**0.05 [0.01 , 0.08]**
Heterogeneity: Chi² = 33.22, df = 31 (P = 0.36); I² = 7%								
Test for overall effect: Z = 2.61 (P = 0.009)								
Test for subgroup differences: Chi² = 0.37, df = 2 (P = 0.83), I² = 0%								



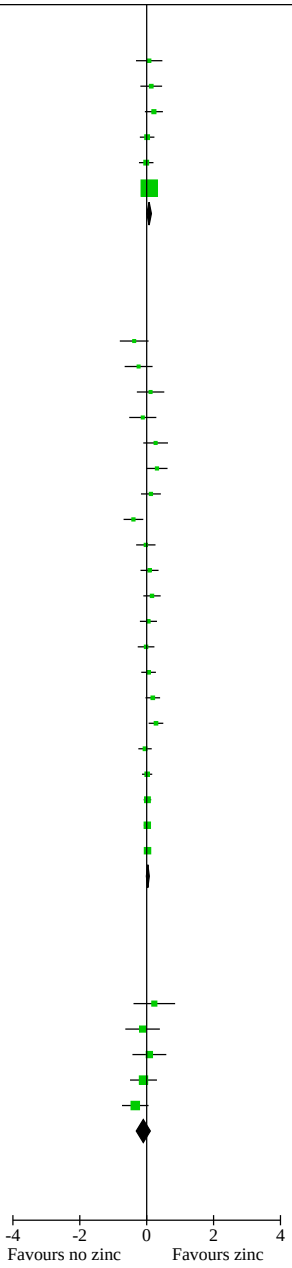
Analysis 2.37. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 37: Weight-to-height ratio: dose subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.37.1 0 to < 5 mg								
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	13.7%	0.12 [-0.29 , 0.53]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	14.0%	-0.12 [-0.52 , 0.29]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	14.8%	0.07 [-0.32 , 0.47]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	26.0%	0.13 [-0.17 , 0.42]
Wuehler 2008	0.09	0.65	103	0.04	0.46	108	31.5%	0.09 [-0.18 , 0.36]
Subtotal (95% CI)			**329**			**342**	**100.0%**	**0.07 [-0.08 , 0.22]**
Heterogeneity: Chi² = 1.02, df = 4 (P = 0.91); I² = 0%								
Test for overall effect: Z = 0.92 (P = 0.36)								
2.37.2 5 to < 10 mg								
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	1.5%	-0.37 [-0.80 , 0.06]
Cavan 1993	0.49	1	76	0.23	0.66	80	2.9%	0.31 [-0.01 , 0.62]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	3.4%	-0.03 [-0.31 , 0.26]
Wuehler 2008	0.05	0.42	100	0.04	0.46	108	3.9%	0.02 [-0.25 , 0.29]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	3.9%	0.09 [-0.18 , 0.35]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	7.1%	-0.05 [-0.25 , 0.15]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	22.7%	0.02 [-0.09 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	27.0%	0.02 [-0.08 , 0.12]
Barffour 2019	-0.72	0.79	739	-0.74	0.82	740	27.5%	0.02 [-0.08 , 0.13]
Subtotal (95% CI)			**2706**			**2676**	**100.0%**	**0.02 [-0.03 , 0.07]**
Heterogeneity: Chi² = 7.19, df = 8 (P = 0.52); I² = 0%								
Test for overall effect: Z = 0.72 (P = 0.47)								
2.37.3 10 to < 15 mg								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	1.7%	0.23 [-0.39 , 0.85]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	2.5%	0.08 [-0.43 , 0.59]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	3.7%	-0.24 [-0.66 , 0.18]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	4.7%	0.27 [-0.10 , 0.64]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	6.1%	0.14 [-0.19 , 0.46]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	7.5%	-0.40 [-0.69 , -0.10]
Wuehler 2008	0.07	0.57	110	0.04	0.46	108	9.2%	0.06 [-0.21 , 0.32]
Gracia 2005	0.12	1.1	115	-0.04	0.9	115	9.6%	0.16 [-0.10 , 0.42]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	13.6%	0.18 [-0.04 , 0.40]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	13.6%	0.28 [0.06 , 0.50]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	27.8%	0.01 [-0.14 , 0.17]
Subtotal (95% CI)			**1196**			**1193**	**100.0%**	**0.08 [-0.01 , 0.16]**
Heterogeneity: Chi² = 18.79, df = 10 (P = 0.04); I² = 47%								
Test for overall effect: Z = 1.83 (P = 0.07)								
2.37.4 15 to < 20 mg								
Rosado 1997	0.25	0.42	48	0.29	0.41	47	49.3%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	50.7%	-0.34 [-0.74 , 0.06]
Subtotal (95% CI)			**97**			**97**	**100.0%**	**-0.22 [-0.50 , 0.06]**
Heterogeneity: Chi² = 0.73, df = 1 (P = 0.39); I² = 0%								
Test for overall effect: Z = 1.53 (P = 0.13)								
2.37.5 20 mg or more								
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	5.9%	0.22 [-0.05 , 0.48]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	6.6%	0.05 [-0.20 , 0.31]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	6.9%	-0.02 [-0.27 , 0.23]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	9.1%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	9.2%	-0.01 [-0.23 , 0.20]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	62.3%	0.08 [-0.01 , 0.16]
Subtotal (95% CI)			**1776**			**1800**	**100.0%**	**0.06 [-0.00 , 0.13]**
Heterogeneity: Chi² = 2.43, df = 5 (P = 0.79); I² = 0%								
Test for overall effect: Z = 1.86 (P = 0.06)								
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%								



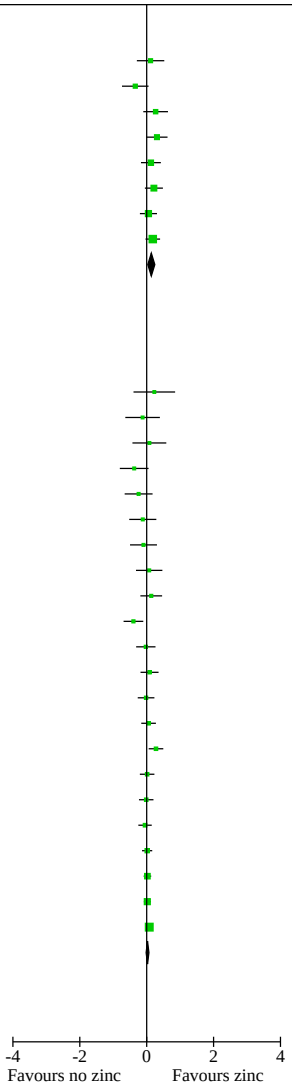
Analysis 2.38. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 38: Weight-to-height ratio: duration subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.38.1 0 to < 6 months								
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	3.0%	0.07 [-0.32 , 0.47]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	4.4%	0.14 [-0.19 , 0.46]
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	6.4%	0.22 [-0.05 , 0.48]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	9.8%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	9.8%	-0.01 [-0.23 , 0.20]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	66.7%	0.08 [-0.01 , 0.16]
Subtotal (95% CI)			**1662**			**1675**	**100.0%**	**0.07 [0.00 , 0.14]**
Heterogeneity: Chi² = 2.14, df = 5 (P = 0.83); I² = 0%								
Test for overall effect: Z = 2.10 (P = 0.04)								
2.38.2 6 to < 12 months								
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	1.0%	-0.37 [-0.80 , 0.06]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	1.1%	-0.24 [-0.66 , 0.18]
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	1.1%	0.12 [-0.29 , 0.53]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	1.1%	-0.12 [-0.52 , 0.29]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	1.4%	0.27 [-0.10 , 0.64]
Cavan 1993	0.49	1	76	0.23	0.66	80	1.9%	0.31 [-0.01 , 0.62]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	2.1%	0.13 [-0.17 , 0.42]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	2.2%	-0.40 [-0.69 , -0.10]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	2.2%	-0.03 [-0.31 , 0.26]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	2.6%	0.09 [-0.18 , 0.35]
Gracia 2005	0.12	1.1	115	-0.04	0.9	115	2.8%	0.16 [-0.10 , 0.42]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	2.9%	0.05 [-0.20 , 0.31]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	3.0%	-0.02 [-0.27 , 0.23]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	3.9%	0.06 [-0.16 , 0.28]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	3.9%	0.18 [-0.04 , 0.40]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	3.9%	0.28 [0.06 , 0.50]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	4.7%	-0.05 [-0.25 , 0.15]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	8.0%	0.01 [-0.14 , 0.17]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	14.8%	0.02 [-0.09 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	17.6%	0.02 [-0.08 , 0.12]
Barffour 2019	-0.72	0.79	739	-0.74	0.82	740	17.9%	0.02 [-0.08 , 0.13]
Subtotal (95% CI)			**4295**			**4070**	**100.0%**	**0.03 [-0.01 , 0.08]**
Heterogeneity: Chi² = 27.72, df = 20 (P = 0.12); I² = 28%								
Test for overall effect: Z = 1.55 (P = 0.12)								
2.38.3 12 months or more								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	11.4%	0.23 [-0.39 , 0.85]
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	16.5%	-0.12 [-0.64 , 0.39]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	17.1%	0.08 [-0.43 , 0.59]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	27.1%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	27.9%	-0.34 [-0.74 , 0.06]
Subtotal (95% CI)			**178**			**174**	**100.0%**	**-0.10 [-0.31 , 0.11]**
Heterogeneity: Chi² = 2.98, df = 4 (P = 0.56); I² = 0%								
Test for overall effect: Z = 0.95 (P = 0.34)								
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%								



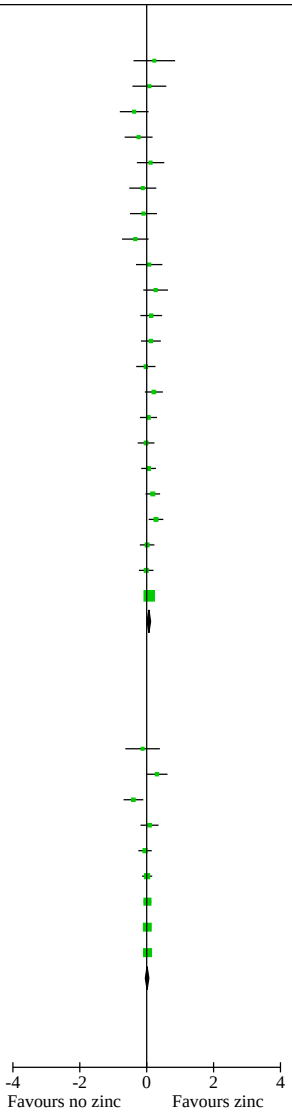
Analysis 2.39. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 39: Weight-to-height ratio: iron co-interventions subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.39.1 Iron co-intervention								
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	6.5%	0.12 [-0.29 , 0.53]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	7.0%	-0.34 [-0.74 , 0.06]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	8.1%	0.27 [-0.10 , 0.64]
Cavan 1993	0.49	1	76	0.23	0.66	80	11.0%	0.31 [-0.01 , 0.62]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	12.4%	0.13 [-0.17 , 0.42]
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	15.1%	0.22 [-0.05 , 0.48]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	16.8%	0.05 [-0.20 , 0.31]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	23.0%	0.18 [-0.04 , 0.40]
Subtotal (95% CI)			**695**			**714**	**100.0%**	**0.14 [0.03 , 0.24]**
Heterogeneity: Chi² = 8.10, df = 7 (P = 0.32); I² = 14%								
Test for overall effect: Z = 2.59 (P = 0.010)								
2.39.2 No iron co-intervention								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	0.5%	0.23 [-0.39 , 0.85]
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	0.7%	-0.12 [-0.64 , 0.39]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	0.7%	0.08 [-0.43 , 0.59]
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	0.9%	-0.37 [-0.80 , 0.06]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	1.0%	-0.24 [-0.66 , 0.18]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	1.1%	-0.12 [-0.52 , 0.29]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	1.1%	-0.10 [-0.50 , 0.31]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	1.1%	0.07 [-0.32 , 0.47]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	1.7%	0.14 [-0.19 , 0.46]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	2.0%	-0.40 [-0.69 , -0.10]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	2.1%	-0.03 [-0.31 , 0.26]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	2.4%	0.09 [-0.18 , 0.35]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	2.8%	-0.02 [-0.27 , 0.23]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	3.6%	0.06 [-0.16 , 0.28]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	3.7%	0.28 [0.06 , 0.50]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	3.7%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	3.7%	-0.01 [-0.23 , 0.20]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	4.4%	-0.05 [-0.25 , 0.15]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	7.5%	0.01 [-0.14 , 0.17]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	13.8%	0.02 [-0.09 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	16.5%	0.02 [-0.08 , 0.12]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	25.2%	0.08 [-0.01 , 0.16]
Subtotal (95% CI)			**4586**			**4350**	**100.0%**	**0.03 [-0.02 , 0.07]**
Heterogeneity: Chi² = 22.69, df = 21 (P = 0.36); I² = 7%								
Test for overall effect: Z = 1.18 (P = 0.24)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%								



Analysis 2.40. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 40: Weight-to-height ratio: formulation subgroup analysis

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	No zinc Mean	No zinc SD	No zinc Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.40.1 Solution								
Walravens 1983	0.29	0.49	20	0.19	0.36	20	0.7%	0.23 [-0.39 , 0.85]
Gibson 1989	0.1	0.27	30	0.08	0.22	30	1.0%	0.08 [-0.43 , 0.59]
Mozaffari-Khosravi 2009	-0.64	0.7	40	-0.38	0.68	45	1.4%	-0.37 [-0.80 , 0.06]
Ruel 1997	-0.28	0.76	45	-0.09	0.8	44	1.5%	-0.24 [-0.66 , 0.18]
Baqui 2003 (2)	-0.8	0.8	43	-0.9	0.9	49	1.5%	0.12 [-0.29 , 0.53]
Baqui 2003	-0.8	0.8	49	-0.7	0.9	45	1.6%	-0.12 [-0.52 , 0.29]
Rosado 1997	0.25	0.42	48	0.29	0.41	47	1.6%	-0.10 [-0.50 , 0.31]
Rosado 1997 (2)	0.19	0.56	49	0.36	0.42	50	1.7%	-0.34 [-0.74 , 0.06]
De Fonseca 2002	-0.19	0.86	51	-0.25	0.73	48	1.7%	0.07 [-0.32 , 0.47]
Meeks Gardner 2005	-1.56	0.51	55	-1.7	0.53	59	1.9%	0.27 [-0.10 , 0.64]
Ninh 1996	-1.18	0.71	73	-1.27	0.6	73	2.5%	0.14 [-0.19 , 0.46]
Brown 2007	-0.47	0.77	83	-0.56	0.65	92	3.0%	0.13 [-0.17 , 0.42]
Umeta 2000	-0.3	3.54	92	-0.21	3.41	92	3.1%	-0.03 [-0.31 , 0.26]
Alarcon 2004	0.29	1.13	109	0.05	1.09	104	3.6%	0.22 [-0.05 , 0.48]
Richard 2006 (2)	-0.01	0.97	119	-0.06	0.94	117	4.0%	0.05 [-0.20 , 0.31]
Richard 2006	-0.02	0.87	119	-0.004	0.85	129	4.2%	-0.02 [-0.27 , 0.23]
Wuehler 2008	0.07	0.55	313	0.04	0.46	108	5.4%	0.06 [-0.16 , 0.28]
Lind 2003 (2)	-0.86	1.06	161	-1.07	1.23	163	5.5%	0.18 [-0.04 , 0.40]
Lind 2003	-0.7	1.06	162	-1.01	1.16	164	5.5%	0.28 [0.06 , 0.50]
Rahman 2001	-1.31	0.76	165	-1.32	0.78	160	5.5%	0.01 [-0.20 , 0.23]
Rahman 2001 (2)	-1.32	0.73	171	-1.31	0.67	157	5.5%	-0.01 [-0.23 , 0.20]
Bhandari 2002	-0.02	0.64	1093	-0.07	0.67	1133	37.7%	0.08 [-0.01 , 0.16]
Subtotal (95% CI)			**3090**			**2929**	**100.0%**	**0.06 [0.01 , 0.12]**
Heterogeneity: Chi² = 20.92, df = 21 (P = 0.46); I² = 0%								
Test for overall effect: Z = 2.49 (P = 0.01)								
2.40.2 Pill/tablet								
Friis 1997	-0.23	1.39	31	-0.07	1.16	27	1.0%	-0.12 [-0.64 , 0.39]
Cavan 1993	0.49	1	76	0.23	0.66	80	2.7%	0.31 [-0.01 , 0.62]
Chen 2012	-0.56	0.98	93	-0.15	1.08	88	3.1%	-0.40 [-0.69 , -0.10]
Shankar 2000	-0.69	0.82	103	-0.76	0.82	109	3.7%	0.09 [-0.18 , 0.35]
Mazariegos 2010	0.05	0.91	188	0.1	1.1	196	6.6%	-0.05 [-0.25 , 0.15]
Müller 2001	-0.09	0.8	332	-0.1	0.7	329	11.4%	0.01 [-0.14 , 0.17]
Hess 2015	-0.7	0.89	617	-0.72	0.89	602	21.0%	0.02 [-0.09 , 0.13]
Becquey 2016	0.08	0.5481	751	0.07	0.5307	704	25.1%	0.02 [-0.08 , 0.12]
Barffour 2019	-0.72	0.79	739	-0.74	0.82	740	25.5%	0.02 [-0.08 , 0.13]
Subtotal (95% CI)			**2930**			**2875**	**100.0%**	**0.01 [-0.04 , 0.06]**
Heterogeneity: Chi² = 11.76, df = 8 (P = 0.16); I² = 32%								
Test for overall effect: Z = 0.45 (P = 0.65)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%								

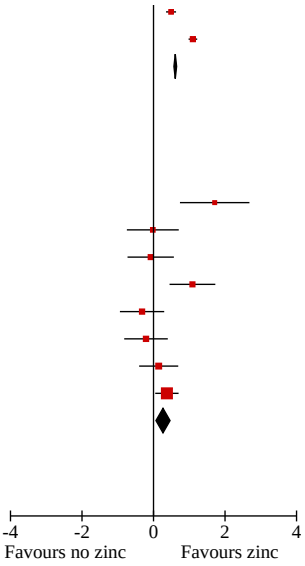


Analysis 2.41. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 41: Serum or plasma zinc concentration: country income level subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.41.1 Low- or middle-income				
Silva 2006	2.12757492	1.10761519	0.0%	2.13 [-0.04 , 4.30]
Sayeg Porto 2000	0.07926742	0.44915102	0.2%	0.08 [-0.80 , 0.96]
Rosales 2004	1.39772302	0.39918356	0.2%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.59178434	0.393349	0.2%	1.59 [0.82 , 2.36]
Garcia 1998	0.61895336	0.34825576	0.3%	0.62 [-0.06 , 1.30]
Smith 1999	1.02871696	0.33059672	0.3%	1.03 [0.38 , 1.68]
Udomkesmalee 1992	2.16724629	0.30343932	0.4%	2.17 [1.57 , 2.76]
Sempértegui 1996	0.94195962	0.30001048	0.4%	0.94 [0.35 , 1.53]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	0.4%	1.81 [1.23 , 2.38]
Tupe 2009	1.2972891	0.28675374	0.4%	1.30 [0.74 , 1.86]
Fallahi 2007	0.39627284	0.28402418	0.5%	0.40 [-0.16 , 0.95]
Mahloudji 1975	-0.165458	0.2788914	0.5%	-0.17 [-0.71 , 0.38]
Ba Lo 2011	0.62542586	0.24941159	0.6%	0.63 [0.14 , 1.11]
Schultink 1997	0.47144486	0.24494512	0.6%	0.47 [-0.01 , 0.95]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	0.6%	0.87 [0.39 , 1.34]
Ruz 1997	-0.0479478	0.23832669	0.6%	-0.05 [-0.52 , 0.42]
Mazariegos 2010	0.3998476	0.23138369	0.7%	0.40 [-0.05 , 0.85]
Müller 2001	0.63830688	0.22576313	0.7%	0.64 [0.20 , 1.08]
Baqui 2003	0.30706347	0.22305208	0.7%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	0.8%	0.00 [-0.43 , 0.43]
Hettiarachchi 2008	0.51369923	0.21562749	0.8%	0.51 [0.09 , 0.94]
Umeta 2000	1.09640714	0.21307062	0.8%	1.10 [0.68 , 1.51]
Hong 1982	1.94421305	0.21124116	0.8%	1.94 [1.53 , 2.36]
Rosado 1997	0.49001387	0.20662869	0.9%	0.49 [0.09 , 0.89]
Kaseb 2013	0.053227	0.205245	0.9%	0.05 [-0.35 , 0.46]
Rosado 1997 (2)	0.62774877	0.20438775	0.9%	0.63 [0.23 , 1.03]
Uçkardeş 2009	0.14435311	0.18964639	1.0%	0.14 [-0.23 , 0.52]
Penny 2004	0.73471063	0.17762983	1.2%	0.73 [0.39 , 1.08]
Wuehler 2008	0.70122941	0.16887846	1.3%	0.70 [0.37 , 1.03]
Cavan 1993	0.51245133	0.1679712	1.3%	0.51 [0.18 , 0.84]
Rahman 2001 (2)	-0.089988	0.16760985	1.3%	-0.09 [-0.42 , 0.24]
Brown 2007	0.53520617	0.16389707	1.4%	0.54 [0.21 , 0.86]
Rahman 2001	-0.1159815	0.16210648	1.4%	-0.12 [-0.43 , 0.20]
Chang 2010	0.36204843	0.15223956	1.6%	0.36 [0.06 , 0.66]
Richard 2006	0.67063373	0.15053466	1.6%	0.67 [0.38 , 0.97]
Chen 2012	0.43585676	0.149852942732796	1.6%	0.44 [0.14 , 0.73]
Richard 2006 (2)	0.27769813	0.14757993	1.7%	0.28 [-0.01 , 0.57]
Caulfield 2013	0.266939	0.139047	1.9%	0.27 [-0.01 , 0.54]
Shankar 2000	-0.1895463	0.13723333	1.9%	-0.19 [-0.46 , 0.08]
Becquey 2016	0.414934	0.132252	2.1%	0.41 [0.16 , 0.67]
Tielsch 2006	0.35339326	0.13023913	2.2%	0.35 [0.10 , 0.61]
Friis 1997	0.40647134	0.1292236	2.2%	0.41 [0.15 , 0.66]
Mandlik 2020	0.0895	0.1284	2.2%	0.09 [-0.16 , 0.34]
Chang 2010 (2)	0.2481705	0.12815887	2.2%	0.25 [-0.00 , 0.50]
Veenemans 2011	1.33657691	0.1276632	2.2%	1.34 [1.09 , 1.59]
Lind 2003 (2)	0.7946871	0.12563884	2.3%	0.79 [0.55 , 1.04]
Lind 2003	0.86027128	0.12535047	2.3%	0.86 [0.61 , 1.11]
Veenemans 2011 (2)	1.11626145	0.12407823	2.4%	1.12 [0.87 , 1.36]
Wessells 2012	1.30076381	0.11129748	3.0%	1.30 [1.08 , 1.52]
Soofi 2013	-0.0581411	0.099716268	3.7%	-0.06 [-0.25 , 0.14]
Sazawal 1996	0.8263088	0.08664303	4.9%	0.83 [0.66 , 1.00]
Abdollahi 2019	-0.1642	0.0833	5.3%	-0.16 [-0.33 , -0.00]
DiGirolamo 2010	0.18538814	0.07877571	5.9%	0.19 [0.03 , 0.34]
Bhandari 2002	1.46023697	0.07309568	6.8%	1.46 [1.32 , 1.60]
Bhandari 2007	0.49031017	0.0714016	7.2%	0.49 [0.35 , 0.63]
Hess 2015	1.101	0.0615	9.7%	1.10 [0.98 , 1.22]

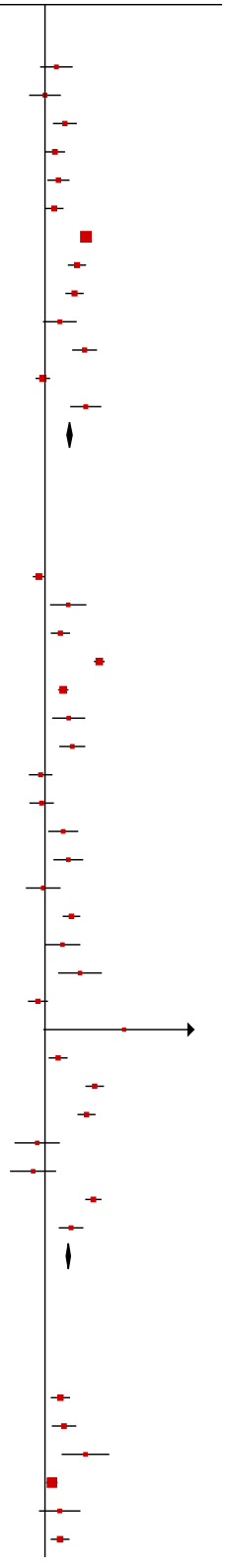
Analysis 2.41. (Continued)

Bhandari 2007	0.49031017	0.0714016	7.2%	0.49 [0.35 , 0.63]
Hess 2015	1.101	0.0615	9.7%	1.10 [0.98 , 1.22]
Subtotal (95% CI)			**100.0%**	**0.61 [0.57 , 0.65]**
Heterogeneity: Chi² = 735.19, df = 55 (P < 0.00001); I² = 93%				
Test for overall effect: Z = 31.80 (P < 0.00001)				
2.41.2 High-income				
Nakamura 1993	1.7108436	0.49561271	4.1%	1.71 [0.74 , 2.68]
Bertinato 2013	-0.019684	0.370193	7.4%	-0.02 [-0.75 , 0.71]
Gibson 1989	-0.0788767	0.33058919	9.2%	-0.08 [-0.73 , 0.57]
Clark 1999	1.08857292	0.32653377	9.5%	1.09 [0.45 , 1.73]
Walravens 1989	-0.3204417	0.3159476	10.1%	-0.32 [-0.94 , 0.30]
Walravens 1983	-0.2100284	0.31083333	10.4%	-0.21 [-0.82 , 0.40]
Sandstead 2008	0.14492933	0.27877714	13.0%	0.14 [-0.40 , 0.69]
Berger 2015	0.374585	0.166471	36.4%	0.37 [0.05 , 0.70]
Subtotal (95% CI)			**100.0%**	**0.27 [0.07 , 0.46]**
Heterogeneity: Chi² = 22.93, df = 7 (P = 0.002); I² = 69%				
Test for overall effect: Z = 2.64 (P = 0.008)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Analysis 2.42. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 42: Serum or plasma zinc concentration: age subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.42.1 6 months to < 1 year				
Baqui 2003	0.30706347	0.22305208	2.5%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	2.6%	0.00 [-0.43 , 0.43]
Brown 2007	0.53520617	0.16389707	4.6%	0.54 [0.21 , 0.86]
Caulfield 2013	0.266939	0.139047	6.5%	0.27 [-0.01 , 0.54]
Chang 2010	0.36204843	0.15223956	5.4%	0.36 [0.06 , 0.66]
Chang 2010 (2)	0.2481705	0.12815887	7.6%	0.25 [-0.00 , 0.50]
Hess 2015	1.101	0.0615	33.0%	1.10 [0.98 , 1.22]
Lind 2003	0.86027128	0.12535047	7.9%	0.86 [0.61 , 1.11]
Lind 2003 (2)	0.7946871	0.12563884	7.9%	0.79 [0.55 , 1.04]
Mazariegos 2010	0.3998476	0.23138369	2.3%	0.40 [-0.05 , 0.85]
Sazawal 1996	1.06488497	0.17037028	4.3%	1.06 [0.73 , 1.40]
Soofi 2013	-0.0581411	0.099716268	12.6%	-0.06 [-0.25 , 0.14]
Umeta 2000	1.09640714	0.21307062	2.7%	1.10 [0.68 , 1.51]
Subtotal (95% CI)			**100.0%**	**0.66 [0.59 , 0.73]**
Heterogeneity: Chi² = 152.53, df = 12 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 18.70 (P < 0.00001)				
2.42.2 1 to < 5 years				
Abdollahi 2019	-0.1642	0.0833	11.4%	-0.16 [-0.33 , -0.00]
Ba Lo 2011	0.62542586	0.24941159	1.3%	0.63 [0.14 , 1.11]
Becquey 2016	0.414934	0.132252	4.5%	0.41 [0.16 , 0.67]
Bhandari 2002	1.46023697	0.07309568	14.8%	1.46 [1.32 , 1.60]
Bhandari 2007	0.49031017	0.0714016	15.5%	0.49 [0.35 , 0.63]
Müller 2001	0.63830688	0.22576313	1.6%	0.64 [0.20 , 1.08]
Penny 2004	0.73471063	0.17762983	2.5%	0.73 [0.39 , 1.08]
Rahman 2001	-0.1159815	0.16210648	3.0%	-0.12 [-0.43 , 0.20]
Rahman 2001 (2)	-0.089988	0.16760985	2.8%	-0.09 [-0.42 , 0.24]
Rosado 1997	0.49001387	0.20662869	1.9%	0.49 [0.09 , 0.89]
Rosado 1997 (2)	0.62774877	0.20438775	1.9%	0.63 [0.23 , 1.03]
Ruz 1997	-0.0479478	0.23832669	1.4%	-0.05 [-0.52 , 0.42]
Sazawal 1996	0.71173994	0.12060246	5.4%	0.71 [0.48 , 0.95]
Schultink 1997	0.47144486	0.24494512	1.3%	0.47 [-0.01 , 0.95]
Sempértegui 1996	0.94195962	0.30001048	0.9%	0.94 [0.35 , 1.53]
Shankar 2000	-0.1895463	0.13723333	4.2%	-0.19 [-0.46 , 0.08]
Silva 2006	2.12757492	1.10761519	0.1%	2.13 [-0.04 , 4.30]
Tielsch 2006	0.35339326	0.13023913	4.7%	0.35 [0.10 , 0.61]
Veenemans 2011	1.33657691	0.1276632	4.9%	1.34 [1.09 , 1.59]
Veenemans 2011 (2)	1.11626145	0.12407823	5.1%	1.12 [0.87 , 1.36]
Walravens 1983	-0.2100284	0.31083333	0.8%	-0.21 [-0.82 , 0.40]
Walravens 1989	-0.3204417	0.3159476	0.8%	-0.32 [-0.94 , 0.30]
Wessells 2012	1.30076381	0.11129748	6.4%	1.30 [1.08 , 1.52]
Wuehler 2008	0.70122941	0.16887846	2.8%	0.70 [0.37 , 1.03]
Subtotal (95% CI)			**100.0%**	**0.63 [0.57 , 0.68]**
Heterogeneity: Chi² = 417.71, df = 23 (P < 0.00001); I² = 94%				
Test for overall effect: Z = 22.29 (P < 0.00001)				
2.42.3 5 to < 13 years				
Becquey 2016	0.414934	0.132252	9.7%	0.41 [0.16 , 0.67]
Cavan 1993	0.51245133	0.1679712	6.0%	0.51 [0.18 , 0.84]
Clark 1999	1.08857292	0.32653377	1.6%	1.09 [0.45 , 1.73]
DiGirolamo 2010	0.18538814	0.07877571	27.2%	0.19 [0.03 , 0.34]
Fallahi 2007	0.39627284	0.28402418	2.1%	0.40 [-0.16 , 0.95]
Friis 1997	0.40647134	0.1292236	10.1%	0.41 [0.15 , 0.66]



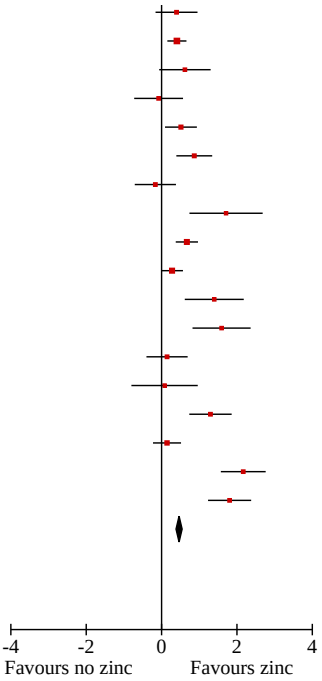
Analysis 2.42. (Continued)

Fallani 2007	0.39627284	0.28402418	2.1%	0.40 [-0.16 , 0.95]
Friis 1997	0.40647134	0.1292236	10.1%	0.41 [0.15 , 0.66]
Garcia 1998	0.61895336	0.34825576	1.4%	0.62 [-0.06 , 1.30]
Gibson 1989	-0.0788767	0.33058919	1.5%	-0.08 [-0.73 , 0.57]
Hettiarachchi 2008	0.51369923	0.21562749	3.6%	0.51 [0.09 , 0.94]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	2.9%	0.87 [0.39 , 1.34]
Mahloudji 1975	-0.165458	0.2788914	2.2%	-0.17 [-0.71 , 0.38]
Nakamura 1993	1.7108436	0.49561271	0.7%	1.71 [0.74 , 2.68]
Richard 2006	0.67063373	0.15053466	7.5%	0.67 [0.38 , 0.97]
Richard 2006 (2)	0.27769813	0.14757993	7.8%	0.28 [-0.01 , 0.57]
Rosales 2004	1.39772302	0.39918356	1.1%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.59178434	0.393349	1.1%	1.59 [0.82 , 2.36]
Sandstead 2008	0.14492933	0.27877714	2.2%	0.14 [-0.40 , 0.69]
Sayeg Porto 2000	0.07926742	0.44915102	0.8%	0.08 [-0.80 , 0.96]
Tupe 2009	1.2972891	0.28675374	2.1%	1.30 [0.74 , 1.86]
Uçkardeş 2009	0.14435311	0.18964639	4.7%	0.14 [-0.23 , 0.52]
Udomkesmalee 1992	2.16724629	0.30343932	1.8%	2.17 [1.57 , 2.76]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	2.0%	1.81 [1.23 , 2.38]
Subtotal (95% CI)			**100.0%**	**0.46 [0.38 , 0.54]**

Heterogeneity: $Chi^2 = 116.91$, df = 21 ($P < 0.00001$); $I^2 = 82\%$

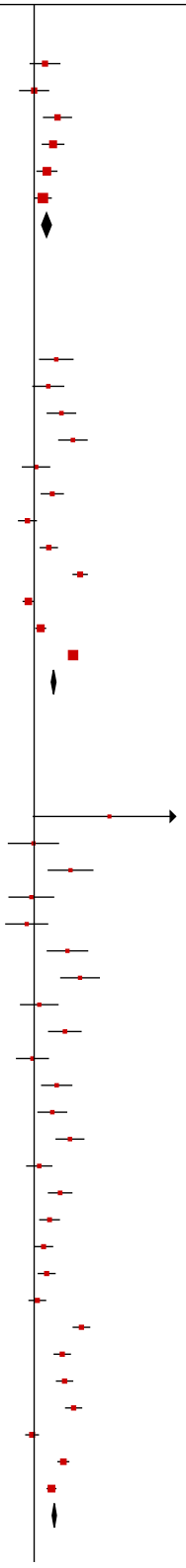
Test for overall effect: $Z = 11.28$ ($P < 0.00001$)

Test for subgroup differences: $Chi^2 = 0.00$, df = 2 ($P < 0.00001$), $I^2 = 0\%$



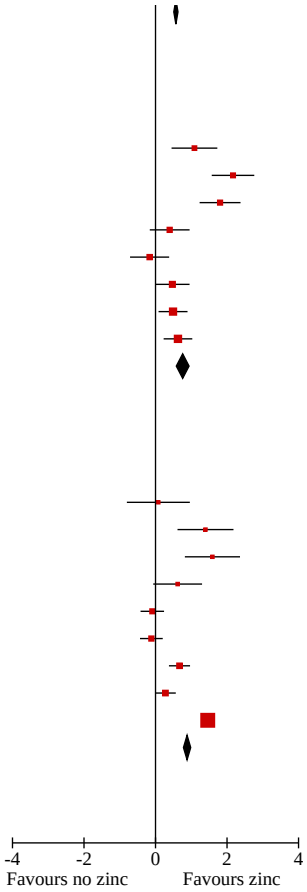
Analysis 2.43. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 43: Serum or plasma zinc concentration: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.43.1 0 to < 5 mg				
Baqui 2003	0.30706347	0.22305208	9.8%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	10.3%	0.00 [-0.43 , 0.43]
Wuehler 2008	0.66041845	0.21037167	11.0%	0.66 [0.25 , 1.07]
Brown 2007	0.53520617	0.16389707	18.2%	0.54 [0.21 , 0.86]
Chang 2010	0.36204843	0.15223956	21.0%	0.36 [0.06 , 0.66]
Chang 2010 (2)	0.2481705	0.12815887	29.7%	0.25 [-0.00 , 0.50]
Subtotal (95% CI)			**100.0%**	**0.35 [0.21 , 0.49]**
Heterogeneity: Chi² = 6.72, df = 5 (P = 0.24); I² = 26%				
Test for overall effect: Z = 5.01 (P < 0.00001)				
2.43.2 5 to < 10 mg				
Ba Lo 2011	0.62542586	0.24941159	1.8%	0.63 [0.14 , 1.11]
Mazariegos 2010	0.3998476	0.23138369	2.1%	0.40 [-0.05 , 0.85]
Wuehler 2008	0.77117766	0.21359493	2.4%	0.77 [0.35 , 1.19]
Umeta 2000	1.09640714	0.21307062	2.5%	1.10 [0.68 , 1.51]
Kaseb 2013	0.053227	0.205245	2.6%	0.05 [-0.35 , 0.46]
Cavan 1993	0.51245133	0.1679712	3.9%	0.51 [0.18 , 0.84]
Shankar 2000	-0.1895463	0.13723333	5.9%	-0.19 [-0.46 , 0.08]
Becquey 2016	0.414934	0.132252	6.4%	0.41 [0.16 , 0.67]
Wessells 2012	1.30076381	0.11129748	9.0%	1.30 [1.08 , 1.52]
Abdollahi 2019	-0.1642	0.0833	16.0%	-0.16 [-0.33 , -0.00]
DiGirolamo 2010	0.18538814	0.07877571	17.9%	0.19 [0.03 , 0.34]
Hess 2015	1.101	0.0615	29.4%	1.10 [0.98 , 1.22]
Subtotal (95% CI)			**100.0%**	**0.55 [0.48 , 0.62]**
Heterogeneity: Chi² = 264.86, df = 11 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 16.48 (P < 0.00001)				
2.43.3 10 to < 15 mg				
Silva 2006	2.12757492	1.10761519	0.1%	2.13 [-0.04 , 4.30]
Bertinato 2013	-0.019684	0.370193	0.6%	-0.02 [-0.75 , 0.71]
Smith 1999	1.02871696	0.33059672	0.8%	1.03 [0.38 , 1.68]
Gibson 1989	-0.0788767	0.33058919	0.8%	-0.08 [-0.73 , 0.57]
Walravens 1983	-0.2100284	0.31083333	0.9%	-0.21 [-0.82 , 0.40]
Sempértegui 1996	0.94195962	0.30001048	1.0%	0.94 [0.35 , 1.53]
Tupe 2009	1.2972891	0.28675374	1.1%	1.30 [0.74 , 1.86]
Sandstead 2008	0.14492933	0.27877714	1.1%	0.14 [-0.40 , 0.69]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	1.5%	0.87 [0.39 , 1.34]
Ruz 1997	-0.0479478	0.23832669	1.6%	-0.05 [-0.52 , 0.42]
Müller 2001	0.63830688	0.22576313	1.7%	0.64 [0.20 , 1.08]
Hettiarachchi 2008	0.51369923	0.21562749	1.9%	0.51 [0.09 , 0.94]
Wuehler 2008	1.01258287	0.20907843	2.0%	1.01 [0.60 , 1.42]
Uçkardeş 2009	0.14435311	0.18964639	2.5%	0.14 [-0.23 , 0.52]
Penny 2004	0.73471063	0.17762983	2.8%	0.73 [0.39 , 1.08]
Chen 2012	0.43585676	0.149852942732796	3.9%	0.44 [0.14 , 0.73]
Caulfield 2013	0.266939	0.139047	4.6%	0.27 [-0.01 , 0.54]
Tielsch 2006	0.35339326	0.13023913	5.2%	0.35 [0.10 , 0.61]
Mandlik 2020	0.0895	0.1284	5.4%	0.09 [-0.16 , 0.34]
Veenemans 2011	1.33657691	0.1276632	5.4%	1.34 [1.09 , 1.59]
Lind 2003 (2)	0.7946871	0.12563884	5.6%	0.79 [0.55 , 1.04]
Lind 2003	0.86027128	0.12535047	5.6%	0.86 [0.61 , 1.11]
Veenemans 2011 (2)	1.11626145	0.12407823	5.7%	1.12 [0.87 , 1.36]
Soofi 2013	-0.0581411	0.099716268	8.9%	-0.06 [-0.25 , 0.14]
Sazawal 1996	0.8263088	0.08664303	11.8%	0.83 [0.66 , 1.00]
Bhandari 2007	0.49031017	0.0714016	17.4%	0.49 [0.35 , 0.63]
Subtotal (95% CI)			**100.0%**	**0.57 [0.51 , 0.63]**
Heterogeneity: Chi² = 181.65, df = 25 (P < 0.00001); I² = 86%				



