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ARTICLE

Role of Zinc Administration in Prevention of Childhood Diarrhea and Respiratory Illnesses: A Meta-analysis

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ABSTRACT

BACKGROUND. The quantified effect of zinc supplementation to prevent childhood diarrhea and respiratory illnesses is unclear. We conducted a meta-analysis of randomized, controlled trials on the subject.

METHODS. We searched PubMed, Science Citation Index, and the Cochrane Database of Controlled Trials and hand-searched the reference lists of identified articles. All randomized, controlled trials of zinc supplementation for ≥3 months for children <5 years of age, using blinded assessment, were eligible. The outcome measures studied were number of episodes of illness, number of days with illness, and number of episodes of severe illness. Data from 17 studies were pooled by using random-effects and fixed-effects models for data with and without significant heterogeneity, respectively.

RESULTS. Children who received a zinc supplement had fewer episodes of diarrhea (rate ratio: 0.86) and respiratory tract infections (rate ratio: 0.92) and significantly fewer attacks of severe diarrhea or dysentery (rate ratio: 0.85), persistent diarrhea (rate ratio: 0.75), and lower respiratory tract infection or pneumonia (rate ratio: 0.80) than did those who received placebo. They also had significantly fewer total days with diarrhea (rate ratio: 0.86) but not days with respiratory illness (rate ratio: 0.95). Published studies showed a publication bias and significant heterogeneity; however, no cause for the latter could be identified.

CONCLUSIONS. Zinc supplementation reduced significantly the frequency and severity of diarrhea and respiratory illnesses and the duration of diarrheal morbidity. The relatively limited reduction in morbidity and the presence of significant heterogeneity and of publication bias indicate the need for larger, high-quality studies to identify subpopulations most likely to benefit.

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Key Words
diarrhea, respiratory illness, meta-analysis, nutrition, supplementation, zinc

Abbreviations
CI—confidence interval
RR—rate ratio

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Zinc is a vital micronutrient in humans and is essential for protein synthesis, cell growth, and differentiation.[1,2] Severe zinc deficiency has been shown to be associated with stunting of growth, hypogonadism, impaired immune function, skin disorders, cognitive dysfunction, and anorexia.[2,3]

Dietary deficiency of zinc is common in several parts of the world, particularly developing countries. This deficiency may arise either from inadequate intake of foods that contain zinc (mainly foods of animal origin) or from inadequate absorption caused by its binding to dietary fiber and phytates, which are commonly found in cereals, nuts, and legumes.[4] Inadequate absorption of zinc may also result from mucosal abnormalities and compromised gut integrity induced by persistent diarrhea attributable to gastrointestinal infections.[5]

Numerous studies have examined the association between childhood morbidity and zinc deficiency.[1,6–9] Those studies suggest that zinc-deficient populations are at increased risk of developing diarrheal diseases, respiratory tract infections, and growth retardation. Using the available data, Caulfield and Black[10] estimated that zinc deficiency is associated with nearly 800 000 excess deaths annually among children <5 years of age throughout the world, including deaths attributable to diarrhea (176 000), pneumonia (406 000), and malaria (207 000). Furthermore, they attributed a global loss of nearly 28 million disability-adjusted life years to zinc deficiency.

Zinc administration has been studied as a tool for the treatment and prevention of diarrhea, respiratory tract infections, pneumonia, acute lower respiratory tract infections, and malaria among children.[11–18] A meta-analysis showed that addition of zinc to the treatment regimen for children with diarrhea led to reductions in the duration of diarrhea and in the frequency of persistent diarrhea, defined as diarrhea lasting >14 days.[19]

Those studies led to the use of zinc supplementation among children in attempts to treat and to prevent common childhood infections. A few studies also examined the effects of zinc supplementation on growth parameters.[20–25] A meta-analysis published in 1999 showed that continuous zinc supplementation was associated with decreased rates of childhood diarrhea and pneumonia.[26] Since then, additional studies that were larger in size and scope than those included in the meta-analysis have been published. Furthermore, the previous meta-analysis included studies with supplementation for periods as short as 2 weeks. Supplementation programs are likely to be provided to children for longer periods (at least a few months). Therefore, we thought that the subject merited reexamination, and we conducted a meta-analysis of studies that examined the efficacy of zinc supplementation lasting ≥3 months in preventing diarrhea and respiratory illnesses among children.

METHODS

Search Protocol and Study Review

To identify studies that examined the effect of zinc supplementation on the occurrence of diarrhea or respiratory tract infections, PubMed, Science Citation Index, and the Cochrane Central Database of Controlled Trials were searched by using the following keywords: "zinc," "supplement," and "diarrhea" or "respiratory illness" or "pneumonia." The searches captured studies published up to November 2005. Two independent reviewers reviewed the search results to identify relevant original human clinical or field trials. Studies that focused on the effects of zinc administration for the treatment of acute or persistent diarrhea or respiratory illnesses were excluded from the analysis. However, studies that enrolled children who had recently recovered from a diarrheal illness and were being observed for subsequent recurrent diarrheal episodes were deemed eligible for inclusion in the meta-analysis. Studies with zinc supplementation for periods of <3 months were excluded. Additional studies were identified through manual searches of reference lists of the originally identified studies on the therapeutic and preventive roles of zinc, as well as reviews on the subject.

