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# Effectiveness of Zinc Supplementation Plus Oral Rehydration Salts Compared With Oral Rehydration Salts Alone as a Treatment for Acute Diarrhea in a Primary Care Setting: A Cluster Randomized Trial

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## What's Known on This Subject

Zinc treatment is efficacious in individually randomized, placebo-controlled trials, but this may not equate to effectiveness under real-life conditions in developing countries, because impact may be altered by community perceptions, methods of intervention delivery, and logistics.

## What This Study Adds

This study shows that education on zinc and promotion of zinc and ORS by health care providers improve diarrhea management in children <5 years of age and reduce unwarranted drug use in a developing-country setting.

## ABSTRACT

**OBJECTIVE.** The purpose of this work was to evaluate whether education about zinc supplements and provision of zinc supplements to caregivers is effective in the treatment of acute diarrhea and whether this strategy adversely affects the use of oral rehydration salts.

**PATIENTS AND METHODS.** Six clusters of 30 000 people each in Haryana, India, were randomly assigned to intervention and control sites. Government and private providers and village health workers were trained to prescribe zinc and oral rehydration salts for use in diarrheal episodes in 1-month-old to 5-year-old children in intervention communities; in the control sites, oral rehydration salts alone was promoted. In 2 cross-sectional surveys commencing 3 months (survey 2) and 6 months (survey 3) after the start of the intervention, care-seeking behavior, drug therapy, and oral rehydration salts use during diarrhea, diarrheal and respiratory morbidity, and hospitalization rates were measured.

**RESULTS.** In the 2 surveys, zinc was used in 36.5% ( $n = 1571$ ) and 59.8% ( $n = 1649$ ) and oral rehydration salts in 34.8% ( $n = 1571$ ) and 59.2% ( $n = 1649$ ) of diarrheal episodes occurring in the 4 weeks preceding interviews in the intervention areas. In control areas, oral rehydration salts were used in 7.8% ( $n = 2209$ ) and 9.8% ( $n = 2609$ ) of episodes. In the intervention communities, care seeking for diarrhea reduced by 34% (survey 3), as did the prescription of drugs of unknown identity (survey 3) and antibiotics (survey 3) for diarrhea. The 24-hour prevalences of diarrhea and acute lower respiratory infections were lower in the intervention communities (survey 3). All-cause, diarrhea, and pneumonia hospitalizations in the preceding 3 months were reduced in the intervention compared with control areas (survey 3).

**CONCLUSIONS.** Diarrhea is more effectively treated when caregivers receive education on zinc supplementation and have ready access to supplies of oral rehydration salts and zinc, and this approach does not adversely affect the use of oral rehydration salts; in fact, it greatly increases use of the same.

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This trial has been registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (identifier NCT00278746).

### Key Words

zinc, diarrhea, cluster randomization, hospitalization

### Abbreviations

ORS—oral rehydration salts  
PHC—primary health center  
WHO—World Health Organization  
ALRI—acute lower respiratory infection  
IQR—interquartile range  
OR—odds ratio  
CI—confidence interval

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**T**HE SAFETY AND efficacy of zinc treatment in children with acute diarrhea and dehydration are well established based on findings of a large number of randomized, placebo-controlled trials conducted under experimental conditions.<sup>1-5</sup> The findings of these efficacy studies, however, may not be the same as effectiveness under real-world conditions. The community's knowledge, attitudes, and perceptions and the way the educational components of the intervention and the zinc supplements are delivered will influence the ultimate benefit to children of this interven-

tion. To help countries decide whether to introduce and scale up such an intervention in national programs, policy-makers need data from effectiveness studies, including the effect on existing diarrhea case management practices, particularly the use of oral rehydration salts (ORS) solution.

We conducted a cluster-randomized trial to test the hypothesis that education about zinc supplementation in acute diarrhea and provision of zinc supplements along with ORS packets to caregivers through public and private health care providers are effective in the treatment of acute diarrhea among children <5 years old. Children in the control communities were not given a placebo, because we wanted to assess any potential negative effect of giving zinc on ORS use rates.

