

## Zinc: From Research to Programs

RCS Presents Seminar Series  
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## Diarrhea and Child Mortality

- 11 million child deaths each year, two thirds of these are preventable
- 2 million child deaths from diarrhea
- 88% of diarrhea deaths are preventable with widespread use of ORS and zinc supplementation for diarrhea treatment

Black, Morris, Bryce. Lancet 2003.  
Jones, Steketee, Black et al. Lancet 2003.

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## Global Diarrhea Treatment Policy

- WHO and UNICEF signed a joint policy for the treatment of diarrhea in children in May 2004
- Treatment should include
  - Liberal use of low-osmolarity Oral Rehydration Solution to correct and prevent dehydration
  - Zinc supplementation for 10-14 days to shorten duration and severity of diarrhea
  - Continued feeding

WHO/UNICEF. Joint statement on the clinical management of acute diarrhea. 2004.

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## WHO and UNICEF Joint Statement

“Many more lives can be saved if these advances are used in conjunction with effective home treatment and use of appropriate health services. To be the most effective these revised recommendations **must become routine practice** both in the home and the health facility.”

WHO/UNICEF. Joint statement on the clinical management of acute diarrhea. 2004.

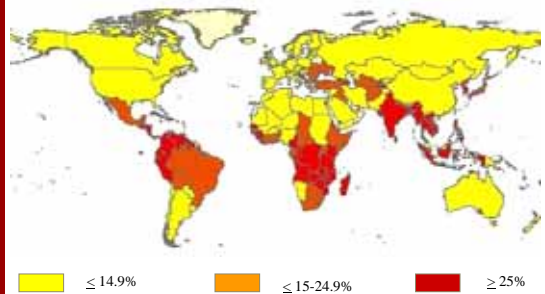
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## Low Osmolarity ORS

- Lower levels of glucose and salt to achieve lower osmolarity (245 mOsm/L)
- Results
  - Improved efficacy of ORS
  - Decreased the need for intravenous therapy
  - Decreased stool output by 20%
  - As safe and effective in children with cholera

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## Global Zinc Deficiency



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Hotz & Brown. Food Nutr Bull 2004.

## Human Zinc Deficiency

- Nutritional dwarfism first recognized among adolescent boys in Iran and Egypt in 1960's
- Zinc deficiency now recognized as causing hypogonadism, growth retardation, dermatitis, decreased immune functions, and increased infections

## Zinc for the Treatment of Diarrhea: History

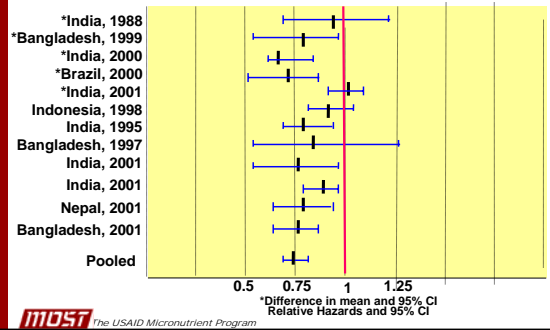
- Research started in the 1980s
- 12 trials in acute diarrhea
- 5 trials in persistent diarrhea
- Age groups: 3-60 mo
- Dose of zinc:  $\approx$  20 mg/d (range 5-45 mg/d)

## Zinc for the Treatment of Diarrhea: Research Findings

- 25% reduction in duration of acute diarrhea
- 29% reduction in duration of persistent diarrhea
- 40% reduction in treatment failure or death in persistent diarrhea

Zinc Investigators' Collaborative Group.  
Am J Clin Nutr 2000.

## Effect of Zinc Supplementation on Duration of Acute Diarrhoea/Time to Recovery



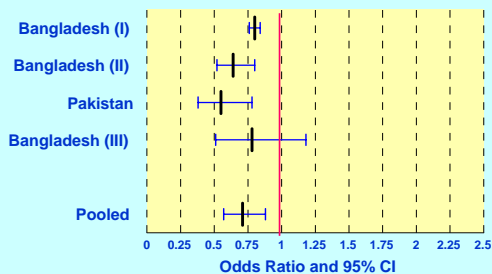
## Therapeutic Effects of Zinc on Diarrhea Severity