All identified studies were reviewed independently by 2 authors (Dr Aggarwal and Mr Sentz), to determine whether they fulfilled the minimal quality criteria, including (1) random allocation of placebo and active interventions, (2) double-blinded assessment of outcomes, and (3) ≥90% follow-up rates. Furthermore, the reviewers identified the parameters for which data were available in the reports, for use in designing a data extraction form. The reviewers extracted data from each of the selected studies independently; any inter-reviewer differences were resolved through a joint review of the article.

Statistical Methods

From the selected studies, data on the number of episodes of diarrhea and respiratory illnesses in the groups receiving zinc supplementation and placebo were extracted. When such data were not provided explicitly, they were calculated by multiplying the mean numbers of episodes of these illnesses per child by the total number of study subjects in each group. From the number of disease episodes and the duration of follow-up monitoring for the supplementation and placebo groups, adjusted rate ratios (RRs) were calculated for each study. In addition, data on rates of severe forms of diseases of interest (eg, persistent diarrhea lasting ≥14 days, severe diarrhea [based on investigator-defined criteria], lower respiratory tract infection, or pneumonia) were retrieved when available.

Statistical analyses and meta-analyses were performed by using Review Manager 4.2.8 software (Nordic

Cochrane Centre, Copenhagen, Denmark). SEs for logarithms of RRs were calculated by using standard statistical methods. Data from different studies were pooled by using a generic inverse variance method, and a pooled RR, SE, and 95% confidence interval (CI) were calculated for each parameter. For each parameter, heterogeneity between studies was tested by using the χ^2 statistic with its degrees of freedom; in addition, the I^2 statistic, measuring the extent of inconsistency of results between various studies, was calculated. Significant heterogeneity was considered to be present if the P value was below .10. Where there was no significant heterogeneity ($P \geq .10$), a fixed-effects model was used for pooling of data from various studies; in cases with significant heterogeneity ($P < .10$), a random-effects model was used to provide a more-conservative estimate of effect. In the latter cases, the data were also analyzed by using subgroup analyses, to assess possible causes of heterogeneity.

Publication bias was examined by using "funnel plot" analysis and was quantified by using the rank correlation method described by Begg and Mazumdar[27] and the regression intercept method described by Egger et al,[28] with P values of $<.10$ being taken as significant. In addition, the trim and fill method described by Duval and Tweedie[29,30] was used to impute missing studies and to recompute the combined effect by adding those missing studies.

RESULTS

Identification of Studies

Table 1 lists the clinical or field trials that were identified in our literature search as having evaluated the role of zinc in the prevention of diarrhea or respiratory illnesses.[15,16,23,24,31–43] Four additional studies[21,22,25,44] that examined the preventive effects of zinc supplementation on these illnesses were excluded for various reasons. Of those, one study was excluded because the assignment of study subjects to zinc or placebo groups was nonrandom.[22] One study was considered ineligible because it studied morbidity outcomes among newborn infants whose mothers had received zinc supplements during pregnancy.[44] A study conducted in Brazil included 2 separate zinc supplementation groups (1 and 5 mg/day); allocation to the latter group was neither random nor concurrent with that to the placebo group, making the group ineligible for the meta-analysis.[21] Data from the other zinc supplementation arm of the study (1 mg/day) had to be excluded because the published data did not permit extraction of the parameters that were used in our analysis. Finally, in one study,[25] zinc and "psychosocial stimulation," an intervention aimed at improving mother-child interaction, were used in a factorial study design, with allocations to the interventions performed in a random manner and a nonrandom manner, respec-

TABLE 1 **Randomized, Placebo-Controlled Studies on the Use of Zinc in the Prevention of Diarrhea, Respiratory Illness, or Both**

Country	No. of Children		Age Group	Criteria for Inclusion of Children in Study	Zinc Dose and Compound Used	Frequency and Duration of Zinc Administration
	Zinc Group	Placebo Group				
Bangladesh[15]	161	157	6 mo	Good general health	20 mg, zinc acetate; riboflavin (1 mg/wk) for both groups	Weekly for 6 mo
Bangladesh[16]	706	768	60 d to 12 mo	Good general health	70 mg, zinc acetate	Weekly for 12 mo
Bangladesh[31]	138	132	4 ± 1 wk	Good general health, had not received vaccines	5 mg, zinc acetate	Daily until 24 wk of age
Burkina Faso[41]	341	344	6–31 mo		12.5 mg, zinc sulfate	Daily for 6 mo
Ethiopia[32]	92	92	6–12 mo	2 subgroups, stunted and not stunted	10 mg, zinc sulfate	6 d/wk for 6 mo
Gambia[33]	55	55	7–28 mo	No long-term illness	70 mg, zinc acetate or gluconate, in fruit drink	Twice weekly for 15 mo
Guatemala[34]	45	44	6–9 mo		10 mg, zinc sulfate	Daily for average of 7 mo
India[38]	286	293	6–35 mo	Recovered from persistent diarrhea (>7 d)	10 mg, zinc gluconate; vitamins for both groups	Daily for 6 mo
India[42]	297	306	6–35 mo	Recovered from persistent diarrhea (>7 d)	10 mg, zinc gluconate; vitamins for both groups	Daily for 6 mo
India[35,43]	1093	1133	6–30 mo	Had not received vitamin A in previous 2 wk	10 mg (infants) or 20 mg (older children), zinc gluconate	6 d/wk for 4 mo
India[36]	(1) 95; (2) 91	94	6–41 mo		(1) 10 mg daily, zinc sulfate; (2) 50 mg weekly, zinc sulfate	(1) 5 d/wk for 16 wk; (2) weekly for 16 wk
India[37]	50	50	<1 y	No major birth defects, low birth weight (<2500 g)	3 mg (<3 mo of age) or 5 mg (>3 mo of age), zinc sulfate; vitamin B syrup for both groups	5 d/wk for 1 y
Indonesia[24]	162	164	6–12 mo	Healthy	10 mg, zinc sulfate	Daily for 6 mo
Vietnam[23]	73	73	4–36 mo	Growth retarded	10 mg, zinc sulfate	Daily for 5 mo
Mexico[39]	54	56	18–36 mo	Healthy	20 mg, zinc methionine	5 d/wk for 12 mo
Peru[40]	81	79	6–36 mo	Recovered from persistent diarrhea	10 mg, zinc gluconate; vitamins and minerals for both groups	Daily for 6 mo