Analysis 2.43. (Continued)

Subtotal (95% CI)			**100.0%**	**0.57 [0.51 , 0.63]**
Heterogeneity: Chi² = 181.65, df = 25 (P < 0.00001); I² = 86%				
Test for overall effect: Z = 19.15 (P < 0.00001)				
2.43.4 15 to < 20 mg				
Clark 1999	1.08857292	0.32653377	7.7%	1.09 [0.45 , 1.73]
Udomkesmalee 1992	2.16724629	0.30343932	9.0%	2.17 [1.57 , 2.76]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	9.7%	1.81 [1.23 , 2.38]
Fallahi 2007	0.39627284	0.28402418	10.2%	0.40 [-0.16 , 0.95]
Mahloudji 1975	-0.165458	0.2788914	10.6%	-0.17 [-0.71 , 0.38]
Schultink 1997	0.47144486	0.24494512	13.7%	0.47 [-0.01 , 0.95]
Rosado 1997	0.49001387	0.20662869	19.3%	0.49 [0.09 , 0.89]
Rosado 1997 (2)	0.62774877	0.20438775	19.7%	0.63 [0.23 , 1.03]
Subtotal (95% CI)			**100.0%**	**0.76 [0.58 , 0.94]**
Heterogeneity: Chi² = 51.51, df = 7 (P < 0.00001); I² = 86%				
Test for overall effect: Z = 8.36 (P < 0.00001)				
2.43.5 20 mg or more				
Sayeg Porto 2000	0.07926742	0.44915102	1.3%	0.08 [-0.80 , 0.96]
Rosales 2004	1.39772302	0.39918356	1.7%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.59178434	0.393349	1.7%	1.59 [0.82 , 2.36]
Garcia 1998	0.61895336	0.34825576	2.2%	0.62 [-0.06 , 1.30]
Rahman 2001 (2)	-0.089988	0.16760985	9.4%	-0.09 [-0.42 , 0.24]
Rahman 2001	-0.1159815	0.16210648	10.1%	-0.12 [-0.43 , 0.20]
Richard 2006	0.67063373	0.15053466	11.7%	0.67 [0.38 , 0.97]
Richard 2006 (2)	0.27769813	0.14757993	12.2%	0.28 [-0.01 , 0.57]
Bhandari 2002	1.46023697	0.07309568	49.7%	1.46 [1.32 , 1.60]
Subtotal (95% CI)			**100.0%**	**0.88 [0.78 , 0.98]**
Heterogeneity: Chi² = 161.54, df = 8 (P < 0.00001); I² = 95%				
Test for overall effect: Z = 17.13 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				

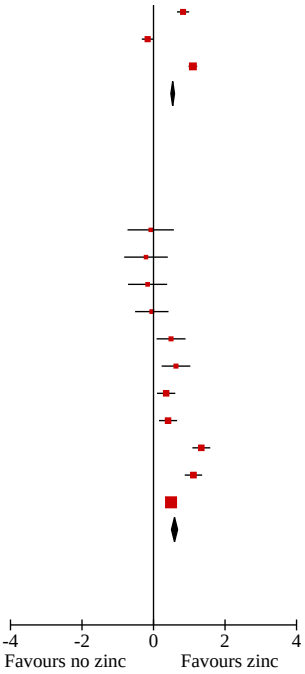


Analysis 2.44. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 44: Serum or plasma zinc concentration: duration subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.44.1 0 to < 6 months				
Silva 2006	2.12757492	1.10761519	0.1%	2.13 [-0.04 , 4.30]
Rosales 2004	1.39772302	0.39918356	0.9%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.59178434	0.393349	0.9%	1.59 [0.82 , 2.36]
Bertinato 2013	-0.019684	0.370193	1.0%	-0.02 [-0.75 , 0.71]
Clark 1999	1.08857292	0.32653377	1.3%	1.09 [0.45 , 1.73]
Sempértegui 1996	0.94195962	0.30001048	1.5%	0.94 [0.35 , 1.53]
Tupe 2009	1.2972891	0.28675374	1.7%	1.30 [0.74 , 1.86]
Fallahi 2007	0.39627284	0.28402418	1.7%	0.40 [-0.16 , 0.95]
Sandstead 2008	0.14492933	0.27877714	1.8%	0.14 [-0.40 , 0.69]
Ba Lo 2011	0.62542586	0.24941159	2.2%	0.63 [0.14 , 1.11]
Schultink 1997	0.47144486	0.24494512	2.3%	0.47 [-0.01 , 0.95]
Hong 1982	1.94421305	0.21124116	3.1%	1.94 [1.53 , 2.36]
Kaseb 2013	0.053227	0.205245	3.3%	0.05 [-0.35 , 0.46]
Uçkardeş 2009	0.14435311	0.18964639	3.8%	0.14 [-0.23 , 0.52]
Rahman 2001 (2)	-0.089988	0.16760985	4.9%	-0.09 [-0.42 , 0.24]
Berger 2015	0.374585	0.166471	5.0%	0.37 [0.05 , 0.70]
Rahman 2001	-0.1159815	0.16210648	5.3%	-0.12 [-0.43 , 0.20]
Wessells 2012	1.30076381	0.11129748	11.1%	1.30 [1.08 , 1.52]
DiGirolamo 2010	0.18538814	0.07877571	22.3%	0.19 [0.03 , 0.34]
Bhandari 2002	1.46023697	0.07309568	25.8%	1.46 [1.32 , 1.60]
Subtotal (95% CI)			**100.0%**	**0.75 [0.68 , 0.82]**
Heterogeneity: Chi² = 308.70, df = 19 (P < 0.00001); I² = 94%				
Test for overall effect: Z = 20.24 (P < 0.00001)				
2.44.2 6 to < 12 months				
Nakamura 1993	1.7108436	0.49561271	0.3%	1.71 [0.74 , 2.68]
Sayeg Porto 2000	0.07926742	0.44915102	0.3%	0.08 [-0.80 , 0.96]
Garcia 1998	0.61895336	0.34825576	0.5%	0.62 [-0.06 , 1.30]
Smith 1999	1.02871696	0.33059672	0.6%	1.03 [0.38 , 1.68]
Walravens 1989	-0.3204417	0.3159476	0.7%	-0.32 [-0.94 , 0.30]
Udomkesmalee 1992	2.16724629	0.30343932	0.7%	2.17 [1.57 , 2.76]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	0.8%	1.81 [1.23 , 2.38]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	1.1%	0.87 [0.39 , 1.34]
Mazariegos 2010	0.3998476	0.23138369	1.2%	0.40 [-0.05 , 0.85]
Müller 2001	0.63830688	0.22576313	1.3%	0.64 [0.20 , 1.08]
Baqui 2003	0.30706347	0.22305208	1.3%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	1.4%	0.00 [-0.43 , 0.43]
Hettiarachchi 2008	0.51369923	0.21562749	1.4%	0.51 [0.09 , 0.94]
Umeta 2000	1.09640714	0.21307062	1.5%	1.10 [0.68 , 1.51]
Penny 2004	0.73471063	0.17762983	2.1%	0.73 [0.39 , 1.08]
Wuehler 2008	0.70122941	0.16887846	2.3%	0.70 [0.37 , 1.03]
Cavan 1993	0.51245133	0.1679712	2.3%	0.51 [0.18 , 0.84]
Brown 2007	0.53520617	0.16389707	2.5%	0.54 [0.21 , 0.86]
Chang 2010	0.36204843	0.15223956	2.8%	0.36 [0.06 , 0.66]
Richard 2006	0.67063373	0.15053466	2.9%	0.67 [0.38 , 0.97]
Chen 2012	0.43585676	0.149852942732796	2.9%	0.44 [0.14 , 0.73]
Richard 2006 (2)	0.27769813	0.14757993	3.0%	0.28 [-0.01 , 0.57]
Shankar 2000	-0.1895463	0.13723333	3.5%	-0.19 [-0.46 , 0.08]
Becquey 2016	0.414934	0.132252	3.8%	0.41 [0.16 , 0.67]
Mandlik 2020	0.0895	0.1284	4.0%	0.09 [-0.16 , 0.34]
Chang 2010 (2)	0.2481705	0.12815887	4.0%	0.25 [-0.00 , 0.50]
Lind 2003 (2)	0.7946871	0.12563884	4.2%	0.79 [0.55 , 1.04]
Lind 2003	0.86027128	0.12535047	4.2%	0.86 [0.61 , 1.11]
Soofi 2013	-0.0581411	0.099716268	6.6%	-0.06 [-0.25 , 0.14]
Sazawal 1996	0.8263088	0.08664303	8.8%	0.83 [0.66 , 1.00]
Abdollahi 2019	-0.1642	0.0833	9.5%	-0.16 [-0.33 , -0.00]

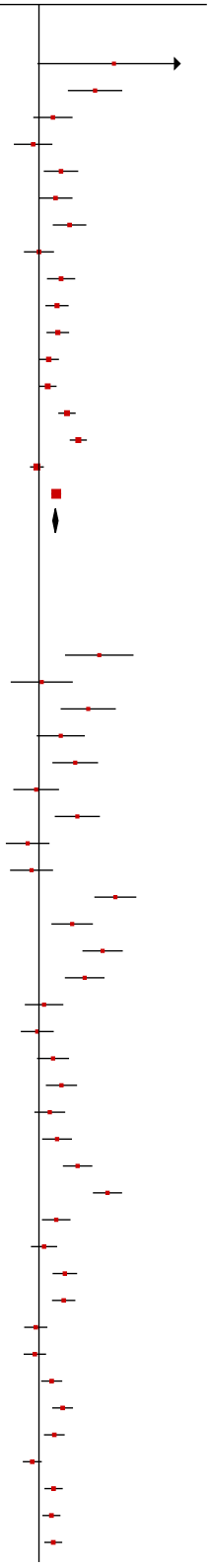
Analysis 2.44. (Continued)

Sazawal 1996	0.8263088	0.08664303	8.8%	0.83 [0.66 , 1.00]
Abdollahi 2019	-0.1642	0.0833	9.5%	-0.16 [-0.33 , -0.00]
Hess 2015	1.101	0.0615	17.4%	1.10 [0.98 , 1.22]
Subtotal (95% CI)			**100.0%**	**0.54 [0.49 , 0.59]**
Heterogeneity: Chi² = 347.05, df = 31 (P < 0.00001); I² = 91%				
Test for overall effect: Z = 20.89 (P < 0.00001)				
2.44.3 12 months or more				
Gibson 1989	-0.0788767	0.33058919	1.7%	-0.08 [-0.73 , 0.57]
Walravens 1983	-0.2100284	0.31083333	1.9%	-0.21 [-0.82 , 0.40]
Mahloudji 1975	-0.165458	0.2788914	2.4%	-0.17 [-0.71 , 0.38]
Ruz 1997	-0.0479478	0.23832669	3.3%	-0.05 [-0.52 , 0.42]
Rosado 1997	0.49001387	0.20662869	4.3%	0.49 [0.09 , 0.89]
Rosado 1997 (2)	0.62774877	0.20438775	4.4%	0.63 [0.23 , 1.03]
Tielsch 2006	0.35339326	0.13023913	10.9%	0.35 [0.10 , 0.61]
Friis 1997	0.40647134	0.1292236	11.1%	0.41 [0.15 , 0.66]
Veenemans 2011	1.33657691	0.1276632	11.4%	1.34 [1.09 , 1.59]
Veenemans 2011 (2)	1.11626145	0.12407823	12.1%	1.12 [0.87 , 1.36]
Bhandari 2007	0.49031017	0.0714016	36.4%	0.49 [0.35 , 0.63]
Subtotal (95% CI)			**100.0%**	**0.59 [0.50 , 0.67]**
Heterogeneity: Chi² = 84.94, df = 10 (P < 0.00001); I² = 88%				
Test for overall effect: Z = 13.64 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.45. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 45: Serum or plasma zinc concentration: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.45.1 Iron co-intervention				
Silva 2006	2.12757492	1.10761519	0.1%	2.13 [-0.04 , 4.30]
Rosales 2004 (2)	1.59178434	0.393349	0.9%	1.59 [0.82 , 2.36]
Fallahi 2007	0.39627284	0.28402418	1.7%	0.40 [-0.16 , 0.95]
Mahloudji 1975	-0.165458	0.2788914	1.8%	-0.17 [-0.71 , 0.38]
Ba Lo 2011	0.62542586	0.24941159	2.2%	0.63 [0.14 , 1.11]
Schultink 1997	0.47144486	0.24494512	2.3%	0.47 [-0.01 , 0.95]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	2.3%	0.87 [0.39 , 1.34]
Baqui 2003 (2)	0	0.21750534	2.9%	0.00 [-0.43 , 0.43]
Rosado 1997 (2)	0.62774877	0.20438775	3.3%	0.63 [0.23 , 1.03]
Cavan 1993	0.51245133	0.1679712	4.8%	0.51 [0.18 , 0.84]
Brown 2007	0.53520617	0.16389707	5.1%	0.54 [0.21 , 0.86]
Richard 2006 (2)	0.27769813	0.14757993	6.3%	0.28 [-0.01 , 0.57]
Chang 2010 (2)	0.2481705	0.12815887	8.3%	0.25 [-0.00 , 0.50]
Lind 2003 (2)	0.7946871	0.12563884	8.7%	0.79 [0.55 , 1.04]
Veenemans 2011 (2)	1.11626145	0.12407823	8.9%	1.12 [0.87 , 1.36]
Soofi 2013	-0.0581411	0.099716268	13.7%	-0.06 [-0.25 , 0.14]
Bhandari 2007	0.49031017	0.0714016	26.8%	0.49 [0.35 , 0.63]
Subtotal (95% CI)			**100.0%**	**0.47 [0.39 , 0.54]**
Heterogeneity: Chi² = 90.82, df = 16 (P < 0.00001); I² = 82%				
Test for overall effect: Z = 12.63 (P < 0.00001)				
2.45.2 No iron co-intervention				
Nakamura 1993	1.7108436	0.49561271	0.2%	1.71 [0.74 , 2.68]
Sayeg Porto 2000	0.07926742	0.44915102	0.3%	0.08 [-0.80 , 0.96]
Rosales 2004	1.39772302	0.39918356	0.3%	1.40 [0.62 , 2.18]
Garcia 1998	0.61895336	0.34825576	0.4%	0.62 [-0.06 , 1.30]
Smith 1999	1.02871696	0.33059672	0.5%	1.03 [0.38 , 1.68]
Gibson 1989	-0.0788767	0.33058919	0.5%	-0.08 [-0.73 , 0.57]
Clark 1999	1.08857292	0.32653377	0.5%	1.09 [0.45 , 1.73]
Walravens 1989	-0.3204417	0.3159476	0.5%	-0.32 [-0.94 , 0.30]
Walravens 1983	-0.2100284	0.31083333	0.5%	-0.21 [-0.82 , 0.40]
Udomkesmalee 1992	2.16724629	0.30343932	0.6%	2.17 [1.57 , 2.76]
Sempértegui 1996	0.94195962	0.30001048	0.6%	0.94 [0.35 , 1.53]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	0.6%	1.81 [1.23 , 2.38]
Tupe 2009	1.2972891	0.28675374	0.6%	1.30 [0.74 , 1.86]
Sandstead 2008	0.14492933	0.27877714	0.7%	0.14 [-0.40 , 0.69]
Ruz 1997	-0.0479478	0.23832669	0.9%	-0.05 [-0.52 , 0.42]
Mazariegos 2010	0.3998476	0.23138369	1.0%	0.40 [-0.05 , 0.85]
Müller 2001	0.63830688	0.22576313	1.0%	0.64 [0.20 , 1.08]
Baqui 2003	0.30706347	0.22305208	1.0%	0.31 [-0.13 , 0.74]
Hettiarachchi 2008	0.51369923	0.21562749	1.1%	0.51 [0.09 , 0.94]
Umeta 2000	1.09640714	0.21307062	1.1%	1.10 [0.68 , 1.51]
Hong 1982	1.94421305	0.21124116	1.2%	1.94 [1.53 , 2.36]
Rosado 1997	0.49001387	0.20662869	1.2%	0.49 [0.09 , 0.89]
Uçkardeş 2009	0.14435311	0.18964639	1.4%	0.14 [-0.23 , 0.52]
Penny 2004	0.73471063	0.17762983	1.7%	0.73 [0.39 , 1.08]
Wuehler 2008	0.70122941	0.16887846	1.8%	0.70 [0.37 , 1.03]
Rahman 2001 (2)	-0.089988	0.16760985	1.9%	-0.09 [-0.42 , 0.24]
Rahman 2001	-0.1159815	0.16210648	2.0%	-0.12 [-0.43 , 0.20]
Chang 2010	0.36204843	0.15223956	2.2%	0.36 [0.06 , 0.66]
Richard 2006	0.67063373	0.15053466	2.3%	0.67 [0.38 , 0.97]
Chen 2012	0.43585676	0.149852942732796	2.3%	0.44 [0.14 , 0.73]
Shankar 2000	-0.1895463	0.13723333	2.8%	-0.19 [-0.46 , 0.08]
Becquey 2016	0.414934	0.132252	3.0%	0.41 [0.16 , 0.67]
Tielsch 2006	0.35339326	0.13023913	3.1%	0.35 [0.10 , 0.61]
Friis 1997	0.40647134	0.1292236	3.1%	0.41 [0.15 , 0.66]



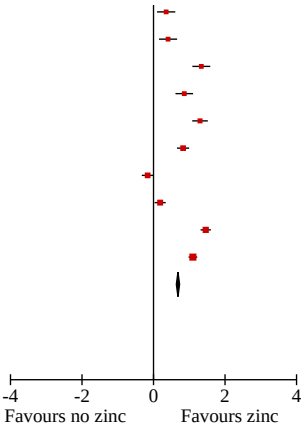
Analysis 2.45. (Continued)

Thelsch 2006	0.35339326	0.13023913	3.1%	0.35 [0.10 , 0.61]
Friis 1997	0.40647134	0.1292236	3.1%	0.41 [0.15 , 0.66]
Veenemans 2011	1.33657691	0.1276632	3.2%	1.34 [1.09 , 1.59]
Lind 2003	0.86027128	0.12535047	3.3%	0.86 [0.61 , 1.11]
Wessells 2012	1.30076381	0.11129748	4.2%	1.30 [1.08 , 1.52]
Sazawal 1996	0.8263088	0.08664303	6.9%	0.83 [0.66 , 1.00]
Abdollahi 2019	-0.1642	0.0833	7.5%	-0.16 [-0.33 , -0.00]
DiGirolamo 2010	0.18538814	0.07877571	8.4%	0.19 [0.03 , 0.34]
Bhandari 2002	1.46023697	0.07309568	9.7%	1.46 [1.32 , 1.60]
Hess 2015	1.101	0.0615	13.8%	1.10 [0.98 , 1.22]
Subtotal (95% CI)			**100.0%**	**0.68 [0.64 , 0.73]**

Heterogeneity: Chi² = 618.86, df = 41 (P < 0.00001); I² = 93%

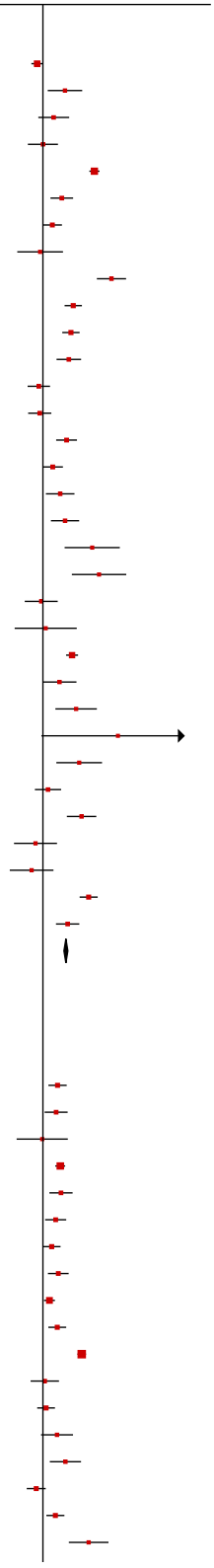
Test for overall effect: Z = 29.97 (P < 0.00001)

Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%



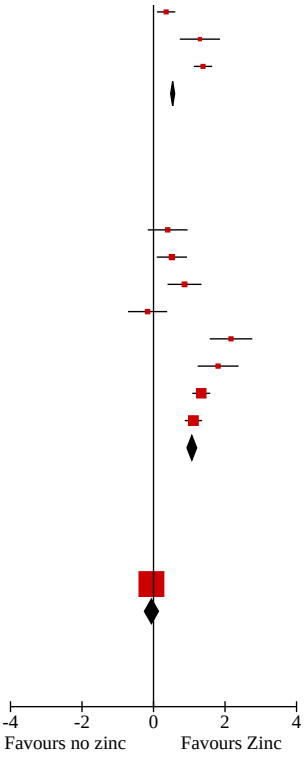
Analysis 2.46. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 46: Serum or plasma zinc concentration: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.46.1 Solution				
Abdollahi 2019	-0.1642	0.0833	11.5%	-0.16 [-0.33 , -0.00]
Ba Lo 2011	0.62542586	0.24941159	1.3%	0.63 [0.14 , 1.11]
Baqui 2003	0.30706347	0.22305208	1.6%	0.31 [-0.13 , 0.74]
Baqui 2003 (2)	0	0.21750534	1.7%	0.00 [-0.43 , 0.43]
Bhandari 2002	1.46023697	0.07309568	15.0%	1.46 [1.32 , 1.60]
Brown 2007	0.53520617	0.16389707	3.0%	0.54 [0.21 , 0.86]
Caulfield 2013	0.266939	0.139047	4.1%	0.27 [-0.01 , 0.54]
Gibson 1989	-0.0788767	0.33058919	0.7%	-0.08 [-0.73 , 0.57]
Hong 1982	1.94421305	0.21124116	1.8%	1.94 [1.53 , 2.36]
Lind 2003	0.86027128	0.12535047	5.1%	0.86 [0.61 , 1.11]
Lind 2003 (2)	0.7946871	0.12563884	5.1%	0.79 [0.55 , 1.04]
Penny 2004	0.73471063	0.17762983	2.5%	0.73 [0.39 , 1.08]
Rahman 2001	-0.1159815	0.16210648	3.0%	-0.12 [-0.43 , 0.20]
Rahman 2001 (2)	-0.089988	0.16760985	2.8%	-0.09 [-0.42 , 0.24]
Richard 2006	0.67063373	0.15053466	3.5%	0.67 [0.38 , 0.97]
Richard 2006 (2)	0.27769813	0.14757993	3.7%	0.28 [-0.01 , 0.57]
Rosado 1997	0.49001387	0.20662869	1.9%	0.49 [0.09 , 0.89]
Rosado 1997 (2)	0.62774877	0.20438775	1.9%	0.63 [0.23 , 1.03]
Rosales 2004	1.39772302	0.39918356	0.5%	1.40 [0.62 , 2.18]
Rosales 2004 (2)	1.59178434	0.393349	0.5%	1.59 [0.82 , 2.36]
Ruz 1997	-0.0479478	0.23832669	1.4%	-0.05 [-0.52 , 0.42]
Sayeg Porto 2000	0.07926742	0.44915102	0.4%	0.08 [-0.80 , 0.96]
Sazawal 1996	0.8263088	0.08664303	10.7%	0.83 [0.66 , 1.00]
Schultink 1997	0.47144486	0.24494512	1.3%	0.47 [-0.01 , 0.95]
Sempértegui 1996	0.94195962	0.30001048	0.9%	0.94 [0.35 , 1.53]
Silva 2006	2.12757492	1.10761519	0.1%	2.13 [-0.04 , 4.30]
Smith 1999	1.02871696	0.33059672	0.7%	1.03 [0.38 , 1.68]
Uçkardeş 2009	0.14435311	0.18964639	2.2%	0.14 [-0.23 , 0.52]
Umeta 2000	1.09640714	0.21307062	1.8%	1.10 [0.68 , 1.51]
Walravens 1983	-0.2100284	0.31083333	0.8%	-0.21 [-0.82 , 0.40]
Walravens 1989	-0.3204417	0.3159476	0.8%	-0.32 [-0.94 , 0.30]
Wessells 2012	1.2975442	0.13056679	4.7%	1.30 [1.04 , 1.55]
Wuehler 2008	0.70122941	0.16887846	2.8%	0.70 [0.37 , 1.03]
Subtotal (95% CI)			**100.0%**	**0.65 [0.60 , 0.71]**
Heterogeneity: Chi² = 414.79, df = 32 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 23.02 (P < 0.00001)				
2.46.2 Pill/tablet				
Becquey 2016	0.414934	0.132252	4.5%	0.41 [0.16 , 0.67]
Berger 2015	0.374585	0.166471	2.8%	0.37 [0.05 , 0.70]
Bertinato 2013	-0.019684	0.370193	0.6%	-0.02 [-0.75 , 0.71]
Bhandari 2007	0.49031017	0.0714016	15.4%	0.49 [0.35 , 0.63]
Cavan 1993	0.51245133	0.1679712	2.8%	0.51 [0.18 , 0.84]
Chang 2010	0.36204843	0.15223956	3.4%	0.36 [0.06 , 0.66]
Chang 2010 (2)	0.2481705	0.12815887	4.8%	0.25 [-0.00 , 0.50]
Chen 2012	0.43585676	0.149852942732796	3.5%	0.44 [0.14 , 0.73]
DiGirolamo 2010	0.18538814	0.07877571	12.7%	0.19 [0.03 , 0.34]
Friis 1997	0.40647134	0.1292236	4.7%	0.41 [0.15 , 0.66]
Hess 2015	1.101	0.0615	20.8%	1.10 [0.98 , 1.22]
Kaseb 2013	0.053227	0.205245	1.9%	0.05 [-0.35 , 0.46]
Mandlik 2020	0.0895	0.1284	4.8%	0.09 [-0.16 , 0.34]
Mazariegos 2010	0.3998476	0.23138369	1.5%	0.40 [-0.05 , 0.85]
Müller 2001	0.63830688	0.22576313	1.5%	0.64 [0.20 , 1.08]
Shankar 2000	-0.1895463	0.13723333	4.2%	-0.19 [-0.46 , 0.08]
Tielsch 2006	0.35339326	0.13023913	4.6%	0.35 [0.10 , 0.61]
Tupe 2009	1.2972891	0.28675374	1.0%	1.30 [0.74 , 1.86]



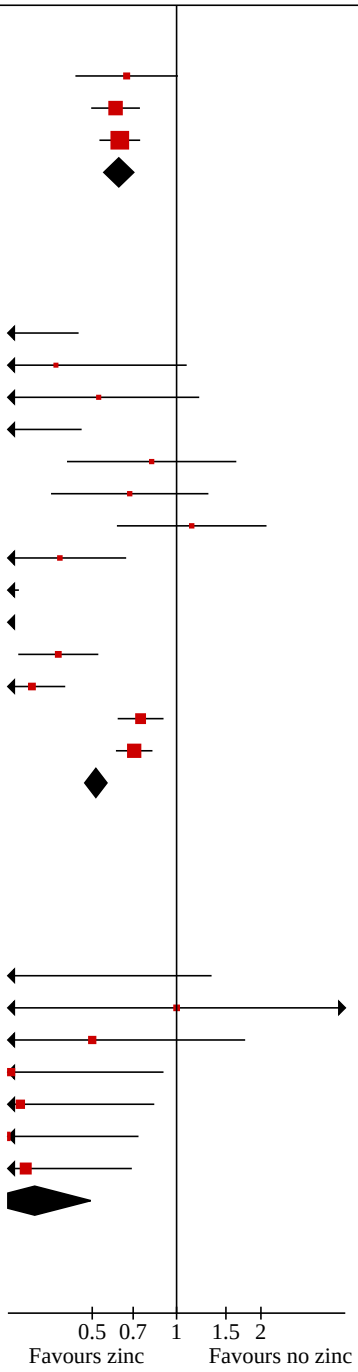
Analysis 2.46. (Continued)

Tielsch 2006	0.35339326	0.13023913	4.6%	0.35 [0.10 , 0.61]
Tupe 2009	1.2972891	0.28675374	1.0%	1.30 [0.74 , 1.86]
Wessells 2012	1.38397957	0.13093544	4.6%	1.38 [1.13 , 1.64]
Subtotal (95% CI)			**100.0%**	**0.54 [0.48 , 0.59]**
Heterogeneity: Chi² = 213.56, df = 18 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 19.09 (P < 0.00001)				
2.46.3 Capsule				
Fallahi 2007	0.39627284	0.28402418	5.8%	0.40 [-0.16 , 0.95]
Hettiarachchi 2008	0.51369923	0.21562749	10.1%	0.51 [0.09 , 0.94]
Hettiarachchi 2008 (2)	0.86739385	0.24267158	8.0%	0.87 [0.39 , 1.34]
Mahloudji 1975	-0.165458	0.2788914	6.0%	-0.17 [-0.71 , 0.38]
Udomkesmalee 1992	2.16724629	0.30343932	5.1%	2.17 [1.57 , 2.76]
Udomkesmalee 1992 (2)	1.80519359	0.29181765	5.5%	1.81 [1.23 , 2.38]
Veenemans 2011	1.33657691	0.1276632	28.9%	1.34 [1.09 , 1.59]
Veenemans 2011 (2)	1.11626145	0.12407823	30.5%	1.12 [0.87 , 1.36]
Subtotal (95% CI)			**100.0%**	**1.07 [0.94 , 1.21]**
Heterogeneity: Chi² = 56.53, df = 7 (P < 0.00001); I² = 88%				
Test for overall effect: Z = 15.62 (P < 0.00001)				
2.46.4 Powder				
Soofi 2013	-0.0581411	0.099716268	100.0%	-0.06 [-0.25 , 0.14]
Subtotal (95% CI)			**100.0%**	**-0.06 [-0.25 , 0.14]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.58 (P = 0.56)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



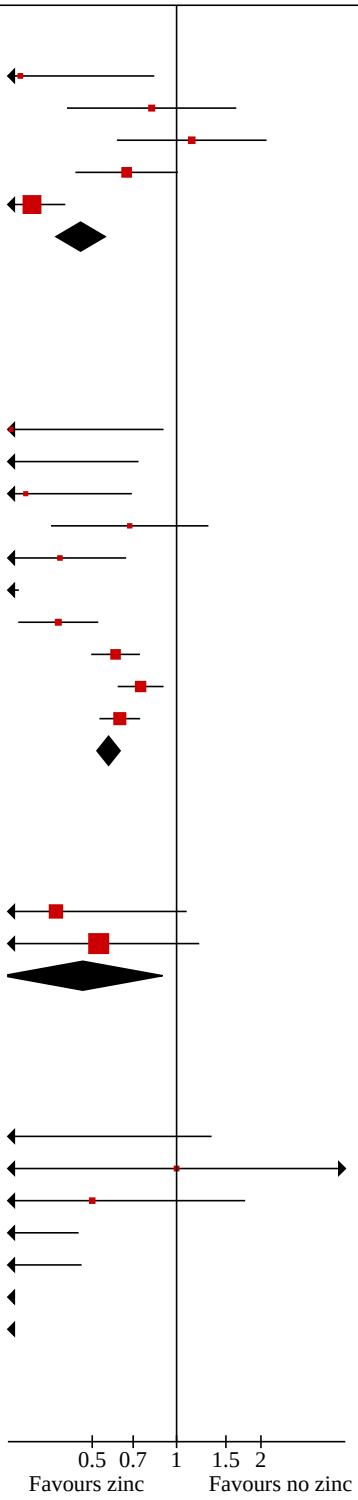
Analysis 2.47. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 47: Prevalence of zinc deficiency: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.47.1 6 months to < 1 year				
Hess 2015	-0.4103	0.2148	8.5%	0.66 [0.44 , 1.01]
Lind 2003	-0.50139064	0.10210941	37.6%	0.61 [0.50 , 0.74]
Lind 2003 (2)	-0.46661953	0.08533585	53.9%	0.63 [0.53 , 0.74]
Subtotal (95% CI)			**100.0%**	**0.62 [0.55 , 0.70]**
Heterogeneity: Chi² = 0.17, df = 2 (P = 0.92); I² = 0%				
Test for overall effect: Z = 7.58 (P < 0.00001)				
2.47.2 1 to < 5 years				
Albert 2003 (2)	-1.96217067	0.59027952	0.6%	0.14 [0.04 , 0.45]
Rosado 1997 (2)	-0.9913982	0.54817965	0.7%	0.37 [0.13 , 1.09]
Rosado 1997	-0.64009262	0.42150954	1.2%	0.53 [0.23 , 1.20]
Albert 2003	-1.51982575	0.37730771	1.5%	0.22 [0.10 , 0.46]
Shankar 2000	-0.20479441	0.35491126	1.7%	0.81 [0.41 , 1.63]
Tielsch 2006	-0.38511439	0.32989001	2.0%	0.68 [0.36 , 1.30]
Abdollahi 2019	0.1243	0.3136	2.2%	1.13 [0.61 , 2.09]
Müller 2001	-0.95900185	0.2779085	2.8%	0.38 [0.22 , 0.66]
Veenemans 2011	-1.77459918	0.24422989	3.6%	0.17 [0.11 , 0.27]
Bhandari 2002	-2.39729649	0.21748349	4.6%	0.09 [0.06 , 0.14]
Veenemans 2011 (2)	-0.97206125	0.16780856	7.7%	0.38 [0.27 , 0.53]
Wessells 2012	-1.18817275	0.13936783	11.1%	0.30 [0.23 , 0.40]
Bhandari 2007	-0.29566242	0.09609274	23.4%	0.74 [0.62 , 0.90]
Barffour 2019	-0.348307	0.076539	36.9%	0.71 [0.61 , 0.82]
Subtotal (95% CI)			**100.0%**	**0.52 [0.47 , 0.56]**
Heterogeneity: Chi² = 153.59, df = 13 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 14.27 (P < 0.00001)				
2.47.3 5 to < 13 years				
Uçkardeş 2009	0	0		Not estimable
Rosales 2004	-2.52305842	1.43399023	2.7%	0.08 [0.00 , 1.33]
Sayeg Porto 2000	0	0.8819171	7.1%	1.00 [0.18 , 5.63]
Rosales 2004 (2)	-0.69314718	0.64117947	13.4%	0.50 [0.14 , 1.76]
Tupe 2009	-1.3600085	0.63908093	13.5%	0.26 [0.07 , 0.90]
DiGirolamo 2010	-1.28372519	0.56145805	17.5%	0.28 [0.09 , 0.83]
Hettiarachchi 2008	-1.40242374	0.55584104	17.9%	0.25 [0.08 , 0.73]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	27.9%	0.29 [0.12 , 0.69]
Subtotal (95% CI)			**100.0%**	**0.31 [0.20 , 0.49]**
Heterogeneity: Chi² = 3.53, df = 6 (P = 0.74); I² = 0%				
Test for overall effect: Z = 4.96 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