Country	Diarrhea Outcome	Percent Reduction
India	Frequency	18
India	Frequency	39
Bangladesh	Output	28
India	Output	38
Brazil	Frequency	59

## Additional Preventive Aspects of Zinc Treatment

- Zinc supplementation for 10-14 days has preventive effect on childhood illnesses in the 2-3 months after treatment
- 25% reduction in diarrhea (9 studies)
- 34% reduction in pneumonia (5 studies)
- 36% reduction in malaria (2 studies)

## Preventive Effect of 10-14 days of Zinc Supplementation on Diarrhea Incidence



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## Community-based Trial Demonstrates Effectiveness of Zinc in Treating Diarrhea

- 30 clusters in rural Bangladesh randomized for health workers to deliver ORS alone or ORS + zinc (20mg/d for 14 days) for diarrhea treatment
- 2-year study with almost 12,000 child-years of observation
- 23% decrease in duration of all diarrhea episodes in zinc treatment clusters compared to control clusters (RH 0.77, 95% CI 0.69-0.86)

Baqui, Black, Arifeen. *BMJ* 2003.

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## Community-based Trial Demonstrates Preventive Benefits of Zinc

- Zinc supplementation decreased . . .
  - Overall diarrhea prevalence by 15% (RR 0.85, 95% CI: 0.76, 0.96)
  - Hospitalization from diarrhea by 19% (RR 0.81, 95% CI: 0.65, 1.00)
  - ALRI prevalence by 7% (RR 0.93, 95% CI: 0.78, 1.10)
  - Hospitalization from ALRI by 19% (RR 0.81, 95% CI: 0.53, 1.23)

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## Community-based Trial Demonstrates Preventive Benefits of Zinc

- Decreased overall mortality (non-injury) by 59% (RR 0.49 95% CI: 0.25, 0.94)
- Decreased inappropriate antibiotic use rate from 34% in control clusters to 13% in zinc clusters (p<0.01)
- Increased ORS use from 50% in control clusters to 75% in zinc clusters (p<0.01)

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## Safety of Zinc Supplementation

- 8,500 children <5 y supplemented in 17 trials
- 11,880 child years of observation in one trial
- Vomiting is the only reported adverse effect
  - 5/7 trials report no differences between zinc and placebo
  - 2 trials report slightly higher vomiting rates in zinc supplemented children
- 4/4 trials show no difference in copper status after 2 weeks of zinc supplementation

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## Cost Effectiveness of ORS and Zinc Supplementation

- Benefit in diarrhea therapy and benefit on mortality indicates cost-effectiveness
- Decreases the need for expensive hospitalization
- Decreases the use of unnecessary antibiotics and other drugs
- Further cost-benefit analyses are needed

Robberstad, Strand, Sommerfelt, and Black. *Bull WHO* 2004.  
Baqui, Black, Arifeen. *J Health Pop Nutr* (In Press).

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## Diarrhea Treatment -- Research to Policy: Accomplishments to Date

- Recognition of the importance of decreasing osmolality in ORS
- Recognition of the positive effect of zinc on duration and severity of diarrhea
- Recognition of the positive effect of zinc on subsequent episodes on diarrhea and pneumonia
- Recognition of the positive joint effect of ORS and zinc on diarrhea mortality

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## Diarrhea Treatment -- Research to Policy: Accomplishments to Date

- Joint policy statement by WHO and UNICEF recommending
  - Low osmolality ORS
  - Zinc supplementation for 10-14 days
- Dispersible tablets developed and used in large-scale research trials
- Applied for inclusion of zinc on the WHO Essential Drug List
- Organization of a Global Task Force for management of diarrhea

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## Diarrhea Treatment -- Policy to Programs

- Developing guidelines/training materials for use in country programs & emergency situations
- Need to establish capacity to produce and procure the zinc supplements & ORS supplies
- Develop delivery mechanisms, designed locally
- Social marketing proposed will require public/private partnerships
- Need to test and perhaps create standards for zinc supplies already on the market (quality control)
- Need continuing donor financial support

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## ORS and Zinc

Treatment of diarrhea is now more effective

This is the chance to make a difference

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## Key references

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## THANK YOU

For more information contact: Phil Harvey, [pharvey@istiinc.com](mailto:pharvey@istiinc.com) or Roy Miller, [rmiller@istiinc.com](mailto:rmiller@istiinc.com)

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