TABLE 2 **Studies Identified During the Initial Search But Excluded Later, With Reasons for Exclusion**

Study	Reasons for Exclusion
Castillo-Duran et al[20]	Zinc supplementation period too short (60 d); did not study effects on diarrhea or respiratory illnesses
Sempertegui et al[48]	Zinc supplementation period too short (60 d)
Roy et al[46]	Zinc supplementation period too short (2 wk)
Rahman et al[45]	Zinc supplementation period too short (2 wk); factorial design with 4 groups receiving (1) placebo, (2) zinc alone, (3) vitamin A alone, or (4) zinc and vitamin A and study data not permitting assessment of the effect of zinc alone
Baqui et al[47]	Zinc supplementation period too short (2 wk)

tively. That study had to be excluded because the published report did not allow extraction of data for groups that received zinc or placebo without psychosocial stimulation. Also, the data were presented as group medians, which precluded calculation of total numbers of illness episodes.

A total of 17 studies[15,16,23,24,31–42] were included in the meta-analysis. Of those, one study[36] had 2 intervention arms, with differing frequencies (daily or weekly) of zinc supplement administration; for analysis, each of the treatment arms was considered a separate study. The subsequent text refers to those as independent studies. Two published studies reported on the same population separately for diarrheal and respiratory morbidity outcomes.[35,43] Data from the 17 studies were analyzed and included 3819 children who received zinc supplementation and 3840 children who received placebo. Table 2 lists some of the other excluded studies, with reasons for their exclusion.[20,45–48]

Prevention of Diarrhea

Of the 17 eligible studies, 15 provided data on the number of episodes of diarrhea among groups that received a zinc supplement or a matched placebo.[15,16,23,24,31–40] Figure 1 shows the results of the meta-analysis for the incidence of diarrhea among children who received zinc supplements or a matched placebo. Of the 15 studies, 3 had RRs of >1.0 and 12 RRs of <1.0. With a random-effects model, our analysis revealed that zinc supplementation was associated with a significant reduction in the occurrence of diarrheal episodes, by 14% (RR: 0.86; 95% CI: 0.79–0.93).

Prevention of Respiratory Illness

Data on the frequency of respiratory illnesses were available in 12 studies, which included 2709 children who received a zinc supplement and 2803 children who received a matched placebo.[15,16,23,24,31–34,37,39,40,43] The pooled data showed an 8% reduction in the occurrence of respiratory illness among children who received a zinc supplement, with a random-effects, pooled RR of 0.92 (95% CI: 0.85–0.99) (Fig 2).

Prevention of Severe Forms of Diarrheal Illness

Data on RRs for the incidence of severe diarrheal disease, including severe diarrhea or dysenteric illness, were available in 5 studies.[15,31,35,36] The fixed-effect pooled RR

