Zinc Supplementation in Children Is Not Associated with Decreases in Hemoglobin Concentrations

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Abstract

Zinc supplementation has proven beneficial in the treatment of acute child diarrhea and appears to enhance linear growth. There is a theoretical risk of anemia in zinc-supplemented children due to inhibited iron transport via decreased copper absorption. Although many zinc supplementation trials have included hematological measures, the potential effect of zinc on these outcomes has not been quantitatively evaluated in a comprehensive review. We performed a systematic review of randomized trials that examined the effect of zinc supplementation on hemoglobin concentrations in apparently healthy children ages 0–15 y and conducted a random effects meta-analysis of weighted mean differences (WMD) of change in hemoglobin concentrations before and after supplementation. Twenty-one randomized, controlled trials representing 3869 participants were included in the meta-analysis. The duration of treatment ranged from 4 to 15 mo; doses were typically 10–20 mg/d. Zinc supplementation did not affect changes in hemoglobin concentrations (pooled WMD: 0.8 g/L; 95% CI: −0.6, 2.2; P = 0.27). There was no evidence for effect modification by age, zinc dosage, duration of treatment, type of control, baseline hemoglobin status, geographical or healthcare setting, or quality of the studies. These results suggest that zinc supplementation at doses typically used in randomized trials is a safe intervention with regards to hemoglobin concentrations. Some benefits might exist among children with severe anemia or zinc deficiency, which warrant further evaluation.

Introduction

Zinc supplementation has been recently recommended as part of the clinical management of acute child diarrhea by prominent international agencies (1). In addition, zinc supplementation appears to be beneficial to other important child health outcomes, including linear growth. Although supplementation is considered to be a relatively safe intervention (2), there is a theoretical risk of anemia in children receiving very high doses of zinc for long periods due to decreases in circulating lipoproteins and diminished copper absorption that inhibits iron transportation (3–5). Many clinical trials of zinc supplementation have included measurements of hematological indicators as endpoints. In a qualitative review of trials published until 2004 (6) and in a meta-analyses limited to 11 clinical trials (7), an adverse effect of zinc supplementation on iron status was not apparent. However, a comprehensive quantitative analysis of all trials reporting the effect of zinc supplementation on hemoglobin concentrations is lacking. In addition, it is unclear whether zinc supplementation could have hematological effects in children with highly increased zinc requirements due to underlying conditions.

We conducted a systematic review and meta-analysis of randomized trials that evaluated the effect of zinc supplementation on hemoglobin concentrations among apparently healthy children. We identified trials published until 2009 in which the interventions provided to the treatment and control groups differed only in the inclusion of zinc.

Methods

Literature search and study identification. The studies considered for possible inclusion in the current meta-analysis were identified through searches in MEDLINE (National Library of Medicine, Bethesda, MD), a computerized bibliographic database spanning the years 1966 to present. The searches were completed on May 14th 2009. In an initial search, all articles that included the key word “zinc” and the words “supplement, supplementation, supplements, or supplemental” were identified. Any clinical trials in which hemoglobin was included as an endpoint were preliminarily selected for evaluation. Next, we conducted a search for all articles that contained the key words hemoglobin or anemia, and merged it with the initial search. Articles were then examined for inclusion or exclusion. Following a similar strategy, we repeated the search using EMBASE (Elsevier, Amsterdam, The Netherlands), and the Cochrane Central Register of Controlled Trials (Wiley InterScience, Hoboken, NJ). The search was limited to humans, but not to the English language. A total of 152 nonoverlapping articles were identified in these databases. To minimize possible publication bias, searches were also conducted on...
distribution of the overall effect size is the sum of each study's true effect difference (WMD) for each study. Weights represent the inverse of the estimated from a random effects model that used the weighted mean of the trials. The overall mean effect of zinc on hemoglobin was then intervention and control groups at baseline, given the randomized nature provided, the effect size was calculated by using postintervention period) divided by their pooled SD. If change in means or SD were not baseline (usually immediately prior to the beginning of supplementation) for studies that had different sample sizes at the beginning and at the end of the intervention, the smallest value was assumed to represent the isolated factor in 1 of the treatment arms compared with the control group, studies conducted in other age groups, and studies that lacked sufficient data on hemoglobin concentrations to calculate the effect size. For the primary aim of examining the effect of zinc on hemoglobin among apparently healthy children (studies not specifically conducted among children with anemia, severe malnutrition, and/or infections), we also included studies among children with diseases including sickle cell disease, malaria, or HIV infections, severe energy-protein malnutrition, or studies that were explicitly done among children with anemia. Complete citations (titles and abstracts) with the appropriate search terms were reviewed to identify the studies that were most likely to meet the inclusion criteria. Manuscripts were then read in full to ensure that they met the criteria.

