

Cost-effectiveness of zinc supplementation as an adjunct treatment for childhood diarrhea

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Background

Recent analyses by WHO estimated that diarrhea causes about 2 million deaths annually in children under five years, about 20% of all such deaths (1). In May 2004, WHO and UNICEF issued a joint statement (2) recommending the incorporation of zinc supplementation together with new low osmolarity ORS and continued feeding as the most effective approach to managing diarrhea. With complete implementation of these new recommendations, it has been estimated that almost 90% of diarrhea deaths could be prevented (3).

The new WHO/UNICEF recommendation to incorporate zinc supplementation into diarrhea management is based on a substantial body of scientific evidence of benefits emerging from 17 studies efficacy studies – 12 on acute and 5 on persistent diarrhea. Together these studies have demonstrated that zinc in addition to ORS reduces both the duration and severity of acute diarrhea relative to treatment with ORS alone (4,5). These benefits are significant both statistically and clinically. Treatment of diarrhea for 10-14 days with zinc supplements also reduces the incidence of diarrhea and pneumonia in the 2-3 months following the treatment (6).

A large community-based study in Bangladesh demonstrated the feasibility of incorporating zinc into diarrhea treatment with ORS into a program setting (7). This effectiveness study recorded a reduction in duration of diarrhea in those given zinc that was comparable to the efficacy studies. The study also noted significant reductions in hospitalizations from diarrhea and overall mortality among children living in villages where zinc in addition to ORS was available relative those living in areas where only ORS was available. Additionally, the use of zinc was associated important indirect benefits. For example, inappropriate use of antibiotics and other medicines was reduced, visits to pharmacies and village drug sellers were also reduced, and the use of ORS was increased (8).

Evidence of cost-effectiveness

Given the effectiveness of zinc therapy in treating diarrhea and that zinc as dispersible tablets (or a syrup) is inexpensive (US\$0.02 per tablet as purchased from Nutriset), is this intervention cost-effective? The published data available to address this question are positive but limited at this time to two studies, Robberstad et al. (9) and Patel et al. (10).

Robberstad et al. (9) investigated the cost effectiveness ratios (CER) in terms of DALYs lost and child deaths averted using a simulation technique with cost data from health facilities in Tanzania. Three alternative management strategies for diarrhea were analyzed: current standard treatment with ORS (I); zinc as adjunct treatment to current standard treatment for children with non-dysenteric diarrhea (II); and, zinc as adjunct treatment to current standard treatment for all children with acute diarrhea, including those with dysentery (III).

Based on evidence from Bangladesh (7), zinc was assumed to reduce case fatality rate for diarrhea by 50% in this analysis. Further the study assumed that there was treatment capacity available at the dispensaries and so the incremental cost of providing zinc was limited to the cost of the zinc tablets. Allowing for the provision of adequate stocks of tablets to dispensaries, each treatment of 14 tablets was estimated to cost US\$0.47.

The mean CER for ORS (I) in this study was US\$113 per lost DALY averted and about US\$3200 per child death averted. The incremental CER of adding zinc to treatment of patients without dysentery (I-II) was \$40 per DALY and roughly \$1200 per death averted. Expanding the program to provide zinc for all acute diarrhea, i.e. including those

with dysentery (II-III), yielded mean incremental CER of \$11 per DALY and \$307 per death averted. The average CER of providing ORS plus zinc to all children with acute diarrhea was \$73 per DALY and \$2100 per death averted. Detailed results and other key assumptions made for this study are listed in the Annex.

Thus adding zinc to ORS for the treatment of all diarrhea reduced the mean CER per lost DALY averted by more than one-third – from \$113 to \$73. This study modeled only direct costs and benefits of zinc and not the indirect benefits. The indirect benefits noted in the Bangladesh effectiveness study, such as decreasing inappropriate use of antibiotics and other ineffective remedies, increased the proportion of patients complying with ORS, will add to the benefits of this intervention to economies both of health systems and of families. Robberstad et al. concluded that there is sufficient evidence to recommend the inclusion of zinc into standard case management of both dysenteric and non-dysenteric acute diarrhea. Since there are no indications of large geographical differences in the efficacy of zinc, these findings are likely applicable to other developing countries.

Patel et al. (10) estimated the average cost of standard treatment for children with acute diarrhea in Nagpur, India, as US \$14 of which the government paid two-thirds. They investigated the costs and effectiveness of adding a zinc/copper mix directly to ORS. Because the addition of the mineral mix shortened the duration of the diarrhea episodes, they estimated that the treatment costs were reduced by 8%.

Conclusion

Available evidence indicates that zinc for diarrhea treatment is highly cost-effective.

Annex: Detailed results, estimates and assumptions from Robberstad et al. (9).

Table 1: Cost-effectiveness ratio (CER) point estimates for management of acute diarrhea in children

	US\$ per DALY averted	US\$ per child death averted
Average CER (I)*	113	3213
Incremental CER (I-II)	40	1176
Incremental CER (II-III)	11	307
Average CER (III)	73	2098

* The management strategies: (I) – standard case management ORS; (I-II) zinc as adjunct treatment to patients without dysentery; (II-III) further expansion of the program to treat all cases of acute diarrhea; (III) the full program.

Table 2: Estimates of case-fatality ratios and effectiveness of zinc used in the Monte-Carlo simulations

Patients with acute diarrhea	Case-fatality ratio	Relative risk when providing zinc as adjunct therapy
Dysentery (bloody stools)		
Without adequate antibiotic Rx	0.58	0.50
With antibiotic Rx	0.14	1.00
Untreated non-dysenteric diarrhea	0.18	0.50

The assumption having greatest impact on the results of the study related to the case fatality rates (CFR) used for diarrhea -- in this study 0.15% for children less than 5 years from a median of 3.2 episodes per child per year and a mortality of 4.9 children per 1000 as reported by Kosek et al. (2003) (1).

Other key assumptions used to model the clinical outcomes of the decision tree treatment protocols included:

- ▲ 7.5 % of all patients with acute diarrhea have dysentery
- ▲ 33% of patients with dysentery receive adequate antibiotic treatment
- ▲ 90% of patients adhere to treatment with zinc and ORS
- ▲ The relative risk for the effectiveness of treatment with ORS is 0.5

References

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