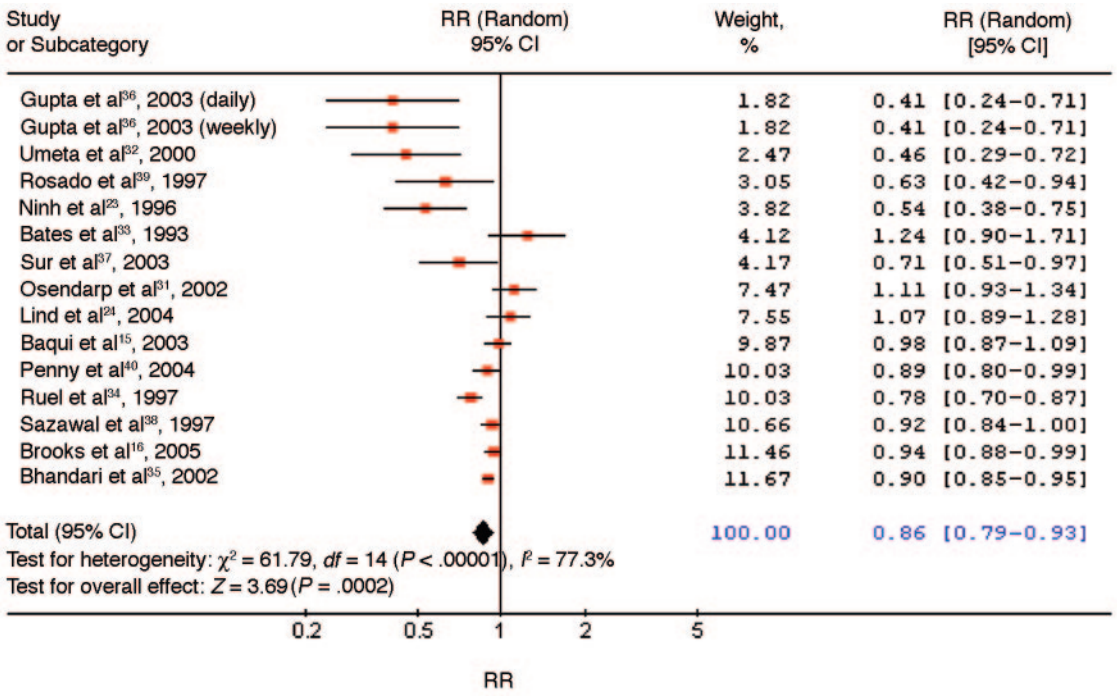

FIGURE 1
Meta-analysis of RRs of incidence of diarrheal episodes in children who received zinc supplementation or a placebo.

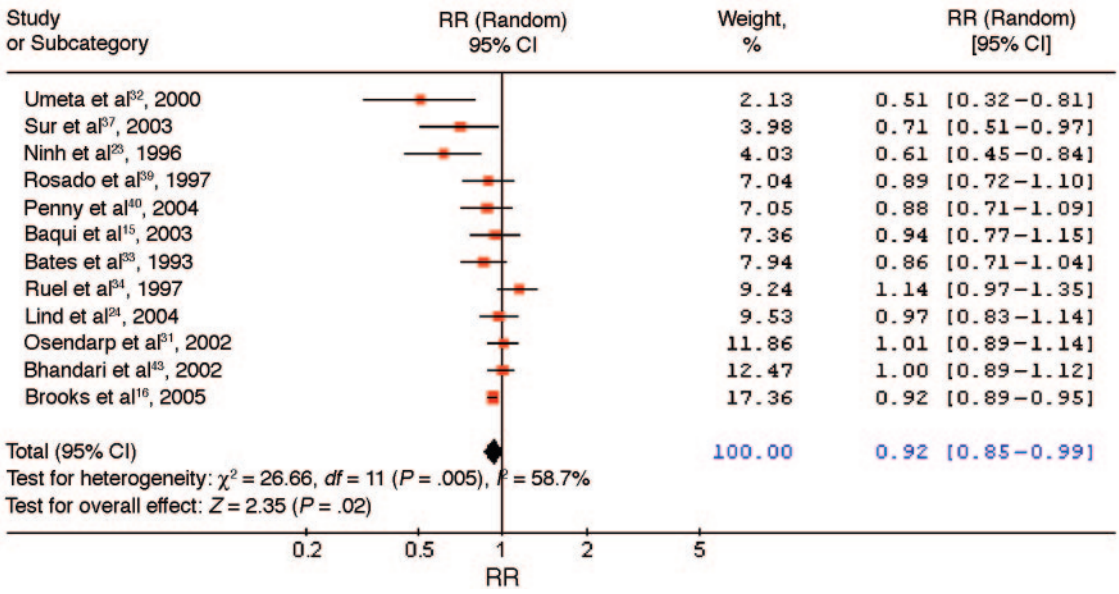

FIGURE 2
Meta-analysis of RRs of incidence of respiratory illness episodes in children who received zinc supplementation or a placebo.

for such illness in the children who received a zinc supplement, compared with the children who received placebo, was 0.85 (95% CI: 0.75–0.95), which indicated a significant reduction in the frequency of severe diarrhea (Fig 3). With the random-effects model, the pooled RR was 0.84 (95% CI: 0.70–1.01).

Three studies provided data on RRs for the incidence of episodes of persistent diarrhea.[31,34,35] A pooled analysis of those studies using a fixed-effect model showed a significant reduction in such illness, with a pooled RR of 0.75 (95% CI: 0.57–0.98) for the occurrence of persistent diarrhea in the children who received a zinc supplement, compared with the children who received a placebo (Fig 4). Use of the random-effects model was not possible because of the small number of available studies.

Prevention of Severe Respiratory Illness

Four studies provided data for comparison of incidence rates of severe respiratory illness, described variably as pneumonia or lower respiratory tract infection.[16,31,42,43] The fixed-effects pooled estimate of the RR for such illness was 0.80 (95% CI: 0.70–0.92) (Fig 5), which indicated a significant reduction in the frequency of such illness. With the random-effects model, the pooled RR was 0.79 (95% CI: 0.65–0.95).

Duration of Diarrhea and Respiratory Illnesses

The pooled efficacies of zinc in the reduction of the number of days with diarrhea or respiratory illnesses were 0.86 (95% CI: 0.79–0.93) and 0.95 (95% CI: 0.84–1.07), respectively (Figs 6 and 7); the latter was not statistically significant.