Data extraction and statistical analyses. Two reviewers independently assessed the suitability of each study for inclusion in the meta-analysis and discrepancies were resolved by consensus after discussion. The primary outcome in this analysis was the difference of change in hemoglobin concentrations before and after supplementation between the zinc and control groups. From each study that met the criteria for inclusion, we extracted information pertaining to the year of the study, study population, geographic location of the study, methods used to measure hemoglobin concentrations, age range of participating children, duration of follow-up, number of participants in each group, the dose of zinc used, the baseline and final hemoglobin values, loss to follow-up rates, and baseline and final serum zinc concentrations. Study quality was assessed using the Jadad level-of-evidence score for randomized controlled trials (8). Scoring is performed on a scale from 0 to 5, in which 1 point is respectively assigned to randomization, blinding, and reporting of participant withdrawals. Two additional points are given for a description of randomization and double-blinding methods.

When several doses of zinc were used in the same study, only the arm with the highest amount of zinc was included, because the highest dose would be most likely to have a hematological effect. If the study used a factorial design in which zinc was given either alone or with some other micronutrient or nutrients, we included the zinc-only and control arms. For studies that had different sample sizes at the beginning and at the end of the intervention, the smallest value was assumed to represent the sample size for change in hemoglobin.

For each study, the effect size was calculated as the treatment group difference between the changes in mean hemoglobin concentrations from baseline (usually immediately prior to the beginning of supplementation) to the end of follow-up (typically at the end of the supplementation period) divided by their pooled SD. If change in means or SD were not provided, the effect size was calculated by using postintervention concentrations, assuming that there were no differences between the intervention and control groups at baseline, given the randomized nature of the trials. The overall mean effect of zinc on hemoglobin was then estimated from a random effects model that used the weighted mean difference (WMD) for each study. Weights represent the inverse of the within-study variance. The random effects model assumes that the distribution of the overall effect size is the sum of each study’s true effect size, which is assumed to follow a normal distribution. Each intercept is the result of a random deviation from an overall mean intercept, independent of the error for a particular observation. Because the total variance of each study effect size varies between studies, the best estimate for the overall mean is a weighted mean effect size, in which the weights are equal to the inverse of the total variance (9).

To test the effect of using postintervention concentrations for those studies that did not report mean changes in hemoglobin concentration and the SD for change, we performed a sensitivity analysis by calculating the mean change in hemoglobin concentration and the SD for change, assuming that the correlation between pre- and post-test variances was equal to the correlation from studies where the SD for change was available.

We determined the presence of outliers by assessing whether studies’ effect sizes were 3–5 times as large as the next largest effect size. Weighted mean effect sizes were calculated with and without outliers. We assessed heterogeneity between the studies by using the chi-square test, as described by Hedges and Pigott (10). In addition, the I² was estimated to evaluate the proportion of any heterogeneity due to between-study variation. On evidence of heterogeneity (P < 0.1), we assessed the role of predefined variables, including mean baseline age of children (<12 or ≥12 mo), baseline hemoglobin concentrations (<110 or ≥110 g/L; only for those trials that reported baseline hemoglobin concentrations), duration of the intervention (≥6 or >6 mo), the use of a placebo or other type of control group, geographical setting, and quality of the trial, with the use of meta-regression models (11).