## METHODS

The study was conducted between January 2005 and September 2006 in 6 primary health centers (PHCs) in district Faridabad in the state of Haryana. Each PHC has a population of ~30 000. The intervention was designed in collaboration with the local health leaders, including those from the Integrated Child Development Services scheme of the government of India. Formative research and pilot testing were done in a distant PHC in the same region.<sup>6</sup> Oral permissions were sought from community leaders to work in their areas. In each household, where interviews were conducted during the surveys, written informed consent was obtained from caregivers. The study was approved by the ethical review committees of the Society for Applied Studies and the World Health Organization (WHO).

### Baseline Survey and Randomization

To obtain data on sociodemographic characteristics, prevalence of diarrhea, ORS use rates, and visits to health care providers during diarrhea, a baseline cross-sectional survey was conducted with a subsample of caregivers (survey 1). This subsample included households with  $\geq 1$  child 1 to 59 months old in areas covered by 10 Anganwadi centers randomly selected from the 30 Anganwadi centers in each PHC. If a surveyed household had multiple children, the youngest one was included to maintain the independence of individual measurements for statistical purposes. A score based on socioeconomic indicators (population size, ownership of farm land, caste, water supply, defecation place, literacy rates, diarrhea rates, care-seeking rates for diarrhea, and hospitalization rates) was computed for each of the 6 PHCs. We then paired PHCs with similar scores. To allocate 1 PHC of each pair to the intervention group, the 2 PHCs in a pair were listed in alphabetical order. A statistician, not otherwise involved with the study, generated 3, single-digit random numbers using a random-numbers table. According to a predecided rule, the first listed PHC in a pair was allocated to the intervention group if the random number was 0 to 4 and the second if it was 5 to 9. The intervention had 3 components: (1) training in diarrhea management based on the current WHO treatment package<sup>7</sup> with the addition of zinc treat-

ment; (2) improvement in the availability of ORS and zinc; and (3) promotion of diarrhea treatment through the primary health care system.

### Intervention Delivery

The channels for delivery of the intervention were defined in partnership with the local government.<sup>6</sup> These included government providers (physicians with a medical degree and auxiliary nurse midwives at the PHC), and Integrated Child Development Services scheme community workers, known as the "Anganwadi workers"; these are community resident workers, 1 for every 1000 people. They are primarily involved in growth monitoring, nutritional supplementation, and preschool education for children aged <6 years of age and are expected to provide ORS to treat diarrhea. Private medical practitioners, >90% of whom do not possess a medical degree but practice indigenous systems of medicine, were also included as channels, because they are commonly used by this population. All of the channels in the intervention communities underwent standard training in diarrhea management; appropriate use of zinc, logistics, and supplies; and referral criteria. The duration was half a day for physicians and a full day for health workers. The strategy was to give 1 blister strip containing 14 dispersible zinc tablets (20 mg each) along with 2 ORS packets (to mix in 1 liter of water each) to all of the children aged 1 month to 4 years with diarrhea. Infants aged <6 months were to receive half a tablet in a teaspoonful of breast milk; older children were to receive 1 tablet dissolved in breast milk or clean water. In the control communities, training on diarrhea management of identical content except for zinc to the intervention areas of similar duration and by the same trainers as in the intervention areas was provided, but zinc treatment was not discussed. Training activities in each pair of PHCs were completed in a month. Post training, the project staff had no role in patient treatment. A poster was designed using insights from formative research and pretested in the pilot study; this provided simple, practical information on zinc and ORS treatment.<sup>6</sup> Posters were pasted on the clinic walls and in the PHC buildings. Formative research had shown that caregivers give treatment for diarrhea only as long as the diarrhea lasts and also prefer "tonics" or multivitamins for young children, because they are perceived to prevent illness. Zinc was, therefore, promoted as a treatment for diarrhea, as well as a "tonic" that prevents diarrhea over the ensuing months; this message was developed so that caregivers would give the full 14-day course of zinc. The zinc supplies were given free of charge by providers to caregivers. Zinc supplies were replenished monthly by supply officers from the study team. Uninterrupted supplies of ORS packets were assured in the intervention and control communities by strengthening logistics in the local health system.