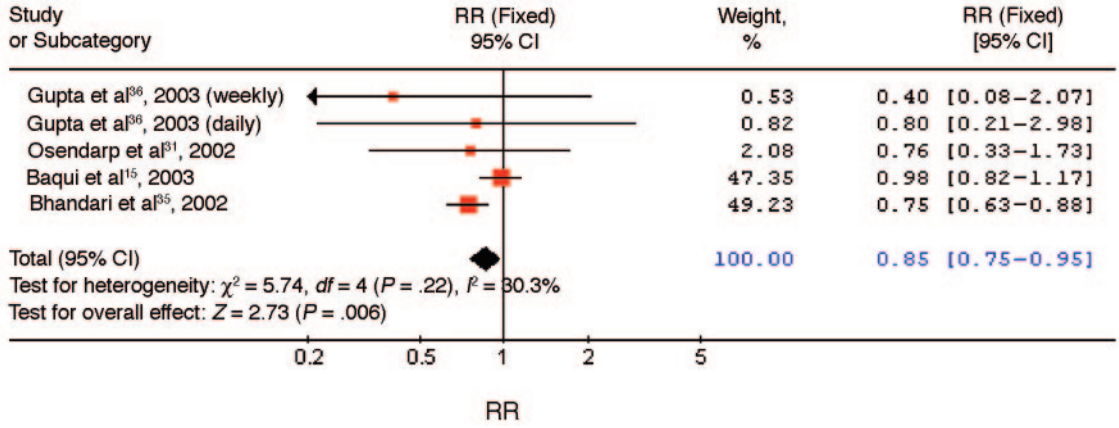

FIGURE 3
Meta-analysis of RRs of incidence of episodes of severe diarrhea and/or dysentery in children who received zinc supplementation or a placebo.

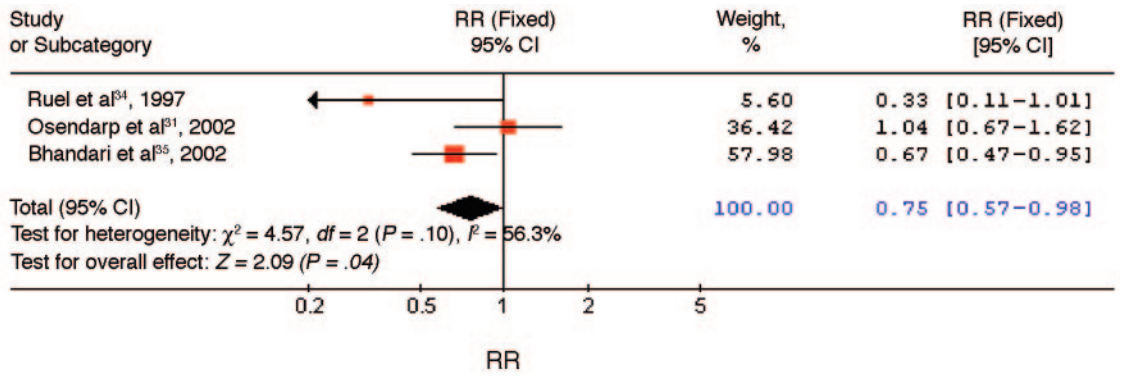

FIGURE 4
Meta-analysis of RRs of incidence of episodes of persistent diarrhea in children who received zinc supplementation or a placebo.

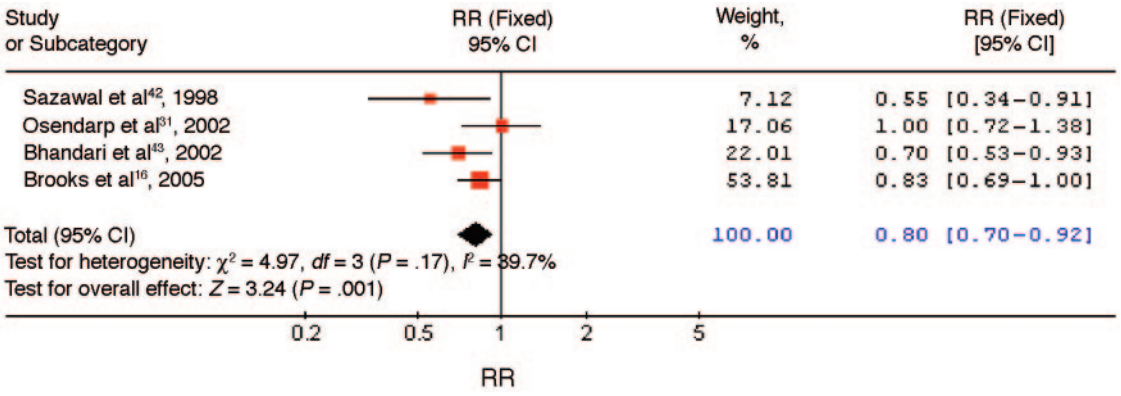

FIGURE 5
Meta-analysis of RRs of incidence of episodes of lower respiratory tract infection or pneumonia in children who received zinc supplementation or a placebo.