Analyses were carried out with using the METAN (12,13) and METAINFO (14) routines for meta-analysis of STATA software, version 10.0 (StataCorp).

Results

Description of studies and study participants. Twenty papers were included in the meta-analysis representing 21 randomized controlled trials (Fig. 1). One study (15) consisted of a trial conducted at 2 different locations [referred to as Bates (15-A) and Bates (15-B)] whose results were reported separately. All studies were conducted between 1993 and 2008 (Table 1). The pooled number of participants was 3869 (range = 53–638). The duration of follow-up ranged from 4 to 15 mo and zinc supplements were provided as 10 or 20 mg/d in most of the studies. Eight studies were conducted in Latin America, 3 in Africa, and 10 in Asia. The baseline age of participating children ranged from 4 to 180 mo. Most studies (n = 12) provided the zinc supplements in the form of zinc sulfate (16–27), 4 studies

![FIGURE 1 Study identification process and reasons for exclusion from the meta-analysis.](image-url)
<table>
<thead>
<tr>
<th>Lead author (citation)</th>
<th>Year</th>
<th>Country</th>
<th>n(^1)</th>
<th>Zinc dose</th>
<th>Control</th>
<th>Male(^2)</th>
<th>Age at baseline</th>
<th>Trial duration</th>
<th>Baseline zinc concentration</th>
<th>Follow-up zinc concentration or change</th>
<th>Baseline hemoglobin concentration</th>
<th>Effect size (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Bates (15)</td>
<td>1993</td>
<td>Gambia</td>
<td>93</td>
<td>20(^1)</td>
<td>Placebo</td>
<td>43.6(^4)</td>
<td>14</td>
<td>15</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bates (15)</td>
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<td>Gambia</td>
<td>105</td>
<td>20(^1)</td>
<td>Placebo</td>
<td>43.6(^4)</td>
<td>6</td>
<td>15</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.0 (6.6, 6.8)</td>
</tr>
<tr>
<td>Ruz (25)</td>
<td>1997</td>
<td>Chile</td>
<td>74</td>
<td>10</td>
<td>Placebo</td>
<td>42.5</td>
<td>39.8</td>
<td>14</td>
<td>17.7</td>
<td>17.2</td>
<td>17.6</td>
<td>1.6 (38.7, 40.7)</td>
</tr>
<tr>
<td>Munoz (31)</td>
<td>2000</td>
<td>Mexico</td>
<td>99</td>
<td>20</td>
<td>Placebo</td>
<td>50.0</td>
<td>28.4</td>
<td>6</td>
<td>13.2</td>
<td>14.2</td>
<td>16.8</td>
<td>0.0 (5.8, 5.8)</td>
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<tr>
<td>Dijkhuizen (22)</td>
<td>2001</td>
<td>Indonesia</td>
<td>184</td>
<td>10</td>
<td>Placebo</td>
<td>59.7</td>
<td>4.2</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>16.1</td>
<td>13.0 (3.2, 3.2)</td>
</tr>
<tr>
<td>Lind (23)</td>
<td>2003</td>
<td>Indonesia</td>
<td>277</td>
<td>10</td>
<td>Placebo</td>
<td>44.0</td>
<td>6.1</td>
<td>6</td>
<td>9.1</td>
<td>9.0</td>
<td>11.6</td>
<td>1.0 (15, 5.9)</td>
</tr>
<tr>
<td>Wieringa (27)</td>
<td>2003</td>
<td>Indonesia</td>
<td>91</td>
<td>10</td>
<td>Placebo</td>
<td>53.2</td>
<td>4.2</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Penny (28)</td>
<td>2004</td>
<td>Peru</td>