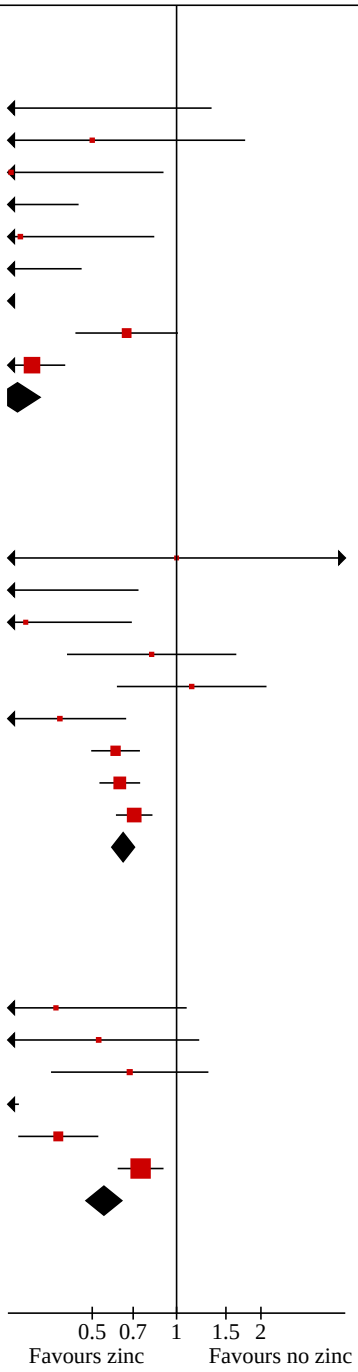
Analysis 2.48. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 48: Prevalence of zinc deficiency: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.48.1 5 to < 10 mg				
DiGirolamo 2010	-1.28372519	0.56145805	3.4%	0.28 [0.09 , 0.83]
Shankar 2000	-0.20479441	0.35491126	8.4%	0.81 [0.41 , 1.63]
Abdollahi 2019	0.1243	0.3136	10.8%	1.13 [0.61 , 2.09]
Hess 2015	-0.4103	0.2148	23.0%	0.66 [0.44 , 1.01]
Wessells 2012	-1.18817275	0.13936783	54.5%	0.30 [0.23 , 0.40]
Subtotal (95% CI)			**100.0%**	**0.45 [0.37 , 0.56]**
Heterogeneity: Chi² = 23.28, df = 4 (P = 0.0001); I² = 83%				
Test for overall effect: Z = 7.67 (P < 0.00001)				
2.48.2 10 to < 15 mg				
Uçkardeş 2009	0	0		Not estimable
Tupe 2009	-1.3600085	0.63908093	0.6%	0.26 [0.07 , 0.90]
Hettiarachchi 2008	-1.40242374	0.55584104	0.8%	0.25 [0.08 , 0.73]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	1.2%	0.29 [0.12 , 0.69]
Tielsch 2006	-0.38511439	0.32989001	2.2%	0.68 [0.36 , 1.30]
Müller 2001	-0.95900185	0.2779085	3.0%	0.38 [0.22 , 0.66]
Veenemans 2011	-1.77459918	0.24422989	3.9%	0.17 [0.11 , 0.27]
Veenemans 2011 (2)	-0.97206125	0.16780856	8.3%	0.38 [0.27 , 0.53]
Lind 2003	-0.50139064	0.10210941	22.5%	0.61 [0.50 , 0.74]
Bhandari 2007	-0.29566242	0.09609274	25.4%	0.74 [0.62 , 0.90]
Lind 2003 (2)	-0.46661953	0.08533585	32.2%	0.63 [0.53 , 0.74]
Subtotal (95% CI)			**100.0%**	**0.57 [0.52 , 0.63]**
Heterogeneity: Chi² = 48.40, df = 9 (P < 0.00001); I² = 81%				
Test for overall effect: Z = 11.55 (P < 0.00001)				
2.48.3 15 to < 20 mg				
Rosado 1997 (2)	-0.9913982	0.54817965	37.2%	0.37 [0.13 , 1.09]
Rosado 1997	-0.64009262	0.42150954	62.8%	0.53 [0.23 , 1.20]
Subtotal (95% CI)			**100.0%**	**0.46 [0.24 , 0.89]**
Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%				
Test for overall effect: Z = 2.31 (P = 0.02)				
2.48.4 20 mg or more				
Rosales 2004	-2.52305842	1.43399023	1.4%	0.08 [0.00 , 1.33]
Sayeg Porto 2000	0	0.8819171	3.6%	1.00 [0.18 , 5.63]
Rosales 2004 (2)	-0.69314718	0.64117947	6.9%	0.50 [0.14 , 1.76]
Albert 2003 (2)	-1.96217067	0.59027952	8.1%	0.14 [0.04 , 0.45]
Albert 2003	-1.51982575	0.37730771	19.9%	0.22 [0.10 , 0.46]
Bhandari 2002	-2.39729649	0.21748349	60.0%	0.09 [0.06 , 0.14]
Subtotal (95% CI)			**100.0%**	**0.14 [0.10 , 0.19]**
Heterogeneity: Chi² = 14.38, df = 5 (P = 0.01); I² = 65%				
Test for overall effect: Z = 11.78 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



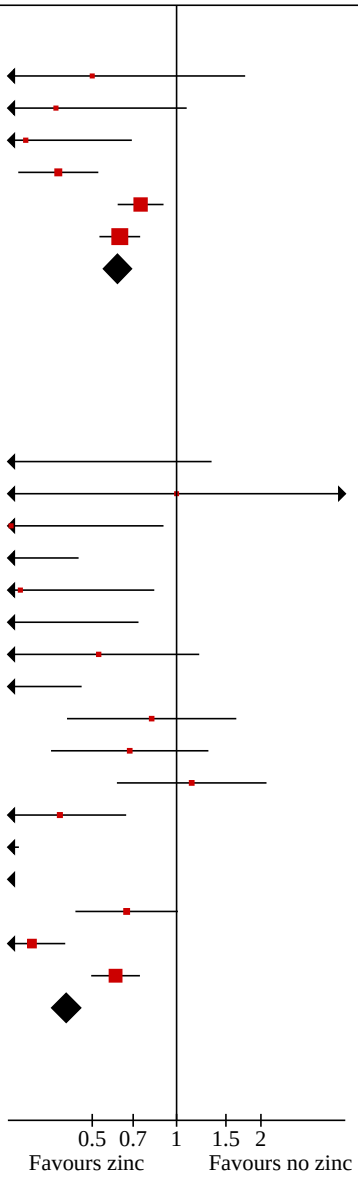
Analysis 2.49. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 49: Prevalence of zinc deficiency: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.49.1 0 to < 6 months				
Uçkardeş 2009	0	0		Not estimable
Rosales 2004	-2.52305842	1.43399023	0.4%	0.08 [0.00 , 1.33]
Rosales 2004 (2)	-0.69314718	0.64117947	2.2%	0.50 [0.14 , 1.76]
Tupe 2009	-1.3600085	0.63908093	2.2%	0.26 [0.07 , 0.90]
Albert 2003 (2)	-1.96217067	0.59027952	2.5%	0.14 [0.04 , 0.45]
DiGirolamo 2010	-1.28372519	0.56145805	2.8%	0.28 [0.09 , 0.83]
Albert 2003	-1.51982575	0.37730771	6.2%	0.22 [0.10 , 0.46]
Bhandari 2002	-2.39729649	0.21748349	18.8%	0.09 [0.06 , 0.14]
Hess 2015	-0.4103	0.2148	19.2%	0.66 [0.44 , 1.01]
Wessells 2012	-1.18817275	0.13936783	45.7%	0.30 [0.23 , 0.40]
Subtotal (95% CI)			**100.0%**	**0.27 [0.22 , 0.33]**
Heterogeneity: Chi² = 46.48, df = 8 (P < 0.00001); I² = 83%				
Test for overall effect: Z = 13.88 (P < 0.00001)				
2.49.2 6 to < 12 months				
Sayeg Porto 2000	0	0.8819171	0.3%	1.00 [0.18 , 5.63]
Hettiarachchi 2008	-1.40242374	0.55584104	0.7%	0.25 [0.08 , 0.73]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	1.1%	0.29 [0.12 , 0.69]
Shankar 2000	-0.20479441	0.35491126	1.8%	0.81 [0.41 , 1.63]
Abdollahi 2019	0.1243	0.3136	2.3%	1.13 [0.61 , 2.09]
Müller 2001	-0.95900185	0.2779085	2.9%	0.38 [0.22 , 0.66]
Lind 2003	-0.50139064	0.10210941	21.6%	0.61 [0.50 , 0.74]
Lind 2003 (2)	-0.46661953	0.08533585	30.9%	0.63 [0.53 , 0.74]
Barffour 2019	-0.348307	0.076539	38.4%	0.71 [0.61 , 0.82]
Subtotal (95% CI)			**100.0%**	**0.64 [0.59 , 0.71]**
Heterogeneity: Chi² = 15.54, df = 8 (P = 0.05); I² = 49%				
Test for overall effect: Z = 9.26 (P < 0.00001)				
2.49.3 12 months or more				
Rosado 1997 (2)	-0.9913982	0.54817965	1.9%	0.37 [0.13 , 1.09]
Rosado 1997	-0.64009262	0.42150954	3.1%	0.53 [0.23 , 1.20]
Tielsch 2006	-0.38511439	0.32989001	5.1%	0.68 [0.36 , 1.30]
Veenemans 2011	-1.77459918	0.24422989	9.4%	0.17 [0.11 , 0.27]
Veenemans 2011 (2)	-0.97206125	0.16780856	19.9%	0.38 [0.27 , 0.53]
Bhandari 2007	-0.29566242	0.09609274	60.6%	0.74 [0.62 , 0.90]
Subtotal (95% CI)			**100.0%**	**0.55 [0.48 , 0.64]**
Heterogeneity: Chi² = 39.02, df = 5 (P < 0.00001); I² = 87%				
Test for overall effect: Z = 7.98 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



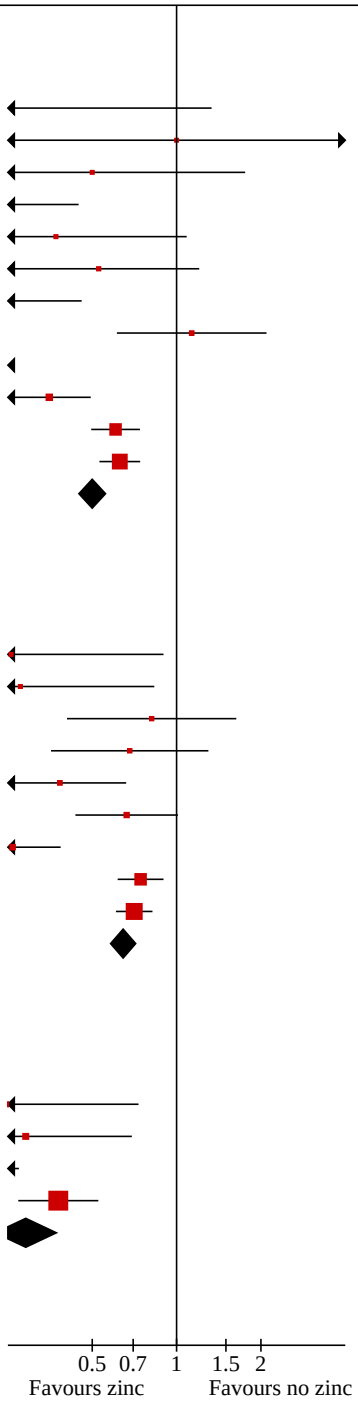
Analysis 2.50. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 50: Prevalence of zinc deficiency: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.50.1 Iron co-intervention				
Rosales 2004 (2)	-0.69314718	0.64117947	0.8%	0.50 [0.14 , 1.76]
Rosado 1997 (2)	-0.9913982	0.54817965	1.1%	0.37 [0.13 , 1.09]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	1.7%	0.29 [0.12 , 0.69]
Veenemans 2011 (2)	-0.97206125	0.16780856	12.2%	0.38 [0.27 , 0.53]
Bhandari 2007	-0.29566242	0.09609274	37.1%	0.74 [0.62 , 0.90]
Lind 2003 (2)	-0.46661953	0.08533585	47.0%	0.63 [0.53 , 0.74]
Subtotal (95% CI)			**100.0%**	**0.62 [0.55 , 0.69]**
Heterogeneity: Chi² = 16.19, df = 5 (P = 0.006); I² = 69%				
Test for overall effect: Z = 8.30 (P < 0.00001)				
2.50.2 No iron co-intervention				
Uçkardeş 2009	0	0		Not estimable
Rosales 2004	-2.52305842	1.43399023	0.2%	0.08 [0.00 , 1.33]
Sayeg Porto 2000	0	0.8819171	0.5%	1.00 [0.18 , 5.63]
Tupe 2009	-1.3600085	0.63908093	0.9%	0.26 [0.07 , 0.90]
Albert 2003 (2)	-1.96217067	0.59027952	1.0%	0.14 [0.04 , 0.45]
DiGirolamo 2010	-1.28372519	0.56145805	1.2%	0.28 [0.09 , 0.83]
Hettiarachchi 2008	-1.40242374	0.55584104	1.2%	0.25 [0.08 , 0.73]
Rosado 1997	-0.64009262	0.42150954	2.1%	0.53 [0.23 , 1.20]
Albert 2003	-1.51982575	0.37730771	2.6%	0.22 [0.10 , 0.46]
Shankar 2000	-0.20479441	0.35491126	2.9%	0.81 [0.41 , 1.63]
Tielsch 2006	-0.38511439	0.32989001	3.4%	0.68 [0.36 , 1.30]
Abdollahi 2019	0.1243	0.3136	3.7%	1.13 [0.61 , 2.09]
Müller 2001	-0.95900185	0.2779085	4.7%	0.38 [0.22 , 0.66]
Veenemans 2011	-1.77459918	0.24422989	6.1%	0.17 [0.11 , 0.27]
Bhandari 2002	-2.39729649	0.21748349	7.7%	0.09 [0.06 , 0.14]
Hess 2015	-0.4103	0.2148	7.9%	0.66 [0.44 , 1.01]
Wessells 2012	-1.18817275	0.13936783	18.8%	0.30 [0.23 , 0.40]
Lind 2003	-0.50139064	0.10210941	35.1%	0.61 [0.50 , 0.74]
Subtotal (95% CI)			**100.0%**	**0.40 [0.36 , 0.45]**
Heterogeneity: Chi² = 112.35, df = 16 (P < 0.00001); I² = 86%				
Test for overall effect: Z = 15.00 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



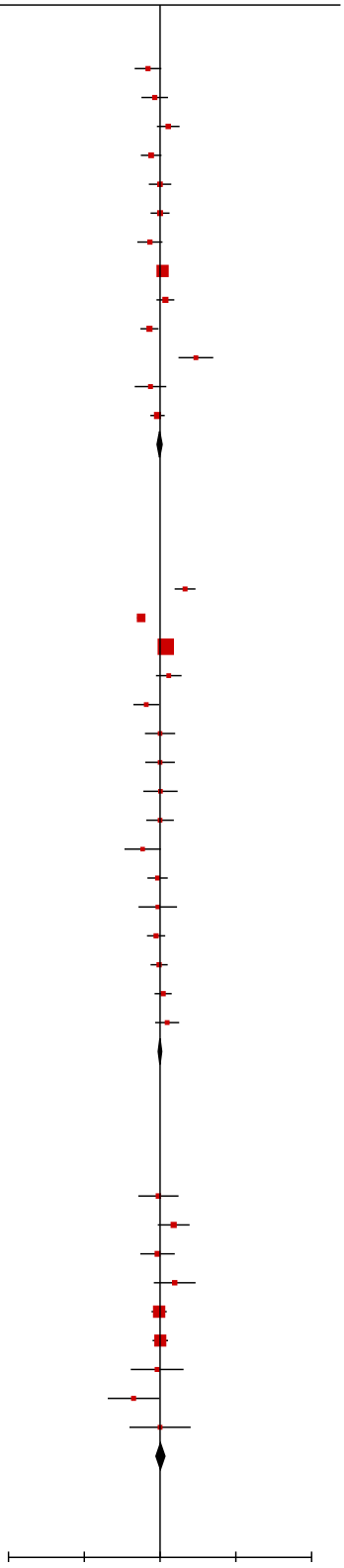
Analysis 2.51. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 51: Prevalence of zinc deficiency: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.51.1 Solution				
Uçkardeş 2009	0	0		Not estimable
Rosales 2004	-2.52305842	1.43399023	0.2%	0.08 [0.00 , 1.33]
Sayeg Porto 2000	0	0.8819171	0.4%	1.00 [0.18 , 5.63]
Rosales 2004 (2)	-0.69314718	0.64117947	0.8%	0.50 [0.14 , 1.76]
Albert 2003 (2)	-1.96217067	0.59027952	0.9%	0.14 [0.04 , 0.45]
Rosado 1997 (2)	-0.9913982	0.54817965	1.0%	0.37 [0.13 , 1.09]
Rosado 1997	-0.64009262	0.42150954	1.8%	0.53 [0.23 , 1.20]
Albert 2003	-1.51982575	0.37730771	2.2%	0.22 [0.10 , 0.46]
Abdollahi 2019	0.1243	0.3136	3.2%	1.13 [0.61 , 2.09]
Bhandari 2002	-2.39729649	0.21748349	6.6%	0.09 [0.06 , 0.14]
Wessells 2012	-1.04603643	0.17370596	10.3%	0.35 [0.25 , 0.49]
Lind 2003	-0.50139064	0.10210941	29.9%	0.61 [0.50 , 0.74]
Lind 2003 (2)	-0.46661953	0.08533585	42.8%	0.63 [0.53 , 0.74]
Subtotal (95% CI)			**100.0%**	**0.50 [0.45 , 0.56]**
Heterogeneity: Chi² = 94.87, df = 11 (P < 0.00001); I² = 88%				
Test for overall effect: Z = 12.42 (P < 0.00001)				
2.51.2 Pill/tablet				
Tupe 2009	-1.3600085	0.63908093	0.7%	0.26 [0.07 , 0.90]
DiGirolamo 2010	-1.28372519	0.56145805	0.9%	0.28 [0.09 , 0.83]
Shankar 2000	-0.20479441	0.35491126	2.2%	0.81 [0.41 , 1.63]
Tielsch 2006	-0.38511439	0.32989001	2.5%	0.68 [0.36 , 1.30]
Müller 2001	-0.95900185	0.2779085	3.6%	0.38 [0.22 , 0.66]
Hess 2015	-0.4103	0.2148	6.0%	0.66 [0.44 , 1.01]
Wessells 2012	-1.34758573	0.20143412	6.8%	0.26 [0.18 , 0.39]
Bhandari 2007	-0.29566242	0.09609274	30.0%	0.74 [0.62 , 0.90]
Barffour 2019	-0.348307	0.076539	47.3%	0.71 [0.61 , 0.82]
Subtotal (95% CI)			**100.0%**	**0.64 [0.58 , 0.71]**
Heterogeneity: Chi² = 32.30, df = 8 (P < 0.0001); I² = 75%				
Test for overall effect: Z = 8.35 (P < 0.00001)				
2.51.3 Capsule				
Hettiarachchi 2008	-1.40242374	0.55584104	5.3%	0.25 [0.08 , 0.73]
Hettiarachchi 2008 (2)	-1.23969089	0.44489251	8.3%	0.29 [0.12 , 0.69]
Veenemans 2011	-1.77459918	0.24422989	27.7%	0.17 [0.11 , 0.27]
Veenemans 2011 (2)	-0.97206125	0.16780856	58.6%	0.38 [0.27 , 0.53]
Subtotal (95% CI)			**100.0%**	**0.29 [0.23 , 0.37]**
Heterogeneity: Chi² = 7.43, df = 3 (P = 0.06); I² = 60%				
Test for overall effect: Z = 9.65 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.52. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 52: Blood hemoglobin concentration: age subgroup analysis

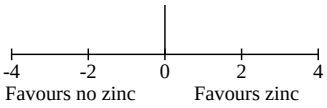
Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.52.1 6 months to < 1 year				
Baqui 2003	-0.3181915	0.17973118	3.5%	-0.32 [-0.67 , 0.03]
Baqui 2003 (2)	-0.1408011	0.1787069	3.5%	-0.14 [-0.49 , 0.21]
Brown 2007	0.21575626	0.15252629	4.9%	0.22 [-0.08 , 0.51]
Caulfield 2013	-0.2349	0.1389	5.8%	-0.23 [-0.51 , 0.04]
Chang 2010	0	0.15099742	4.9%	0.00 [-0.30 , 0.30]
Chang 2010 (2)	0	0.12771313	6.9%	0.00 [-0.25 , 0.25]
Chhagan 2009	-0.2685948	0.1695139	3.9%	-0.27 [-0.60 , 0.06]
Hess 2015	0.0666	0.0573	34.4%	0.07 [-0.05 , 0.18]
Lind 2003	0.14047671	0.12005207	7.8%	0.14 [-0.09 , 0.38]
Lind 2003 (2)	-0.2797198	0.12152387	7.6%	-0.28 [-0.52 , -0.04]
Sazawal 2006	0.94537655	0.2338561	2.1%	0.95 [0.49 , 1.40]
Sazawal 2006 (2)	-0.2525775	0.21260589	2.5%	-0.25 [-0.67 , 0.16]
Soofi 2013	-0.0669424	0.096656017	12.1%	-0.07 [-0.26 , 0.12]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.08 , 0.05]**
Heterogeneity: Chi² = 37.24, df = 12 (P = 0.0002); I² = 68%				
Test for overall effect: Z = 0.37 (P = 0.71)				
2.52.2 1 to < 5 years				
Alarcon 2004	0.65988387	0.14027963	2.7%	0.66 [0.38 , 0.93]
Barffour 2019	-0.499741	0.053375	18.6%	-0.50 [-0.60 , -0.40]
Becquey 2016	0.150661	0.031845	52.1%	0.15 [0.09 , 0.21]
Larson 2010	0.22945555	0.17236099	1.8%	0.23 [-0.11 , 0.57]
Penny 2004	-0.3643812	0.17330205	1.8%	-0.36 [-0.70 , -0.02]
Rosado 1997	0	0.20354768	1.3%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	1.3%	0.00 [-0.39 , 0.39]
Ruz 1997	0.01134939	0.23082689	1.0%	0.01 [-0.44 , 0.46]
Sazawal 1996	0	0.18560454	1.5%	0.00 [-0.36 , 0.36]
Schultink 1997	-0.4592705	0.24477245	0.9%	-0.46 [-0.94 , 0.02]
Shankar 2000	-0.0656005	0.13696131	2.8%	-0.07 [-0.33 , 0.20]
Silva 2006	-0.0604796	0.259294937	0.8%	-0.06 [-0.57 , 0.45]
Tielsch 2006 (2)	-0.1046182	0.12265454	3.5%	-0.10 [-0.35 , 0.14]
Veenemans 2011	-0.0252519	0.11537593	4.0%	-0.03 [-0.25 , 0.20]
Veenemans 2011 (2)	0.08122736	0.11542427	4.0%	0.08 [-0.15 , 0.31]
Wuehler 2008	0.18697864	0.16202415	2.0%	0.19 [-0.13 , 0.50]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.05 , 0.04]**
Heterogeneity: Chi² = 144.76, df = 15 (P < 0.00001); I² = 90%				
Test for overall effect: Z = 0.12 (P = 0.90)				
2.52.3 5 to < 13 years				
Fallahi 2007	-0.0431949	0.27074191	4.9%	-0.04 [-0.57 , 0.49]
Hettiarachchi 2008	0.3595858	0.21415043	7.9%	0.36 [-0.06 , 0.78]
Hettiarachchi 2008 (2)	-0.0668533	0.23201837	6.7%	-0.07 [-0.52 , 0.39]
Mahloudji 1975	0.38607155	0.28106433	4.6%	0.39 [-0.16 , 0.94]
Richard 2006	-0.0245774	0.10239943	34.5%	-0.02 [-0.23 , 0.18]
Richard 2006 (2)	0.00653118	0.10404523	33.4%	0.01 [-0.20 , 0.21]
Rosales 2004	-0.0767944	0.3554178	2.9%	-0.08 [-0.77 , 0.62]
Rosales 2004 (2)	-0.6986394	0.34771623	3.0%	-0.70 [-1.38 , -0.02]
Tupe 2009	0	0.41177862	2.1%	0.00 [-0.81 , 0.81]
Subtotal (95% CI)			**100.0%**	**0.01 [-0.11 , 0.13]**
Heterogeneity: Chi² = 8.93, df = 8 (P = 0.35); I² = 10%				
Test for overall effect: Z = 0.17 (P = 0.87)				



Analysis 2.52. (Continued)

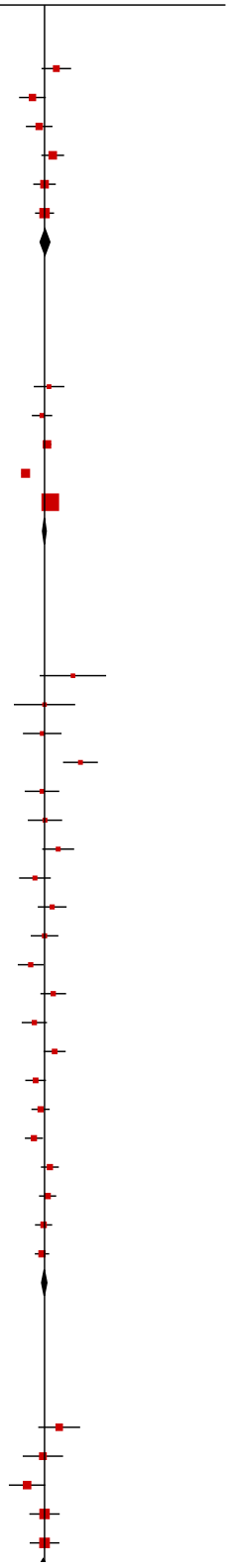
Test for overall effect: Z = 0.17 (P = 0.87)

Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%



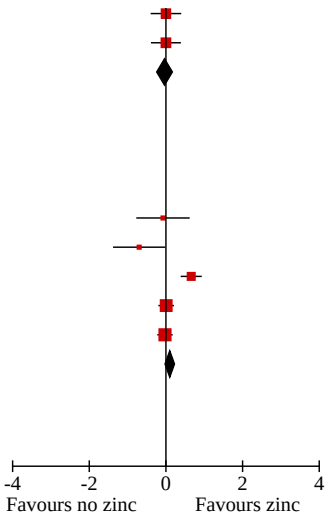
Analysis 2.53. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 53: Blood hemoglobin concentration: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.53.1 0 to < 5 mg				
Wuehler 2008	0.31019802	0.19870793	10.7%	0.31 [-0.08 , 0.70]
Baqui 2003	-0.3181915	0.17973118	13.1%	-0.32 [-0.67 , 0.03]
Baqui 2003 (2)	-0.1408011	0.1787069	13.3%	-0.14 [-0.49 , 0.21]
Brown 2007	0.21575626	0.15252629	18.2%	0.22 [-0.08 , 0.51]
Chang 2010	0	0.15099742	18.6%	0.00 [-0.30 , 0.30]
Chang 2010 (2)	0	0.12771313	26.0%	0.00 [-0.25 , 0.25]
Subtotal (95% CI)			**100.0%**	**0.01 [-0.12 , 0.14]**
Heterogeneity: Chi² = 8.16, df = 5 (P = 0.15); I² = 39%				
Test for overall effect: Z = 0.19 (P = 0.85)				
2.53.2 5 to < 10 mg				
Wuehler 2008	0.1191155	0.2055267	1.4%	0.12 [-0.28 , 0.52]
Shankar 2000	-0.0656005	0.13696131	3.1%	-0.07 [-0.33 , 0.20]
Hess 2015	0.0666	0.0573	17.7%	0.07 [-0.05 , 0.18]
Barffour 2019	-0.499741	0.053375	20.4%	-0.50 [-0.60 , -0.40]
Becquey 2016	0.150661	0.031845	57.4%	0.15 [0.09 , 0.21]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.05 , 0.04]**
Heterogeneity: Chi² = 111.93, df = 4 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 0.17 (P = 0.86)				
2.53.3 10 to < 15 mg				
Smith 1999	0.74647108	0.44636222	0.6%	0.75 [-0.13 , 1.62]
Tupe 2009	0	0.41177862	0.7%	0.00 [-0.81 , 0.81]
Silva 2006	-0.0604796	0.259294937	1.8%	-0.06 [-0.57 , 0.45]
Sazawal 2006	0.94537655	0.2338561	2.2%	0.95 [0.49 , 1.40]
Hettiarachchi 2008 (2)	-0.0668533	0.23201837	2.2%	-0.07 [-0.52 , 0.39]
Ruz 1997	0.01134939	0.23082689	2.2%	0.01 [-0.44 , 0.46]
Hettiarachchi 2008	0.3595858	0.21415043	2.6%	0.36 [-0.06 , 0.78]
Sazawal 2006 (2)	-0.2525775	0.21260589	2.6%	-0.25 [-0.67 , 0.16]
Wuehler 2008	0.20080601	0.19348251	3.2%	0.20 [-0.18 , 0.58]
Sazawal 1996	0	0.18560454	3.5%	0.00 [-0.36 , 0.36]
Penny 2004	-0.3643812	0.17330205	4.0%	-0.36 [-0.70 , -0.02]
Larson 2010	0.22945555	0.17236099	4.0%	0.23 [-0.11 , 0.57]
Chhagan 2009	-0.2685948	0.1695139	4.1%	-0.27 [-0.60 , 0.06]
Chen 2012	0.26446978	0.148742524	5.4%	0.26 [-0.03 , 0.56]
Caulfield 2013	-0.2349	0.1389	6.2%	-0.23 [-0.51 , 0.04]
Tielsch 2006 (2)	-0.1046182	0.12265454	7.9%	-0.10 [-0.35 , 0.14]
Lind 2003 (2)	-0.2797198	0.12152387	8.1%	-0.28 [-0.52 , -0.04]
Lind 2003	0.14047671	0.12005207	8.3%	0.14 [-0.09 , 0.38]
Veenemans 2011 (2)	0.08122736	0.11542427	8.9%	0.08 [-0.15 , 0.31]
Veenemans 2011	-0.0252519	0.11537593	8.9%	-0.03 [-0.25 , 0.20]
Soofi 2013	-0.0669424	0.096656017	12.7%	-0.07 [-0.26 , 0.12]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.08 , 0.06]**
Heterogeneity: Chi² = 47.68, df = 20 (P = 0.0005); I² = 58%				
Test for overall effect: Z = 0.22 (P = 0.83)				
2.53.4 15 to < 20 mg				
Mahloudji 1975	0.38607155	0.28106433	13.7%	0.39 [-0.16 , 0.94]
Fallahi 2007	-0.0431949	0.27074191	14.8%	-0.04 [-0.57 , 0.49]
Schultink 1997	-0.4592705	0.24477245	18.1%	-0.46 [-0.94 , 0.02]
Rosado 1997	0	0.20354768	26.2%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	27.2%	0.00 [-0.39 , 0.39]



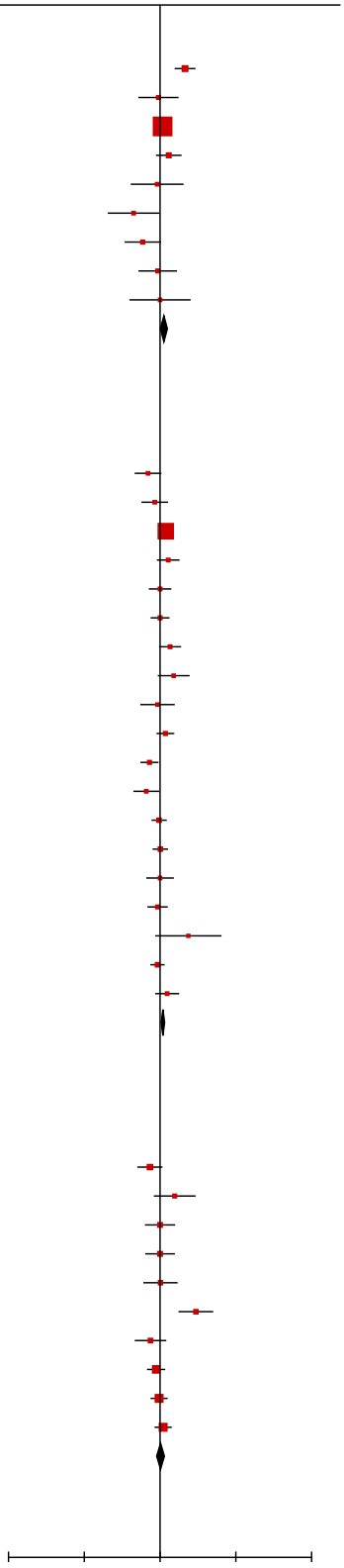
Analysis 2.53. (Continued)

Rosado 1997	0	0.20334768	26.2%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	27.2%	0.00 [-0.39 , 0.39]
Subtotal (95% CI)			**100.0%**	**-0.04 [-0.24 , 0.17]**
Heterogeneity: Chi² = 5.31, df = 4 (P = 0.26); I² = 25%				
Test for overall effect: Z = 0.35 (P = 0.73)				
2.53.5 20 mg or more				
Rosales 2004	-0.0767944	0.3554178	3.1%	-0.08 [-0.77 , 0.62]
Rosales 2004 (2)	-0.6986394	0.34771623	3.2%	-0.70 [-1.38 , -0.02]
Alarcon 2004	0.65988387	0.14027963	19.9%	0.66 [0.38 , 0.93]
Richard 2006 (2)	0.00653118	0.10404523	36.3%	0.01 [-0.20 , 0.21]
Richard 2006	-0.0245774	0.10239943	37.4%	-0.02 [-0.23 , 0.18]
Subtotal (95% CI)			**100.0%**	**0.10 [-0.02 , 0.22]**
Heterogeneity: Chi² = 23.74, df = 4 (P < 0.0001); I² = 83%				
Test for overall effect: Z = 1.59 (P = 0.11)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				



Analysis 2.54. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 54: Blood hemoglobin concentration: duration subgroup analysis

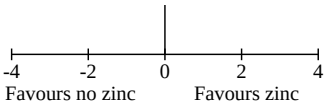
Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.54.1 0 to < 6 months				
Alarcon 2004	0.65988387	0.14027963	11.1%	0.66 [0.38 , 0.93]
Fallahi 2007	-0.0431949	0.27074191	3.0%	-0.04 [-0.57 , 0.49]
Hess 2015	0.0666	0.0573	66.7%	0.07 [-0.05 , 0.18]
Larson 2010	0.22945555	0.17236099	7.4%	0.23 [-0.11 , 0.57]
Rosales 2004	-0.0767944	0.3554178	1.7%	-0.08 [-0.77 , 0.62]
Rosales 2004 (2)	-0.6986394	0.34771623	1.8%	-0.70 [-1.38 , -0.02]
Schultink 1997	-0.4592705	0.24477245	3.7%	-0.46 [-0.94 , 0.02]
Silva 2006	-0.0604796	0.259294937	3.3%	-0.06 [-0.57 , 0.45]
Tupe 2009	0	0.41177862	1.3%	0.00 [-0.81 , 0.81]
Subtotal (95% CI)			**100.0%**	**0.10 [0.01 , 0.19]**
Heterogeneity: Chi² = 28.30, df = 8 (P = 0.0004); I² = 72%				
Test for overall effect: Z = 2.15 (P = 0.03)				
2.54.2 6 to < 12 months				
Baqui 2003	-0.3181915	0.17973118	1.7%	-0.32 [-0.67 , 0.03]
Baqui 2003 (2)	-0.1408011	0.1787069	1.7%	-0.14 [-0.49 , 0.21]
Becquey 2016	0.150661	0.031845	52.7%	0.15 [0.09 , 0.21]
Brown 2007	0.21575626	0.15252629	2.3%	0.22 [-0.08 , 0.51]
Chang 2010	0	0.15099742	2.3%	0.00 [-0.30 , 0.30]
Chang 2010 (2)	0	0.12771313	3.3%	0.00 [-0.25 , 0.25]
Chen 2012	0.26446978	0.148742524	2.4%	0.26 [-0.03 , 0.56]
Hettiarachchi 2008	0.3595858	0.21415043	1.2%	0.36 [-0.06 , 0.78]
Hettiarachchi 2008 (2)	-0.0668533	0.23201837	1.0%	-0.07 [-0.52 , 0.39]
Lind 2003	0.14047671	0.12005207	3.7%	0.14 [-0.09 , 0.38]
Lind 2003 (2)	-0.2797198	0.12152387	3.6%	-0.28 [-0.52 , -0.04]
Penny 2004	-0.3643812	0.17330205	1.8%	-0.36 [-0.70 , -0.02]
Richard 2006	-0.0245774	0.10239943	5.1%	-0.02 [-0.23 , 0.18]
Richard 2006 (2)	0.00653118	0.10404523	4.9%	0.01 [-0.20 , 0.21]
Sazawal 1996	0	0.18560454	1.6%	0.00 [-0.36 , 0.36]
Shankar 2000	-0.0656005	0.13696131	2.8%	-0.07 [-0.33 , 0.20]
Smith 1999	0.74647108	0.44636222	0.3%	0.75 [-0.13 , 1.62]
Soofi 2013	-0.0669424	0.096656017	5.7%	-0.07 [-0.26 , 0.12]
Wuehler 2008	0.18697864	0.16202415	2.0%	0.19 [-0.13 , 0.50]
Subtotal (95% CI)			**100.0%**	**0.07 [0.03 , 0.12]**
Heterogeneity: Chi² = 39.83, df = 18 (P = 0.002); I² = 55%				
Test for overall effect: Z = 3.22 (P = 0.001)				
2.54.3 12 months or more				
Chhagan 2009	-0.2685948	0.1695139	9.3%	-0.27 [-0.60 , 0.06]
Mahloudji 1975	0.38607155	0.28106433	3.4%	0.39 [-0.16 , 0.94]
Rosado 1997	0	0.20354768	6.5%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	6.7%	0.00 [-0.39 , 0.39]
Ruz 1997	0.01134939	0.23082689	5.0%	0.01 [-0.44 , 0.46]
Sazawal 2006	0.94537655	0.2338561	4.9%	0.95 [0.49 , 1.40]
Sazawal 2006 (2)	-0.2525775	0.21260589	5.9%	-0.25 [-0.67 , 0.16]
Tielsch 2006 (2)	-0.1046182	0.12265454	17.8%	-0.10 [-0.35 , 0.14]
Veenemans 2011	-0.0252519	0.11537593	20.2%	-0.03 [-0.25 , 0.20]
Veenemans 2011 (2)	0.08122736	0.11542427	20.1%	0.08 [-0.15 , 0.31]
Subtotal (95% CI)			**100.0%**	**0.01 [-0.09 , 0.11]**
Heterogeneity: Chi² = 23.36, df = 9 (P = 0.005); I² = 61%				
Test for overall effect: Z = 0.24 (P = 0.81)				



Analysis 2.54. (Continued)