### Measurement of Outcomes

The effectiveness of the program was assessed through 2 cross-sectional surveys in which caregivers of all house-

holds with a child aged 1 month to 4 years were interviewed; if multiple children were available in a household, information was obtained on the youngest. The first evaluation survey commenced concurrently in 1 intervention and control area 3 months (survey 2) after training was completed, and zinc supplies were available with all of the channels in the intervention area. Subsequent to completion of the survey in all of the 6 PHCs, a second cross-sectional survey was conducted (survey 3) ~6 months after start of the intervention. During the surveys, sociodemographic characteristics of the family were assessed, and caregivers were queried on history of diarrhea, cough, fast breathing, or difficult breathing in the past 24 hours, 2 weeks, and 4 weeks, and on hospitalizations anytime during the last 3 months. If a child had diarrhea in the last 4 weeks, information was obtained on the type of health care provider visited; the use of antibiotics, antidiarrheals, or drugs of unknown identity; and ORS and zinc prescription and use. The identity of the reported drug was confirmed through examination of leftover medication, bottles or strips, and prescription slips whenever possible. The formative research revealed that syrups, tablets, and powders of unknown identity prescribed in this setting were often antibiotics. If a child had >1 diarrheal episode in the last 4 weeks, information was collected on the most recent episode. If a child had been hospitalized more than once in the last 3 months, information was obtained for the most recent hospitalization.

The intervention was monitored by local health authorities at their routine monthly meetings to review programs. Feedback at the time of the meeting was given directly by the authorities to the health workers. Consistent with an effectiveness design, the project team's role was restricted to the measurement of specific outcomes.

### Sample Size and Statistical Analysis

We estimated that the 8000 to 9000 children aged 1 month to 4 years available from 3 PHCs would be adequate to detect a 30% change in ORS use rates during diarrhea occurring in the last 4 weeks, a 15% reduction in drug use rates during diarrhea, and a 20% reduction in care-seeking rates from health care providers for diarrhea with 90% power and 95% confidence.

Forms were created in the computer using Fox Pro software (Microsoft Corp, Redmond, WA) with range and consistency checks built in. Subsequent to double data entry and validation, files were merged into the main database daily. We analyzed data using Stata 8 (Stata Corp, College Station, TX). Because randomization was by community, we adjusted for cluster randomization.<sup>8</sup>

Analysis related to treatment-seeking behaviors, sources of care, treatment prescriptions by health care providers, ORS and zinc prescriptions and use, and out-of-pocket expenses incurred on the episode was based on the most recent diarrheal episode in the 4-week interval preceding the date of interview. The data on duration of use of the 14-day course of zinc are based on those diarrheal episodes for which zinc had been prescribed and 14 days had elapsed since the day of prescription.

### Definitions Used

In infants aged <2 months, diarrhea was defined based on caregiver's report of recent change in consistency and/or frequency of stools; for older children, caregiver's report of  $\geq 3$  loose or watery stools in a 24-hour period constituted a diarrheal illness.

Acute lower respiratory infection (ALRI) was defined as the presence of cough or difficult breathing along with fast breathing as reported by the mother.<sup>9</sup> To label a child as suffering from pneumonia, the caregiver use of local term "pneumonia" or "pasli chalna" was necessary.

Sources of care were categorized as Anganwadi workers, private providers, and others. The latter included the PHC physicians, auxiliary nurse midwives, and pharmacies. A "hospitalization" was defined as an inpatient admission to a government or private facility irrespective of the length of stay.

### RESULTS

The characteristics in the households included in the baseline survey were similar in the intervention and control areas with the exception of ALRI prevalence, which was significantly higher in the control areas ( $P = .0001$ ; Table 1). Caregivers were available for interview in >93% of eligible households in the 2 evaluation surveys (surveys 2 and 3; Fig 1). The median interval between the start of the intervention and survey 2 was 141 days (interquartile range [IQR]: 112–158 days) and 151 days (IQR: 136–165 days) in the intervention and control communities, respectively. The median interval between the end of surveys 2 and 3 was 120 days (IQR: 106–139 days) and 113 days (IQR: 99–123 days) in the intervention and control communities, respectively.

