Evidence Snapshot

1. Zinc is part of the WHO recommended treatment

- Mother and other caregivers should prevent dehydration through the early administration of increased amounts of appropriate fluids available in the home, and ORS solution, if on hand:
    - Continue feeding (or increase breastfeeding) during, and increase all feeding after the episode
    - Recognize the signs of dehydration and take the child to a health-care provider for ORS or intravenous electrolyte solution, as well as familiarize themselves with other symptoms requiring medical treatment (e.g., bloody diarrhea)
    - **Provide children with 20 mg per day of zinc supplementation for 10–14 days (10 mg per day for infants under six months old).**

Source:

All info from: World Health Organization. WHO/UNICEF Joint Statement: Clinical Management of Acute Diarrhea (WHO/FCH/CAH/04.7). Geneva, Switzerland: World Health Organization;

2. Zinc is effective in treating diarrhea

- **16%** decrease in frequency of severe diarrhea in acute cases
- **14%** decrease in the number of days of diarrhea
- **25%** decrease in frequency of persistent cases
- **16%** decrease in duration of acute diarrhea cases and 24% decrease in persistent cases

Sources:

Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. Pediatrics. 2007 Jun;119(6):1120-30. PubMed PMID: 17545379.

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Bhutta ZA, Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A, Khatun F, Martorell R, Ninh NX, Penny ME, Rosado JL, Roy SK, Ruel M, Sazawal S, Shankar A. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. Am J Clin Nutr. 2000 Dec;72(6):1516-22. PubMed PMID: 11101480.

3. Zinc can prevent future incidence of diarrhea

- **14%** reduction in new diarrheal episodes

Sources:

Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: a meta-analysis. Pediatrics. 2007 Jun;119(6):1120-30. PubMed PMID: 17545379.

4. Zinc is safe to use

- **No reports of severe adverse reactions from any form of zinc supplementation** used in the treatment of diarrhea.
- **A zinc dose of 40 mg has been approved as being safe to use by the Food and Drug Administration** (FDA), and a zinc dosage of more than this can pose certain risks.

Sources:

Role of zinc in pediatric diarrhea. Chaitali Bajait, Vijay Thawani Indian J Pharmacol. 2011 May-Jun; 43(3): 232–235. doi: 10.4103/0253-7613.81495 PMCID: PMC3113371

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5. Adverse effects of zinc are minimal

Treatment with zinc was associated with an **increase in vomiting**, **although the reduction in diarrhea duration seems to outweigh this**. Trial reported that **vomiting was limited to one episode** in most children and mainly occurred within 10 minutes of administration

- Oral zinc sulfate supplements can also cause side effects such as stomach upset, heartburn, and nausea. Rare side effects include fever, sore throat, mouth sores, weakness, and fatigue.
    - **One large effectiveness trial found no differences in adverse reactions based on the different zinc salts** were noted in the supplementation trials.
    - **One trial reported higher vomiting in the zinc versus the control group, when zinc was given with multiple micronutrients, but not when given alone.**
    - The copper status has been evaluated in four trials. Three of these have not found a difference in the serum copper status after supplementation. However, one trial did find a significant trend of decreased copper level when comparing zinc-supplemented children with non-zinc supplemented children. However, these children were malnourished with persistent diarrhea at baseline. **Overall, there is no substantial evidence of short-term zinc supplementation for the treatment of diarrhea adversely affecting the copper status**

Source:

Entire bullet: Role of zinc in pediatric diarrhea. Chaitali Bajait, Vijay Thawani Indian J Pharmacol. 2011 May-Jun; 43(3): 232–235. doi: 10.4103/0253-7613.81495 PMCID: PMC3113371

(Primary Source: Larson CP, Hoque AB, Larson CP, Khan AM, Saha UR. Initiation of zinc treatment for acute childhood diarrhea and risk for vomiting or regurgitation: a randomized, double-blind, placebo-controlled trial. Journal of Health, Population, and Nutrition 2005;23(4):311–9.)

Alternate Source: Fischer C, Harvey P. Low risk of adverse effects from zinc supplementation. Arlington (VA): International Science and Technology Institute, MOST; 2005.

6. Zinc is a cost-effective treatment for diarrhea

- CER for ORS is US$ 113 (2001 dollars) per DALY averted/US$ 3200 per child death averted. **The mean incremental CER of adding zinc to treatment of non-dysenteric patients is US$40/DALY averted and US$1200/death averted**
- Mean CERs of providing ORS and zinc to all children with acute diarrhea is US$ 73 per DALY and about US$ 2100 per death averted. **The mean CER is reduced by more than 1/3 when ORS was combined with zinc for treatment of all children with acute diarrhea**
- Is there any way to compare this with e.g., cost-effectiveness of malaria treatment? Just to get a better sense of how zinc stacks up to other treatments.