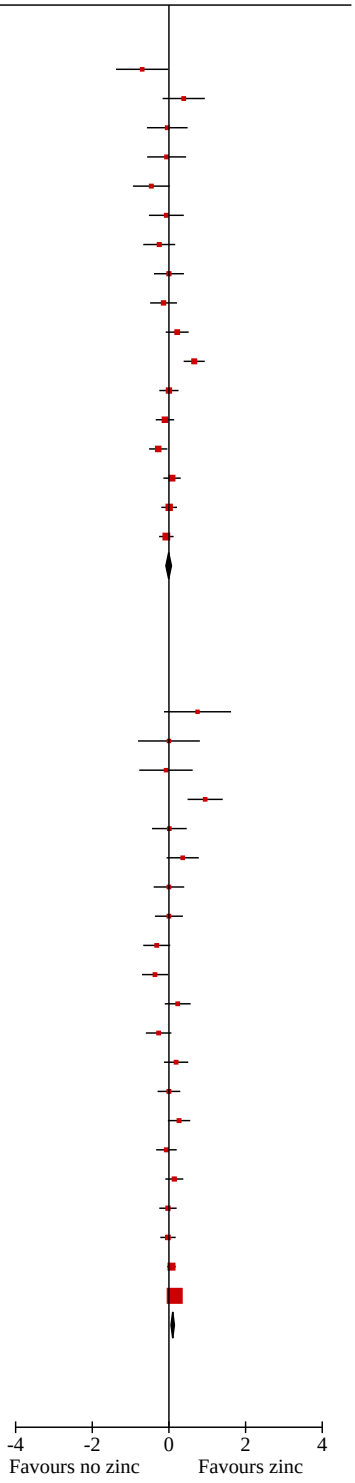
Test for overall effect: Z = 0.24 (P = 0.81)

Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%



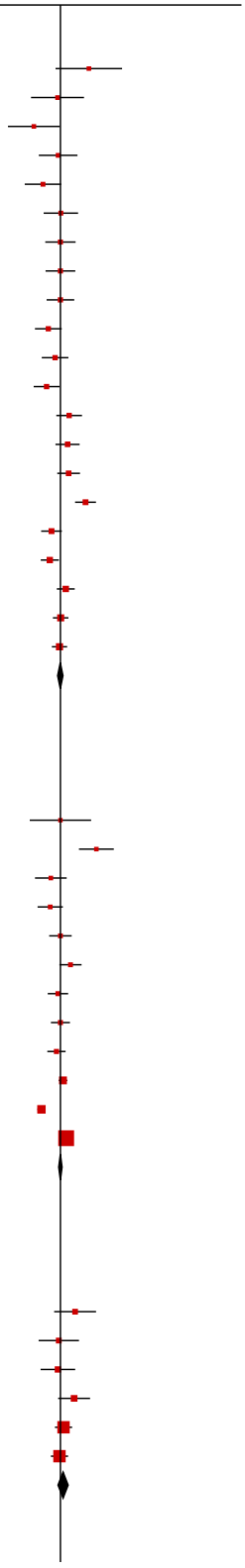
Analysis 2.55. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 55: Blood hemoglobin concentration: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.55.1 Iron co-intervention				
Rosales 2004 (2)	-0.6986394	0.34771623	1.1%	-0.70 [-1.38 , -0.02]
Mahloudji 1975	0.38607155	0.28106433	1.7%	0.39 [-0.16 , 0.94]
Fallahi 2007	-0.0431949	0.27074191	1.9%	-0.04 [-0.57 , 0.49]
Silva 2006	-0.0604796	0.259294937	2.0%	-0.06 [-0.57 , 0.45]
Schultink 1997	-0.4592705	0.24477245	2.3%	-0.46 [-0.94 , 0.02]
Hettiarachchi 2008 (2)	-0.0668533	0.23201837	2.6%	-0.07 [-0.52 , 0.39]
Sazawal 2006 (2)	-0.2525775	0.21260589	3.0%	-0.25 [-0.67 , 0.16]
Rosado 1997 (2)	0	0.19945954	3.5%	0.00 [-0.39 , 0.39]
Baqui 2003 (2)	-0.1408011	0.1787069	4.3%	-0.14 [-0.49 , 0.21]
Brown 2007	0.21575626	0.15252629	5.9%	0.22 [-0.08 , 0.51]
Alarcon 2004	0.65988387	0.14027963	7.0%	0.66 [0.38 , 0.93]
Chang 2010 (2)	0	0.12771313	8.4%	0.00 [-0.25 , 0.25]
Tielsch 2006 (2)	-0.1046182	0.12265454	9.1%	-0.10 [-0.35 , 0.14]
Lind 2003 (2)	-0.2797198	0.12152387	9.3%	-0.28 [-0.52 , -0.04]
Veenemans 2011 (2)	0.08122736	0.11542427	10.3%	0.08 [-0.15 , 0.31]
Richard 2006 (2)	0.00653118	0.10404523	12.7%	0.01 [-0.20 , 0.21]
Soofi 2013	-0.0669424	0.096656017	14.7%	-0.07 [-0.26 , 0.12]
Subtotal (95% CI)			**100.0%**	**-0.01 [-0.08 , 0.07]**
Heterogeneity: Chi² = 42.74, df = 16 (P = 0.0003); I² = 63%				
Test for overall effect: Z = 0.18 (P = 0.86)				
2.55.2 No iron co-intervention				
Smith 1999	0.74647108	0.44636222	0.3%	0.75 [-0.13 , 1.62]
Tupe 2009	0	0.41177862	0.3%	0.00 [-0.81 , 0.81]
Rosales 2004	-0.0767944	0.3554178	0.4%	-0.08 [-0.77 , 0.62]
Sazawal 2006	0.94537655	0.2338561	0.9%	0.95 [0.49 , 1.40]
Ruz 1997	0.01134939	0.23082689	1.0%	0.01 [-0.44 , 0.46]
Hettiarachchi 2008	0.3595858	0.21415043	1.1%	0.36 [-0.06 , 0.78]
Rosado 1997	0	0.20354768	1.2%	0.00 [-0.40 , 0.40]
Sazawal 1996	0	0.18560454	1.5%	0.00 [-0.36 , 0.36]
Baqui 2003	-0.3181915	0.17973118	1.6%	-0.32 [-0.67 , 0.03]
Penny 2004	-0.3643812	0.17330205	1.7%	-0.36 [-0.70 , -0.02]
Larson 2010	0.22945555	0.17236099	1.7%	0.23 [-0.11 , 0.57]
Chhagan 2009	-0.2685948	0.1695139	1.8%	-0.27 [-0.60 , 0.06]
Wuehler 2008	0.18697864	0.16202415	1.9%	0.19 [-0.13 , 0.50]
Chang 2010	0	0.15099742	2.2%	0.00 [-0.30 , 0.30]
Chen 2012	0.26446978	0.148742524	2.3%	0.26 [-0.03 , 0.56]
Shankar 2000	-0.0656005	0.13696131	2.7%	-0.07 [-0.33 , 0.20]
Lind 2003	0.14047671	0.12005207	3.5%	0.14 [-0.09 , 0.38]
Veenemans 2011	-0.0252519	0.11537593	3.8%	-0.03 [-0.25 , 0.20]
Richard 2006	-0.0245774	0.10239943	4.8%	-0.02 [-0.23 , 0.18]
Hess 2015	0.0666	0.0573	15.4%	0.07 [-0.05 , 0.18]
Becquey 2016	0.150661	0.031845	49.9%	0.15 [0.09 , 0.21]
Subtotal (95% CI)			**100.0%**	**0.10 [0.05 , 0.14]**
Heterogeneity: Chi² = 44.56, df = 20 (P = 0.001); I² = 55%				
Test for overall effect: Z = 4.38 (P < 0.0001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Analysis 2.56. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 56: Blood hemoglobin concentration: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.56.1 Solution				
Smith 1999	0.74647108	0.44636222	0.6%	0.75 [-0.13 , 1.62]
Rosales 2004	-0.0767944	0.3554178	1.0%	-0.08 [-0.77 , 0.62]
Rosales 2004 (2)	-0.6986394	0.34771623	1.1%	-0.70 [-1.38 , -0.02]
Silva 2006	-0.0604796	0.259294937	1.9%	-0.06 [-0.57 , 0.45]
Schultink 1997	-0.4592705	0.24477245	2.1%	-0.46 [-0.94 , 0.02]
Ruz 1997	0.01134939	0.23082689	2.4%	0.01 [-0.44 , 0.46]
Rosado 1997	0	0.20354768	3.1%	0.00 [-0.40 , 0.40]
Rosado 1997 (2)	0	0.19945954	3.2%	0.00 [-0.39 , 0.39]
Sazawal 1996	0	0.18560454	3.7%	0.00 [-0.36 , 0.36]
Baqui 2003	-0.3181915	0.17973118	3.9%	-0.32 [-0.67 , 0.03]
Baqui 2003 (2)	-0.1408011	0.1787069	4.0%	-0.14 [-0.49 , 0.21]
Penny 2004	-0.3643812	0.17330205	4.2%	-0.36 [-0.70 , -0.02]
Larson 2010	0.22945555	0.17236099	4.3%	0.23 [-0.11 , 0.57]
Wuehler 2008	0.18697864	0.16202415	4.8%	0.19 [-0.13 , 0.50]
Brown 2007	0.21575626	0.15252629	5.5%	0.22 [-0.08 , 0.51]
Alarcon 2004	0.65988387	0.14027963	6.5%	0.66 [0.38 , 0.93]
Caulfield 2013	-0.2349	0.1389	6.6%	-0.23 [-0.51 , 0.04]
Lind 2003 (2)	-0.2797198	0.12152387	8.6%	-0.28 [-0.52 , -0.04]
Lind 2003	0.14047671	0.12005207	8.8%	0.14 [-0.09 , 0.38]
Richard 2006 (2)	0.00653118	0.10404523	11.7%	0.01 [-0.20 , 0.21]
Richard 2006	-0.0245774	0.10239943	12.1%	-0.02 [-0.23 , 0.18]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.07 , 0.07]**
Heterogeneity: Chi² = 55.45, df = 20 (P < 0.0001); I² = 64%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2.56.2 Pill/tablet				
Tupe 2009	0	0.41177862	0.3%	0.00 [-0.81 , 0.81]
Sazawal 2006	0.94537655	0.2338561	0.9%	0.95 [0.49 , 1.40]
Sazawal 2006 (2)	-0.2525775	0.21260589	1.1%	-0.25 [-0.67 , 0.16]
Chhagan 2009	-0.2685948	0.1695139	1.7%	-0.27 [-0.60 , 0.06]
Chang 2010	0	0.15099742	2.2%	0.00 [-0.30 , 0.30]
Chen 2012	0.26446978	0.148742524	2.3%	0.26 [-0.03 , 0.56]
Shankar 2000	-0.0656005	0.13696131	2.7%	-0.07 [-0.33 , 0.20]
Chang 2010 (2)	0	0.12771313	3.1%	0.00 [-0.25 , 0.25]
Tielsch 2006 (2)	-0.1046182	0.12265454	3.3%	-0.10 [-0.35 , 0.14]
Hess 2015	0.0666	0.0573	15.3%	0.07 [-0.05 , 0.18]
Barffour 2019	-0.499741	0.053375	17.6%	-0.50 [-0.60 , -0.40]
Becquey 2016	0.150661	0.031845	49.5%	0.15 [0.09 , 0.21]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.05 , 0.04]**
Heterogeneity: Chi² = 135.78, df = 11 (P < 0.00001); I² = 92%				
Test for overall effect: Z = 0.06 (P = 0.95)				
2.56.3 Capsule				
Mahloudji 1975	0.38607155	0.28106433	5.8%	0.39 [-0.16 , 0.94]
Fallahi 2007	-0.0431949	0.27074191	6.3%	-0.04 [-0.57 , 0.49]
Hettiarachchi 2008 (2)	-0.0668533	0.23201837	8.6%	-0.07 [-0.52 , 0.39]
Hettiarachchi 2008	0.3595858	0.21415043	10.1%	0.36 [-0.06 , 0.78]
Veenemans 2011 (2)	0.08122736	0.11542427	34.6%	0.08 [-0.15 , 0.31]
Veenemans 2011	-0.0252519	0.11537593	34.6%	-0.03 [-0.25 , 0.20]
Subtotal (95% CI)			**100.0%**	**0.07 [-0.06 , 0.20]**
Heterogeneity: Chi² = 4.31, df = 5 (P = 0.51); I² = 0%				
Test for overall effect: Z = 1.03 (P = 0.31)				



Analysis 2.56. (Continued)

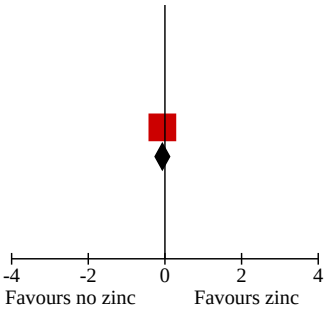
Heterogeneity: Chi² = 4.31, df = 3 (P = 0.31), I² = 0%
Test for overall effect: Z = 1.03 (P = 0.31)

2.56.4 Powder

Soofi 2013	-0.0669424	0.096656017	100.0%	-0.07 [-0.26 , 0.12]
Subtotal (95% CI)			**100.0%**	**-0.07 [-0.26 , 0.12]**

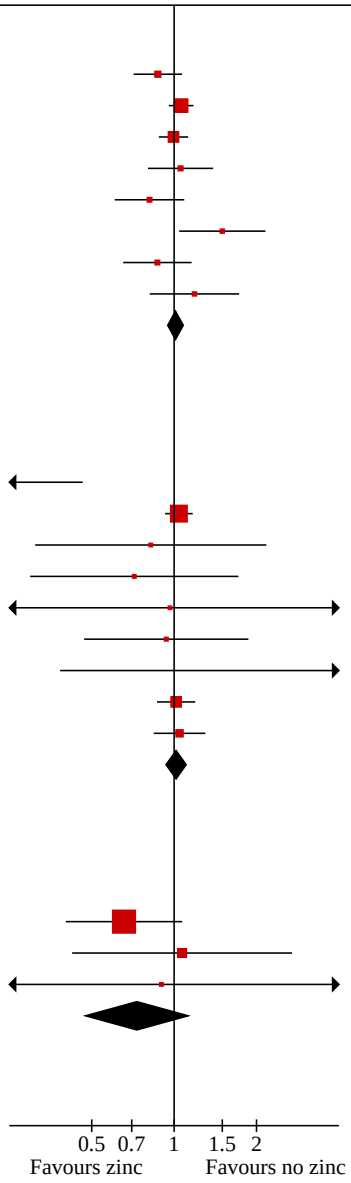
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%



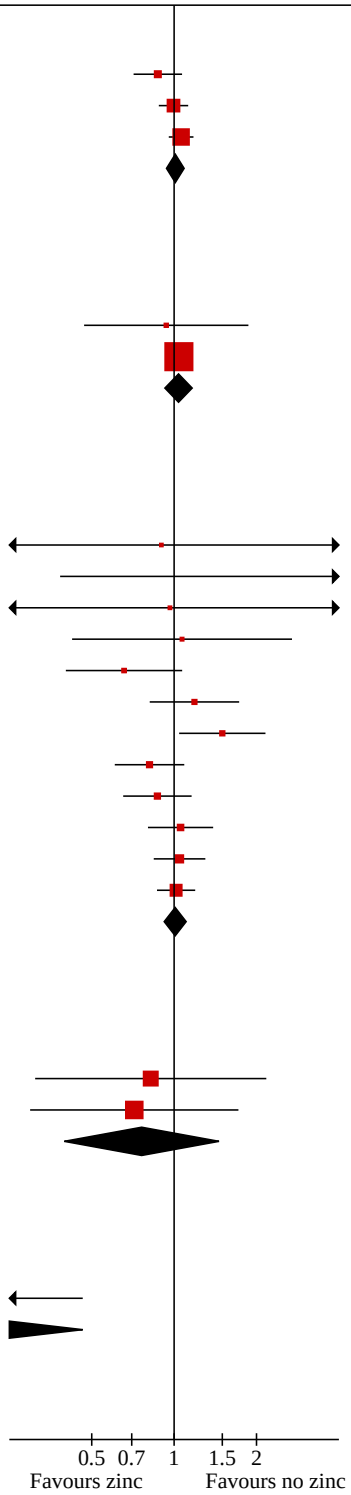
Analysis 2.57. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 57: Prevalence of anemia: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.57.1 6 months to < 1 year				
Brown 2007	-0.13703855	0.10402621	10.3%	0.87 [0.71 , 1.07]
Chang 2010	0.05888852	0.05297985	39.6%	1.06 [0.96 , 1.18]
Chang 2010 (2)	-0.0052113	0.06303318	28.0%	0.99 [0.88 , 1.13]
Chhagan 2009	0.05427392	0.13991047	5.7%	1.06 [0.80 , 1.39]
Lind 2003	-0.20692889	0.14916654	5.0%	0.81 [0.61 , 1.09]
Lind 2003 (2)	0.40546511	0.18523964	3.2%	1.50 [1.04 , 2.16]
Sazawal 2006	-0.14064043	0.14680505	5.2%	0.87 [0.65 , 1.16]
Soofi 2013	0.170994927	0.191953448	3.0%	1.19 [0.81 , 1.73]
Subtotal (95% CI)			**100.0%**	**1.01 [0.95 , 1.08]**
Heterogeneity: Chi² = 11.43, df = 7 (P = 0.12); I² = 39%				
Test for overall effect: Z = 0.35 (P = 0.73)				
2.57.2 1 to < 5 years				
Alarcon 2004	-1.79615684	0.5241074	0.7%	0.17 [0.06 , 0.46]
Barffour 2019	0.040065	0.05932	52.9%	1.04 [0.93 , 1.17]
Rosado 1997	-0.19671029	0.49610282	0.8%	0.82 [0.31 , 2.17]
Rosado 1997 (2)	-0.33516874	0.44703626	0.9%	0.72 [0.30 , 1.72]
Sazawal 2006 (2)	-0.03509132	0.78550816	0.3%	0.97 [0.21 , 4.50]
Shankar 2000	-0.0661398	0.35260528	1.5%	0.94 [0.47 , 1.87]
Tielsch 2006 (2)	1.42931175	1.21856809	0.1%	4.18 [0.38 , 45.50]
Veenemans 2011	0.01673932	0.0819935	27.7%	1.02 [0.87 , 1.19]
Veenemans 2011 (2)	0.04570999	0.11075183	15.2%	1.05 [0.84 , 1.30]
Subtotal (95% CI)			**100.0%**	**1.02 [0.93 , 1.11]**
Heterogeneity: Chi² = 14.40, df = 8 (P = 0.07); I² = 44%				
Test for overall effect: Z = 0.39 (P = 0.70)				
2.57.3 5 to < 13 years				
Hettiarachchi 2008	-0.42159449	0.24965948	77.6%	0.66 [0.40 , 1.07]
Hettiarachchi 2008 (2)	0.06669137	0.47195062	21.7%	1.07 [0.42 , 2.70]
Tupe 2009	-0.10724553	2.6517494	0.7%	0.90 [0.00 , 162.40]
Subtotal (95% CI)			**100.0%**	**0.73 [0.47 , 1.12]**
Heterogeneity: Chi² = 0.84, df = 2 (P = 0.66); I² = 0%				
Test for overall effect: Z = 1.43 (P = 0.15)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



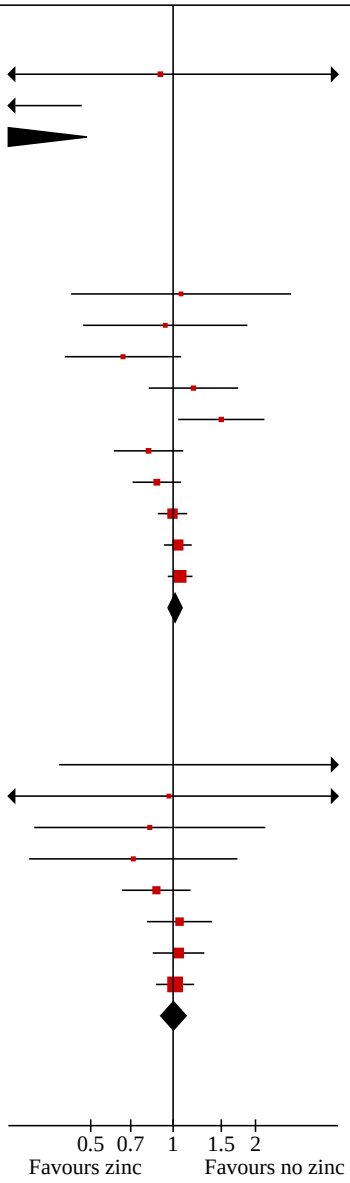
Analysis 2.58. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 58: Prevalence of anemia: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.58.1 0 to < 5 mg				
Brown 2007	-0.13703855	0.10402621	13.2%	0.87 [0.71 , 1.07]
Chang 2010 (2)	-0.0052113	0.06303318	35.9%	0.99 [0.88 , 1.13]
Chang 2010	0.05888852	0.05297985	50.9%	1.06 [0.96 , 1.18]
Subtotal (95% CI)			**100.0%**	**1.01 [0.94 , 1.09]**
Heterogeneity: Chi² = 2.91, df = 2 (P = 0.23); I² = 31%				
Test for overall effect: Z = 0.26 (P = 0.79)				
2.58.2 5 to < 10 mg				
Shankar 2000	-0.0661398	0.35260528	2.8%	0.94 [0.47 , 1.87]
Barffour 2019	0.040065	0.05932	97.2%	1.04 [0.93 , 1.17]
Subtotal (95% CI)			**100.0%**	**1.04 [0.93 , 1.16]**
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.77); I² = 0%				
Test for overall effect: Z = 0.63 (P = 0.53)				
2.58.3 10 to < 15 mg				
Tupe 2009	-0.10724553	2.6517494	0.0%	0.90 [0.00 , 162.40]
Tielsch 2006 (2)	1.42931175	1.21856809	0.1%	4.18 [0.38 , 45.50]
Sazawal 2006 (2)	-0.03509132	0.78550816	0.4%	0.97 [0.21 , 4.50]
Hettiarachchi 2008 (2)	0.06669137	0.47195062	1.0%	1.07 [0.42 , 2.70]
Hettiarachchi 2008	-0.42159449	0.24965948	3.5%	0.66 [0.40 , 1.07]
Soofi 2013	0.170994927	0.191953448	6.0%	1.19 [0.81 , 1.73]
Lind 2003 (2)	0.40546511	0.18523964	6.4%	1.50 [1.04 , 2.16]
Lind 2003	-0.20692889	0.14916654	9.9%	0.81 [0.61 , 1.09]
Sazawal 2006	-0.14064043	0.14680505	10.3%	0.87 [0.65 , 1.16]
Chhagan 2009	0.05427392	0.13991047	11.3%	1.06 [0.80 , 1.39]
Veenemans 2011 (2)	0.04570999	0.11075183	18.0%	1.05 [0.84 , 1.30]
Veenemans 2011	0.01673932	0.0819935	32.9%	1.02 [0.87 , 1.19]
Subtotal (95% CI)			**100.0%**	**1.01 [0.92 , 1.11]**
Heterogeneity: Chi² = 13.00, df = 11 (P = 0.29); I² = 15%				
Test for overall effect: Z = 0.19 (P = 0.85)				
2.58.4 15 to < 20 mg				
Rosado 1997	-0.19671029	0.49610282	44.8%	0.82 [0.31 , 2.17]
Rosado 1997 (2)	-0.33516874	0.44703626	55.2%	0.72 [0.30 , 1.72]
Subtotal (95% CI)			**100.0%**	**0.76 [0.40 , 1.46]**
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%				
Test for overall effect: Z = 0.82 (P = 0.41)				
2.58.5 20 mg or more				
Alarcon 2004	-1.79615684	0.5241074	100.0%	0.17 [0.06 , 0.46]
Subtotal (95% CI)			**100.0%**	**0.17 [0.06 , 0.46]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 3.43 (P = 0.0006)				
Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%				



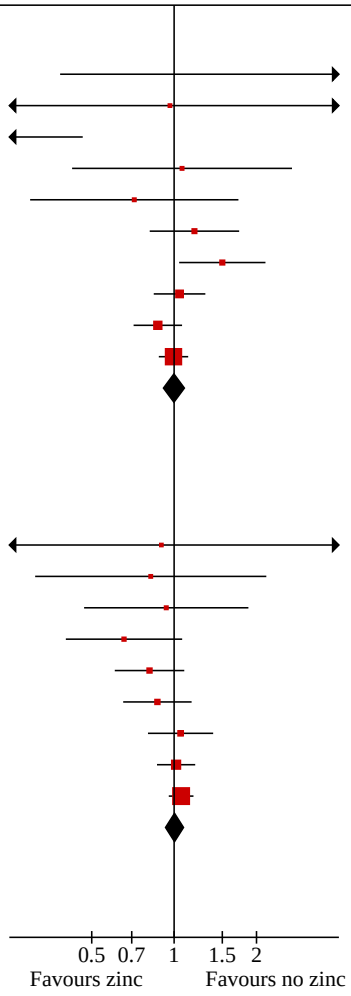
Analysis 2.59. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 59: Prevalence of anemia: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.59.1 0 to < 6 months				
Tupe 2009	-0.10724553	2.6517494	3.8%	0.90 [0.00 , 162.40]
Alarcon 2004	-1.79615684	0.5241074	96.2%	0.17 [0.06 , 0.46]
Subtotal (95% CI)			**100.0%**	**0.18 [0.06 , 0.48]**
Heterogeneity: Chi² = 0.39, df = 1 (P = 0.53); I² = 0%				
Test for overall effect: Z = 3.37 (P = 0.0008)				
2.59.2 6 to < 12 months				
Hettiarachchi 2008 (2)	0.06669137	0.47195062	0.4%	1.07 [0.42 , 2.70]
Shankar 2000	-0.0661398	0.35260528	0.7%	0.94 [0.47 , 1.87]
Hettiarachchi 2008	-0.42159449	0.24965948	1.4%	0.66 [0.40 , 1.07]
Soofi 2013	0.170994927	0.191953448	2.4%	1.19 [0.81 , 1.73]
Lind 2003 (2)	0.40546511	0.18523964	2.6%	1.50 [1.04 , 2.16]
Lind 2003	-0.20692889	0.14916654	4.0%	0.81 [0.61 , 1.09]
Brown 2007	-0.13703855	0.10402621	8.3%	0.87 [0.71 , 1.07]
Chang 2010 (2)	-0.0052113	0.06303318	22.6%	0.99 [0.88 , 1.13]
Barffour 2019	0.040065	0.05932	25.5%	1.04 [0.93 , 1.17]
Chang 2010	0.05888852	0.05297985	32.0%	1.06 [0.96 , 1.18]
Subtotal (95% CI)			**100.0%**	**1.02 [0.96 , 1.08]**
Heterogeneity: Chi² = 13.54, df = 9 (P = 0.14); I² = 34%				
Test for overall effect: Z = 0.56 (P = 0.58)				
2.59.3 12 months or more				
Tielsch 2006 (2)	1.42931175	1.21856809	0.2%	4.18 [0.38 , 45.50]
Sazawal 2006 (2)	-0.03509132	0.78550816	0.5%	0.97 [0.21 , 4.50]
Rosado 1997	-0.19671029	0.49610282	1.2%	0.82 [0.31 , 2.17]
Rosado 1997 (2)	-0.33516874	0.44703626	1.5%	0.72 [0.30 , 1.72]
Sazawal 2006	-0.14064043	0.14680505	13.7%	0.87 [0.65 , 1.16]
Chhagan 2009	0.05427392	0.13991047	15.1%	1.06 [0.80 , 1.39]
Veenemans 2011 (2)	0.04570999	0.11075183	24.0%	1.05 [0.84 , 1.30]
Veenemans 2011	0.01673932	0.0819935	43.9%	1.02 [0.87 , 1.19]
Subtotal (95% CI)			**100.0%**	**1.00 [0.90 , 1.12]**
Heterogeneity: Chi² = 3.38, df = 7 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.05 (P = 0.96)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



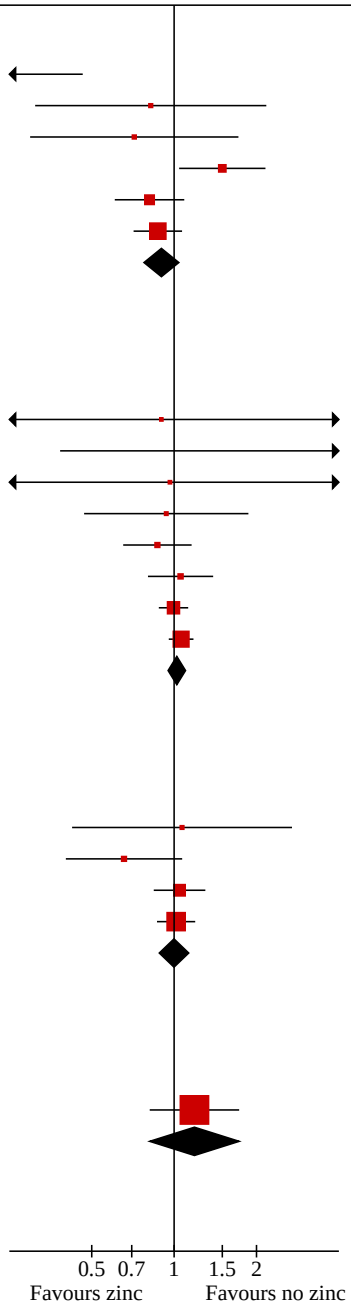
Analysis 2.60. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 60: Prevalence of anemia: iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.60.1 Iron co-intervention				
Tielsch 2006 (2)	1.42931175	1.21856809	0.1%	4.18 [0.38 , 45.50]
Sazawal 2006 (2)	-0.03509132	0.78550816	0.3%	0.97 [0.21 , 4.50]
Alarcon 2004	-1.79615684	0.5241074	0.7%	0.17 [0.06 , 0.46]
Hettiarachchi 2008 (2)	0.06669137	0.47195062	0.9%	1.07 [0.42 , 2.70]
Rosado 1997 (2)	-0.33516874	0.44703626	1.0%	0.72 [0.30 , 1.72]
Soofi 2013	0.170994927	0.191953448	5.5%	1.19 [0.81 , 1.73]
Lind 2003 (2)	0.40546511	0.18523964	5.9%	1.50 [1.04 , 2.16]
Veenemans 2011 (2)	0.04570999	0.11075183	16.4%	1.05 [0.84 , 1.30]
Brown 2007	-0.13703855	0.10402621	18.6%	0.87 [0.71 , 1.07]
Chang 2010 (2)	-0.0052113	0.06303318	50.6%	0.99 [0.88 , 1.13]
Subtotal (95% CI)			**100.0%**	**1.00 [0.91 , 1.09]**
Heterogeneity: Chi² = 21.20, df = 9 (P = 0.01); I² = 58%				
Test for overall effect: Z = 0.04 (P = 0.97)				
2.60.2 No iron co-intervention				
Tupe 2009	-0.10724553	2.6517494	0.0%	0.90 [0.00 , 162.40]
Rosado 1997	-0.19671029	0.49610282	0.6%	0.82 [0.31 , 2.17]
Shankar 2000	-0.0661398	0.35260528	1.2%	0.94 [0.47 , 1.87]
Hettiarachchi 2008	-0.42159449	0.24965948	2.4%	0.66 [0.40 , 1.07]
Lind 2003	-0.20692889	0.14916654	6.7%	0.81 [0.61 , 1.09]
Sazawal 2006	-0.14064043	0.14680505	6.9%	0.87 [0.65 , 1.16]
Chhagan 2009	0.05427392	0.13991047	7.6%	1.06 [0.80 , 1.39]
Veenemans 2011	0.01673932	0.0819935	22.0%	1.02 [0.87 , 1.19]
Chang 2010	0.05888852	0.05297985	52.7%	1.06 [0.96 , 1.18]
Subtotal (95% CI)			**100.0%**	**1.00 [0.93 , 1.08]**
Heterogeneity: Chi² = 7.31, df = 8 (P = 0.50); I² = 0%				
Test for overall effect: Z = 0.09 (P = 0.93)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



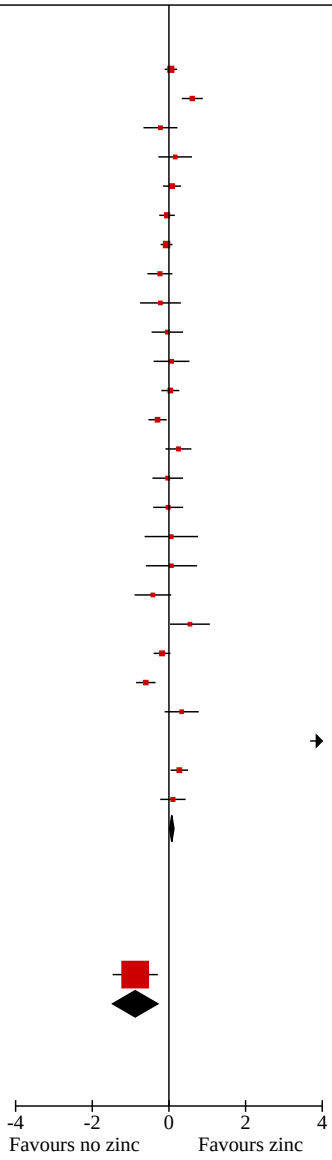
Analysis 2.61. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 61: Prevalence of anemia: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.61.1 Solution				
Alarcon 2004	-1.79615684	0.5241074	2.0%	0.17 [0.06 , 0.46]
Rosado 1997	-0.19671029	0.49610282	2.3%	0.82 [0.31 , 2.17]
Rosado 1997 (2)	-0.33516874	0.44703626	2.8%	0.72 [0.30 , 1.72]
Lind 2003 (2)	0.40546511	0.18523964	16.3%	1.50 [1.04 , 2.16]
Lind 2003	-0.20692889	0.14916654	25.1%	0.81 [0.61 , 1.09]
Brown 2007	-0.13703855	0.10402621	51.6%	0.87 [0.71 , 1.07]
Subtotal (95% CI)			**100.0%**	**0.90 [0.78 , 1.04]**
Heterogeneity: Chi² = 18.87, df = 5 (P = 0.002); I² = 73%				
Test for overall effect: Z = 1.43 (P = 0.15)				
2.61.2 Pill/tablet				
Tupe 2009	-0.10724553	2.6517494	0.0%	0.90 [0.00 , 162.40]
Tielsch 2006 (2)	1.42931175	1.21856809	0.1%	4.18 [0.38 , 45.50]
Sazawal 2006 (2)	-0.03509132	0.78550816	0.2%	0.97 [0.21 , 4.50]
Shankar 2000	-0.0661398	0.35260528	1.1%	0.94 [0.47 , 1.87]
Sazawal 2006	-0.14064043	0.14680505	6.5%	0.87 [0.65 , 1.16]
Chhagan 2009	0.05427392	0.13991047	7.1%	1.06 [0.80 , 1.39]
Chang 2010 (2)	-0.0052113	0.06303318	35.2%	0.99 [0.88 , 1.13]
Chang 2010	0.05888852	0.05297985	49.8%	1.06 [0.96 , 1.18]
Subtotal (95% CI)			**100.0%**	**1.02 [0.95 , 1.10]**
Heterogeneity: Chi² = 3.36, df = 7 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.61 (P = 0.54)				
2.61.3 Capsule				
Hettiarachchi 2008 (2)	0.06669137	0.47195062	1.8%	1.07 [0.42 , 2.70]
Hettiarachchi 2008	-0.42159449	0.24965948	6.4%	0.66 [0.40 , 1.07]
Veenemans 2011 (2)	0.04570999	0.11075183	32.5%	1.05 [0.84 , 1.30]
Veenemans 2011	0.01673932	0.0819935	59.3%	1.02 [0.87 , 1.19]
Subtotal (95% CI)			**100.0%**	**1.00 [0.88 , 1.13]**
Heterogeneity: Chi² = 3.08, df = 3 (P = 0.38); I² = 3%				
Test for overall effect: Z = 0.02 (P = 0.99)				
2.61.4 Powder				
Soofi 2013	0.170994927	0.191953448	100.0%	1.19 [0.81 , 1.73]
Subtotal (95% CI)			**100.0%**	**1.19 [0.81 , 1.73]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.89 (P = 0.37)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