Treatment seeking for diarrhea, overall ( $P = .046$ ) and outside the village of residence ( $P < .0001$ ), was significantly less in intervention than in control communities (Table 2, survey 3). With the passage of time, treatment was increasingly sought from Anganwadi workers, and the private providers were used less (Table 2). As hypothesized, the prescription of drugs of unknown identity ( $P < .0001$ ) and of oral antibiotics was also less ( $P < .0001$ ) in the intervention areas (survey 3, Table 3). The median (IQR) out-of-pocket cost for treatment of a diarrheal episode was 25 rupees (IQR: 8–60 rupees) and 50 rupees (IQR: 25–100 rupees) in survey 2 and nil (IQR: 0–28 rupees) and 40 rupees (IQR: 20–85 rupees) in survey 3 in the intervention and control communities, respectively.

The diarrhea treatment prescription and actual use rates were ascertained for the 4-week window preceding the date of interview at the 2 surveys (2 and 3). The prescription rates of ORS were significantly higher in the intervention communities than in control communities at surveys 2 ( $P < .0001$ ) and 3 ( $P < .0001$ ; Table 3). Zinc was prescribed in 35.9% and 60.0% episodes in the 2 surveys, respectively, in the intervention communities. The use rates of ORS were higher in the intervention communities than in control communities in survey 2 (odds ratio [OR]: 6.33; 95% confidence interval [CI]: 2.38–16.80;  $P < .0001$ ; Fig 2) and in survey 3 (OR: 13.36; 95% CI: 9.00–19.80;  $P < .0001$ ; Fig 2). Zinc

**TABLE 1** Baseline Characteristics of Randomly Selected Households With  $\geq 1$  Child Aged 1 Month to 5 Years in the Intervention and Control Communities

Characteristics	Intervention ( <i>n</i> = 3083)	Control ( <i>n</i> = 3034)
Socioeconomic characteristics		
No. of family members, median (IQR)	6 (5–8)	6 (4–8)
Household income per year in rupees, median (IQR)	36 000 (24 000–60 000)	36 000 (24 000–60 000)
Caregivers who do not work outside home, <i>n</i> (%)	2956 (95.9)	2847 (93.8)
Mothers who have never been to school, <i>n</i> (%)	1514 (49.1)	1444 (47.6)
Mothers years of schooling, mean (SD)	4.1 (4.9)	4.2 (4.6)
Previous 24-h morbidity in children aged 1 mo to 5 y, <i>n</i> (%)		
Diarrhea <sup>a</sup>	241 (7.8)	210 (6.9)
ALRI <sup>b</sup>	21 (0.7)	48 (1.6)
Pneumonia <sup>c</sup>	29 (0.9)	49 (1.6)
Children hospitalized in last 3 mo, <i>n</i> (%)	108 (3.5)	116 (3.8)
Children with diarrhea in last 24 h and ORS was used, <i>n</i> (%)	4 (1.6)	10 (4.7)

<sup>a</sup> Diarrhea was defined as caregiver's report of recent change in consistency and/or frequency of stools in infants aged <2 months and caregiver's report of  $\geq 3$  loose or watery stools in a 24-hour period for older children.

<sup>b</sup> ALRI indicates the presence of cough or difficult breathing along with fast breathing as reported by mother.

<sup>c</sup> Pneumonia indicates the caregiver's use of local term "pneumonia" or "pasli chalna."