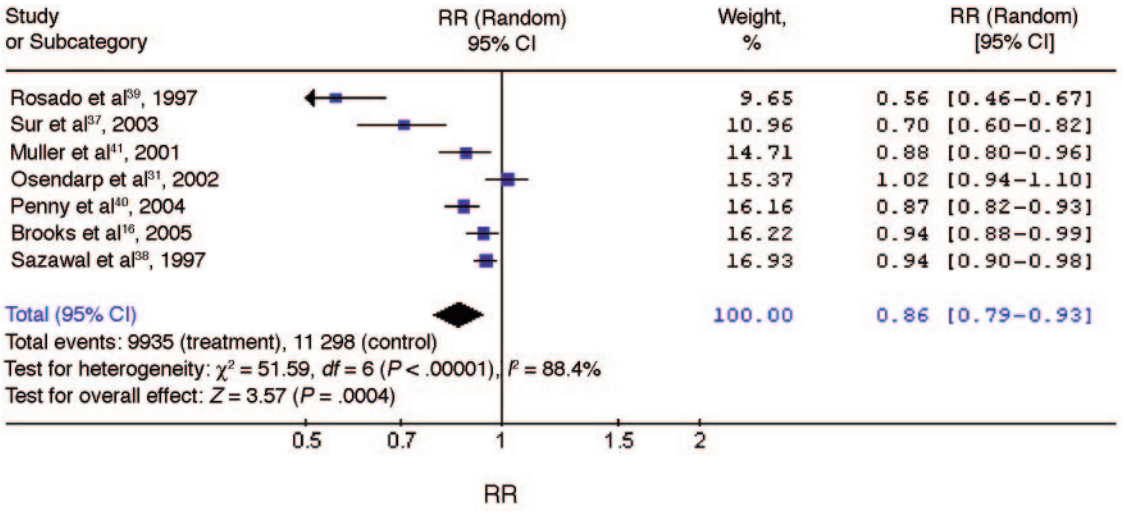

FIGURE 6
Meta-analysis of RRs of number of days with diarrhea in children who received zinc supplementation or a placebo.

Reasons for Heterogeneity Among Studies

Subgroup analyses for the type of zinc compound used, the total dosage of zinc per week (≥70 mg versus <70 mg), and the frequency of zinc administration (daily or less frequently) did not explain the heterogeneity between studies. The available data did not permit evaluation of the effects of zinc supplementation separately for children with good versus poor nutrition or children with zinc deficiency versus no zinc deficiency at the time of inclusion in the study.

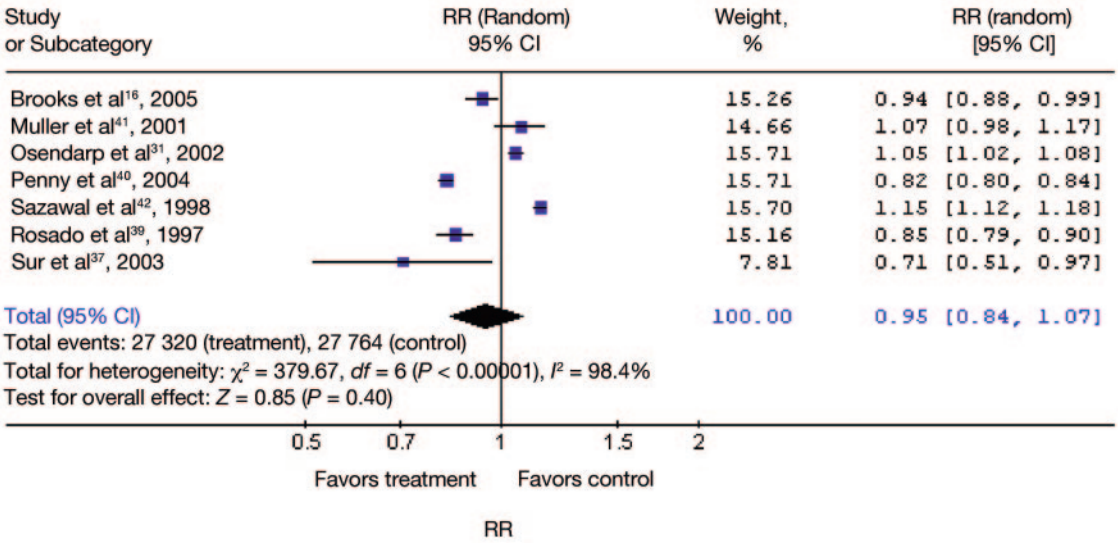

FIGURE 7
Meta-analysis of RRs of number of days with respiratory illness in children who received zinc supplementation or a placebo. OR indicates odds ratio.

Publication Bias

To assess whether there was a bias in the published literature toward studies with positive outcomes, we plotted the effect size of each trial versus variance of the effect for reduction in the number of episodes of diarrhea or respiratory illnesses. In the absence of a publication bias, such a plot is expected to have a shape resembling an inverted funnel.[28] The funnel plots for both parameters were nearly identical (Fig 8), with an excess of favorable studies with high variance and an apparently limited number of published studies of small size and negative effect, which indicated the existence of a publication bias.

The regression intercept method described by Egger et al[28] indicated the presence of significant publication bias in studies on the effects of zinc supplementation on diarrhea (P = .070) but not respiratory illnesses (P = .340). The rank correlation method described by Begg and Mazumdar[27] failed to show the presence of significant publication bias in studies on diarrhea (P = .138) but found evidence of such bias in studies on respiratory illnesses (P = .029). The trim and fill analysis for studies on diarrhea showed 3 missing studies in the right lower portion; with the addition of those studies, a summary RR of 0.90 (95% CI: 0.82–0.98) was obtained. Similarly, there were 3 missing studies for respiratory illnesses; with the addition of those studies, the summary RR was estimated as 0.95 (95% CI: 0.87–1.04).