<td>100</td>
<td>20</td>
<td>Placebo</td>
<td>38.0</td>
<td>19.3</td>
<td>6</td>
<td>10.8</td>
<td>10.7</td>
<td>4.2(^8)</td>
<td>0.9(^8)</td>
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<tr>
<td>Sazawal (29)</td>
<td>2004</td>
<td>India</td>
<td>115</td>
<td>10</td>
<td>Multi vitamins without zinc</td>
<td>49.2</td>
<td>8.5</td>
<td>4</td>
<td>10.0</td>
<td>9.6</td>
<td>14.2</td>
<td>9.3</td>
</tr>
<tr>
<td>Baqui (34)</td>
<td>2005</td>
<td>Bangladesh</td>
<td>124</td>
<td>2.9(^9)</td>
<td>Riboflavin</td>
<td>46.5</td>
<td>6.4</td>
<td>6</td>
<td>10.8</td>
<td>9.9</td>
<td>1.3(^9)</td>
<td>0.6(^9)</td>
</tr>
<tr>
<td>Brooks (30)</td>
<td>2006</td>
<td>Bangladesh</td>
<td>638</td>
<td>10(^10)</td>
<td>Placebo</td>
<td>55.0</td>
<td>5.3</td>
<td>10</td>
<td>9.9</td>
<td>9.7</td>
<td>11.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Olney (33)</td>
<td>2006</td>
<td>Zanzibar</td>
<td>102</td>
<td>10</td>
<td>Placebo</td>
<td>47.2</td>
<td>9.0</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>91</td>
</tr>
<tr>
<td>Silva (26)</td>
<td>2006</td>
<td>Brazil</td>
<td>58</td>
<td>10</td>
<td>Placebo</td>
<td>43.1</td>
<td>23.5</td>
<td>4</td>
<td>9.3</td>
<td>7.9</td>
<td>13.4</td>
<td>8.0</td>
</tr>
<tr>
<td>Rosado (32)</td>
<td>2006</td>
<td>Mexico</td>
<td>252</td>
<td>30</td>
<td>Placebo</td>
<td>57.3</td>
<td>72–84(^11)</td>
<td>6</td>
<td>12.5</td>
<td>12.5</td>
<td>13.8</td>
<td>10.4 (1.6, 1.8)</td>
</tr>
<tr>
<td>Richard (24)</td>
<td>2006</td>
<td>Peru</td>
<td>380</td>
<td>20</td>
<td>Placebo</td>
<td>43.6</td>
<td>6–180(^11)</td>
<td>7</td>
<td>10.8</td>
<td>10.7</td>
<td>13.8</td>
<td>10.4 (1.6, 1.8)</td>
</tr>
<tr>
<td>Berger (21)</td>
<td>2006</td>
<td>Vietnam</td>
<td>386</td>
<td>10</td>
<td>Placebo</td>
<td>49.7</td>
<td>5.9</td>
<td>6</td>
<td>14.4</td>
<td>14.6</td>
<td>23.1</td>
<td>15.8 (3.7, 2.7)</td>
</tr>
<tr>
<td>Wasonwisut (20)</td>
<td>2006</td>
<td>Thailand</td>
<td>124</td>
<td>10</td>
<td>Placebo</td>
<td>51.0</td>
<td>4.5</td>
<td>6</td>
<td>11.5</td>
<td>11.1</td>
<td>16.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Brown (19)</td>
<td>2007</td>
<td>Peru</td>
<td>144</td>
<td>3</td>
<td>Iron-fortified porridge</td>
<td>48.5</td>
<td>7.6</td>
<td>6</td>
<td>11.7</td>
<td>12.0</td>
<td>0.7(^9)</td>
<td>—(^6)</td>
</tr>
<tr>
<td>Fallahi (18)</td>
<td>2007</td>
<td>Iran</td>
<td>53</td>
<td>20</td>
<td>Iron</td>
<td>38.0</td>
<td>134</td>
<td>4</td>
<td>9.7</td>
<td>9.9</td>
<td>4.5(^9)</td>
<td>3.6(^9)</td>
</tr>
<tr>
<td>Hettiarachchi (17)</td>
<td>2008</td>
<td>Sri Lanka</td>
<td>382</td>
<td>14</td>
<td>Placebo</td>
<td>40.4</td>
<td>159</td>
<td>6</td>
<td>7.3</td>
<td>10.2</td>
<td>12.0</td>
<td>10.8 (2.3, 9.8)</td>
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<tr>
<td>Wachler (16)</td>
<td>2008</td>
<td>Ecuador</td>
<td>88</td>
<td>10</td>
<td>Placebo</td>
<td>53.2</td>
<td>20.8</td>
<td>6</td>
<td>10.8</td>
<td>10.6</td>
<td>3.2(^8)</td>
<td>0.0(^8)</td>
</tr>
</tbody>
</table>