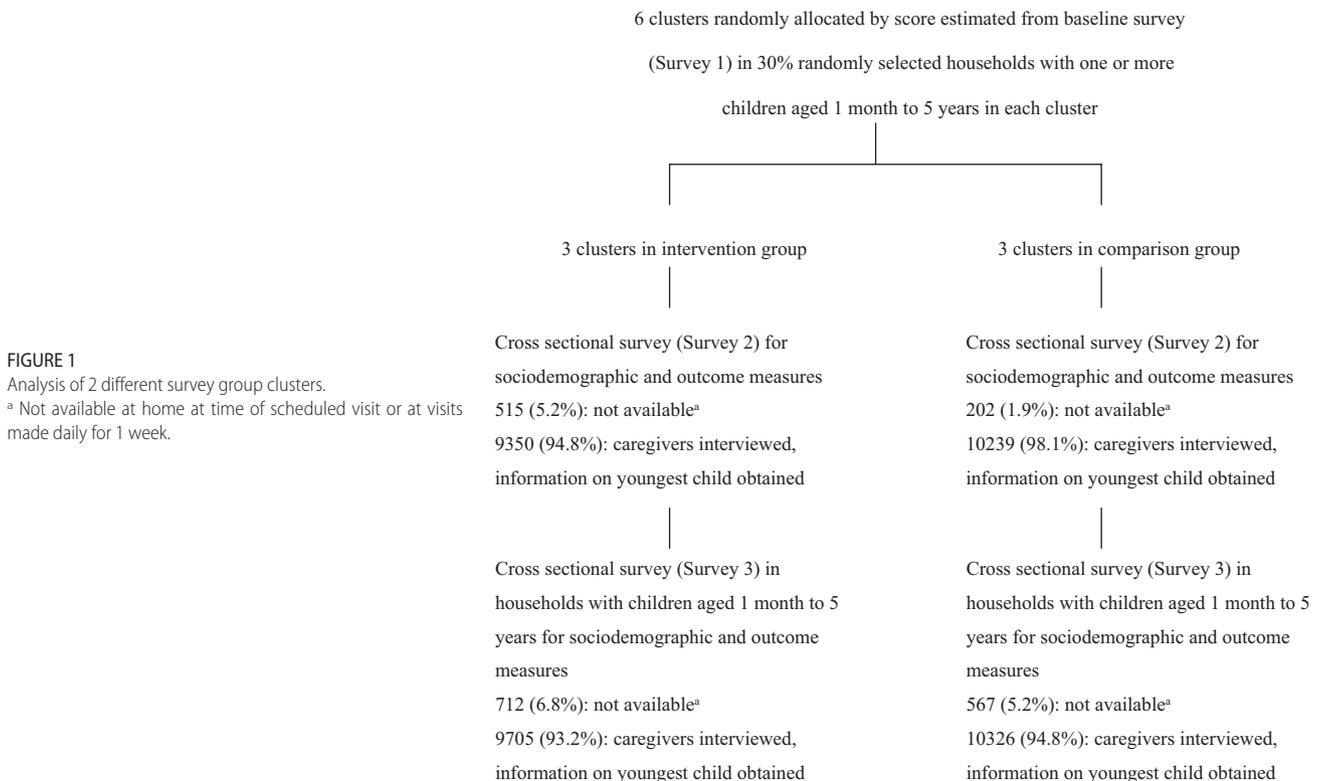
tablets had been used in 36.5% (*n* = 1571) and 59.8% (*n* = 1649) of diarrheal episodes in survey 2 and 3, respectively. Zinc was not reported to be used in any of the episodes in the control communities (Fig 2). Among those administered zinc by caregivers, 70.0% and 61.9% in the 2 surveys were given the complete 14-day course.

There was a significantly lower prevalence of diarrhea in the intervention versus the control communities (Table 4) in the 24-hour ( $P = .003$ ) and 2-week ( $P < .0001$ ) time intervals in survey 3. Using the local term for pneumonia or the WHO definition of ALRI,<sup>9</sup> the 24-hour prevalence was lower ( $P < .0001$ ) in the intervention

areas compared with control areas in survey 3 (Table 4). Hospital admissions because of any cause were also significantly lower in the intervention areas than control areas in survey 3 ( $P < .0001$ ), as were hospitalizations because of diarrhea ( $P = .023$ ) and pneumonia ( $P < .0001$ ; Table 4).

## DISCUSSION

An intervention that included caregiver education on the use of zinc and ORS during childhood diarrhea and provision of both zinc and ORS by public and private health care providers to caregivers was associated with



**FIGURE 1**

Analysis of 2 different survey group clusters.

<sup>a</sup> Not available at home at time of scheduled visit or at visits made daily for 1 week.

**TABLE 2 Treatment-Seeking Behavior and Sources of Care for the Most Recent Diarrheal Episode Occurring in the Last 4 Weeks in the Intervention and Control Communities**