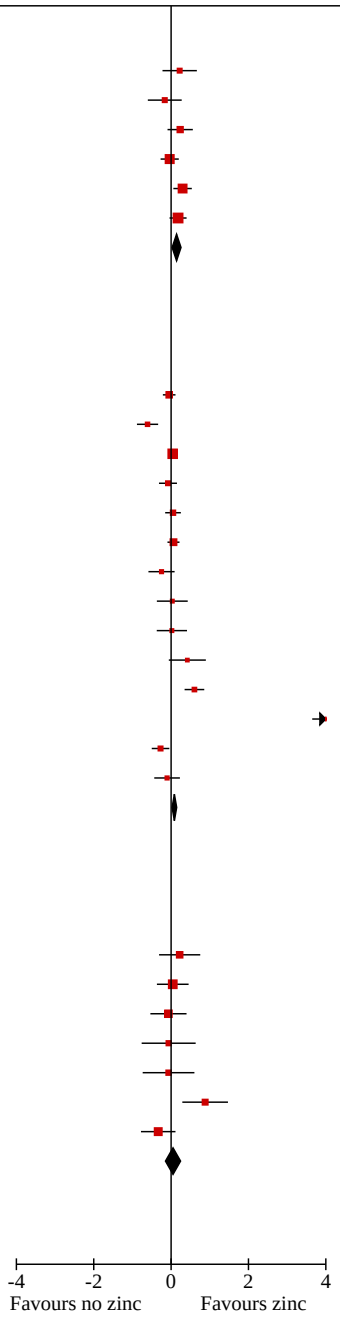
Analysis 2.62. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 62: Serum or plasma ferritin concentration: country income level subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.62.1 Low- or middle-income				
Abdollahi 2019	0.0499	0.0832	11.9%	0.05 [-0.11 , 0.21]
Alarcon 2004	0.609097	0.13973937	4.2%	0.61 [0.34 , 0.88]
Baqui 2003	-0.22141	0.22650955	1.6%	-0.22 [-0.67 , 0.22]
Baqui 2003 (2)	0.164061	0.22336122	1.7%	0.16 [-0.27 , 0.60]
Becquey 2016	0.08108	0.118537	5.9%	0.08 [-0.15 , 0.31]
Bhandari 2002	-0.04944	0.1033257	7.7%	-0.05 [-0.25 , 0.15]
Bhandari 2007	-0.06163	0.07921676	13.2%	-0.06 [-0.22 , 0.09]
Brown 2007	-0.23437	0.16675888	3.0%	-0.23 [-0.56 , 0.09]
Fallahi 2007	-0.22115	0.27156027	1.1%	-0.22 [-0.75 , 0.31]
Hettiarachchi 2008	-0.04255	0.20891616	1.9%	-0.04 [-0.45 , 0.37]
Hettiarachchi 2008 (2)	0.068376	0.23842946	1.5%	0.07 [-0.40 , 0.54]
Lind 2003	0.036753	0.1199138	5.8%	0.04 [-0.20 , 0.27]
Lind 2003 (2)	-0.29683	0.12159844	5.6%	-0.30 [-0.54 , -0.06]
Penny 2004	0.247714	0.17253156	2.8%	0.25 [-0.09 , 0.59]
Rosado 1997	-0.03062	0.20355981	2.0%	-0.03 [-0.43 , 0.37]
Rosado 1997 (2)	-0.01974	0.19946448	2.1%	-0.02 [-0.41 , 0.37]
Rosales 2004	0.063304	0.35616542	0.7%	0.06 [-0.63 , 0.76]
Rosales 2004 (2)	0.066212	0.34117341	0.7%	0.07 [-0.60 , 0.73]
Schultink 1997	-0.41923	0.24423569	1.4%	-0.42 [-0.90 , 0.06]
Silva 2006	0.548783	0.264194167	1.2%	0.55 [0.03 , 1.07]
Soofi 2013	-0.17988	0.11229157	6.6%	-0.18 [-0.40 , 0.04]
Tielsch 2006 (2)	-0.60298	0.12976071	4.9%	-0.60 [-0.86 , -0.35]
Tupe 2009	0.333026	0.22748483	1.6%	0.33 [-0.11 , 0.78]
Veenemans 2011	4.078946	0.20163249	2.0%	4.08 [3.68 , 4.47]
Veenemans 2011 (2)	0.271917	0.11591617	6.2%	0.27 [0.04 , 0.50]
Wuehler 2008	0.103987	0.16907035	2.9%	0.10 [-0.23 , 0.44]
Subtotal (95% CI)			**100.0%**	**0.07 [0.02 , 0.13]**
Heterogeneity: Chi² = 475.19, df = 25 (P < 0.00001); I² = 95%				
Test for overall effect: Z = 2.57 (P = 0.01)				
2.62.2 High-income				
Sandstead 2008	-0.87998	0.30091972	100.0%	-0.88 [-1.47 , -0.29]
Subtotal (95% CI)			**100.0%**	**-0.88 [-1.47 , -0.29]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.92 (P = 0.003)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



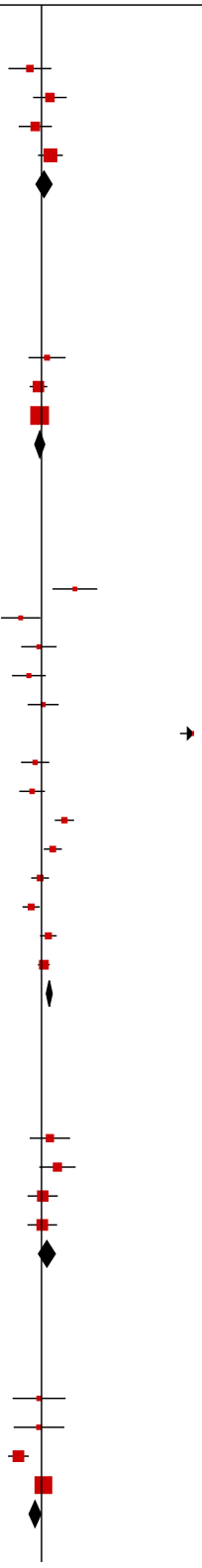
Analysis 2.63. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 63: Serum or plasma ferritin concentration: age subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.63.1 6 months to < 1 year				
Baqui 2003	0.221412	0.22650955	6.7%	0.22 [-0.22 , 0.67]
Baqui 2003 (2)	-0.16406	0.22336122	6.9%	-0.16 [-0.60 , 0.27]
Brown 2007	0.234369	0.16675888	12.3%	0.23 [-0.09 , 0.56]
Lind 2003	-0.03675	0.1199138	23.8%	-0.04 [-0.27 , 0.20]
Lind 2003 (2)	0.296827	0.12159844	23.2%	0.30 [0.06 , 0.54]
Soofi 2013	0.179884	0.11229157	27.2%	0.18 [-0.04 , 0.40]
Subtotal (95% CI)			**100.0%**	**0.14 [0.03 , 0.26]**
Heterogeneity: Chi² = 6.26, df = 5 (P = 0.28); I² = 20%				
Test for overall effect: Z = 2.41 (P = 0.02)				
2.63.2 1 to < 5 years				
Abdollahi 2019	-0.0499	0.0832	13.2%	-0.05 [-0.21 , 0.11]
Alarcon 2004	-0.6091	0.13973937	4.7%	-0.61 [-0.88 , -0.34]
Barffour 2019	0.040065	0.05932	25.9%	0.04 [-0.08 , 0.16]
Becquey 2016	-0.08108	0.118537	6.5%	-0.08 [-0.31 , 0.15]
Bhandari 2002	0.049442	0.1033257	8.5%	0.05 [-0.15 , 0.25]
Bhandari 2007	0.061631	0.07921676	14.5%	0.06 [-0.09 , 0.22]
Penny 2004	-0.24771	0.17253156	3.1%	-0.25 [-0.59 , 0.09]
Rosado 1997	0.030621	0.20355981	2.2%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	0.019744	0.19946448	2.3%	0.02 [-0.37 , 0.41]
Schultink 1997	0.419234	0.24423569	1.5%	0.42 [-0.06 , 0.90]
Tielsch 2006 (2)	0.602978	0.12976071	5.4%	0.60 [0.35 , 0.86]
Veenemans 2011	4.043808	0.20163249	2.2%	4.04 [3.65 , 4.44]
Veenemans 2011 (2)	-0.27322	0.11591617	6.8%	-0.27 [-0.50 , -0.05]
Wuehler 2008	-0.10399	0.16907035	3.2%	-0.10 [-0.44 , 0.23]
Subtotal (95% CI)			**100.0%**	**0.08 [0.03 , 0.14]**
Heterogeneity: Chi² = 448.03, df = 13 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 2.81 (P = 0.005)				
2.63.3 5 to < 13 years				
Fallahi 2007	0.221153	0.27156027	13.4%	0.22 [-0.31 , 0.75]
Hettiarachchi 2008	0.04255	0.20891616	22.7%	0.04 [-0.37 , 0.45]
Hettiarachchi 2008 (2)	-0.06838	0.23842946	17.4%	-0.07 [-0.54 , 0.40]
Rosales 2004	-0.0633	0.35616542	7.8%	-0.06 [-0.76 , 0.63]
Rosales 2004 (2)	-0.06621	0.34117341	8.5%	-0.07 [-0.73 , 0.60]
Sandstead 2008	0.879976	0.30091972	10.9%	0.88 [0.29 , 1.47]
Tupe 2009	-0.33303	0.22748483	19.2%	-0.33 [-0.78 , 0.11]
Subtotal (95% CI)			**100.0%**	**0.05 [-0.15 , 0.24]**
Heterogeneity: Chi² = 11.30, df = 6 (P = 0.08); I² = 47%				
Test for overall effect: Z = 0.50 (P = 0.62)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



Analysis 2.64. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 64: Serum or plasma ferritin concentration: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.64.1 0 to < 5 mg				
Wuehler 2008	-0.30632	0.28870484	13.7%	-0.31 [-0.87 , 0.26]
Baqui 2003	0.221412	0.22650955	22.3%	0.22 [-0.22 , 0.67]
Baqui 2003 (2)	-0.16406	0.22336122	22.9%	-0.16 [-0.60 , 0.27]
Brown 2007	0.234369	0.16675888	41.1%	0.23 [-0.09 , 0.56]
Subtotal (95% CI)			**100.0%**	**0.07 [-0.14 , 0.28]**
Heterogeneity: Chi² = 4.21, df = 3 (P = 0.24); I² = 29%				
Test for overall effect: Z = 0.62 (P = 0.54)				
2.64.2 5 to < 10 mg				
Abdollahi 2014	0	0		Not estimable
Wuehler 2008	0.14566	0.24939969	6.9%	0.15 [-0.34 , 0.63]
Becquey 2016	-0.08108	0.118537	30.7%	-0.08 [-0.31 , 0.15]
Abdollahi 2019	-0.0499	0.0832	62.3%	-0.05 [-0.21 , 0.11]
Subtotal (95% CI)			**100.0%**	**-0.05 [-0.17 , 0.08]**
Heterogeneity: Chi² = 0.68, df = 2 (P = 0.71); I² = 0%				
Test for overall effect: Z = 0.70 (P = 0.48)				
2.64.3 10 to < 15 mg				
Sandstead 2008	0.879976	0.30091972	1.6%	0.88 [0.29 , 1.47]
Silva 2006	-0.54878	0.264194167	2.1%	-0.55 [-1.07 , -0.03]
Hettiarachchi 2008 (2)	-0.06838	0.23842946	2.6%	-0.07 [-0.54 , 0.40]
Tupe 2009	-0.33303	0.22748483	2.8%	-0.33 [-0.78 , 0.11]
Hettiarachchi 2008	0.04255	0.20891616	3.4%	0.04 [-0.37 , 0.45]
Veenemans 2011	4.043808	0.20163249	3.6%	4.04 [3.65 , 4.44]
Wuehler 2008	-0.16795	0.18973469	4.1%	-0.17 [-0.54 , 0.20]
Penny 2004	-0.24771	0.17253156	4.9%	-0.25 [-0.59 , 0.09]
Tielsch 2006 (2)	0.602978	0.12976071	8.7%	0.60 [0.35 , 0.86]
Lind 2003 (2)	0.296827	0.12159844	9.9%	0.30 [0.06 , 0.54]
Lind 2003	-0.03675	0.1199138	10.2%	-0.04 [-0.27 , 0.20]
Veenemans 2011 (2)	-0.27322	0.11591617	10.9%	-0.27 [-0.50 , -0.05]
Soofi 2013	0.179884	0.11229157	11.6%	0.18 [-0.04 , 0.40]
Bhandari 2007	0.061631	0.07921676	23.4%	0.06 [-0.09 , 0.22]
Subtotal (95% CI)			**100.0%**	**0.20 [0.13 , 0.28]**
Heterogeneity: Chi² = 428.29, df = 13 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 5.32 (P < 0.00001)				
2.64.4 15 to < 20 mg				
Fallahi 2007	0.221153	0.27156027	17.0%	0.22 [-0.31 , 0.75]
Schultink 1997	0.419234	0.24423569	21.1%	0.42 [-0.06 , 0.90]
Rosado 1997	0.030621	0.20355981	30.3%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	0.019744	0.19946448	31.6%	0.02 [-0.37 , 0.41]
Subtotal (95% CI)			**100.0%**	**0.14 [-0.08 , 0.36]**
Heterogeneity: Chi² = 2.05, df = 3 (P = 0.56); I² = 0%				
Test for overall effect: Z = 1.26 (P = 0.21)				
2.64.5 20 mg or more				
Rosales 2004	-0.0633	0.35616542	4.9%	-0.06 [-0.76 , 0.63]
Rosales 2004 (2)	-0.06621	0.34117341	5.3%	-0.07 [-0.73 , 0.60]
Alarcon 2004	-0.6091	0.13973937	31.7%	-0.61 [-0.88 , -0.34]
Bhandari 2002	0.049442	0.1033257	58.1%	0.05 [-0.15 , 0.25]
Subtotal (95% CI)			**100.0%**	**-0.17 [-0.33 , -0.02]**
Heterogeneity: Chi² = 14.57, df = 3 (P = 0.002); I² = 79%				



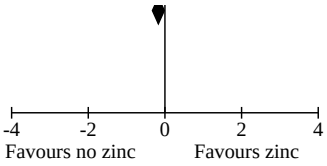
Analysis 2.64. (Continued)

Subtotal (95% CI) **100.0%** **-0.17 [-0.33 , -0.02]**

Heterogeneity: Chi² = 14.57, df = 3 (P = 0.002); I² = 79%

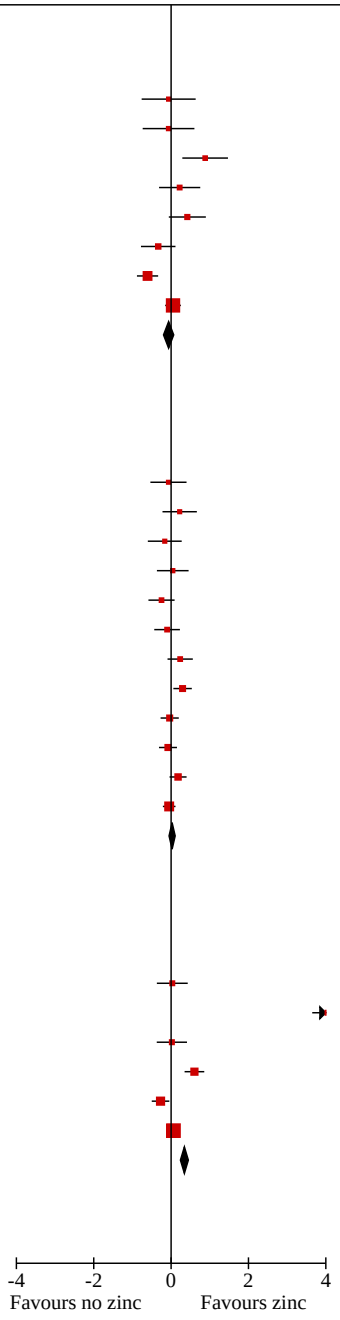
Test for overall effect: Z = 2.18 (P = 0.03)

Test for subgroup differences: Chi² = 0.00, df = 4 (P < 0.00001), I² = 0%



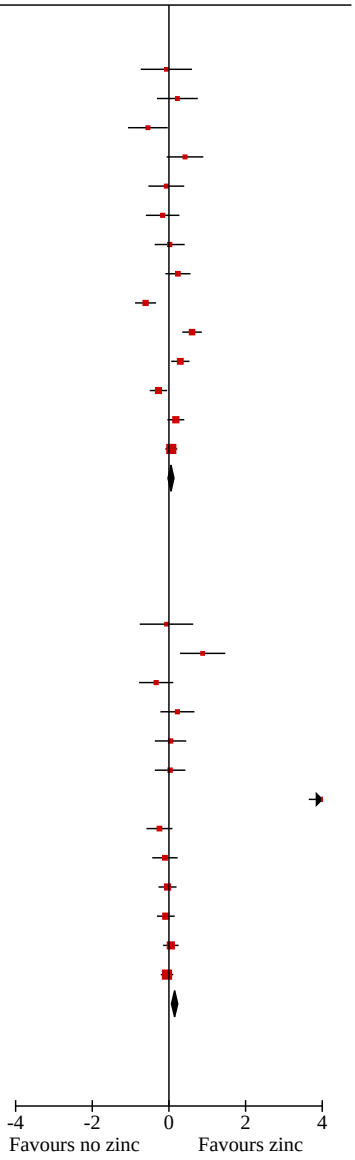
Analysis 2.65. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 65: Serum or plasma ferritin concentration: duration subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.65.1 0 to < 6 months				
Abdollahi 2014	0	0		Not estimable
Rosales 2004	-0.0633	0.35616542	3.6%	-0.06 [-0.76 , 0.63]
Rosales 2004 (2)	-0.06621	0.34117341	3.9%	-0.07 [-0.73 , 0.60]
Sandstead 2008	0.879976	0.30091972	5.0%	0.88 [0.29 , 1.47]
Fallahi 2007	0.221153	0.27156027	6.1%	0.22 [-0.31 , 0.75]
Schultink 1997	0.419234	0.24423569	7.5%	0.42 [-0.06 , 0.90]
Tupe 2009	-0.33303	0.22748483	8.7%	-0.33 [-0.78 , 0.11]
Alarcon 2004	-0.6091	0.13973937	23.1%	-0.61 [-0.88 , -0.34]
Bhandari 2002	0.049442	0.1033257	42.2%	0.05 [-0.15 , 0.25]
Subtotal (95% CI)			**100.0%**	**-0.06 [-0.20 , 0.07]**
Heterogeneity: Chi² = 32.68, df = 7 (P < 0.0001); I² = 79%				
Test for overall effect: Z = 0.96 (P = 0.34)				
2.65.2 6 to < 12 months				
Hettiarachchi 2008 (2)	-0.06838	0.23842946	2.9%	-0.07 [-0.54 , 0.40]
Baqui 2003	0.221412	0.22650955	3.2%	0.22 [-0.22 , 0.67]
Baqui 2003 (2)	-0.16406	0.22336122	3.3%	-0.16 [-0.60 , 0.27]
Hettiarachchi 2008	0.04255	0.20891616	3.7%	0.04 [-0.37 , 0.45]
Penny 2004	-0.24771	0.17253156	5.4%	-0.25 [-0.59 , 0.09]
Wuehler 2008	-0.10399	0.16907035	5.7%	-0.10 [-0.44 , 0.23]
Brown 2007	0.234369	0.16675888	5.8%	0.23 [-0.09 , 0.56]
Lind 2003 (2)	0.296827	0.12159844	11.0%	0.30 [0.06 , 0.54]
Lind 2003	-0.03675	0.1199138	11.3%	-0.04 [-0.27 , 0.20]
Becquey 2016	-0.08108	0.118537	11.5%	-0.08 [-0.31 , 0.15]
Soofi 2013	0.179884	0.11229157	12.9%	0.18 [-0.04 , 0.40]
Abdollahi 2019	-0.0499	0.0832	23.4%	-0.05 [-0.21 , 0.11]
Subtotal (95% CI)			**100.0%**	**0.03 [-0.05 , 0.10]**
Heterogeneity: Chi² = 15.06, df = 11 (P = 0.18); I² = 27%				
Test for overall effect: Z = 0.65 (P = 0.52)				
2.65.3 12 months or more				
Rosado 1997	0.030621	0.20355981	6.6%	0.03 [-0.37 , 0.43]
Veenemans 2011	4.043808	0.20163249	6.7%	4.04 [3.65 , 4.44]
Rosado 1997 (2)	0.019744	0.19946448	6.8%	0.02 [-0.37 , 0.41]
Tielsch 2006 (2)	0.602978	0.12976071	16.2%	0.60 [0.35 , 0.86]
Veenemans 2011 (2)	-0.27322	0.11591617	20.3%	-0.27 [-0.50 , -0.05]
Bhandari 2007	0.061631	0.07921676	43.4%	0.06 [-0.09 , 0.22]
Subtotal (95% CI)			**100.0%**	**0.34 [0.24 , 0.45]**
Heterogeneity: Chi² = 386.75, df = 5 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 6.58 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



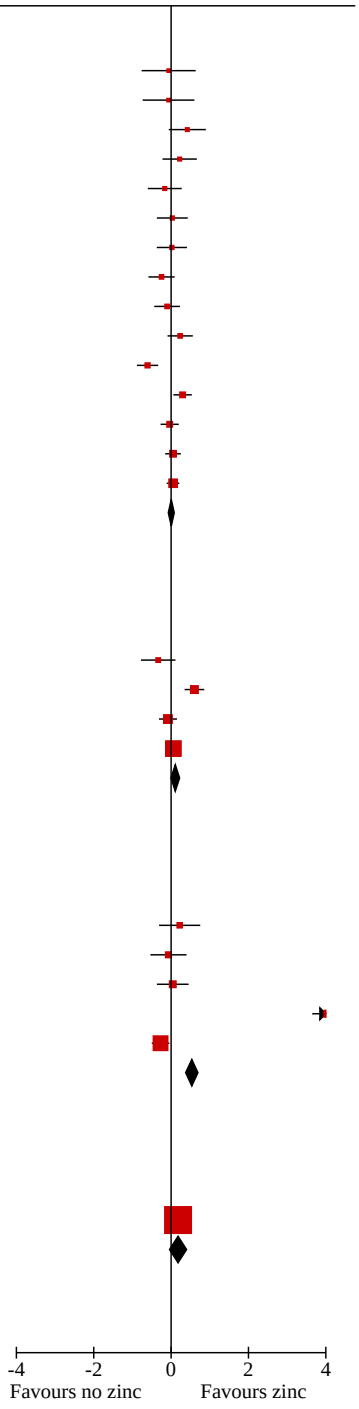
Analysis 2.66. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 66: Serum or plasma ferritin concentration: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.66.1 Iron co-intervention				
Rosales 2004 (2)	-0.06621	0.34117341	1.3%	-0.07 [-0.73 , 0.60]
Fallahi 2007	0.221153	0.27156027	2.1%	0.22 [-0.31 , 0.75]
Silva 2006	-0.54878	0.264194167	2.2%	-0.55 [-1.07 , -0.03]
Schultink 1997	0.419234	0.24423569	2.6%	0.42 [-0.06 , 0.90]
Hettiarachchi 2008 (2)	-0.06838	0.23842946	2.7%	-0.07 [-0.54 , 0.40]
Baqui 2003 (2)	-0.16406	0.22336122	3.1%	-0.16 [-0.60 , 0.27]
Rosado 1997 (2)	0.019744	0.19946448	3.9%	0.02 [-0.37 , 0.41]
Brown 2007	0.234369	0.16675888	5.6%	0.23 [-0.09 , 0.56]
Alarcon 2004	-0.6091	0.13973937	8.0%	-0.61 [-0.88 , -0.34]
Tielsch 2006 (2)	0.602978	0.12976071	9.2%	0.60 [0.35 , 0.86]
Lind 2003 (2)	0.296827	0.12159844	10.5%	0.30 [0.06 , 0.54]
Veenemans 2011 (2)	-0.27322	0.11591617	11.6%	-0.27 [-0.50 , -0.05]
Soofi 2013	0.179884	0.11229157	12.3%	0.18 [-0.04 , 0.40]
Bhandari 2007	0.061631	0.07921676	24.8%	0.06 [-0.09 , 0.22]
Subtotal (95% CI)			**100.0%**	**0.05 [-0.02 , 0.13]**
Heterogeneity: Chi² = 64.00, df = 13 (P < 0.00001); I² = 80%				
Test for overall effect: Z = 1.36 (P = 0.17)				
2.66.2 No iron co-intervention				
Rosales 2004	-0.0633	0.35616542	1.4%	-0.06 [-0.76 , 0.63]
Sandstead 2008	0.879976	0.30091972	1.9%	0.88 [0.29 , 1.47]
Tupe 2009	-0.33303	0.22748483	3.4%	-0.33 [-0.78 , 0.11]
Baqui 2003	0.221412	0.22650955	3.4%	0.22 [-0.22 , 0.67]
Hettiarachchi 2008	0.04255	0.20891616	4.0%	0.04 [-0.37 , 0.45]
Rosado 1997	0.030621	0.20355981	4.2%	0.03 [-0.37 , 0.43]
Veenemans 2011	4.043808	0.20163249	4.3%	4.04 [3.65 , 4.44]
Penny 2004	-0.24771	0.17253156	5.8%	-0.25 [-0.59 , 0.09]
Wuehler 2008	-0.10399	0.16907035	6.1%	-0.10 [-0.44 , 0.23]
Lind 2003	-0.03675	0.1199138	12.1%	-0.04 [-0.27 , 0.20]
Becquey 2016	-0.08108	0.118537	12.3%	-0.08 [-0.31 , 0.15]
Bhandari 2002	0.049442	0.1033257	16.2%	0.05 [-0.15 , 0.25]
Abdollahi 2019	-0.0499	0.0832	25.0%	-0.05 [-0.21 , 0.11]
Subtotal (95% CI)			**100.0%**	**0.15 [0.07 , 0.23]**
Heterogeneity: Chi² = 404.90, df = 12 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 3.56 (P = 0.0004)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



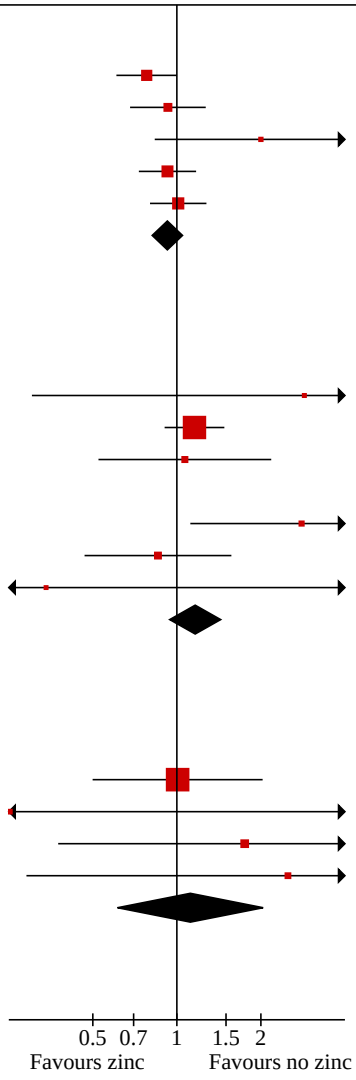
Analysis 2.67. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 67: Serum or plasma ferritin concentration: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.67.1 Solution				
Rosales 2004	-0.0633	0.35616542	1.2%	-0.06 [-0.76 , 0.63]
Rosales 2004 (2)	-0.06621	0.34117341	1.3%	-0.07 [-0.73 , 0.60]
Schultink 1997	0.419234	0.24423569	2.6%	0.42 [-0.06 , 0.90]
Baqui 2003	0.221412	0.22650955	3.0%	0.22 [-0.22 , 0.67]
Baqui 2003 (2)	-0.16406	0.22336122	3.1%	-0.16 [-0.60 , 0.27]
Rosado 1997	0.030621	0.20355981	3.7%	0.03 [-0.37 , 0.43]
Rosado 1997 (2)	0.019744	0.19946448	3.8%	0.02 [-0.37 , 0.41]
Penny 2004	-0.24771	0.17253156	5.1%	-0.25 [-0.59 , 0.09]
Wuehler 2008	-0.10399	0.16907035	5.4%	-0.10 [-0.44 , 0.23]
Brown 2007	0.234369	0.16675888	5.5%	0.23 [-0.09 , 0.56]
Alarcon 2004	-0.6091	0.13973937	7.8%	-0.61 [-0.88 , -0.34]
Lind 2003 (2)	0.296827	0.12159844	10.4%	0.30 [0.06 , 0.54]
Lind 2003	-0.03675	0.1199138	10.6%	-0.04 [-0.27 , 0.20]
Bhandari 2002	0.049442	0.1033257	14.3%	0.05 [-0.15 , 0.25]
Abdollahi 2019	0.0499	0.0832	22.1%	0.05 [-0.11 , 0.21]
Subtotal (95% CI)			**100.0%**	**0.00 [-0.07 , 0.08]**
Heterogeneity: Chi² = 34.59, df = 14 (P = 0.002); I² = 60%				
Test for overall effect: Z = 0.11 (P = 0.91)				
2.67.2 Pill/tablet				
Tupe 2009	-0.33303	0.22748483	6.2%	-0.33 [-0.78 , 0.11]
Tielsch 2006 (2)	0.602978	0.12976071	19.2%	0.60 [0.35 , 0.86]
Becquey 2016	-0.08108	0.118537	23.0%	-0.08 [-0.31 , 0.15]
Bhandari 2007	0.061631	0.07921676	51.5%	0.06 [-0.09 , 0.22]
Subtotal (95% CI)			**100.0%**	**0.11 [-0.00 , 0.22]**
Heterogeneity: Chi² = 21.20, df = 3 (P < 0.0001); I² = 86%				
Test for overall effect: Z = 1.90 (P = 0.06)				
2.67.3 Capsule				
Fallahi 2007	0.221153	0.27156027	8.9%	0.22 [-0.31 , 0.75]
Hettiarachchi 2008 (2)	-0.06838	0.23842946	11.5%	-0.07 [-0.54 , 0.40]
Hettiarachchi 2008	0.04255	0.20891616	15.0%	0.04 [-0.37 , 0.45]
Veenemans 2011	4.043808	0.20163249	16.1%	4.04 [3.65 , 4.44]
Veenemans 2011 (2)	-0.27322	0.11591617	48.6%	-0.27 [-0.50 , -0.05]
Subtotal (95% CI)			**100.0%**	**0.54 [0.38 , 0.69]**
Heterogeneity: Chi² = 364.74, df = 4 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 6.62 (P < 0.00001)				
2.67.4 Powder				
Soofi 2013	0.179884	0.11229157	100.0%	0.18 [-0.04 , 0.40]
Subtotal (95% CI)			**100.0%**	**0.18 [-0.04 , 0.40]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.60 (P = 0.11)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



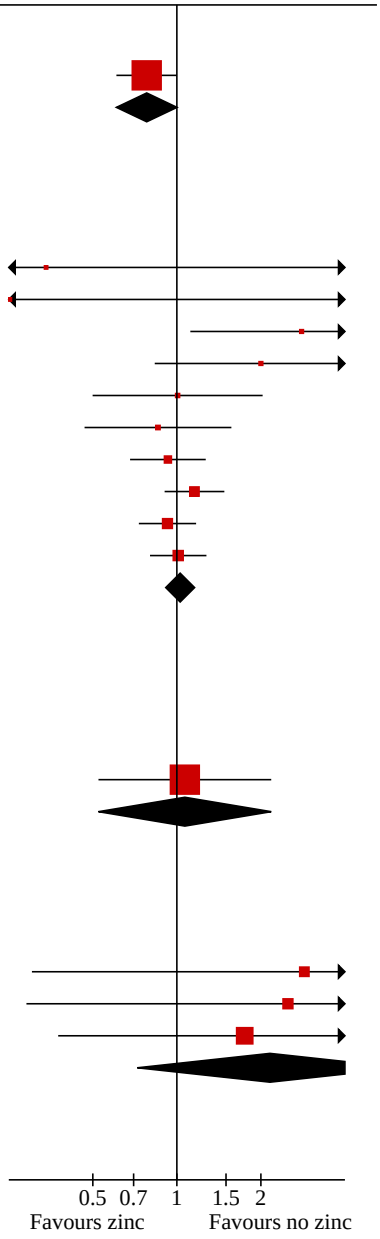
Analysis 2.68. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 68: Prevalence of iron deficiency: age subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.68.1 6 months to < 1 year				
Brown 2007	-0.24865273	0.12751685	25.0%	0.78 [0.61 , 1.00]
Lind 2003	-0.07383161	0.15918361	16.1%	0.93 [0.68 , 1.27]
Lind 2003 (2)	0.69314718	0.44674359	2.0%	2.00 [0.83 , 4.80]
Sazawal 2006	-0.07738666	0.12047289	28.0%	0.93 [0.73 , 1.17]
Sazawal 2006 (2)	0.0112604	0.11869286	28.9%	1.01 [0.80 , 1.28]
Subtotal (95% CI)			**100.0%**	**0.92 [0.82 , 1.05]**
Heterogeneity: Chi² = 5.34, df = 4 (P = 0.25); I² = 25%				
Test for overall effect: Z = 1.23 (P = 0.22)				
2.68.2 1 to < 5 years				
Alarcon 2004	1.05165531	1.14653549	0.9%	2.86 [0.30 , 27.08]
Bhandari 2007	0.145356	0.12569767	72.7%	1.16 [0.90 , 1.48]
Rosado 1997	0.06595797	0.36350034	8.7%	1.07 [0.52 , 2.18]
Rosado 1997 (2)	0	0		Not estimable
Tielsch 2006 (2)	1.0288725	0.46819442	5.2%	2.80 [1.12 , 7.00]
Veenemans 2011	-0.15582994	0.30894248	12.0%	0.86 [0.47 , 1.57]
Veenemans 2011 (2)	-1.07867807	1.62891875	0.4%	0.34 [0.01 , 8.28]
Subtotal (95% CI)			**100.0%**	**1.16 [0.94 , 1.44]**
Heterogeneity: Chi² = 5.75, df = 5 (P = 0.33); I² = 13%				
Test for overall effect: Z = 1.41 (P = 0.16)				
2.68.3 5 to < 13 years				
Hettiarachchi 2008	0.00628086	0.35773941	73.4%	1.01 [0.50 , 2.03]
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	3.6%	0.25 [0.01 , 5.96]
Rosales 2004	0.55961579	0.78490218	15.2%	1.75 [0.38 , 8.15]
Rosales 2004 (2)	0.91629073	1.10050493	7.8%	2.50 [0.29 , 21.61]
Subtotal (95% CI)			**100.0%**	**1.12 [0.61 , 2.04]**
Heterogeneity: Chi² = 1.80, df = 3 (P = 0.62); I² = 0%				
Test for overall effect: Z = 0.36 (P = 0.72)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



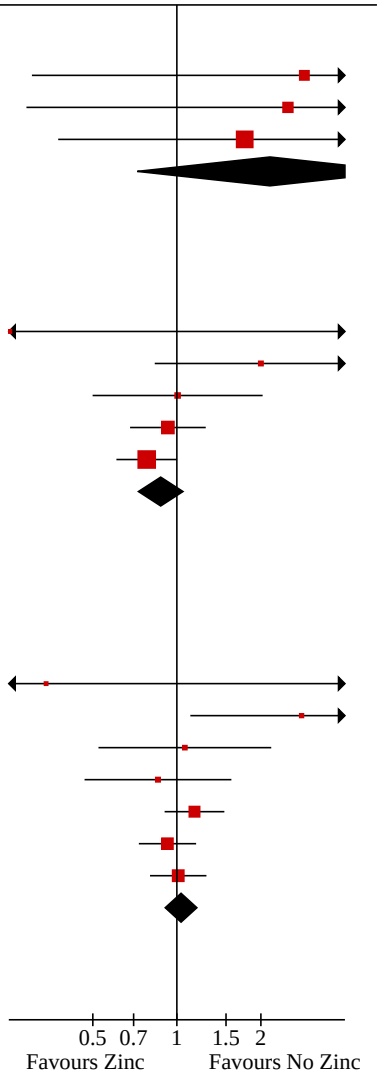
Analysis 2.69. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 69: Prevalence of iron deficiency: dose subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.69.1 0 to < 5 mg				
Brown 2007	-0.24865273	0.12751685	100.0%	0.78 [0.61 , 1.00]
Subtotal (95% CI)			**100.0%**	**0.78 [0.61 , 1.00]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.95 (P = 0.05)				
2.69.2 10 to < 15 mg				
Veenemans 2011 (2)	-1.07867807	1.62891875	0.1%	0.34 [0.01 , 8.28]
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	0.1%	0.25 [0.01 , 5.96]
Tielsch 2006 (2)	1.0288725	0.46819442	1.7%	2.80 [1.12 , 7.00]
Lind 2003 (2)	0.69314718	0.44674359	1.8%	2.00 [0.83 , 4.80]
Hettiarachchi 2008	0.00628086	0.35773941	2.9%	1.01 [0.50 , 2.03]
Veenemans 2011	-0.15582994	0.30894248	3.9%	0.86 [0.47 , 1.57]
Lind 2003	-0.07383161	0.15918361	14.5%	0.93 [0.68 , 1.27]
Bhandari 2007	0.145356	0.12569767	23.3%	1.16 [0.90 , 1.48]
Sazawal 2006	-0.07738666	0.12047289	25.4%	0.93 [0.73 , 1.17]
Sazawal 2006 (2)	0.0112604	0.11869286	26.2%	1.01 [0.80 , 1.28]
Subtotal (95% CI)			**100.0%**	**1.03 [0.91 , 1.16]**
Heterogeneity: Chi² = 10.43, df = 9 (P = 0.32); I² = 14%				
Test for overall effect: Z = 0.45 (P = 0.65)				
2.69.3 15 to < 20 mg				
Rosado 1997 (2)	0	0		Not estimable
Rosado 1997	0.06595797	0.36350034	100.0%	1.07 [0.52 , 2.18]
Subtotal (95% CI)			**100.0%**	**1.07 [0.52 , 2.18]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.18 (P = 0.86)				
2.69.4 20 mg or more				
Alarcon 2004	1.05165531	1.14653549	23.7%	2.86 [0.30 , 27.08]
Rosales 2004 (2)	0.91629073	1.10050493	25.7%	2.50 [0.29 , 21.61]
Rosales 2004	0.55961579	0.78490218	50.6%	1.75 [0.38 , 8.15]
Subtotal (95% CI)			**100.0%**	**2.16 [0.72 , 6.44]**
Heterogeneity: Chi² = 0.15, df = 2 (P = 0.93); I² = 0%				
Test for overall effect: Z = 1.38 (P = 0.17)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