1. Includes participants in the treatment groups used in the meta-analysis only, who did not have missing values of hemoglobin at follow-up. When ranges of participants with missing values were reported (16,19,28), the smallest sample sizes were selected.

2. In the intervention group at baseline.

3. 70 mg twice/wk.

4. In the 2 sites combined.

5. Baseline hemoglobin values not reported. Follow-up hemoglobin concentrations were used to calculate the effect size, assuming that there were no differences between the intervention and control groups at baseline, given the randomized nature of the trials.

6. Baseline hemoglobin values not reported. Follow-up hemoglobin concentrations were used to calculate the effect size, assuming that there were no differences between the intervention and control groups at baseline, given the randomized nature of the trials.

7. Reported baseline and follow-up hemoglobin concentrations but not SD for change. Follow-up hemoglobin concentrations were used to calculate the effect size, assuming that there were no differences between the intervention and control groups at baseline, given the randomized nature of the trials.

8. Reported mean and SD for change in hemoglobin concentrations from baseline to follow-up in zinc and control groups.

9. Change in zinc concentrations from baseline.

10. 20 mg/wk.

11. 70 mg/wk.

12. Range.
used zinc gluconate (15,28,29), 2 studies used zinc acetate (30,34), 1 study used zinc methionine (31), 1 study used zinc oxide (32), and 1 study did not explicitly report in which form they provided zinc (33). Most studies used a placebo as control. Ten studies (16,18–20,26,28,31–34) reported the mean change in hemoglobin levels and a SD for change in each treatment group. Follow-up mean values of hemoglobin and their SD were used for the other 11 studies (15,17,21–25,27,29,30) (Table 1). Of those 11 studies, 5 did not report baseline hemoglobin concentrations (15,22,27,29). Although we aimed to include only studies conducted among apparently healthy children, in 7 trials, mean baseline hemoglobin concentrations were <110 g/L (19,21,28,30,31,33,34).

**Effect of zinc supplementation on change in hemoglobin concentrations.** The pooled WMD was 0.8 g/L (95% CI: −0.6, 2.2; P = 0.27) (Fig. 2). In this model, there was no evidence for influential studies: weights ranged from 0.1 to 7.8%. However, the trials by Olney et al. (33) and Hettiarachchi et al. (17) were considered as outliers, because their effect sizes were 3–5 times as large as the next largest effect size. After exclusion of those 2 studies from the analysis, the WMD was −0.2 g/L (95% CI: −0.9, 0.5; P = 0.59) and there was no evidence of heterogeneity between studies (I² = 0%; P = 0.60).

We next performed sensitivity analysis to examine the effect of using postintervention values for studies that did not report mean changes in hemoglobin concentration and the SD for change. These analyses included 14 trials that reported mean hemoglobin values at baseline and follow-up, after excluding the 2 outliers (16,18–21,23–26,28,30–32,34). We calculated the SD for change, assuming that the correlation between pre- and post-intervention values was equal to the correlation from studies where change was reported. The pooled WMD using this method was 0.4 g/L (95% CI: −0.4, 1.3; P = 0.33) and there was no evidence of heterogeneity across the studies.