Caregivers Interviewed	Survey 2			Survey 3		
	Intervention (n = 9350), n (%)	Control (n = 10 239), n (%)	OR (95% CI) <sup>a</sup>	Intervention in the last 4 wk (n = 9706), n (%)	Control in the last 4 wk (n = 10 326), n (%)	OR (95% CI) <sup>a</sup>
Children with ≥1 diarrheal episode in the last 4 wk	1571 (16.8)	2209 (21.6)	0.73 (0.56–0.96)	1649 (17.0)	2609 (25.3)	0.60 (0.43–0.84)
Children with diarrhea who sought treatment outside home	1023 (10.9)	1357 (13.2)	0.80 (0.64–1.01)	1135 (11.7)	1731 (16.8)	0.66 (0.43–0.99)
First source from where treatment was sought						
Village based						
Anganwadi worker	156 (9.9)	5 (0.2)	48.6 (10.6–221.64)	449 (27.2)	25 (1.0)	38.67 (13.8–108.12)
Private providers	505 (32.1)	860 (38.9)	0.74 (0.42–1.30)	461 (28.0)	968 (37.1)	0.66 (0.46–0.94)
Others <sup>b</sup>	76 (4.8)	55 (2.5)	1.99 (1.67–2.38)	93 (5.6)	160 (6.1)	0.91 (0.42–1.99)
Any of the above	737 (46.9)	920 (41.6)	1.24 (0.64–2.39)	1003 (60.8)	1153 (44.2)	1.96 (1.58–2.44)
Outside village						
Private providers	278 (17.7)	414 (18.7)	0.93 (0.38–2.31)	130 (7.9)	553 (21.2)	0.32 (0.17–0.60)
Government sources	8 (0.5)	23 (1.0)	0.49 (0.13–1.74)	2 (0.1)	25 (1.0)	0.12 (0.03–0.56)
Others <sup>b</sup>	0	4 (0.2)		0	12 (0.5)	
Any of the above	286 (18.2)	441 (20.0)	0.89 (0.37–2.13)	132 (8.0)	590 (22.6)	0.30 (0.16–0.56)

<sup>a</sup> Data were adjusted for cluster randomization.

<sup>b</sup> Others include PHC physicians, auxiliary nurse midwives, and drugstores.

substantial health benefits to children. These benefits included reduction in the prevalence of diarrhea and pneumonia, and in all-cause, diarrhea, and pneumonia hospitalizations. The intervention also resulted in easier access to diarrhea case management within the village itself, reduction in the use of unwarranted oral and injectable drugs during diarrhea, and reduction in the out-of-pocket costs for care of diarrhea to the family. ORS use increased substantially in the intervention areas, and there was no indication that use of zinc during diarrhea compromised the use of ORS, which is the mainstay of diarrhea treatment.

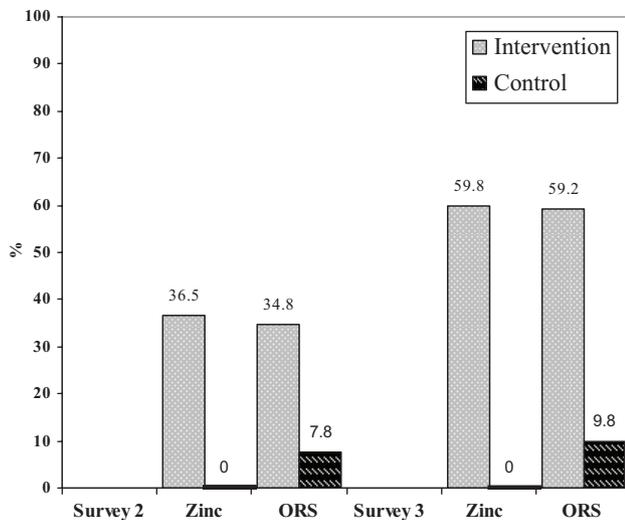
Several factors may have contributed to wide acceptance of this intervention. Studies have shown that communities desire a specific treatment for diarrhea in addition to ORS.<sup>10</sup> Promotion of zinc and ORS together, availability of both in the community, and effective ed-

ucation to caregivers may have led to higher rates of care seeking for diarrhea and, therefore, in increased ORS use rates. Families may have also been more likely to visit health care providers to seek a new treatment. In the intervention communities, families were sensitized to the benefits of zinc treatment for acute diarrhea and its availability with the village workers and private providers through awareness activities, such as posters in public places and announcements in the village. The engagement of private providers in the program was an important factor in achieving high rates of intervention compliance. The reduction in the use of unwarranted drug therapy during diarrhea may have resulted from the more frequent use of village-based health workers for source of treatment, a decrease in episode severity,<sup>1–2</sup> and reduction in diarrhea morbidity.<sup>11</sup> The reduction in drug prescriptions by private providers is consistent with