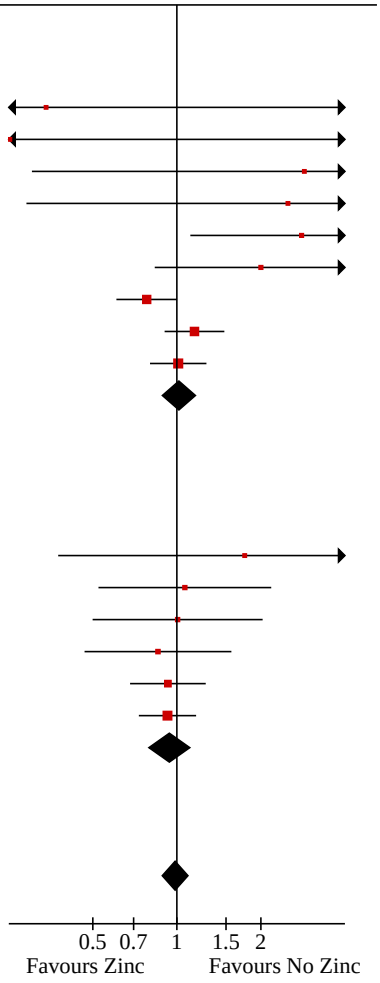
Analysis 2.70. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 70: Prevalence of iron deficiency: duration subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.70.1 0 to < 6 months				
Alarcon 2004	1.05165531	1.14653549	23.7%	2.86 [0.30 , 27.08]
Rosales 2004 (2)	0.91629073	1.10050493	25.7%	2.50 [0.29 , 21.61]
Rosales 2004	0.55961579	0.78490218	50.6%	1.75 [0.38 , 8.15]
Subtotal (95% CI)			**100.0%**	**2.16 [0.72 , 6.44]**
Heterogeneity: Chi² = 0.15, df = 2 (P = 0.93); I² = 0%				
Test for overall effect: Z = 1.38 (P = 0.17)				
2.70.2 6 to < 12 months				
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	0.3%	0.25 [0.01 , 5.96]
Lind 2003 (2)	0.69314718	0.44674359	4.4%	2.00 [0.83 , 4.80]
Hettiarachchi 2008	0.00628086	0.35773941	6.8%	1.01 [0.50 , 2.03]
Lind 2003	-0.07383161	0.15918361	34.6%	0.93 [0.68 , 1.27]
Brown 2007	-0.24865273	0.12751685	53.9%	0.78 [0.61 , 1.00]
Subtotal (95% CI)			**100.0%**	**0.88 [0.73 , 1.05]**
Heterogeneity: Chi² = 5.13, df = 4 (P = 0.27); I² = 22%				
Test for overall effect: Z = 1.42 (P = 0.15)				
2.70.3 12 months or more				
Rosado 1997 (2)	0	0		Not estimable
Veenemans 2011 (2)	-1.07867807	1.62891875	0.2%	0.34 [0.01 , 8.28]
Tielsch 2006 (2)	1.0288725	0.46819442	2.0%	2.80 [1.12 , 7.00]
Rosado 1997	0.06595797	0.36350034	3.3%	1.07 [0.52 , 2.18]
Veenemans 2011	-0.15582994	0.30894248	4.6%	0.86 [0.47 , 1.57]
Bhandari 2007	0.145356	0.12569767	28.0%	1.16 [0.90 , 1.48]
Sazawal 2006	-0.07738666	0.12047289	30.5%	0.93 [0.73 , 1.17]
Sazawal 2006 (2)	0.0112604	0.11869286	31.4%	1.01 [0.80 , 1.28]
Subtotal (95% CI)			**100.0%**	**1.04 [0.91 , 1.18]**
Heterogeneity: Chi² = 7.04, df = 6 (P = 0.32); I² = 15%				
Test for overall effect: Z = 0.52 (P = 0.60)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



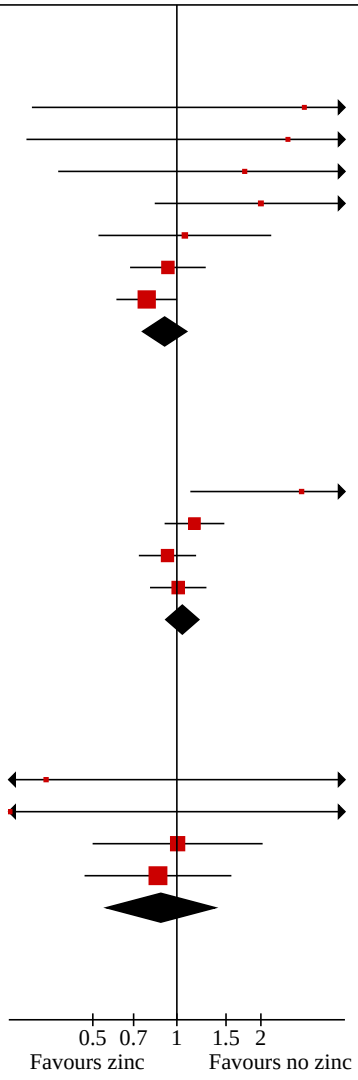
Analysis 2.71. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 71: Prevalence of iron deficiency: Iron co-interventions subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.71.1 Iron co-intervention				
Rosado 1997 (2)	0	0		Not estimable
Veenemans 2011 (2)	-1.07867807	1.62891875	0.1%	0.34 [0.01 , 8.28]
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	0.1%	0.25 [0.01 , 5.96]
Alarcon 2004	1.05165531	1.14653549	0.2%	2.86 [0.30 , 27.08]
Rosales 2004 (2)	0.91629073	1.10050493	0.2%	2.50 [0.29 , 21.61]
Tielsch 2006 (2)	1.0288725	0.46819442	1.3%	2.80 [1.12 , 7.00]
Lind 2003 (2)	0.69314718	0.44674359	1.5%	2.00 [0.83 , 4.80]
Brown 2007	-0.24865273	0.12751685	17.9%	0.78 [0.61 , 1.00]
Bhandari 2007	0.145356	0.12569767	18.4%	1.16 [0.90 , 1.48]
Sazawal 2006 (2)	0.0112604	0.11869286	20.7%	1.01 [0.80 , 1.28]
Subtotal (95% CI)			**60.5%**	**1.02 [0.89 , 1.17]**
Heterogeneity: Chi² = 15.03, df = 8 (P = 0.06); I² = 47%				
Test for overall effect: Z = 0.24 (P = 0.81)				
2.71.2 No iron co-intervention				
Rosales 2004	0.55961579	0.78490218	0.5%	1.75 [0.38 , 8.15]
Rosado 1997	0.06595797	0.36350034	2.2%	1.07 [0.52 , 2.18]
Hettiarachchi 2008	0.00628086	0.35773941	2.3%	1.01 [0.50 , 2.03]
Veenemans 2011	-0.15582994	0.30894248	3.0%	0.86 [0.47 , 1.57]
Lind 2003	-0.07383161	0.15918361	11.5%	0.93 [0.68 , 1.27]
Sazawal 2006	-0.07738666	0.12047289	20.1%	0.93 [0.73 , 1.17]
Subtotal (95% CI)			**39.5%**	**0.94 [0.79 , 1.11]**
Heterogeneity: Chi² = 0.90, df = 5 (P = 0.97); I² = 0%				
Test for overall effect: Z = 0.72 (P = 0.47)				
Total (95% CI)			**100.0%**	**0.99 [0.89 , 1.10]**
Heterogeneity: Chi² = 16.44, df = 14 (P = 0.29); I² = 15%				
Test for overall effect: Z = 0.27 (P = 0.79)				
Test for subgroup differences: Chi² = 0.51, df = 1 (P = 0.48), I² = 0%				



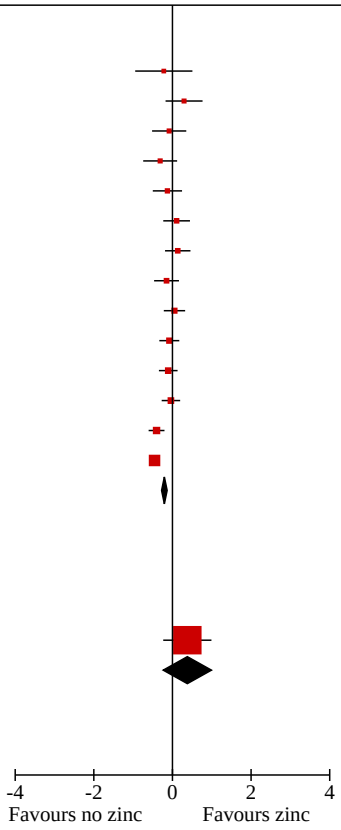
Analysis 2.72. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 72: Prevalence of iron deficiency: formulation subgroup analysis

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
2.72.1 Solution				
Rosado 1997 (2)	0	0		Not estimable
Alarcon 2004	1.05165531	1.14653549	0.7%	2.86 [0.30 , 27.08]
Rosales 2004 (2)	0.91629073	1.10050493	0.7%	2.50 [0.29 , 21.61]
Rosales 2004	0.55961579	0.78490218	1.4%	1.75 [0.38 , 8.15]
Lind 2003 (2)	0.69314718	0.44674359	4.3%	2.00 [0.83 , 4.80]
Rosado 1997	0.06595797	0.36350034	6.5%	1.07 [0.52 , 2.18]
Lind 2003	-0.07383161	0.15918361	33.8%	0.93 [0.68 , 1.27]
Brown 2007	-0.24865273	0.12751685	52.7%	0.78 [0.61 , 1.00]
Subtotal (95% CI)			**100.0%**	**0.90 [0.75 , 1.08]**
Heterogeneity: Chi² = 7.31, df = 6 (P = 0.29); I² = 18%				
Test for overall effect: Z = 1.09 (P = 0.28)				
2.72.2 Pill/tablet				
Tielsch 2006 (2)	1.0288725	0.46819442	2.2%	2.80 [1.12 , 7.00]
Bhandari 2007	0.145356	0.12569767	30.5%	1.16 [0.90 , 1.48]
Sazawal 2006	-0.07738666	0.12047289	33.2%	0.93 [0.73 , 1.17]
Sazawal 2006 (2)	0.0112604	0.11869286	34.2%	1.01 [0.80 , 1.28]
Subtotal (95% CI)			**100.0%**	**1.05 [0.91 , 1.20]**
Heterogeneity: Chi² = 6.17, df = 3 (P = 0.10); I² = 51%				
Test for overall effect: Z = 0.65 (P = 0.52)				
2.72.3 Capsule				
Veenemans 2011 (2)	-1.07867807	1.62891875	2.0%	0.34 [0.01 , 8.28]
Hettiarachchi 2008 (2)	-1.3776363	1.61333167	2.0%	0.25 [0.01 , 5.96]
Hettiarachchi 2008	0.00628086	0.35773941	41.0%	1.01 [0.50 , 2.03]
Veenemans 2011	-0.15582994	0.30894248	55.0%	0.86 [0.47 , 1.57]
Subtotal (95% CI)			**100.0%**	**0.88 [0.56 , 1.37]**
Heterogeneity: Chi² = 1.09, df = 3 (P = 0.78); I² = 0%				
Test for overall effect: Z = 0.58 (P = 0.56)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



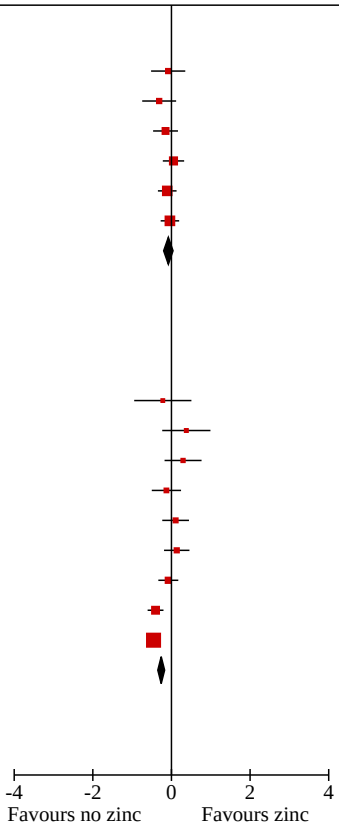
Analysis 2.73. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 73: Serum or plasma copper concentration: country income level subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.73.1 Low- or middle-income				
Abdollahi 2014	-0.219911	0.371172	0.9%	-0.22 [-0.95 , 0.51]
Ruz 1997	0.29516255	0.24001271	2.2%	0.30 [-0.18 , 0.77]
Baqui 2003	-0.0831867	0.22182466	2.6%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.3123873	0.22014163	2.7%	-0.31 [-0.74 , 0.12]
Sazawal 1996	-0.1280763	0.189844	3.6%	-0.13 [-0.50 , 0.24]
Bhandari 2007	0.1059698	0.1732339	4.3%	0.11 [-0.23 , 0.45]
Wuehler 2008	0.13464314	0.16487845	4.8%	0.13 [-0.19 , 0.46]
Brown 2007	-0.1503591	0.16126262	5.0%	-0.15 [-0.47 , 0.17]
Caulfield 2013	0.051391	0.138444	6.8%	0.05 [-0.22 , 0.32]
Tielsch 2006	-0.0797641	0.12950733	7.7%	-0.08 [-0.33 , 0.17]
Lind 2003 (2)	-0.1071722	0.12101791	8.8%	-0.11 [-0.34 , 0.13]
Lind 2003	-0.0391086	0.11991514	9.0%	-0.04 [-0.27 , 0.20]
Wessells 2012	-0.4043988	0.10290265	12.2%	-0.40 [-0.61 , -0.20]
Bhandari 2002	-0.455432	0.0664687	29.3%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.21 [-0.28 , -0.14]**
Heterogeneity: Chi² = 37.51, df = 13 (P = 0.0003); I² = 65%				
Test for overall effect: Z = 5.72 (P < 0.00001)				
2.73.2 High-income				
Walravens 1983	0.37851699	0.31282088	100.0%	0.38 [-0.23 , 0.99]
Subtotal (95% CI)			**100.0%**	**0.38 [-0.23 , 0.99]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.21 (P = 0.23)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



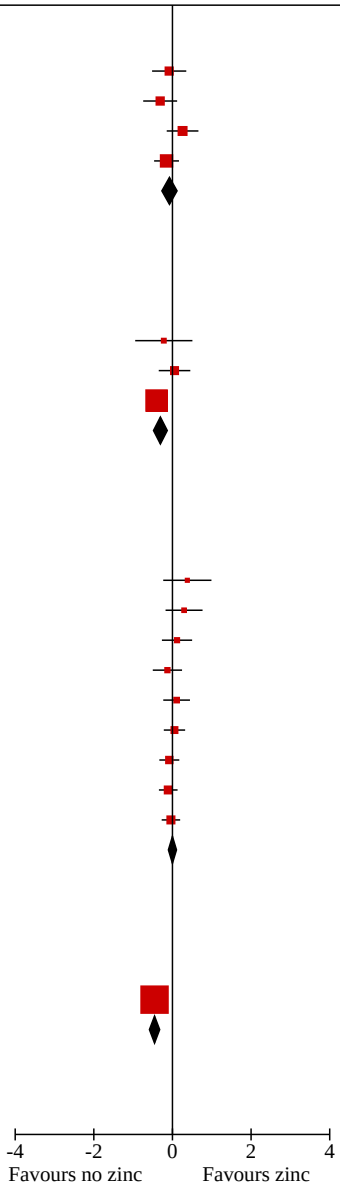
Analysis 2.74. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 74: Serum or plasma copper concentration: age subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.74.1 6 months to < 1 year				
Baqui 2003	-0.0831867	0.22182466	7.5%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.3123873	0.22014163	7.7%	-0.31 [-0.74 , 0.12]
Brown 2007	-0.1503591	0.16126262	14.3%	-0.15 [-0.47 , 0.17]
Caulfield 2013	0.051391	0.138444	19.4%	0.05 [-0.22 , 0.32]
Lind 2003 (2)	-0.1071722	0.12101791	25.3%	-0.11 [-0.34 , 0.13]
Lind 2003	-0.0391086	0.11991514	25.8%	-0.04 [-0.27 , 0.20]
Subtotal (95% CI)			**100.0%**	**-0.08 [-0.20 , 0.04]**
Heterogeneity: Chi² = 2.37, df = 5 (P = 0.80); I² = 0%				
Test for overall effect: Z = 1.30 (P = 0.19)				
2.74.2 1 to < 5 years				
Abdollahi 2014	-0.219911	0.371172	1.4%	-0.22 [-0.95 , 0.51]
Walravens 1983	0.37851699	0.31282088	2.0%	0.38 [-0.23 , 0.99]
Ruz 1997	0.29516255	0.24001271	3.4%	0.30 [-0.18 , 0.77]
Sazawal 1996	-0.1280763	0.189844	5.4%	-0.13 [-0.50 , 0.24]
Bhandari 2007	0.1059698	0.1732339	6.5%	0.11 [-0.23 , 0.45]
Wuehler 2008	0.13464314	0.16487845	7.2%	0.13 [-0.19 , 0.46]
Tielsch 2006	-0.0797641	0.12950733	11.6%	-0.08 [-0.33 , 0.17]
Wessells 2012	-0.4043988	0.10290265	18.4%	-0.40 [-0.61 , -0.20]
Bhandari 2002	-0.455432	0.0664687	44.1%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.26 [-0.35 , -0.17]**
Heterogeneity: Chi² = 32.75, df = 8 (P < 0.0001); I² = 76%				
Test for overall effect: Z = 5.90 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



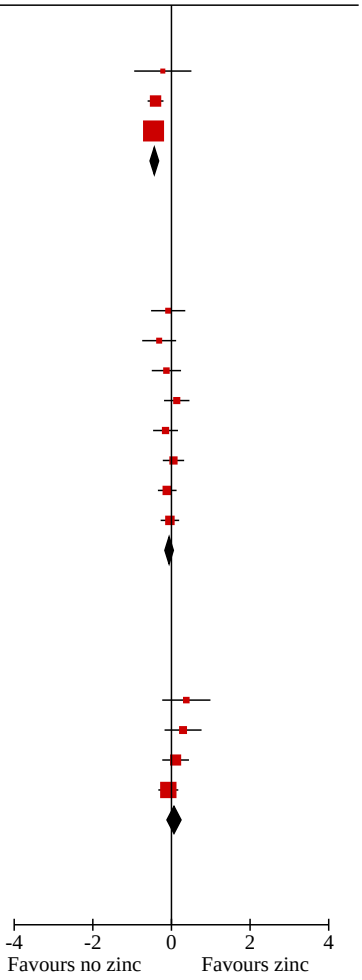
Analysis 2.75. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 75: Serum or plasma copper concentration: dose subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.75.1 0 to < 5 mg				
Baqui 2003	-0.0831867	0.22182466	19.7%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.3123873	0.22014163	20.0%	-0.31 [-0.74 , 0.12]
Wuehler 2008	0.25743494	0.20564239	22.9%	0.26 [-0.15 , 0.66]
Brown 2007	-0.1503591	0.16126262	37.3%	-0.15 [-0.47 , 0.17]
Subtotal (95% CI)			**100.0%**	**-0.08 [-0.27 , 0.12]**
Heterogeneity: Chi² = 4.00, df = 3 (P = 0.26); I² = 25%				
Test for overall effect: Z = 0.77 (P = 0.44)				
2.75.2 5 to < 10 mg				
Abdollahi 2014	-0.219911	0.371172	5.8%	-0.22 [-0.95 , 0.51]
Wuehler 2008	0.05269646	0.20481956	19.0%	0.05 [-0.35 , 0.45]
Wessells 2012	-0.4043988	0.10290265	75.2%	-0.40 [-0.61 , -0.20]
Subtotal (95% CI)			**100.0%**	**-0.31 [-0.48 , -0.13]**
Heterogeneity: Chi² = 4.04, df = 2 (P = 0.13); I² = 50%				
Test for overall effect: Z = 3.44 (P = 0.0006)				
2.75.3 10 to < 15 mg				
Walravens 1983	0.37851699	0.31282088	2.8%	0.38 [-0.23 , 0.99]
Ruz 1997	0.29516255	0.24001271	4.8%	0.30 [-0.18 , 0.77]
Wuehler 2008	0.11626404	0.1959972	7.1%	0.12 [-0.27 , 0.50]
Sazawal 1996	-0.1280763	0.189844	7.6%	-0.13 [-0.50 , 0.24]
Bhandari 2007	0.1059698	0.1732339	9.1%	0.11 [-0.23 , 0.45]
Caulfield 2013	0.051391	0.138444	14.3%	0.05 [-0.22 , 0.32]
Tielsch 2006	-0.0797641	0.12950733	16.4%	-0.08 [-0.33 , 0.17]
Lind 2003 (2)	-0.1071722	0.12101791	18.7%	-0.11 [-0.34 , 0.13]
Lind 2003	-0.0391086	0.11991514	19.1%	-0.04 [-0.27 , 0.20]
Subtotal (95% CI)			**100.0%**	**-0.00 [-0.10 , 0.10]**
Heterogeneity: Chi² = 5.57, df = 8 (P = 0.70); I² = 0%				
Test for overall effect: Z = 0.01 (P = 1.00)				
2.75.4 20 mg or more				
Bhandari 2002	-0.455432	0.0664687	100.0%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.46 [-0.59 , -0.33]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 6.85 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 3 (P < 0.00001), I² = 0%				



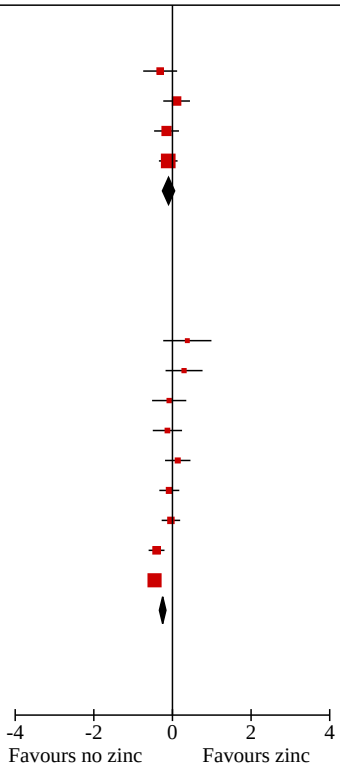
Analysis 2.76. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 76: Serum or plasma copper concentration: duration subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.76.1 0 to < 6 months				
Abdollahi 2014	-0.219911	0.371172	2.2%	-0.22 [-0.95 , 0.51]
Wessells 2012	-0.4043988	0.10290265	28.8%	-0.40 [-0.61 , -0.20]
Bhandari 2002	-0.455432	0.0664687	69.0%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.44 [-0.54 , -0.33]**
Heterogeneity: Chi² = 0.52, df = 2 (P = 0.77); I² = 0%				
Test for overall effect: Z = 7.89 (P < 0.00001)				
2.76.2 6 to < 12 months				
Baqui 2003	-0.0831867	0.22182466	6.1%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.3123873	0.22014163	6.2%	-0.31 [-0.74 , 0.12]
Sazawal 1996	-0.1280763	0.189844	8.3%	-0.13 [-0.50 , 0.24]
Wuehler 2008	0.13464314	0.16487845	11.0%	0.13 [-0.19 , 0.46]
Brown 2007	-0.1503591	0.16126262	11.5%	-0.15 [-0.47 , 0.17]
Caulfield 2013	0.051391	0.138444	15.6%	0.05 [-0.22 , 0.32]
Lind 2003 (2)	-0.1071722	0.12101791	20.4%	-0.11 [-0.34 , 0.13]
Lind 2003	-0.0391086	0.11991514	20.8%	-0.04 [-0.27 , 0.20]
Subtotal (95% CI)			**100.0%**	**-0.06 [-0.17 , 0.05]**
Heterogeneity: Chi² = 3.99, df = 7 (P = 0.78); I² = 0%				
Test for overall effect: Z = 1.09 (P = 0.28)				
2.76.3 12 months or more				
Walravens 1983	0.37851699	0.31282088	8.5%	0.38 [-0.23 , 0.99]
Ruz 1997	0.29516255	0.24001271	14.4%	0.30 [-0.18 , 0.77]
Bhandari 2007	0.1059698	0.1732339	27.6%	0.11 [-0.23 , 0.45]
Tielsch 2006	-0.0797641	0.12950733	49.5%	-0.08 [-0.33 , 0.17]
Subtotal (95% CI)			**100.0%**	**0.06 [-0.11 , 0.24]**
Heterogeneity: Chi² = 3.23, df = 3 (P = 0.36); I² = 7%				
Test for overall effect: Z = 0.71 (P = 0.48)				
Test for subgroup differences: Chi² = 0.00, df = 2 (P < 0.00001), I² = 0%				



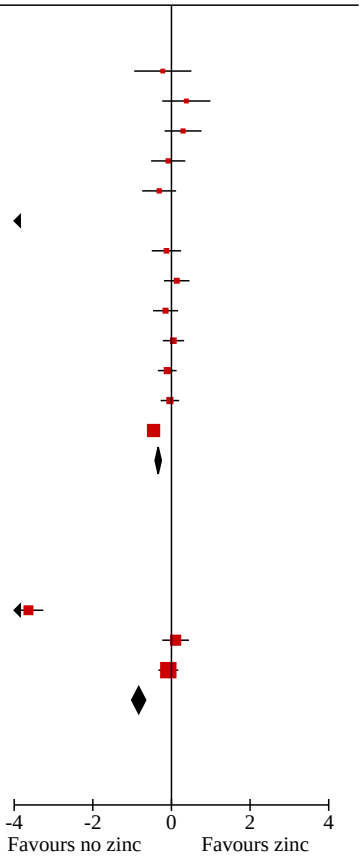
Analysis 2.77. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 77: Serum or plasma copper concentration: iron co-interventions subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.77.1 Iron co-intervention				
Baqui 2003 (2)	-0.3123873	0.22014163	12.8%	-0.31 [-0.74 , 0.12]
Bhandari 2007	0.1059698	0.1732339	20.7%	0.11 [-0.23 , 0.45]
Brown 2007	-0.1503591	0.16126262	23.9%	-0.15 [-0.47 , 0.17]
Lind 2003 (2)	-0.1071722	0.12101791	42.5%	-0.11 [-0.34 , 0.13]
Subtotal (95% CI)			**100.0%**	**-0.10 [-0.25 , 0.05]**
Heterogeneity: Chi² = 2.45, df = 3 (P = 0.49); I² = 0%				
Test for overall effect: Z = 1.26 (P = 0.21)				
2.77.2 No iron co-intervention				
Walravens 1983	0.37851699	0.31282088	1.8%	0.38 [-0.23 , 0.99]
Ruz 1997	0.29516255	0.24001271	3.1%	0.30 [-0.18 , 0.77]
Baqui 2003	-0.0831867	0.22182466	3.6%	-0.08 [-0.52 , 0.35]
Sazawal 1996	-0.1280763	0.189844	4.9%	-0.13 [-0.50 , 0.24]
Wuehler 2008	0.13464314	0.16487845	6.5%	0.13 [-0.19 , 0.46]
Tielsch 2006	-0.0797641	0.12950733	10.6%	-0.08 [-0.33 , 0.17]
Lind 2003	-0.0391086	0.11991514	12.4%	-0.04 [-0.27 , 0.20]
Wessells 2012	-0.4043988	0.10290265	16.8%	-0.40 [-0.61 , -0.20]
Bhandari 2002	-0.455432	0.0664687	40.2%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.25 [-0.33 , -0.17]**
Heterogeneity: Chi² = 32.24, df = 8 (P < 0.0001); I² = 75%				
Test for overall effect: Z = 5.91 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Analysis 2.78. Comparison 2: Zinc versus no zinc: subgroup analyses, Outcome 78: Serum or plasma copper concentration: formulation subgroup analysis

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.78.1 Solution				
Abdollahi 2014	-0.219911	0.371172	1.2%	-0.22 [-0.95 , 0.51]
Walravens 1983	0.37851699	0.31282088	1.7%	0.38 [-0.23 , 0.99]
Ruz 1997	0.29516255	0.24001271	2.8%	0.30 [-0.18 , 0.77]
Baqui 2003	-0.0831867	0.22182466	3.3%	-0.08 [-0.52 , 0.35]
Baqui 2003 (2)	-0.3123873	0.22014163	3.3%	-0.31 [-0.74 , 0.12]
Wessells 2012	-4.2649498	0.21496638	3.5%	-4.26 [-4.69 , -3.84]
Sazawal 1996	-0.1280763	0.189844	4.5%	-0.13 [-0.50 , 0.24]
Wuehler 2008	0.13464314	0.16487845	6.0%	0.13 [-0.19 , 0.46]
Brown 2007	-0.1503591	0.16126262	6.2%	-0.15 [-0.47 , 0.17]
Caulfield 2013	0.051391	0.138444	8.5%	0.05 [-0.22 , 0.32]
Lind 2003 (2)	-0.1071722	0.12101791	11.1%	-0.11 [-0.34 , 0.13]
Lind 2003	-0.0391086	0.11991514	11.3%	-0.04 [-0.27 , 0.20]
Bhandari 2002	-0.455432	0.0664687	36.7%	-0.46 [-0.59 , -0.33]
Subtotal (95% CI)			**100.0%**	**-0.34 [-0.42 , -0.26]**
Heterogeneity: Chi² = 379.03, df = 12 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 8.37 (P < 0.00001)				
2.78.2 Pill/Tablet				
Wessells 2012	-3.6377848	0.1918164	22.6%	-3.64 [-4.01 , -3.26]
Bhandari 2007	0.1059698	0.1732339	27.7%	0.11 [-0.23 , 0.45]
Tielsch 2006	-0.0797641	0.12950733	49.6%	-0.08 [-0.33 , 0.17]
Subtotal (95% CI)			**100.0%**	**-0.83 [-1.01 , -0.65]**
Heterogeneity: Chi² = 277.02, df = 2 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 9.13 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P < 0.00001), I² = 0%				



Comparison 3. Zinc versus zinc plus iron

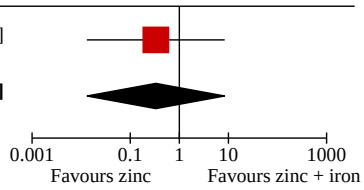
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 All-cause mortality	1	323	Risk Ratio (IV, Fixed, 95% CI)	0.33 [0.01, 8.39]
3.2 All-cause hospitalization	1	399	Risk Ratio (IV, Fixed, 95% CI)	1.09 [0.53, 2.24]
3.3 Incidence of all-cause diarrhea	5	1530	Risk Ratio (IV, Fixed, 95% CI)	0.91 [0.84, 0.97]
3.4 Prevalence of all-cause diarrhea	1	399	Risk Ratio (IV, Fixed, 95% CI)	1.11 [0.94, 1.31]
3.5 Incidence of severe diarrhea	1	323	Risk Ratio (IV, Fixed, 95% CI)	1.28 [0.96, 1.69]
3.6 Hospitalisation due to all-cause diarrhea	1	399	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.26, 4.00]
3.7 Incidence of LRTI	3	1065	Risk Ratio (IV, Fixed, 95% CI)	1.08 [0.97, 1.20]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.8 Incidence of malaria	1	419	Risk Ratio (IV, Fixed, 95% CI)	1.17 [0.81, 1.69]
3.9 Height	6	1551	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.04, 0.16]
3.10 Weight	5	944	Std. Mean Difference (IV, Fixed, 95% CI)	0.12 [-0.01, 0.25]
3.11 Weight-to-height ratio	4	933	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.07, 0.19]
3.12 Prevalence of stunting	2	462	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [1.01, 1.17]
3.13 Serum or plasma zinc concentration	8	1337	Std. Mean Difference (IV, Fixed, 95% CI)	0.16 [0.05, 0.27]
3.14 Prevalence of zinc deficiency	3	350	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.37, 1.33]
3.15 Study withdrawal	2	557	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.46, 1.10]
3.16 Blood hemoglobin concentration	8	1341	Std. Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.34, -0.12]
3.17 Serum or plasma ferritin concentration	6	945	Std. Mean Difference (IV, Fixed, 95% CI)	-1.78 [-1.99, -1.56]
3.18 Prevalence of iron deficiency	2	434	Risk Ratio (M-H, Fixed, 95% CI)	5.23 [3.10, 8.83]
3.19 Serum or plasma copper concentration	2	353	Std. Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.15, 0.27]
3.20 Prevalence of anemia	3	482	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [1.09, 1.49]

Analysis 3.1. Comparison 3: Zinc versus zinc plus iron, Outcome 1: All-cause mortality

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc + iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	-1.10476615	1.6491	161	162	100.0%	0.33 [0.01 , 8.39]
Total (95% CI)			**161**	**162**	**100.0%**	**0.33 [0.01 , 8.39]**

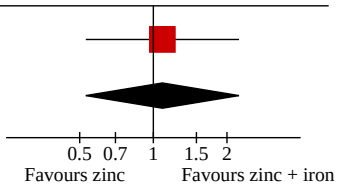
Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.50)
Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3: Zinc versus zinc plus iron, Outcome 2: All-cause hospitalization

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc + iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Chang 2010	0.08530402	0.3679	198	201	100.0%	1.09 [0.53 , 2.24]
Total (95% CI)			**198**	**201**	**100.0%**	**1.09 [0.53 , 2.24]**

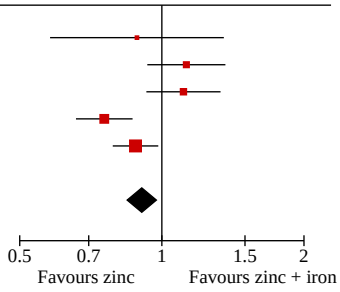
Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)
Test for subgroup differences: Not applicable



Analysis 3.3. Comparison 3: Zinc versus zinc plus iron, Outcome 3: Incidence of all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc + iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Rosado 1997	-0.1214128	0.216192346	54	55	2.8%	0.89 [0.58 , 1.35]
Chang 2010	0.11953719	0.097156627	198	201	14.0%	1.13 [0.93 , 1.36]
Lind 2003	0.10536052	0.092242766	162	161	15.5%	1.11 [0.93 , 1.33]
Richard 2006	-0.28081941	0.070392286	191	185	26.6%	0.76 [0.66 , 0.87]
Baqui 2003	-0.12842579	0.056625424	161	162	41.1%	0.88 [0.79 , 0.98]
Total (95% CI)			**766**	**764**	**100.0%**	**0.91 [0.84 , 0.97]**

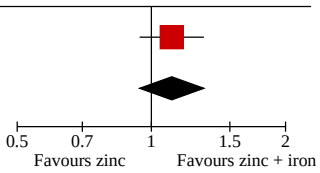
Heterogeneity: Chi² = 16.92, df = 4 (P = 0.002); I² = 76%
Test for overall effect: Z = 2.70 (P = 0.007)
Test for subgroup differences: Not applicable



Analysis 3.4. Comparison 3: Zinc versus zinc plus iron, Outcome 4: Prevalence of all-cause diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc + iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Chang 2010	0.10536052	0.0846196951304905	198	201	100.0%	1.11 [0.94 , 1.31]
Total (95% CI)			**198**	**201**	**100.0%**	**1.11 [0.94 , 1.31]**

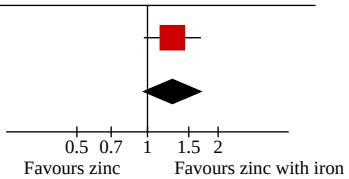
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 3.5. Comparison 3: Zinc versus zinc plus iron, Outcome 5: Incidence of severe diarrhea

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc with iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	0.244	0.143	161	162	100.0%	1.28 [0.96 , 1.69]
Total (95% CI)			**161**	**162**	**100.0%**	**1.28 [0.96 , 1.69]**

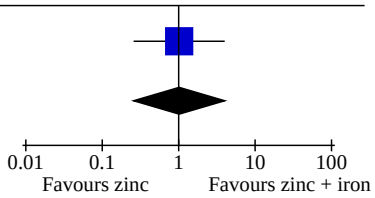
Heterogeneity: Not applicable
Test for overall effect: Z = 1.71 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 3.6. Comparison 3: Zinc versus zinc plus iron, Outcome 6: Hospitalisation due to all-cause diarrhea

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chang 2010	4	198	4	201	100.0%	1.02 [0.26 , 4.00]
Total (95% CI)		**198**		**201**	**100.0%**	**1.02 [0.26 , 4.00]**
Total events:	4		4			

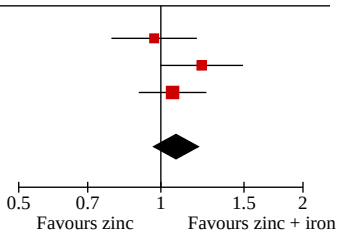
Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.98)
Test for subgroup differences: Not applicable



Analysis 3.7. Comparison 3: Zinc versus zinc plus iron, Outcome 7: Incidence of LRTI

Study or Subgroup	log[Risk Ratio]	SE	Zinc Total	Zinc + iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Baqui 2003	-0.03265596	0.106277326	161	162	27.3%	0.97 [0.79 , 1.19]
Richard 2006	0.199	0.103	209	210	29.1%	1.22 [1.00 , 1.49]
Lind 2003	0.05715841	0.084160505	162	161	43.6%	1.06 [0.90 , 1.25]
Total (95% CI)			**532**	**533**	**100.0%**	**1.08 [0.97 , 1.20]**

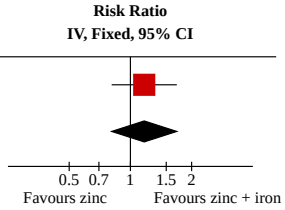
Heterogeneity: Chi² = 2.52, df = 2 (P = 0.28); I² = 21%
Test for overall effect: Z = 1.33 (P = 0.18)
Test for subgroup differences: Not applicable



Analysis 3.8. Comparison 3: Zinc versus zinc plus iron, Outcome 8: Incidence of malaria

Study or Subgroup	log[Risk Ratio]	SE	Favours zinc Total	Favours zinc with iron Total	Weight	Risk Ratio IV, Fixed, 95% CI
Richard 2006	0.15647258	0.188042020540181	209	210	100.0%	1.17 [0.81 , 1.69]
Total (95% CI)			**209**	**210**	**100.0%**	**1.17 [0.81 , 1.69]**

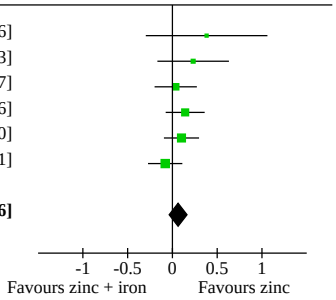
Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)
Test for subgroup differences: Not applicable



Analysis 3.9. Comparison 3: Zinc versus zinc plus iron, Outcome 9: Height

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Kusumastuti 2018	-1.7	0.9	17	-2.05	0.89	17	2.2%	0.38 [-0.30 , 1.06]
Rosado 1997	0.16	0.34641016	48	0.07	0.42	49	6.2%	0.23 [-0.17 , 0.63]
Baqui 2003	70.9	2.8	141	70.8	2.6	135	17.8%	0.04 [-0.20 , 0.27]
Lind 2003	-0.77	0.92	162	-0.9	0.9	163	20.9%	0.14 [-0.08 , 0.36]
Hettiarachchi 2008	-1.14	0.99	201	-1.24	0.98	199	25.8%	0.10 [-0.09 , 0.30]
Richard 2006	-2.11	0.88	209	-2.04	0.85	210	27.0%	-0.08 [-0.27 , 0.11]
Total (95% CI)			**778**			**773**	**100.0%**	**0.06 [-0.04 , 0.16]**

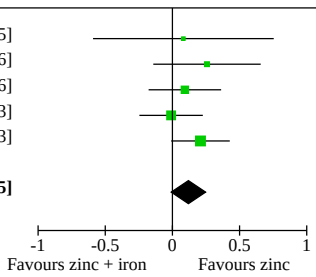
Heterogeneity: Chi² = 4.40, df = 5 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 3.10. Comparison 3: Zinc versus zinc plus iron, Outcome 10: Weight