DISCUSSION

Our meta-analysis indicated that zinc supplementation for young children led to reductions in the risk of diarrhea and respiratory tract infections (14% and 8%, respectively). Zinc supplementation was also associated with reductions in the rates of serious forms of these illnesses and in the number of days of diarrhea per child. However, there was no significant reduction in the number of days with respiratory illness. The published literature showed significant heterogeneity regarding the preventive effects of zinc administration, with evidence of publication bias.

The current meta-analysis focused on estimating the

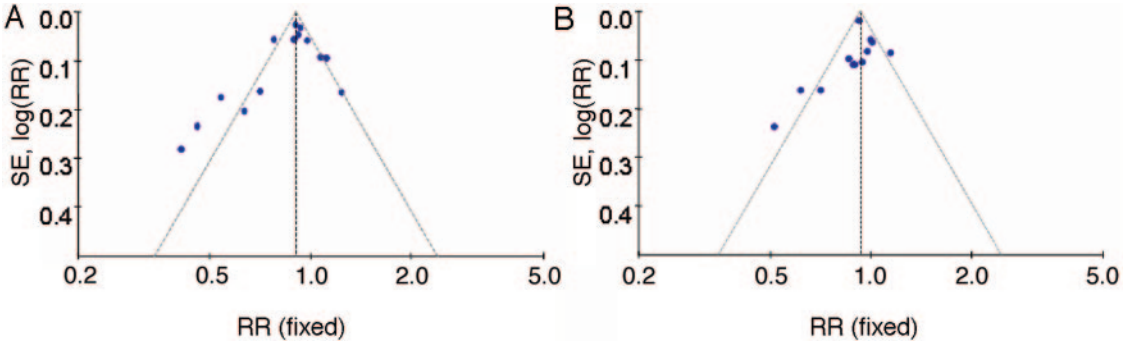

FIGURE 8
Funnel plot of studies on zinc supplementation for prevention of diarrhea (A) and respiratory illnesses (B) to assess the presence of publication bias.

effect of zinc supplementation on the reduction of childhood morbidity. Zinc deficiency, arising from inadequate dietary intake or poor absorption, is common in many developing countries.[4] It is thought to be 1 of the 10 greatest factors contributing to disease burden among children in developing countries[49] and has led to calls for the initiation of supplementation and food fortification programs. Although several studies have assessed the efficacy of zinc supplementation in preventing infections among children, the results of those studies were quite variable. The current meta-analysis provides a structured review to summarize the effects of zinc supplementation and provides quantified effectiveness data, to aid in policy formulation regarding the implementation of large-scale zinc supplementation programs. It provides evidence that zinc supplementation programs are likely to reduce morbidity attributable to diarrhea and respiratory tract infections, although the proportions prevented are likely to be small.

Our findings of reduced frequency of diarrhea and respiratory illnesses in children receiving zinc supplementation indicate that this intervention could be useful in developing countries where zinc deficiency is common and mortality rates are high. Although the effects of zinc supplementation on the morbidity attributable to childhood infections were modest, the absolute number of illness episodes prevented would be large, given that most children <5 years of age suffer several episodes per year, on average. Given that >3.5 million children are estimated to die as a result of either diarrhea or respiratory illnesses,[49] even small effects could translate into major absolute reductions in childhood morbidity and mortality rates.[49]

The estimates provided by the current meta-analysis should allow for better estimation of the benefits of zinc supplementation. Throughout the world, nearly 2 billion episodes of diarrhea are estimated to occur every year among children <5 years of age.[50] With the pooled estimate from our study, zinc supplementation might be expected to prevent 280 million episodes of diarrhea each year.[50] Furthermore, the data from this meta-analysis should be useful for calculation of cost-effectiveness and cost/benefit ratios for administration of zinc supplements in developing countries.

The relatively modest effect of zinc supplementation observed in the current meta-analysis implies that this intervention should be combined with other interventions aimed at reducing childhood morbidity. The relative financial feasibility and cost-effectiveness of such interventions could help determine their priority for implementation. Alternatively, a combination of interventions may be synergistic, with the combination providing greater benefits than the sum of benefits expected from the measures applied individually, thus enhancing their cost-effectiveness.

Our meta-analysis has several strengths. First, it included only studies that were deemed high quality by meeting strict inclusion criteria. It included only randomized, placebo-controlled studies in which assessors were unaware of treatment allocation. Blinded assessment prevents observer bias; this may be particularly important in studies pertaining to zinc supplementation, because major outcome measurements in such studies (ie, occurrence of diarrhea or respiratory illnesses and their severe forms) are subjective in nature. Second, we took care to exclude studies in which zinc administration was performed with a therapeutic intent, whereas a previous meta-analysis on this subject[26] included such studies, which might have led to an overestimation of the potential preventative effects of zinc. Furthermore, our meta-analysis included the results of larger studies on the subject. In addition, we used a more-robust, random-effects model for pooling the results of published studies if their results had significant heterogeneity.

Our analysis has some inherent limitations. It did not take into consideration the beneficial effect of zinc supplementation on linear growth, which is often cited as another benefit of zinc supplementation. We also did not consider the effect of zinc supplementation on malaria. The effect of zinc supplementation on malaria has been examined in only a few studies in Africa,[18,33] which were too limited, compared with those for diarrhea and respiratory illnesses. Also, our results may not be applicable to children with HIV infection, although diarrhea and respiratory illnesses are common in such children. Furthermore, our meta-analysis addressed only prophylactic effects of zinc and did not review studies on the therapeutic effects of zinc.