**TABLE 3 Treatment Prescribed by Health Care Providers for the Most Recent Episode of Diarrhea in the Last 4 Weeks in the Intervention and Control Communities Reported by Caregivers**

Children With ≥1 Diarrheal Episode in the Last 4 Weeks: Type of Treatment Prescribed by the First Source of Care	Survey 2			Survey 3		
	Intervention (n = 1571)	Control (n = 2209)	OR (95% CI) <sup>a</sup>	Intervention (n = 1649)	Control (n = 2609)	OR (95% CI) <sup>a</sup>
Syrup or tablet or powder of unknown identity	704 (44.8)	1182 (53.5)	0.70 (0.49–1.02)	361 (21.9)	1450 (55.6)	0.22 (0.15–0.34)
Oral antibiotics	59 (3.8)	356 (16.1)	0.20 (0.13–0.32)	34 (2.1)	382 (14.6)	0.12 (0.05–0.32)
Oral antidiarrheals	4 (0.2)	32 (1.4)	0.17 (0.02–1.27)	0	31 (1.2)	
Injections	234 (14.9)	304 (13.8)	1.10 (0.52–2.29)	81 (4.9)	286 (11.0)	0.42 (0.17–1.01)
Intravenous fluids	7 (0.4)	14 (0.6)	0.70 (0.51–0.96)	6 (0.4)	19 (0.7)	0.50 (0.22–1.14)
ORS prescribed	498 (31.7)	140 (6.3)	6.86 (2.91–16.19)	875 (53.1)	217 (8.3)	12.46 (8.95–17.35)
Zinc prescribed	564 (35.9)	0		997 (60.5)	0	

<sup>a</sup> Data were adjusted for cluster randomization.



**FIGURE 2**  
Use rates of zinc and ORS during the most recent diarrheal episode in the previous 4 weeks in the intervention and control communities.

provider beliefs that prescribing zinc and ORS together would be perceived by families of affected children as closer to their expectations of a satisfactory treatment package.<sup>11</sup>

Attributing observed benefits to individual components of the intervention is neither feasible nor was it the purpose of the trial. Some assumptions in this direction can, however, be made. The reduction in diarrhea and pneumonia morbidity is perhaps associated with the introduction of zinc treatment, because improving compliance with the standard WHO diarrhea management regimen, including ORS, is not associated with such an effect. In addition, some of the previous individually randomized trials of zinc treatment for diarrhea have shown reduction in subsequent morbidity.<sup>11,12</sup> The re-

duction in the use of antidiarrheal agents may be an indirect effect of zinc treatment, because training in routine case management, including judicious use of antibiotics, was provided in the intervention and control communities. This is plausible, because families desire a drug in addition to ORS, and this influences prescribing practices. It is notable that years of effort have not succeeded in achieving a substantial decline in the use of antibiotics and antidiarrheal agents in India.<sup>13–15</sup>

The reduction in hospitalizations related to diarrhea may have resulted from several factors, such as ready availability of treatment in the village itself, increase in ORS use rates and zinc treatment, and the overall education on early care seeking and diarrhea treatment. That zinc treatment also contributed significantly to reduced hospitalizations is indirectly supported by the decline in pneumonia hospitalizations, because no specific treatment for pneumonia was provided.

The findings of this study are consistent with observations from a community-based intervention trial in Bangladesh, India, which reported that diarrhea treatment education and easy community access to zinc and ORS among caregivers are associated with reduced diarrhea morbidity and overall mortality in children.<sup>11</sup> In this trial, increased use of ORS and decreased use of drugs for diarrhea were also reported.<sup>16</sup>

The low ORS use rate in the control communities is a matter of concern. The national average ORS use rate is ~18% for childhood diarrhea, and it tends to be higher in urban areas.<sup>17</sup>

Several important limitations of this study need to be noted. It is possible that the observed effects may be influenced by factors other than zinc treatment. The private providers contributed significantly to the observed effects when zinc tablets were provided to them free of cost, and they could refer their patients to village-level workers to obtain ORS packets. In future programs,

**TABLE 4** Impact of the Intervention on Prevalence of Morbidity and Hospitalizations in the Intervention and Control Communities