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Kusumastuti 2018	-1.79	0.72	17	-1.88	1.34	17	3.6%	0.08 [-0.59 , 0.75]
Rosado 1997	0.26	0.34641016	48	0.16	0.42	49	10.2%	0.26 [-0.14 , 0.66]
Hettiarachchi 2008	-1.34	0.85	113	-1.42	0.87	99	22.4%	0.09 [-0.18 , 0.36]
Baqui 2003	8.08	1.07	141	8.09	0.98	135	29.3%	-0.01 [-0.25 , 0.23]
Lind 2003	-1.46	1.08	163	-1.68	1.02	162	34.4%	0.21 [-0.01 , 0.43]
Total (95% CI)			**482**			**462**	**100.0%**	**0.12 [-0.01 , 0.25]**

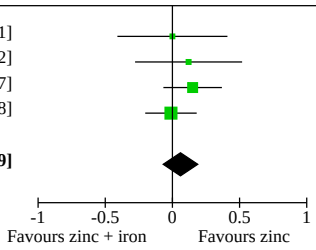
Heterogeneity: Chi² = 2.30, df = 4 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.83 (P = 0.07)
Test for subgroup differences: Not applicable



Analysis 3.11. Comparison 3: Zinc versus zinc plus iron, Outcome 11: Weight-to-height ratio

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Baqui 2003	-0.8	0.8	49	-0.8	0.8	43	9.8%	0.00 [-0.41 , 0.41]
Rosado 1997	0.25	0.41569219	48	0.19	0.56	49	10.4%	0.12 [-0.28 , 0.52]
Lind 2003	-0.7	1.06	162	-0.86	1.06	163	34.8%	0.15 [-0.07 , 0.37]
Richard 2006	-0.02	0.87	209	-0.01	0.97	210	45.0%	-0.01 [-0.20 , 0.18]
Total (95% CI)			**468**			**465**	**100.0%**	**0.06 [-0.07 , 0.19]**

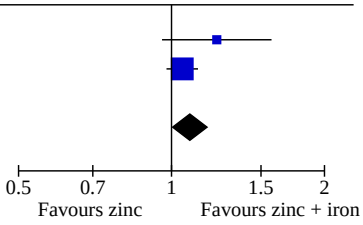
Heterogeneity: Chi² = 1.36, df = 3 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.92 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 3.12. Comparison 3: Zinc versus zinc plus iron, Outcome 12: Prevalence of stunting

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio (Non-event) M-H, Fixed, 95% CI
Hettiarachchi 2008	20	99	14	40	20.6%	1.23 [0.96 , 1.57]
Lind 2003	12	162	19	161	79.4%	1.05 [0.98 , 1.13]
Total (95% CI)		**261**		**201**	**100.0%**	**1.09 [1.01 , 1.17]**
Total events:	32		33			

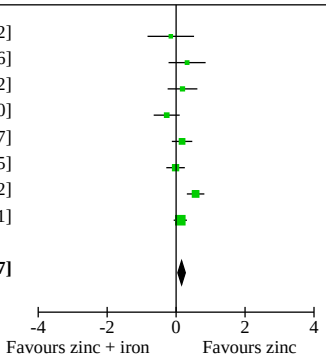
Heterogeneity: Chi² = 1.82, df = 1 (P = 0.18); I² = 45%
Test for overall effect: Z = 2.09 (P = 0.04)
Test for subgroup differences: Not applicable



Analysis 3.13. Comparison 3: Zinc versus zinc plus iron, Outcome 13: Serum or plasma zinc concentration

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Rosales 2004	13.9	1.9	16	14.2	1.9	18	2.6%	-0.15 [-0.83 , 0.52]
Fallahi 2007	14.8	1.6	28	14.2	2.1	26	4.0%	0.32 [-0.22 , 0.86]
Baqui 2003	0.79	0.28	42	0.75	0.11	41	6.2%	0.19 [-0.25 , 0.62]
Rosado 1997	16.8	5.8	54	18.3	5.1	55	8.2%	-0.27 [-0.65 , 0.10]
Chang 2010	10.3	1.1	85	10.1	1.2	91	13.2%	0.17 [-0.12 , 0.47]
Hettiarachchi 2008	12.33	2.76	100	12.37	2.33	114	16.1%	-0.02 [-0.28 , 0.25]
Lind 2003	11.58	1.41	123	10.8	1.34	125	18.0%	0.57 [0.31 , 0.82]
Richard 2006	13.82	6.14	209	13.19	3.98	210	31.6%	0.12 [-0.07 , 0.31]
Total (95% CI)			**657**			**680**	**100.0%**	**0.16 [0.05 , 0.27]**

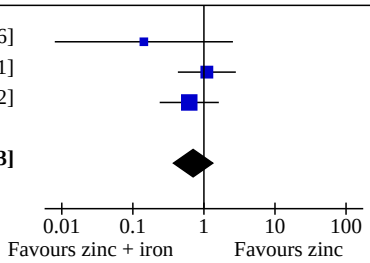
Heterogeneity: Chi² = 17.84, df = 7 (P = 0.01); I² = 61%
Test for overall effect: Z = 2.89 (P = 0.004)
Test for subgroup differences: Not applicable



Analysis 3.14. Comparison 3: Zinc versus zinc plus iron, Outcome 14: Prevalence of zinc deficiency

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosales 2004	0	16	3	16	16.7%	0.14 [0.01 , 2.56]
Rosado 1997	8	53	7	51	34.1%	1.10 [0.43 , 2.81]
Hettiarachchi 2008	6	100	11	114	49.2%	0.62 [0.24 , 1.62]
Total (95% CI)		**169**		**181**	**100.0%**	**0.70 [0.37 , 1.33]**
Total events:	14		21			

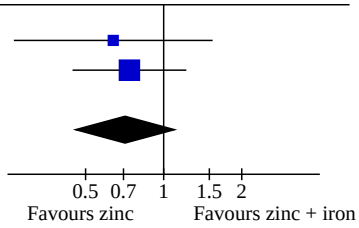
Heterogeneity: Chi² = 2.10, df = 2 (P = 0.35); I² = 5%
Test for overall effect: Z = 1.08 (P = 0.28)
Test for subgroup differences: Not applicable



Analysis 3.15. Comparison 3: Zinc versus zinc plus iron, Outcome 15: Study withdrawal

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Hettiarachchi 2008	7	107	13	127	28.4%	0.64 [0.26 , 1.54]
Baqui 2003	22	161	30	162	71.6%	0.74 [0.45 , 1.22]
Total (95% CI)		**268**		**289**	**100.0%**	**0.71 [0.46 , 1.10]**
Total events:	29		43			

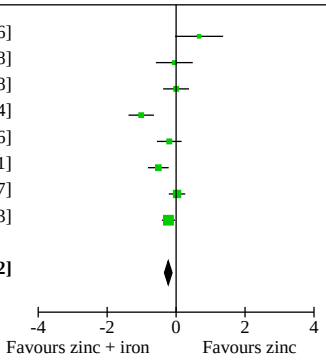
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 1.53 (P = 0.13)
Test for subgroup differences: Not applicable



Analysis 3.16. Comparison 3: Zinc versus zinc plus iron, Outcome 16: Blood hemoglobin concentration

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Rosales 2004	153.3	10.1	15	145.2	13.1	19	2.5%	0.67 [-0.03 , 1.36]
Fallahi 2007	135.4	6.7	28	135.8	8.6	26	4.2%	-0.05 [-0.59 , 0.48]
Rosado 1997	118	51	54	118	51	55	8.5%	0.00 [-0.38 , 0.38]
Hettiarachchi 2008	38.58	19.69	43	62.18	24.36	115	8.8%	-1.01 [-1.38 , -0.64]
Baqui 2003	101.3	12	64	103.7	12	57	9.3%	-0.20 [-0.56 , 0.16]
Chang 2010	93	13	85	100	14	91	13.2%	-0.52 [-0.82 , -0.21]
Lind 2003	115.7	15.2	134	115.3	13.9	136	21.0%	0.03 [-0.21 , 0.27]
Richard 2006	116.61	11.88	209	119.09	10.49	210	32.4%	-0.22 [-0.41 , -0.03]
Total (95% CI)			**632**			**709**	**100.0%**	**-0.23 [-0.34 , -0.12]**

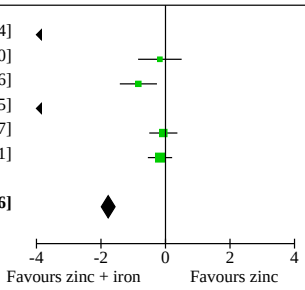
Heterogeneity: Chi² = 33.53, df = 7 (P < 0.0001); I² = 79%
Test for overall effect: Z = 4.08 (P < 0.0001)
Test for subgroup differences: Not applicable



Analysis 3.17. Comparison 3: Zinc versus zinc plus iron, Outcome 17: Serum or plasma ferritin concentration

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Hettiarachchi 2008	34.54	1.69	201	55.07	1.52	199	5.5%	-12.75 [-13.65 , -11.84]
Rosales 2004	38.1	23.7037037	16	44	39.55555556	18	9.9%	-0.17 [-0.85 , 0.50]
Fallahi 2007	25.1	11.6	24	41.6	24.2	27	13.7%	-0.84 [-1.42 , -0.26]
Lind 2003	13.3	3.6	134	32.3	2.9	136	15.1%	-5.80 [-6.35 , -5.25]
Baqui 2003	-15.3	22.6	40	-13.7	24.7	41	23.8%	-0.07 [-0.50 , 0.37]
Rosado 1997	19.7	99.2	54	43.6	169.8	55	32.0%	-0.17 [-0.55 , 0.21]
Total (95% CI)			**469**			**476**	**100.0%**	**-1.78 [-1.99 , -1.56]**

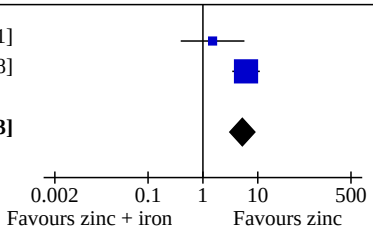
Heterogeneity: Chi² = 927.92, df = 5 (P < 0.00001); I² = 99%
Test for overall effect: Z = 16.36 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 3.18. Comparison 3: Zinc versus zinc plus iron, Outcome 18: Prevalence of iron deficiency

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosales 2004	4	16	3	18	19.0%	1.50 [0.39 , 5.71]
Hettiarachchi 2008	74	201	12	199	81.0%	6.11 [3.43 , 10.88]
Total (95% CI)		**217**		**217**	**100.0%**	**5.23 [3.10 , 8.83]**
Total events:	78		15			

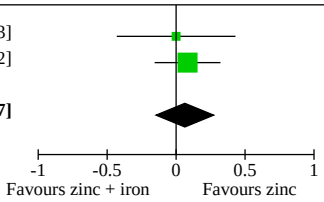
Heterogeneity: Chi² = 3.63, df = 1 (P = 0.06); I² = 72%
Test for overall effect: Z = 6.20 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 3.19. Comparison 3: Zinc versus zinc plus iron, Outcome 19: Serum or plasma copper concentration

Study or Subgroup	Zinc Mean	Zinc SD	Zinc Total	Zinc + iron Mean	Zinc + iron SD	Zinc + iron Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Baqui 2003	-0.9	3.8	42	-0.9	2.7	41	23.5%	0.00 [-0.43 , 0.43]
Lind 2003	15.1	5.1	134	14.7	4.5	136	76.5%	0.08 [-0.16 , 0.32]
Total (95% CI)			**176**			**177**	**100.0%**	**0.06 [-0.15 , 0.27]**

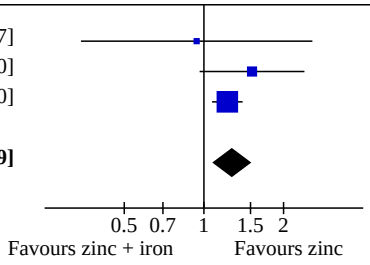
Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 3.20. Comparison 3: Zinc versus zinc plus iron, Outcome 20: Prevalence of anemia

Study or Subgroup	Zinc Events	Zinc Total	Zinc + iron Events	Zinc + iron Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosado 1997	6	42	7	46	6.9%	0.94 [0.34 , 2.57]
Hettiarachchi 2008	32	100	24	114	23.2%	1.52 [0.96 , 2.40]
Chang 2010	84	91	67	89	69.9%	1.23 [1.07 , 1.40]
Total (95% CI)		**233**		**249**	**100.0%**	**1.27 [1.09 , 1.49]**
Total events:	122		98			

Heterogeneity: Chi² = 1.25, df = 2 (P = 0.54); I² = 0%
Test for overall effect: Z = 2.99 (P = 0.003)
Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. Outcome measure definitions

Diarrhea

We defined diarrhea according to the World Health Organization (WHO) definition ("the passage of three or more loose or liquid stools per day, or more frequent passage than is normal for the individual") (WHO 2022). If a trial presented data on diarrhea overall, undifferentiated by severity level, then we included these data in meta-analyses for all-cause diarrhea outcomes. We did the same for outcomes that trial authors defined as acute diarrhea. We defined persistent diarrhea, per WHO, as "diarrhea lasting 14 days or longer" (WHO 2022). We defined diarrhea as severe if it was defined this way by trial authors.

Lower respiratory tract infection (LRTI)

Several systematic reviews have found that LRTI is often defined inconsistently across studies (Bhutta 1999; Imdad 2010; Roth 2010). To deal with this inconsistency, we only included LRTI data from a study if the study's LRTI definition matched any of the following definitions. The first two of these definitions could have been diagnosed by someone who was not a medical professional (for example, a field worker). The third definition must have been diagnosed by a medical professional (for example, a physician).

- Difficulty breathing or rapid breathing, or both
- Difficulty breathing or cough, along with one or more of the following: age-specific rapid breathing rates, lower chest wall indrawing, chest auscultation signs of pneumonia (decreased breath sounds, bronchial breath sounds, crackles, abnormal voice resonance, pleural rub), nasal flaring, grunting, fever, central cyanosis, inability to breastfeed or drink, vomiting everything, convulsions, lethargy, unconsciousness, or severe respiratory distress (for example, head nodding; WHO/UNICEF 2000; WHO/UNICEF 2005)
- Clinical evidence of LRTI based on chest auscultation (decreased breath sounds, bronchial breath sounds, crackles, abnormal voice resonance, pleural rub) or chest radiograph.

We gave preference to more severe or rigorously diagnosed LRTI outcome data. For example, if a study provided LRTI data based on rapid breathing and LRTI data based on both rapid breathing and symptoms such as chest indrawing, then we extracted the latter. If a study provided data from caregivers of children and from study field workers, then we extracted the latter. If a study provided fieldworker-

reported and physician-reported data, we extracted the latter. If a trial reported LRTI outcomes and pneumonia outcomes separately, then we used the LRTI outcomes. We did not include upper respiratory tract infection data.

Malaria

As with LRTI, we gave preference to more virulent forms of malaria (for example, preference was given to *Plasmodium falciparum* rather than *Plasmodium vivax*) if it was not possible to extract all forms.

Growth

Height data could be described in terms of raw lengths (for example, in units of centimeter [cm]), or in terms of height-for-age z-scores (HAZ scores). HAZ scores describe a child's height as a standard deviation score in a height distribution from a reference population of children of similar ages. If a study reported height outcomes as both raw lengths and HAZ scores, then we preferentially extracted the HAZ scores. However, if a study only reported raw lengths, then we extracted these. We did the same for raw weights and weight-for-age z-scores (WAZ scores). We defined stunting as "height that is more than two standard deviations below the WHO child growth standards median" (WHO 2022).

Zinc and other micronutrient status and adverse events

We included measures of anemia and iron deficiency as follows, consistent with WHO definitions (WHO 2022).

- Anemia: blood hemoglobin level of < 110 g/L, 115 g/L, or 120 g/L for children aged 6 to 59 months, 5 to 11 years, and 12 to 14 years, respectively
- Iron deficiency: blood ferritin concentrations of < 15 µg/L

We included measures of zinc and copper deficiency as defined by trial authors, given that there are no standard WHO definitions for these conditions.

If trial authors reported more than one measure for a particular outcome, then we gave preference to the one defined as most severe.

Appendix 2. Search strategies

Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library; searched 30 April 2021

#1 MeSH descriptor: [Zinc] explode all trees
#2 MeSH descriptor: [Zinc Compounds] explode all trees
#3 MeSH descriptor: [Zinc Oxide] explode all trees
#4 MeSH descriptor: [Zinc Sulfate] explode all trees
#5 MeSH descriptor: [Zinc Acetate] explode all trees
#6 (Zinc):ti,ab,kw
#7 (Zn):ti,ab,kw
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9 MeSH descriptor: [Infant] explode all trees
#10 MeSH descriptor: [Child] explode all trees
#11 MeSH descriptor: [Adolescent] explode all trees
#12 (newborn* or neonat* or neo-nat* or (neo next nat*) or infan* or baby or babies or toddler* or preschool* or pre-school* or (pre next school*) or pediatric* or paediatric* or child* or girl* or boy* or preteen* or pre-teen* or (pre next teen*) or teen* or preadolescen* or pre-adolescen* or (pre next adolescen*) or adolescen* or prepubert* or pre-pubert* or (pre next pubert*) or pubert*):ti,ab,kw
#13 #9 OR #10 OR #11 OR #12
#14 #8 AND #13

Date 2013 to 2021

Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library; searched 2 February 2022

#1 MeSH descriptor: [Zinc] explode all trees
#2 MeSH descriptor: [Zinc Compounds] explode all trees
#3 MeSH descriptor: [Zinc Oxide] explode all trees
#4 MeSH descriptor: [Zinc Sulfate] explode all trees
#5 MeSH descriptor: [Zinc Acetate] explode all trees
#6 (Zinc):ti,ab,kw
#7 (Zn):ti,ab,kw
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9 MeSH descriptor: [Infant] explode all trees
#10 MeSH descriptor: [Child] explode all trees
#11 MeSH descriptor: [Adolescent] explode all trees

#12 (newborn* or neonat* or neo-nat* or (neo next nat*) or infan* or baby or babies or toddler* or preschool* or pre-school* or (pre next school*) or pediatric* or paediatric* or child* or girl* or boy* or preteen* or pre-teen* or (pre next teen*) or teen* or preadolescen* or pre-adolescen* or (pre next adolescen*) or adolescen* or prepubert* or pre-pubert* or (pre next pubert*) or pubert*):ti,ab,kw
#13 #9 OR #10 OR #11 OR #12
#14 #8 AND #13

Date 2021 -2022

MEDLINE Ovid (R); searched 30 April 2021

1 zinc/ or zinc compounds/ or zinc oxide/ or zinc sulfate/ or zinc acetate/
2 (zinc or Zn).tw.
3 1 or 2
4 exp infant/ or exp child/ or adolescent/
5 (newborn$ or neonat$ or neo-nat$ or infan$ or baby or babies or toddler$ or preschool$ or pre- school$ or pediatric$ or paediatric$ or child$ or girl$ or boy$ or preteen$ or pre-teen$ or teen$ or preadolescen$ or pre-adolescen$ or adolescen$ or prepubert$ or pre-pubert $ or pubert$).tw.
6 4 or 5
7 exp placebos/
8 exp volunteer/
9randomized controlled clinical trial.pt
10 controlled clinical trial.pt.
11 randomi#ed.ab.
12 random.ab.
13 randomly.ab.
14 placebo$.ab.
15 drug therapy.fs.
16 trial.ab.
17 trials.ab.
18 group.ab.
19 groups.ab.
20 volunteer$.ab.
21 factorial$.ab.
22 assign$.ab.
23 allocat$.ab.
24 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 3 and 6 and 24
26 exp animals/ not humans.sh.
27 25 not 26
28 limit 27 to yr="2013-Current"

MEDLINE Ovid (R); searched 2 February 2022

1 zinc/ or zinc compounds/ or zinc oxide/ or zinc sulfate/ or zinc acetate/
2 (zinc or Zn).tw.
3 1 or 2
4 exp infant/ or exp child/ or adolescent/
5 (newborn$ or neonat$ or neo-nat$ or infan$ or baby or babies or toddler$ or preschool$ or pre- school$ or pediatric$ or paediatric$ or child$ or girl$ or boy$ or preteen$ or pre-teen$ or teen$ or preadolescen$ or pre-adolescen$ or adolescen$ or prepubert$ or pre-pubert $ or pubert$).tw.
6 4 or 5
7 exp placebos/
8 exp volunteer/
9randomized controlled clinical trial.pt
10 controlled clinical trial.pt.
11 randomi#ed.ab.
12 random.ab.
13 randomly.ab.
14 placebo$.ab.
15 drug therapy.fs.
16 trial.ab.
17 trials.ab.
18 group.ab.

19 groups.ab.
20 volunteer$.ab.
21 factorial$.ab.
22 assign$.ab.
23 allocat$.ab.
24 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 3 and 6 and 24
26 exp animals/ not humans.sh.
27 25 not 26
28 limit 27 to dt=20210430-20220202

MEDLINE Ovid (R) In-Process & Other Non-Indexed Citations; searched 30 April 2021

1 (zinc or Zn).tw.
2 (newborn$ or neonat$ or neo-nat$ or infan$ or baby or babies or toddler$ or preschool$ or pre- school$ or pre school$ or pediatric$ or paediatric$ or child$ or girl$ or boy$ or preteen$ or pre-teen$ or teen$ or preadolescen$ or pre-adolescen$ or adolescen$ or prepubert $ or pre-pubert$ or pubert$).tw.
3 1 and 2
4 randomized controlled trial.pt.
5 controlled clinical trial.pt.
6 randomi#ed.ab.
7 random.ab.
8 randomly.ab.
9 placebo$.ab.
10 drug therapy.fs.
11 trial.ab.
12 trials.ab.
13 group.ab.
14 groups.ab.
15 (crossover or cross-over).ab.
16 ((singl$ or doubl$) adj1 (blind$)).ab.
17 volunteer.ab.
18 factorial$.ab.
19 assign$.ab.
20 allocat$.ab.
21 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22 exp animals/ not humans.sh.
23 3 and 21
24 23 not 22
25 limit 24 to yr="2013-Current"

MEDLINE Ovid (R) In-Process & Other Non-Indexed Citations; searched 2 February 2022

1 (zinc or Zn).tw.
2 (newborn$ or neonat$ or neo-nat$ or infan$ or baby or babies or toddler$ or preschool$ or pre- school$ or pre school$ or pediatric$ or paediatric$ or child$ or girl$ or boy$ or preteen$ or pre-teen$ or teen$ or preadolescen$ or pre-adolescen$ or adolescen$ or prepubert $ or pre-pubert$ or pubert$).tw.
3 1 and 2
4 randomized controlled trial.pt.
5 controlled clinical trial.pt.
6 randomi#ed.ab.
7 random.ab.
8 randomly.ab.
9 placebo$.ab.
10 drug therapy.fs.
11 trial.ab.
12 trials.ab.
13 group.ab.
14 groups.ab.
15 (crossover or cross-over).ab.
16 ((singl$ or doubl$) adj1 (blind$)).ab.
17 volunteer.ab.
18 factorial$.ab.

19 assign$.ab.
20 allocat$.ab.
21 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22 exp animals/ not humans.sh.
23 3 and 21
24 23 not 22
25 limit 24 to dt=20210430-20220202

Embase Elsevier; searched 30 April 2021

#1'zinc'/exp
#2'zinc derivative'/exp
#3 'zinc oxide'/exp
#4 'zinc sulfate'/exp
#5 'zinc acetate'/exp
#6 zinc OR zn
#7#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8 'infant'/exp
#9 'child'/exp
#10 'adolescent'/exp
#11 newborn* OR neonat* OR 'neo nat*' OR infan* OR baby OR babies OR toddler* OR preschool* OR 'pre school*' OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR 'pre teen*' OR teen* OR preadolescen* OR 'pre adolescen*' OR adolescen* OR prepubert* OR 'pre pubert*' OR pubert*
#12 #8 OR #9 OR #10 OR #11
#13 'crossover procedure'/exp
#14 'double blind procedure'/exp
#15 'randomized controlled trial'/exp
#16 'single blind procedure'/exp
#17 'placebo'/exp
#18 'volunteer'/exp
#19 'drug therapy'/exp
#20 crossover OR 'cross over'
#21 (singl* OR doubl*) NEXT/1 blind*
#22 random* OR placebo* OR 'drug therap*' OR trial OR trials OR group OR groups OR factorial* OR assign* OR allocat* OR volunteer*
#23 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24 #7 AND #12 AND #23
#25 #24 NOT ([animals]/lim NOT [humans]/lim)
#26 #25 AND [2013-2021]/py
#27 #26 NOT [medline]/lim

Embase Elsevier; searched 2 February 2022

#1'zinc'/exp
#2'zinc derivative'/exp
#3 'zinc oxide'/exp
#4 'zinc sulfate'/exp
#5 'zinc acetate'/exp
#6 zinc OR zn
#7#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8 'infant'/exp
#9 'child'/exp
#10 'adolescent'/exp
#11 newborn* OR neonat* OR 'neo nat*' OR infan* OR baby OR babies OR toddler* OR preschool* OR 'pre school*' OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR 'pre teen*' OR teen* OR preadolescen* OR 'pre adolescen*' OR adolescen* OR prepubert* OR 'pre pubert*' OR pubert*
#12 #8 OR #9 OR #10 OR #11
#13 'crossover procedure'/exp
#14 'double blind procedure'/exp
#15 'randomized controlled trial'/exp
#16 'single blind procedure'/exp
#17 'placebo'/exp
#18 'volunteer'/exp
#19 'drug therapy'/exp

#20 crossover OR 'cross over'
#21 (singl* OR doubl*) NEXT/1 blind*
#22 random* OR placebo* OR 'drug therap*' OR trial OR trials OR group OR groups OR factorial* OR assign* OR allocat* OR volunteer*
#23 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24 #7 AND #12 AND #23
#25 #24 NOT ([animals]/lim NOT [humans]/lim)
#26 #25 AND NOT [medline]/lim AND [30-04-2021]/sd NOT [03-02-2022]/sd

World Health Organization International Clinical Trials Registry Platform(ICTRP); searched 30 April 2021 and 2 February 2022

(Zinc AND Child) OR (Zinc AND Infant) OR (Zinc AND Adolescent)

Web of Science (Science Citation Index and Conference Proceedings Citation Index-Science); searched 30 April 2021

#1 TS=(Zinc OR Zn)
#2 TS=(newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*)
#3 TS=(random* OR placebo* OR “drug therap*” OR trial OR trials OR group OR groups OR crossover* OR cross-over* OR double-blind* OR “doubl* blind*” OR single-blind* OR “singl* blind*” OR factorial* OR assign* OR allocat* OR volunteer*)
#4 #3 AND #2 AND #1
#5 #4 Timespan=2013-2021

Web of Science (Science Citation Index and Conference Proceedings Citation Index-Science); searched 2 February 2022

#1 TS=(Zinc OR Zn)
#2 TS=(newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*)
#3 TS=(random* OR placebo* OR “drug therap*” OR trial OR trials OR group OR groups OR crossover* OR cross-over* OR double-blind* OR “doubl* blind*” OR single-blind* OR “singl* blind*” OR factorial* OR assign* OR allocat* OR volunteer*)
#4 #3 AND #2 AND #1
#5 #4 Timespan=2021-2022

Scopus Elsevier; searched 30 April 2021

(TITLE-ABS-KEY (zinc OR zn)) AND (TITLE-ABS-KEY (newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*)) AND ((TITLE-ABS-KEY (random* OR placebo* OR "drug therap*" OR trial OR trials OR group OR groups OR crossover OR cross-over OR factorial* OR allocat* OR assign* OR volunteer*)) OR (TITLE-ABS-KEY (singl* OR doubl*) PRE/1 TITLE-ABS-KEY (blind*))) AND NOT INDEX (medline) AND (LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR, 2013))

Scopus Elsevier; searched 2 February 2022

((TITLE-ABS-KEY (zinc OR zn)) AND (TITLE-ABS-KEY (newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*)) AND ((TITLE-ABS-KEY (random* OR placebo* OR "drug therap*" OR trial OR trials OR group OR groups OR crossover OR cross-over OR factorial* OR allocat* OR assign* OR volunteer*)) OR (TITLE-ABS-KEY (singl* OR doubl*) PRE/1 TITLE-ABS-KEY (blind*))) AND NOT INDEX(medline)) AND ORIG-LOAD-DATE > 20210430

Cochrane Database of Systematic Reviews (CDSR) in the Cochrane Library ; searched 30 April 2021

#1 MeSH descriptor: [Zinc] explode all trees
#2 MeSH descriptor: [Zinc Compounds] explode all trees
#3 MeSH descriptor: [Zinc Oxide] explode all trees
#4 MeSH descriptor: [Zinc Sulfate] explode all trees
#5 MeSH descriptor: [Zinc Acetate] explode all trees
#6 (Zinc):ti,ab,kw
#7 (Zn):ti,ab,kw
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9 MeSH descriptor: [Infant] explode all trees
#10 MeSH descriptor: [Child] explode all trees

#11 MeSH descriptor: [Adolescent] explode all trees
#12 (newborn* or neonat* or neo-nat* or (neo next nat*) or infan* or baby or babies or toddler* or preschool* or pre-school* or (pre next school*) or pediatric* or paediatric* or child* or girl* or boy* or preteen* or pre-teen* or (pre next teen*) or teen* or preadolescen* or pre-adolescen* or (pre next adolescen*) or adolescen* or prepubert* or pre-pubert* or (pre next pubert*) or pubert*):ti,ab,kw
#13 #9 OR #10 OR #11 OR #12
#14 #8 AND #13

Date 01/01/13 -30/04/21

Cochrane Database of Systematic Reviews (CDSR) in the Cochrane Library ; searched 2 February 2022

#1 MeSH descriptor: [Zinc] explode all trees
#2 MeSH descriptor: [Zinc Compounds] explode all trees
#3 MeSH descriptor: [Zinc Oxide] explode all trees
#4 MeSH descriptor: [Zinc Sulfate] explode all trees
#5 MeSH descriptor: [Zinc Acetate] explode all trees
#6 (Zinc):ti,ab,kw
#7 (Zn):ti,ab,kw
#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9 MeSH descriptor: [Infant] explode all trees
#10 MeSH descriptor: [Child] explode all trees
#11 MeSH descriptor: [Adolescent] explode all trees
#12 (newborn* or neonat* or neo-nat* or (neo next nat*) or infan* or baby or babies or toddler* or preschool* or pre-school* or (pre next school*) or pediatric* or paediatric* or child* or girl* or boy* or preteen* or pre-teen* or (pre next teen*) or teen* or preadolescen* or pre-adolescen* or (pre next adolescen*) or adolescen* or prepubert* or pre-pubert* or (pre next pubert*) or pubert*):ti,ab,kw
#13 #9 OR #10 OR #11 OR #12
#14 #8 AND #13

Date 30/04/21 -02/02/22

Global Index Medicus (WPRIM, LILACS, IMSEAR, IMEMR, AIM); searched 30 April 2021

(mh:(zinc)) OR ((zinc OR zn)) AND ((mh:(child)) OR ((mh:(infant))) OR ((mh:(adolescent))) OR ((newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR "pre school*" OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR "pre teen*" OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*))) AND ((mh:(placebos)) OR ((mh:(volunteer))) OR ((random* OR placebo* OR trial OR trials OR group OR groups OR crossover OR cross-over OR factorial* OR assign* OR allocat* OR volunteer*)) OR ((singl* OR doubl*) AND ((blind*)))) AND NOT ((mh:(animals)) AND NOT ((mh:(animals)) AND ((mh:(humans))))) AND (year_cluster:[2013 TO 2021])

Global Index Medicus (WPRIM, LILACS, IMSEAR, IMEMR, AIM); searched 2 February 2022

(mh:(zinc)) OR ((zinc OR zn)) AND ((mh:(child)) OR ((mh:(infant))) OR ((mh:(adolescent))) OR ((newborn* OR neonat* OR neo-nat* OR infan* OR baby OR babies OR toddler* OR preschool* OR pre-school* OR "pre school*" OR pediatric* OR paediatric* OR child* OR girl* OR boy* OR preteen* OR pre-teen* OR "pre teen*" OR teen* OR preadolescen* OR pre-adolescen* OR adolescen* OR prepubert* OR pre-pubert* OR pubert*))) AND ((mh:(placebos)) OR ((mh:(volunteer))) OR ((random* OR placebo* OR trial OR trials OR group OR groups OR crossover OR cross-over OR factorial* OR assign* OR allocat* OR volunteer*)) OR ((singl* OR doubl*) AND ((blind*)))) AND NOT ((mh:(animals)) AND NOT ((mh:(animals)) AND ((mh:(humans))))) AND (year_cluster:[2021 TO 2022])

Appendix 3. Unused methods archived for use in future updates of this review

We will conduct the following sensitivity analyses to examine whether or not our findings are robust to certain decisions made while conducting the review.

- We will repeat the primary meta-analysis excluding studies at high risk of bias due to incomplete outcome data.
- We will repeat the meta-analysis using an intracluster correlation coefficient (ICC) value at least as large as the largest observed ICC.

Appendix 4. Funnel plots for selected pooled analysis

Publication bias

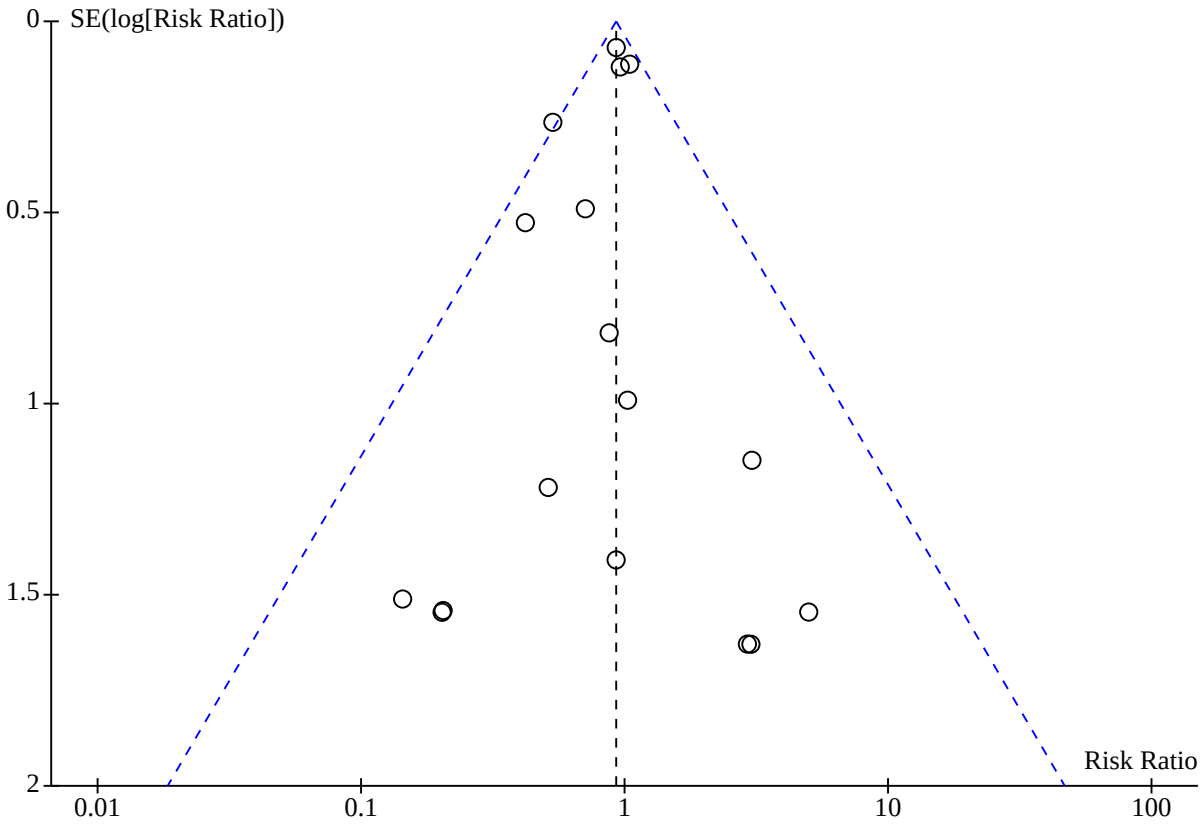
Comparison 1: Zinc versus no zinc

Primary outcomes

1. All-cause mortality

The funnel plot for all-cause mortality appeared symmetrical (Figure 7).

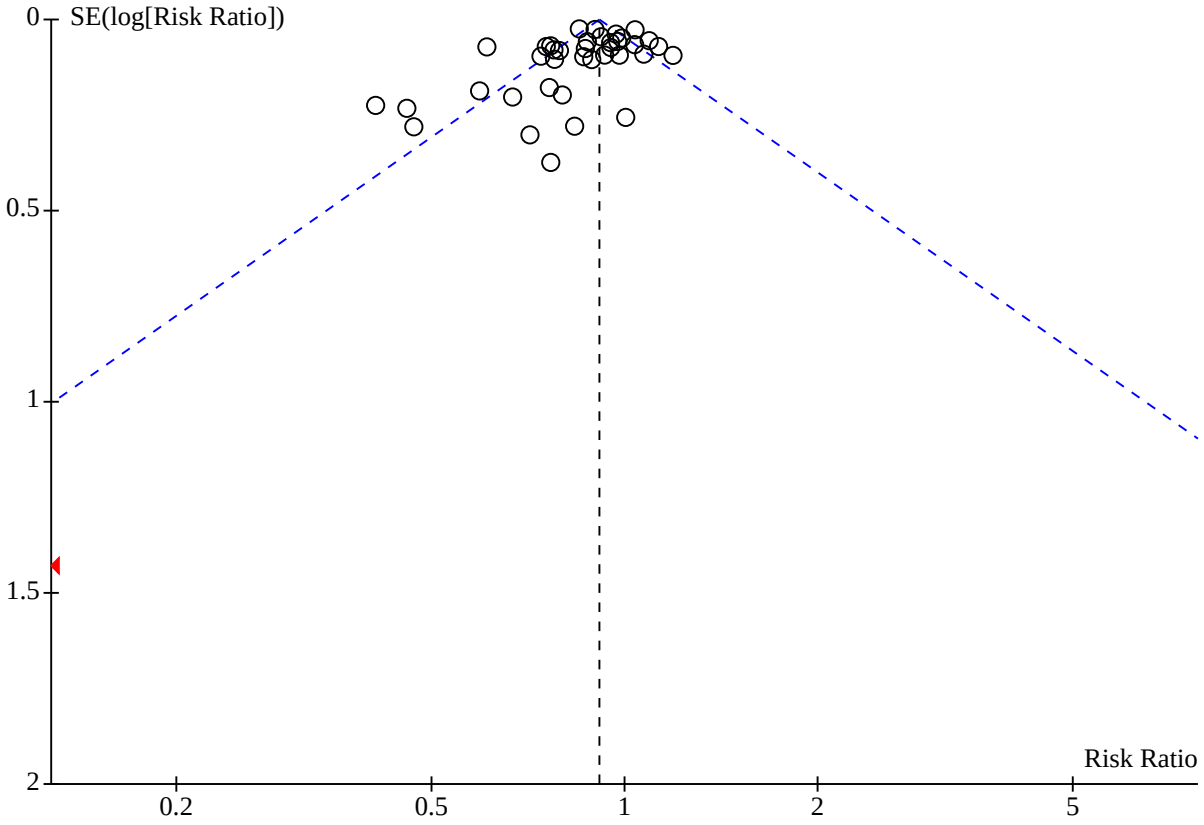
Figure 7. Funnel plot of comparison 1: zinc versus no zinc, outcome 1.1, all-cause mortality RR: risk ratio; SE: standard error



4.1. Incidence of all-cause diarrhea

The funnel plot for incidence of all-cause diarrhea had evidence of funnel plot asymmetry (Figure 8).