Source:

Robberstad B, Strand T, Black RE, Sommerfelt H. Cost-effectiveness of zinc as adjunct therapy for acute childhood diarrhoea in developing countries. Bull World Health Organ. 2004 Jul;82(7):523-31. PubMed PMID: 15500284; PubMed Central PMCID: PMC2622915.

7. Zinc has the potential to reduce misuse of antimicrobials

A study of antimicrobial use in a rural area of Bangladesh found that 26% of the purchased medicines were antimicrobials, which were most frequently purchased for children aged 0 – 4 years to use for diarrhea. A community-based, 30-cluster controlled trial was conducted in Bangladesh in which **there was a significant reduction in antimicrobial use and related behavior in the intervention area (where households were given zinc supplements for diarrhea)**

Source:

Baqui AH, Black RE, El Arifeen S, Yunus M, Zaman K, Begum N, Roess AA, Santosham M. Zinc therapy for diarrhoea increased the use of oral rehydration therapy and reduced the use of antibiotics in Bangladeshi children. J Health Popul Nutr. 2004 Dec;22(4):440-2. PubMed PMID: 15663177.

Fact Sheet

1. U-5 diarrheal deaths

- 1.34 million or 15% of all under-5 deaths (Black et al., 2010)
- Alternate figures range from 1.7-2.2 million; note that new figures are expected in early 2012 that may be lower

Source:

Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, Jha P, Campbell H, Walker CF, Cibulskis R, Eisele T, Liu L, Mathers C; Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 2010 Jun 5;375(9730):1969-87. Epub 2010 May 11. PubMed PMID: 20466419.

2. ORS efficacy/effectiveness

- May prevent up to 93% of diarrhea deaths (Munos et al, 2010)
- Failure of ORT, defined as the need to rehydrate children intravenously, has a failure rate of 3.6% (Gavin et al., 1996)
- Patients with oral maintenance therapy required 70% less intravenous fluid (Cash et al., 1997)

Source:

Munos MK, Walker CL, Black RE. The effect of oral rehydration solution and recommended home fluids on diarrhoea mortality. Int J Epidemiol. 2010 Apr;39 Suppl 1:i75-87. Review. PubMed PMID: 20348131; PubMed Central PMCID: PMC2845864.150

Gavin N, Merrick N, Davidson B. Efficacy of glucose-based oral rehydration therapy. Pediatrics. 1996 Jul;98(1):45-51. PubMed PMID: 8668411.

Cash RA, Nalin DR, Rochat R, Reller LB, Haque ZA, Rahman AS. A clinical trial of oral therapy in a rural cholera-treatment center. Am J Trop Med Hyg. 1970 Jul;19(4):653-6. PubMed PMID: 5425504.

3. Caregiver willingness to use zinc again

- 83.5% in Bangladesh (ICDDR,B, 2004)
- 94% in Benin (PSI)

Source:

ICDDR,B. Acceptability and Adherence to Zinc Dispersible Tablet Treatment of Acute Childhood Diarrhea.
PSI (USAID/POUZN). A Public-Private Partnership for the Introduction of Zinc for Diarrhea Treatment in Benin.

4. ORS-Zinc Coverage

- ORS Coverage Global 39% (UNICEFWHO, 2009)
- ORS+ Zinc Coverage Global <1%; only Bangladesh is higher than 1%

Source:

Fischer Walker CL, Friberg IK, Binkin N, Young M, Walker N, et al. (2011) Scaling Up Diarrhea Prevention and Treatment Interventions: A Lives Saved Tool Analysis. PLoS Med 8(3): e1000428.

5. Cost-effectiveness of ORS and Zinc

- CER for ORS is US$ 113 (2001 dollars) per DALY averted/US$ 3200 per child death averted (Robberstad et al., 2004)
- The mean incremental CER of adding zinc to treatment of non-dysenteric patients is US$40/DALY averted and US$1200/death averted (Robberstad et al., 2004)
- Mean CERs of providing ORS and zinc to all children with acute diarrhea is US$ 73 per DALY and about US$ 2100 per death averted. The mean CER is reduced by more than 1/3 when ORS was combined with zinc for treatment of all children with acute diarrhea (Robberstad et al., 2004)

Source:

Robberstad B, Strand T, Black RE, Sommerfelt H. Cost-effectiveness of zinc as adjunct therapy for acute childhood diarrhoea in developing countries. Bull World Health Organ. 2004 Jul;82(7):523-31. PubMed PMID: 15500284; PubMed Central PMCID: PMC2622915.

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Robberstad B, Strand T, Black RE, Sommerfelt H. Cost-effectiveness of zinc as adjunct therapy for acute childhood diarrhoea in developing countries. Bull World Health Organ. 2004 Jul;82(7):523-31. PubMed PMID: 15500284; PubMed Central PMCID: PMC2622915.