The benefits of any supplementation program, including those for zinc administration, may be expected to be disproportionately larger for subjects with marginal or poor nutritional status. In 2 studies, children who were enrolled with initially low serum zinc levels seemed to experience greater reductions in the incidence and prevalence rates of diarrhea after receiving zinc, compared with children with higher baseline serum zinc levels.[32,38] However, it was not possible to analyze data on diarrhea and respiratory illnesses for children with varying degrees of malnutrition, because such stratified data were not available in the other studies that met our inclusion criteria. In fact, in trials in which zinc supplementation was tried for the treatment of diarrhea, it seemed to have greater value for children with poor nutritional status and serum zinc levels.[19] Future studies that could analyze the different effects of zinc on children who are deemed zinc deficient or not would be useful for identifying subpopulations that could most benefit in resource-limited settings. It should be noted that the diagnosis of zinc deficiency remains difficult, and serum zinc levels are not necessarily accurate for this purpose. Furthermore, most of the zinc supplemen-

tation studies were performed in developing countries, and the results of our meta-analysis may not be applicable to children in developed regions. Several large, randomized, controlled studies undertaken after the 1999 meta-analysis supported the results presented in the current meta-analysis.[16,35,40]

The existence of significant heterogeneity in the results of various published studies may distract from the conclusions of our meta-analysis. We accounted for this by using random-effects, meta-analysis techniques for analyses in which studies showed significant heterogeneity. The fixed-effects model was used only for some analyses; in those analyses, we also pooled data by using the random-effects model, and we found the results to be largely similar.

The funnel plot analysis indicated the presence of publication bias. This visual impression was supported by quantitative measures of publication bias; the discordance between the results of the methods for measuring publication bias described by Begg and Mazumdar[27] and by Egger et al[28] can be explained by the relatively low sensitivity of these methods, whereby nonsignificant results with these tests do not rule out the presence of bias. The presence of heterogeneity and publication bias suggests the need for additional large, randomized, controlled studies to examine the benefits of zinc supplementation. It will also be important to monitor the populations for which prophylactic zinc supplementation has already been introduced, to study trends in disease morbidity rates and to estimate the effectiveness of this intervention under field conditions.

The studies included in our meta-analysis used zinc doses of 15 to 140 mg/week. Although our subgroup analyses failed to show any effect of dose on the benefits seen with zinc supplementation, this might have been related to the limited sensitivity of such analyses and the small number of studies using various doses. The large variation in the doses used in various studies, at times exceeding the recommended daily allowance for zinc (11 mg/day for men and 8 mg/day for women), suggests the need for additional studies on optimal supplementation doses, particular because high zinc intakes have been shown to be associated with inhibition of absorption of other micronutrients[51] and with poorer survival rates for children with HIV infection.[52]

CONCLUSIONS

Pooled data from our meta-analysis indicated that zinc supplementation in healthy children led to significant but modest reductions in the frequency of diarrhea and respiratory illnesses. This intervention also led to reductions in the frequency of severe diarrhea and lower respiratory tract infections and in the number of days with diarrhea per child; however, there was no significant reduction in the number of days with respiratory illness per child in the pooled data from the included studies. These data may have public health significance, and they provide support for the implementation of zinc supplementation programs in developing countries in an attempt to improve child health. Furthermore, the results of our analysis emphasize the need for additional data collection pertaining to zinc in larger studies, especially those in which study subjects are stratified according to baseline nutritional status. Such data would be important in evaluating differences in the responses of well-nourished and poorly nourished children to zinc supplements and might thus enable better targeting of this intervention.

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PATIENTS' VIEWS ON FINANCIAL CONFLICTS OF INTEREST IN CANCER RESEARCH TRIALS

Background: Financial ties between researchers or medical centers and companies whose drugs are being tested have come under increasing scrutiny.
Methods: We conducted in-person interviews with 253 patients in cancer-research trials (a 93% response rate) at five US medical centers to determine their attitudes regarding potential financial conflicts of interest among researchers and medical centers.
Results: More than 90% of patients expressed little or no worry about financial ties that researchers or institutions might have with drug companies. Most patients said they would have enrolled in the trial even if the drug company had paid the researcher for speaking (82% of those interviewed) or consulting (75%) or if the researcher had received royalty payments (70%) or owned stock in the company (76%). Similarly, most patients would have enrolled in the trial if their cancer center had owned stock in the drug company (77%) or received royalty payments from the company (79%). Most patients believed it was ethical for researchers to receive speaking fees (81%) or consulting fees (82%) from the company. However, a substantial minority of patients wanted disclosure of the oversight system for researchers (40%) and of researchers' financial interests (31%); 17% thought no disclosure to patients was necessary.
Conclusions: Most patients in cancer-research trials were not worried about financial ties between researchers or medical centers and drug companies and would still have enrolled in the trial if they had known about such financial ties. A substantial minority wanted to be informed about the oversight system to protect against financial conflicts of interest and about researchers' financial interests.

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Role of Zinc Administration in Prevention of Childhood Diarrhea and Respiratory Illnesses: A Meta-analysis

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