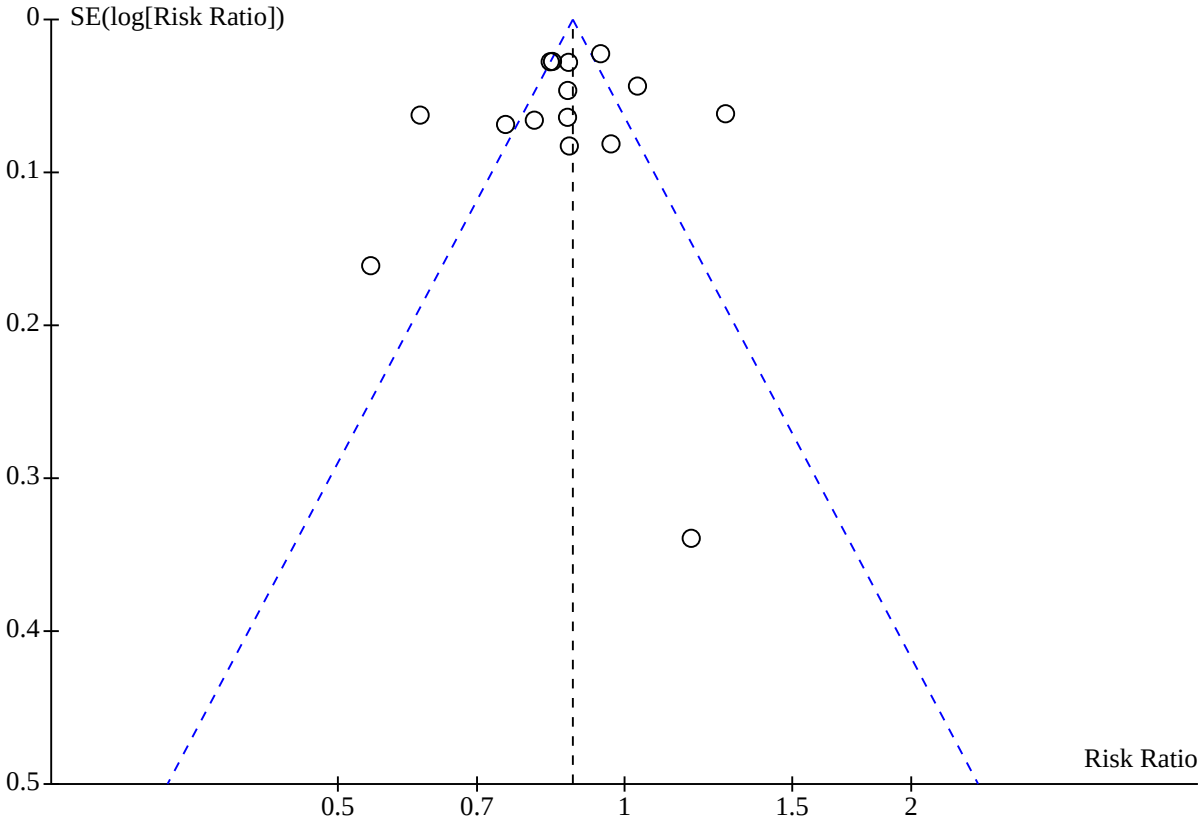
Figure 8. Funnel plot for effect of zinc supplementation on call-cause diarrhea



4.2. Prevalence of all-cause diarrhea

The funnel plot for prevalence of all-cause diarrhea appeared symmetrical (Figure 9).

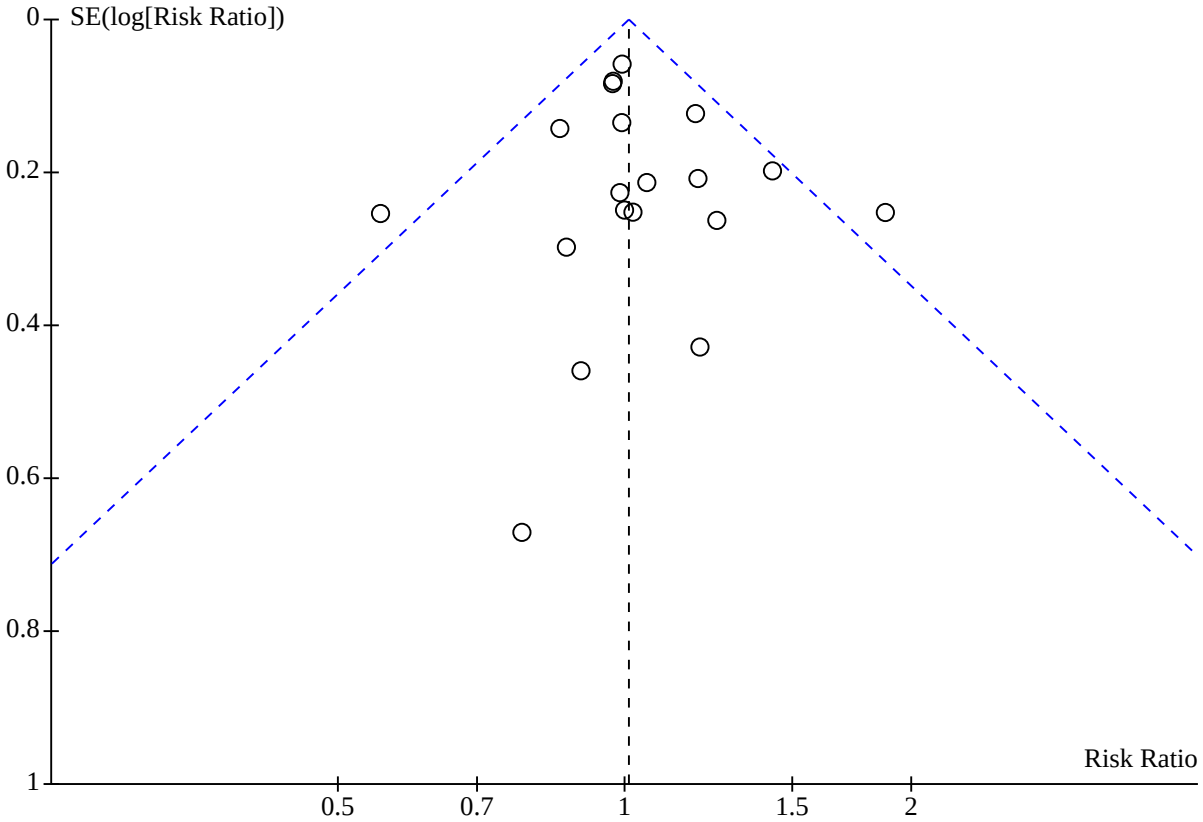
Figure 9. Funnel plot for effect of zinc supplementation on prevalance of all-cause diarrhea



5.1. Incidence of lower respiratory tract infection (LRTI)

The funnel plot for incidence of LRTI appeared symmetrical (Figure 10).

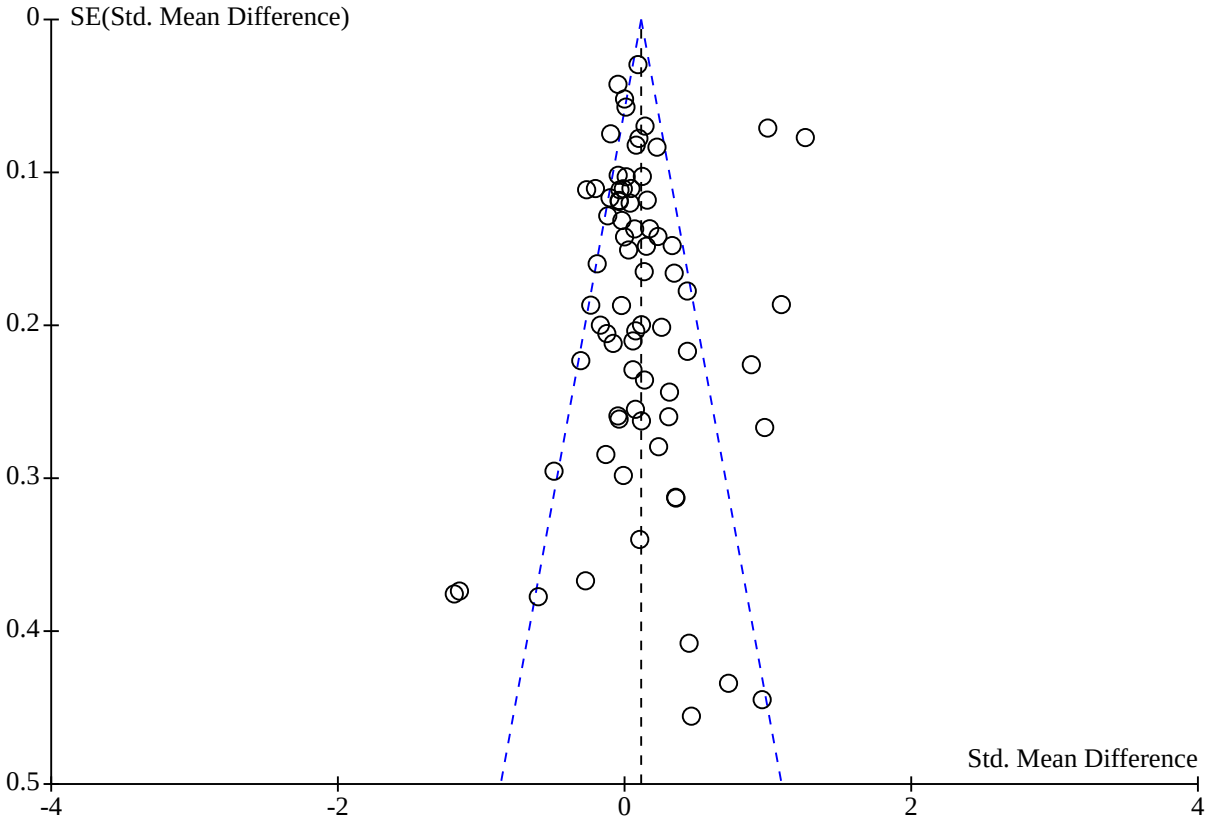
Figure 10. Funnel plot for effect of zinc supplementation on incidence of lower respiratory tract infection (LRTI) RR-relative risk SE: Standard error



7.1. Height

The funnel plot for height appeared symmetrical (Figure 11).

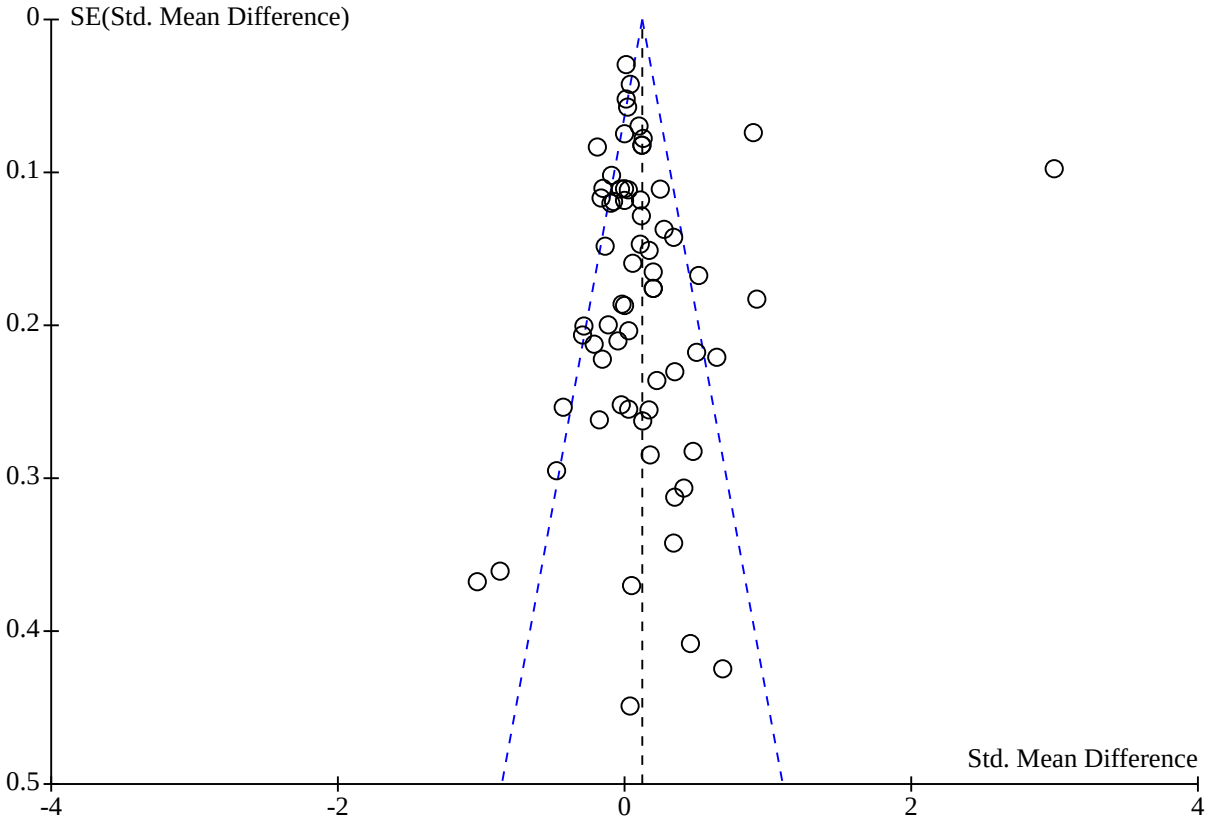
Figure 11. Funnel plot for effect of zinc supplementation on height



7.2. Weight

There was some visual asymmetry in the funnel plot for the analysis of weight (Figure 12), suggesting small-study effects or reporting bias.

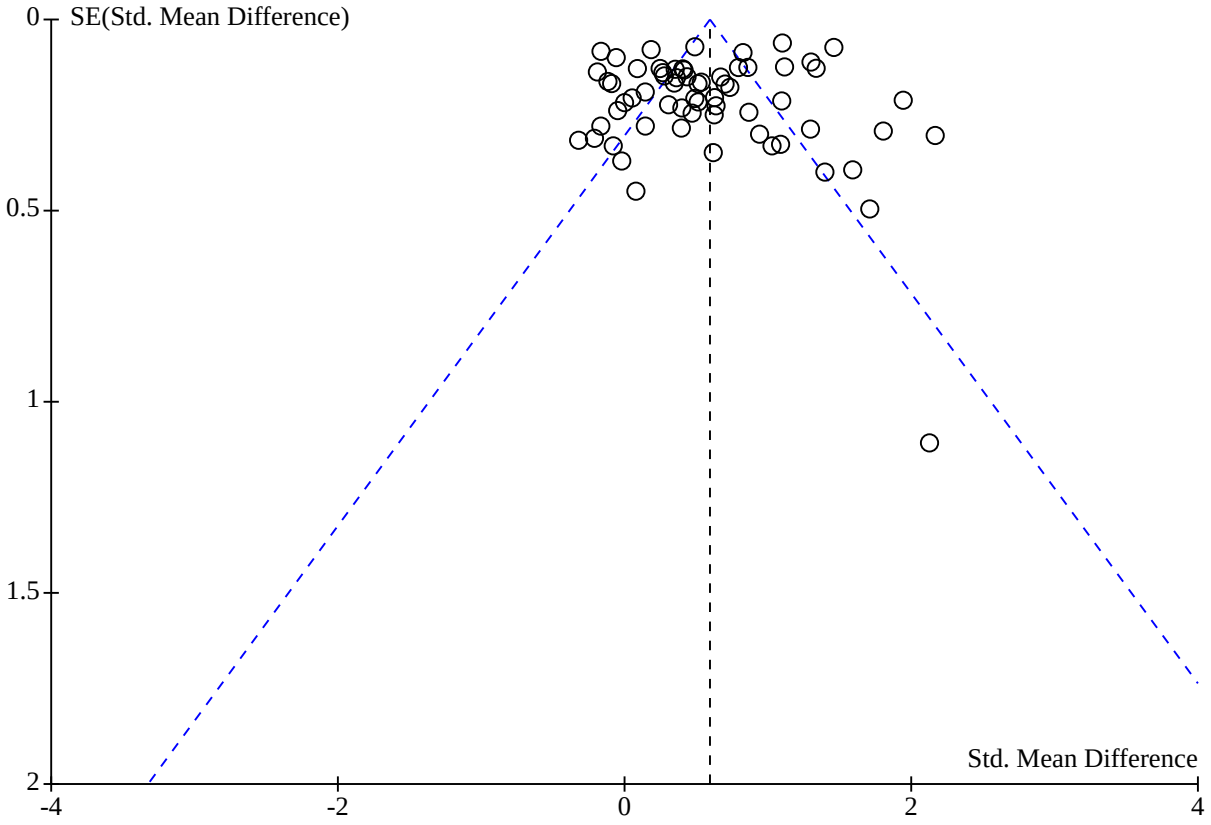
Figure 12. Funnel plot for effect of zinc supplementation on weight



8.1 Serum or plasma zinc concentration

The funnel plot for the analysis of plasma zinc concentration did not appear to have any substantive asymmetry (Figure 13).

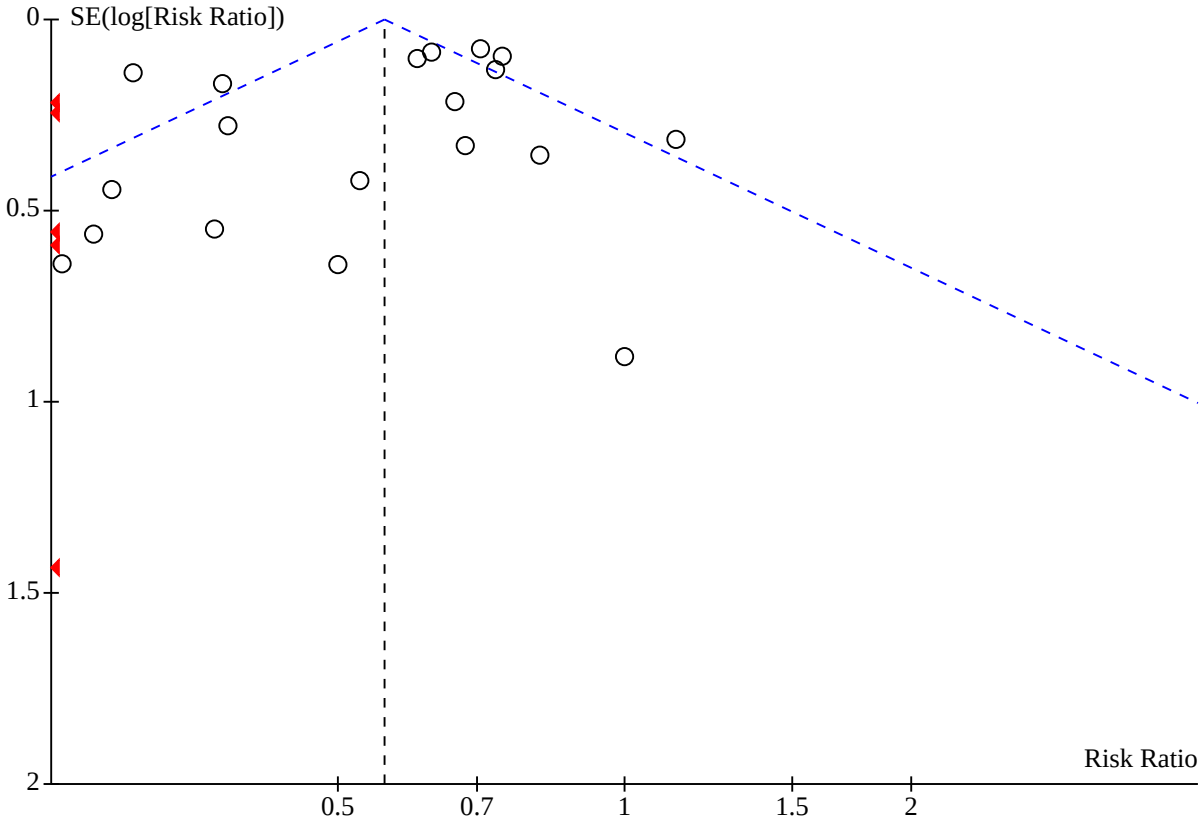
Figure 13. Funnel plot for effect of zinc supplementation on serum zinc



8.2 Prevalence of zinc deficiency

The funnel plot for publication bias appeared to be skewed for the analysis of prevalence of zinc deficiency (Figure 14).

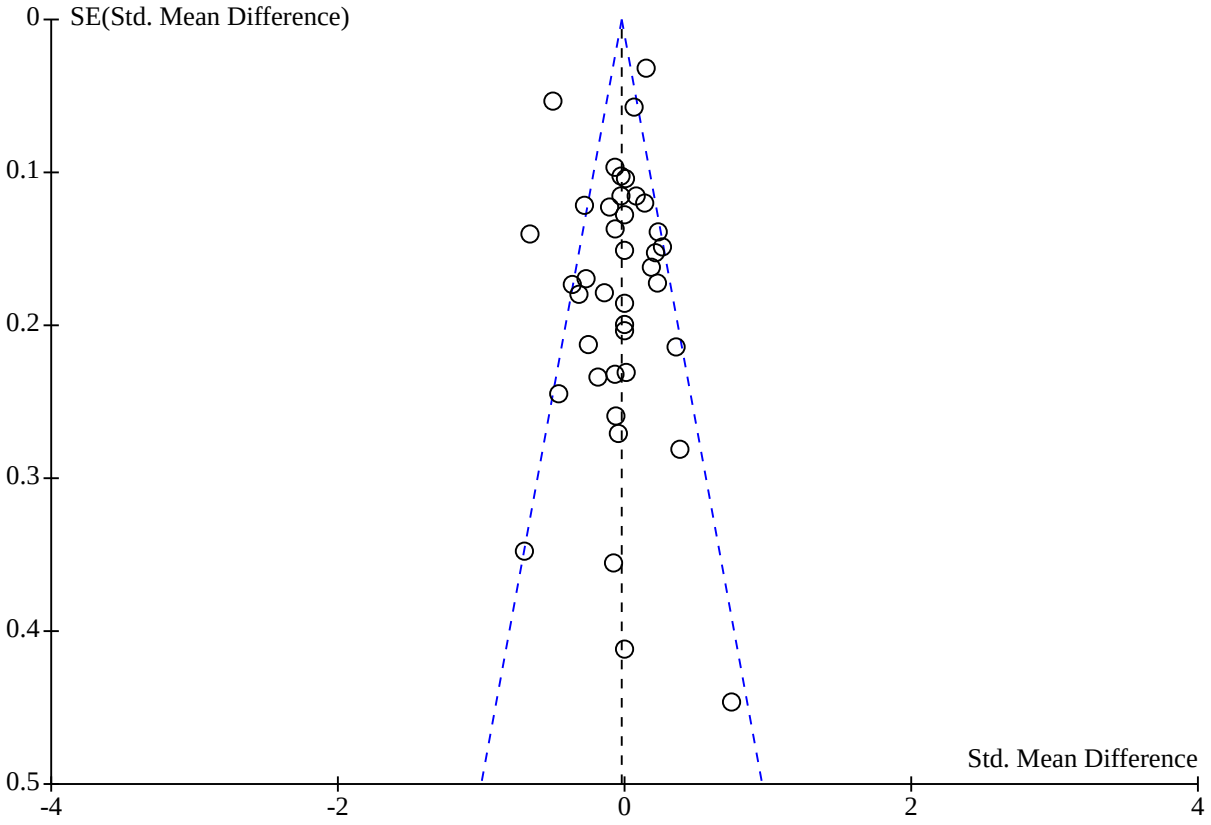
Figure 14. Funnel plot for effect of zinc supplementation on prevalance of zinc deficiency



10.1 Blood hemoglobin concentration

The funnel plot for blood hemoglobin concentration appeared symmetrical (Figure 15).

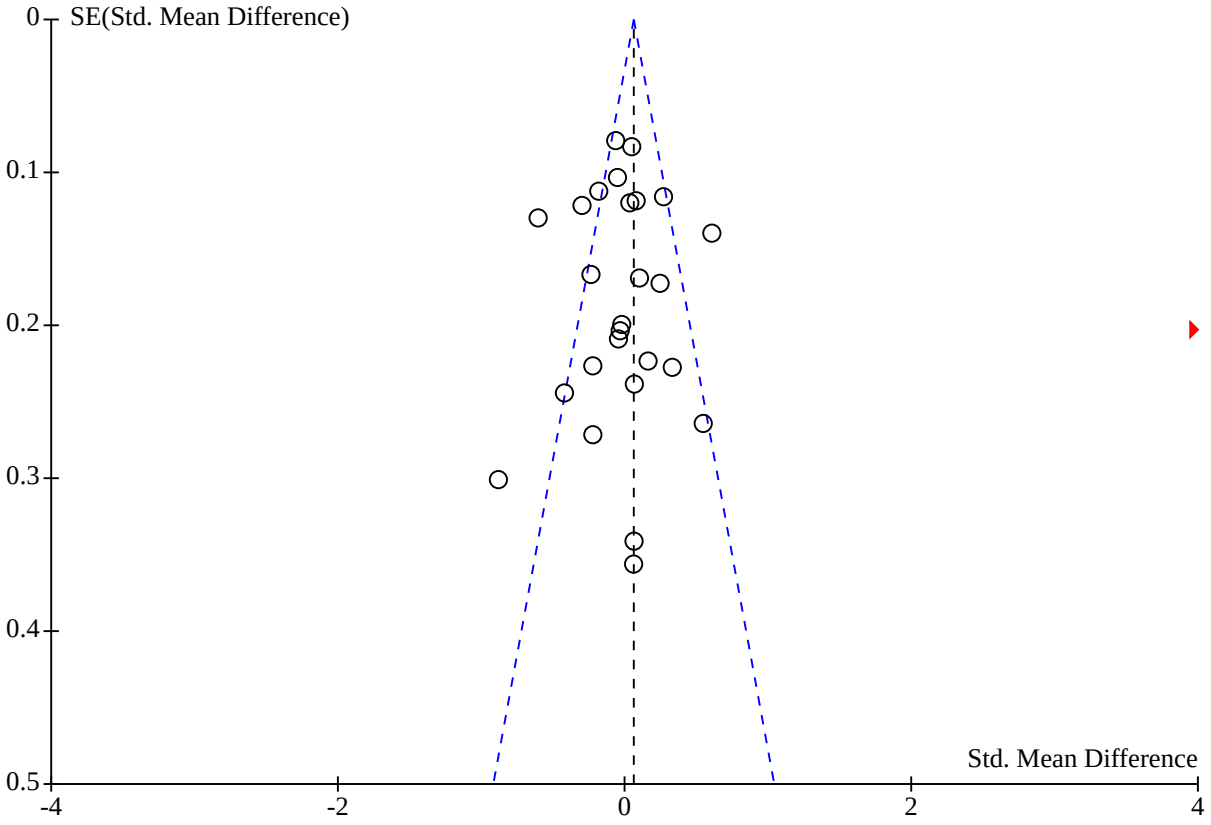
Figure 15. Funnel plot for effect of zinc supplementation on blood hemoglobin concentration



11.1 Serum or plasma ferritin concentration

The funnel plot for ferritin concentration appeared symmetrical (Figure 16).

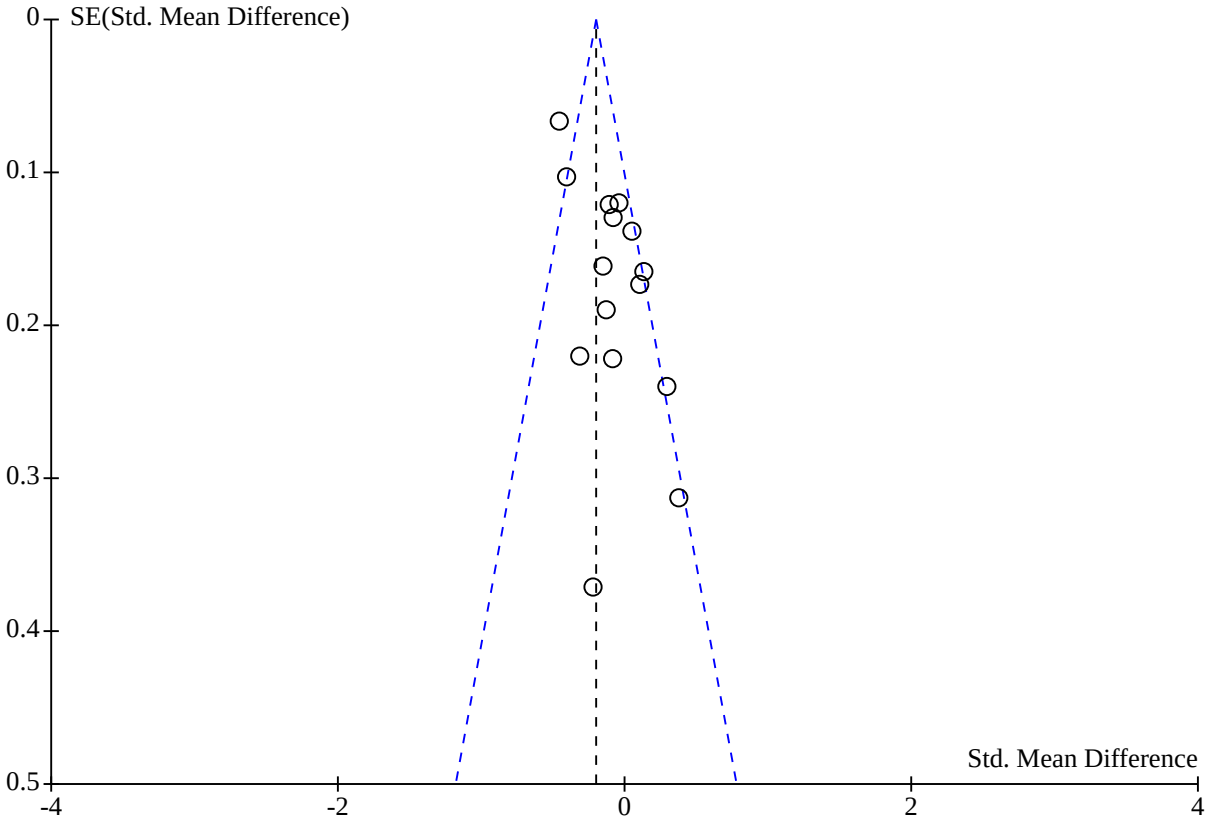
Figure 16. Funnel plot for effect of zinc supplementation on plasma ferritin



12.1. Serum or plasma copper concentration

There was evidence of funnel plot asymmetry for the analysis of plasma copper concentration (Figure 17).

Figure 17. Funnel plot for effect of zinc supplementation on serum copper



WHAT'S NEW

Date	Event	Description
29 March 2023	New citation required but conclusions have not changed	16 new studies added. Conclusions of the review remain unchanged.
29 March 2023	New search has been performed	Updated following a new search in May 2021 and a top-up search in February 2022.

HISTORY

Protocol first published: Issue 10, 2011
Review first published: Issue 5, 2014

CONTRIBUTIONS OF AUTHORS

For this update, AI conceptualized, designed and co-ordinated the review. AI, JS, MH, AR, and JR screened records, extracted data, and performed the risk of bias assessment. AI, JR, and RS analyzed the data. AI did the GRADE analysis. AI, JR, and RS wrote the manuscript. AS and OT conducted the literature search. XHC contributed to the last version of the review and approved this version. EMW and ZB contributed to the writing and interpretation of findings. AI is the guarantor of the review.

DECLARATIONS OF INTEREST

Evan Mayo-Wilson has declared that he has no conflicts of interest.

Allison Regan has declared that she has no conflicts of interest.

Jaimie Rogner has declared that she has no conflicts of interest.

Aamer Imdad has declared that he has no conflicts of interest.

Zulfiqar A Bhutta has published previous reviews about zinc. ZB was involved in some of the included trials but did not assess their eligibility, extract data, assess the risk of bias or grade the certainty of the evidence from these studies.

Xin Chan has declared that she has no conflicts of interest.

Maya Haykal has declared that she has no conflicts of interest.

Rida Sherwani is a Pediatric Resident at SUNY Upstate Medical University. She has declared that she has no conflicts of interest.

Jasleen Sidhu has declared that she has no conflicts of interest.

Abigail Smith has declared that she has no conflicts of interest.

Olivia Tsistinas has declared that she has no conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- Aga Khan University, Pakistan

  Zulfiqar A Bhutta is supported by Aga Khan University, Karachi, Pakistan

External sources

- External support, Other

  No external support was available for this review

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- We eliminated the outcomes, 'hospitalization due to severe diarrhea' and 'hospitalization due to persistent diarrhea'. (Studies only reported hospitalization due to all-cause diarrhea, undifferentiated by the level of severity or persistence. However, if a child was hospitalized for a diarrhea episode, this episode would likely be severe or persistent, or both.)
- We re-specified the outcome, 'Side effects (for example, abdominal pain, nausea, vomiting, diarrhea)' as: "Study withdrawal, participants with one or more side effects, vomiting episodes, and participants with one or more vomiting episodes". We only included 'participants with one or more vomiting episodes' in the summary of findings table. We made these changes to be specific about the side effects as the earlier definition included multiple domains, which were difficult to classify.
- We did not include the incidence of severe diarrhea and persistent diarrhea in the summary of findings table to avoid displaying too many outcomes in the table. Another reason was to avoid more than one outcome for the outcome measure of 'Diarrhea'. Also, incidence of diarrhea would capture most of the cases of severe diarrhea.
- Given a large number of excluded studies, we did not search all excluded study reference lists to identify additional studies.
- We changed the age subgroup analysis from, "children six months to under five years versus five years to 13 years" to "children six months to under one year, versus one to under five years, versus five years to under 13 years." We made this change because we thought that these age groups might have different physiologic needs and zinc might have a differential effect on outcomes in these age subgroups.
- We clarified the exclusion of mixed micronutrients. We added 'powder' as a category to the subgroup analysis for formulation so we could include studies that used zinc in the powder form. We still excluded the studies in which zinc was given with other multiple micronutrients in the form of powder or sprinkles.
- We included an additional comparison for 'zinc versus zinc plus iron' to evaluate the effect of providing zinc and iron simultaneously.
- We did not undertake a sensitivity analysis excluding studies from the primary analysis for risk of bias due to incomplete outcome data. Effects were more likely to be underestimated than overestimated as a result of dropout, so we considered the primary result to be a conservative estimate.
- We did not undertake the sensitivity analysis based on computation of intracluster correlation coefficient (ICC). This was because neither of the two studies for which ICCs were imputed reported any of the primary outcomes for this review.

Differences between the last version of the review and this version of the review

- We took height data in Dehbozorgi 2007 from Table 1 of the published manuscript. We think there is a typo in the table for height data in the zinc group between stages 1 to 3. The mean at the end of stage of 3 should be 6.26 rather than 2.26, as the same group gained about 4.25 and 2.41 cm in stage 1 to 2 and 2 to 3, respectively. We revised the data in this update (year 2022).
- There was a typo in the data for hemoglobin in Caulfield 2013. We corrected it in this version of the review.
- The summary of findings table in the last version of the review contained nine outcomes (Mayo-Wilson 2014). We reduced this to seven outcomes in this version per Cochrane policy.
- In the previous version of the review (Mayo-Wilson 2014), we entered the data for continuous outcomes in a way such that a summary effect of less than zero indicated an effect in favor of intervention and vice versa. We have switched this to a summary effect greater than 0 favoring the intervention in this version of the review. We did this based on feedback from readers who reported that it was confusing to see a negative sign with growth outcomes, for example, when the intervention increased weight and height.
- We reduced the number of excluded studies from the previous version per suggestions from the editors.
- We searched IndMed in the previous version but not the current version, because we could not access the website.
- SCOPUS became available to the review team, so we added it to the list of databases to search more comprehensively.
- We searched the Cochrane Database of Systematic Reviews in this update.
- We were unable to search the metaRegister of Controlled Trials for this update because the service has been discontinued.
- We were unable to search WHO Library & Information Networks for Knowledge Database (WHOLIS) because of repeated issues accessing the resource
- We were unable to search Global Health or PROQUEST Dissertations in this update as we did not have access to these databases. We did search Global Index Medicus, which, much like Global Health Library, has a public health literature focus.
- We were not able to use all of our preplanned methods. We direct the reader to Appendix 3 for the text describing these methods.
- One study, referred to as Cole 2012, in the last version of the review was unpublished. This study has now been published and is included in this version as Sampaio 2013.
- In the previous version of the review, Vakili 2015 was included as Vakili 2009. Vakili 2009 did not contribute any data but an additional report was available as Vakili 2015 and data were available for growth outcomes. We updated the reference to Vakili 2015 in this version of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Cause of Death; Child Mortality; Diarrhea [mortality]; Growth Disorders [*prevention & control]; Infant Mortality; Malaria [mortality]; Morbidity; Randomized Controlled Trials as Topic; Respiratory Tract Infections [mortality]; Trace Elements [*administration & dosage] [adverse effects]; Zinc [*administration & dosage] [adverse effects] [*deficiency]

MeSH check words

Child; Child, Preschool; Female; Humans; Infant; Male