- **Discussion**

We conducted a quantitative analysis of the effect of zinc supplements on children’s hemoglobin concentrations, based on a comprehensive, systematic review of the literature. Our results confirm that there is no consistent evidence for an adverse effect of zinc supplementation on hemoglobin among apparently healthy children. Compared with control groups, zinc supplementation resulted in a nonstatistically significant pooled effect on hemoglobin concentration of 0.8 g/L, which is unlikely to have clinical relevance. Likewise, there was no evidence for an effect of zinc on hemoglobin within the subgroup of children with high zinc requirements for zinc due to high underlying prevalence of diarrheal, malarial, or other infections.

These results need to be interpreted in light of some considerations. First, treatment effects independent of baseline hemoglobin differences between groups (i.e., effects on hemoglobin change over time) were only reported in a minority of the trials meta-analyzed. Thus, the pooled estimate of effect is partially based on follow-up values. These values may not represent the true effect of zinc, because there were differences in baseline hemoglobin concentrations between treatment arms in some trials (17,20,26). Second, although the exclusion of 2 outliers did not substantially change the conclusions of the meta-analysis, it is noteworthy that both of these trials were conducted in populations with high rates of zinc deficiency and/or anemia and both suggest a large positive effect of zinc supplementation on hemoglobin concentrations. Similarly, 1 study conducted among anemic children reported a positive effect of zinc on hemoglobin (35). It is therefore possible that zinc supplements may provide hematological benefits in populations that are severely zinc deficient or that have increased requirements for zinc due to high underlying prevalence of diarrheal, malarial, or other infections. Third, there may be a possibility for publication bias if the report of results on hemoglobin was related to the effect of zinc.

Zinc supplementation did not result in adverse effects on hemoglobin concentrations in this meta-analysis. Zinc toxicity...
(nausea, vomiting) can occur with very high doses, and sideroblastic anemia due to zinc-induced copper deficiency has been documented with doses around 300–600 mg/d in adults (7.5–15 times the tolerable upper intake level) (4). A 13-mo-old child whose daily intake ranged from 120 to 180 mg/d (17–26 mg/d; 7.5–15 times the tolerable upper intake level) (4). A 13-mo-old child whose daily intake ranged from 120 to 180 mg/d (17–26 times the upper intake level of 7 mg/d) was also reported to have sideroblastic anemia (5). However, those doses are much higher than doses typically used in supplementation studies (≤20 mg/d) and the range of zinc doses presented in this meta-analysis. In addition, short-term zinc supplementation, as in the treatment of diarrhea, is unlikely to be prolonged enough to have any hematological consequences.

In summary, our results suggest that zinc supplementation does not appear to affect hemoglobin concentrations among apparently healthy children. Despite the lack of an effect on hemoglobin concentrations, zinc supplementation has proven beneficial to other relevant child health outcomes, including diarrheal diseases (45) and linear growth (46), and is an important public health tool. The hematological benefits of zinc supplementation among children with increased zinc requirements deserve further investigation.

Acknowledgments

L.H.D. conducted the literature search, data extraction, data analyses, and wrote the first draft of the manuscript. E.V. proposed the meta-analysis, contributed to literature review and interpretation of results, and critically reviewed the manuscript. Both authors read and approved the final manuscript.