Caregivers Interviewed	Survey 2			Survey 3		
	Intervention (n = 9350), n (%)	Control (n = 10 239), n (%)	OR (95% CI) <sup>a</sup>	Intervention (n = 9706), n (%)	Control (n = 10 326), n (%)	OR (95% CI) <sup>a</sup>
Morbidity in the previous 24 h						
Diarrhea <sup>b</sup>	429 (4.6)	639 (6.2)	0.72 (0.50–1.04)	592 (6.1)	822 (8.0)	0.75 (0.62–0.91)
Pneumonia <sup>c</sup>	165 (1.8)	235 (2.3)	0.76 (0.54–1.08)	37 (0.4)	105 (1.0)	0.37 (0.22–0.64)
ALRI <sup>d</sup>	147 (1.6)	171 (1.8)	0.94 (0.74–1.20)	26 (0.3)	97 (0.9)	0.28 (0.19–0.42)
Morbidity in the previous 14 days						
Diarrhea	1217 (13.0)	1851 (18.1)	0.68 (0.50–0.91)	1384 (14.3)	2368 (22.9)	0.56 (0.41–0.75)
Pneumonia	497 (5.3)	651 (6.4)	0.83 (0.55–1.24)	231 (2.4)	434 (4.2)	0.55 (0.25–1.25)
ALRI	411 (4.4)	474 (4.6)	0.95 (0.71–1.26)	175 (1.8)	391 (3.8)	0.47 (0.20–1.06)
Hospital admissions						
All cause	365 (3.9)	517 (5.0)	0.76 (0.48–1.21)	268 (2.8)	674 (6.5)	0.41 (0.29–0.57)
Diarrhea	157 (1.7)	180 (1.8)	0.95 (0.68–1.34)	105 (1.1)	162 (1.6)	0.69 (0.50–0.95)
Pneumonia	150 (1.6)	306 (3.0)	0.53 (0.25–1.10)	132 (1.4)	470 (4.5)	0.29 (0.15–0.54)

<sup>a</sup> Data were adjusted for cluster randomization.

<sup>b</sup> Diarrhea was defined as caregiver's report of recent change in consistency and/or frequency of stools in infants aged <2 months and caregiver's report of ≥3 loose or watery stools in a 24-hour period for older children.

<sup>c</sup> ALRI indicates the presence of cough or difficult breathing along with fast breathing as reported by mother.

<sup>d</sup> Pneumonia indicates the caregiver's use of local term "pneumonia" or "pasli chalna."

if the private providers are not engaged in diarrhea treatment and given access to zinc and ORS, the actual effects may be less than was observed in this trial. We cannot exclude the possibility of a reporting bias in favor of the intervention communities for diarrhea and pneumonia prevalence. Because case management, including zinc treatment, was only provided for diarrhea, and an impact was observed for pneumonia as well, it is unlikely that reporting bias was a major problem. The possibility of families moving among clusters during the study cannot be excluded, but this possible contamination would likely reduce the apparent intervention effect. However, because use of zinc was not reported in the control areas, this may not be a substantial issue. The results reported in this study are in children aged 1 month to 4 years. In individually randomized efficacy trials, a beneficial impact of zinc supplementation in acute diarrhea has only been reported for children >6 months of age and not in younger infants.<sup>18</sup> Additional studies are required to assess the impact of zinc treatment in early infancy, particularly in settings where the prevalence of low birth weight rates is high. Finally, the baseline ALRI prevalence was significantly higher in control communities than in intervention communities. Because these data were obtained in only one third of subjects, it is possible that these findings are a chance occurrence. Adjustment for baseline characteristics would be appropriate but was not feasible, because outcomes were measured through periodic cross-sectional surveys with different sample households in each survey.

## CONCLUSIONS

This study demonstrates that an intervention to improve diarrhea management with ORS and zinc is feasible and highly acceptable in rural Indian communities. The resulting health benefits are substantial and accomplished with a reduction in the cost to families for diarrhea treatment from current practice. Further scaling up of this intervention should be given priority in India and other countries with high disease burden because of diarrhea and pneumonia.

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## Effectiveness of Zinc Supplementation Plus Oral Rehydration Salts Compared With Oral Rehydration Salts Alone as a Treatment for Acute Diarrhea in a Primary Care Setting: A Cluster Randomized Trial

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