Literature Cited

17. Hettiarachchi M, Liyanage C, Wickremasinghe R, Hilmers DC, Abrams SA. The efficacy of micronutrient supplementation in reducing the preva-

TABLE 2 Characteristics of randomized controlled trials of zinc supplementation and hemoglobin concentrations among children with underlying illnesses or malnutrition

<table>
<thead>
<tr>
<th>Lead author (citation)</th>
<th>Underlying condition</th>
<th>Country</th>
<th>n</th>
<th>Zinc dose</th>
<th>Age range</th>
<th>Trial duration</th>
<th>Baseline hemoglobin concentration</th>
<th>Change in hemoglobin concentration</th>
<th>Zinc</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alarcon (35)</td>
<td>Anemic</td>
<td>Peru</td>
<td>213</td>
<td>3/8 kg</td>
<td>6–35 mo</td>
<td>4 mo</td>
<td>95</td>
<td>95</td>
<td>FeZn 24</td>
<td>Fe 20</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Zlotkin (44)</td>
<td>Anemic</td>
<td>Ghana</td>
<td>239</td>
<td>10</td>
<td>6–18 mo</td>
<td>2 mo</td>
<td>87</td>
<td>87</td>
<td>FeZn 104</td>
<td>Fe 108</td>
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</tr>
<tr>
<td>Fahmida (37)</td>
<td>Anemic and stunted</td>
<td>Indonesia</td>
<td>303</td>
<td>10</td>
<td>3–6 mo</td>
<td>6 mo</td>
<td>97</td>
<td>96</td>
<td>Zn –6</td>
<td>Placebo –5</td>
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<tr>
<td>Zeba (43)</td>
<td>Malaria</td>
<td>Burkina Faso</td>
<td>148</td>
<td>10</td>
<td>6–72 mo</td>
<td>6 mo</td>
<td>93</td>
<td>94</td>
<td>Zn 101</td>
<td>Placebo 102</td>
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<td>The Zinc Against</td>
<td>Malaria</td>
<td>Ecuador, Ghana, Tanzania, Uganda, Zambia</td>
<td>927</td>
<td>40 (20 if &lt;12 mo)</td>
<td>6–60 mo</td>
<td>4 d</td>
<td>92</td>
<td>93</td>
<td>Zn 9</td>
<td>Placebo 8</td>
<td>&lt;0.05</td>
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<tr>
<td>Plasmodium Study Group (42)</td>
<td>Anemic and stunted</td>
<td>3 mo</td>
<td>95</td>
<td>95</td>
<td>FeZn 24</td>
<td>Fe 20</td>
<td>&lt;0.05</td>
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</tr>
<tr>
<td>Shankar (41)</td>
<td>Anemic</td>
<td>Papua New Guinea</td>
<td>212</td>
<td>10</td>
<td>6–60 mo</td>
<td>10 mo</td>
<td>104</td>
<td>105</td>
<td>Zn 86</td>
<td>Placebo 87</td>
<td>0.4</td>
</tr>
<tr>
<td>Bobat (36)</td>
<td>HIV-1</td>
<td>South Africa</td>
<td>85</td>
<td>10</td>
<td>6–60 mo</td>
<td>6 mo</td>
<td>98</td>
<td>103</td>
<td>Zn 0</td>
<td>Placebo 4</td>
<td>0.2</td>
</tr>
<tr>
<td>Penny (40)</td>
<td>Diarrhea</td>
<td>Peru</td>
<td>276</td>
<td>20</td>
<td>6–36 mo</td>
<td>15 d</td>
<td>102</td>
<td>101</td>
<td>Zn 0</td>
<td>Placebo 2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Makonnen (39)</td>
<td>Protein-energy</td>
<td>Lesotho</td>
<td>300</td>
<td>10</td>
<td>6–60 mo</td>
<td>3 mo</td>
<td>92</td>
<td>91</td>
<td>Zn 104</td>
<td>Placebo 98</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mahloudji (38)</td>
<td>Zinc deficient</td>
<td>Iran</td>
<td>40</td>
<td>20</td>
<td>6–144 mo</td>
<td>3 mo</td>
<td>130</td>
<td>134</td>
<td>FeZn 143</td>
<td>Fe 138</td>
<td>&lt;0.05</td>
</tr>
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</tr>
</tbody>
</table>

1 Unless noted otherwise.
2 Follow-up hemoglobin concentrations.
3 All children received 200,000 IU (60 mg) vitamin A.
4 At d 28.


