Effect of Intensive Handwashing Promotion on Childhood Diarrhea in High-Risk Communities in Pakistan

A Randomized Controlled Trial

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Context Washing hands with soap prevents diarrhea, but children at the highest risk of death from diarrhea are younger than 1 year, too young to wash their own hands. Previous studies lacked sufficient power to assess the impact of household handwashing on diarrhea in infants.

Objective To evaluate the effect of promoting household handwashing with soap among children at the highest risk of death from diarrhea.

Design, Setting, and Participants A cluster randomized controlled trial of 36 low-income neighborhoods in urban squatter settlements in Karachi, Pakistan. Field workers visited participating households at least weekly from April 15, 2002, to April 5, 2003. Eligible households located in the study area had at least 2 children younger than 15 years, at least 1 of whom was younger than 5 years.

Interventions Weekly visits in 25 neighborhoods to promote handwashing with soap after defecation and before preparing food, eating, and feeding a child. Within intervention neighborhoods, 300 households (1523 children) received a regular supply of antibacterial soap and 300 households (1640 children) received plain soap. Eleven neighborhoods (306 households and 1528 children) comprised the control group.

Main Outcome Measure Incidence density of diarrhea among children, defined as the number of diarrheal episodes per 100 person-weeks of observation.

Results Children younger than 15 years living in households that received handwashing promotion and plain soap had a 53% lower incidence of diarrhea (95% confidence interval [CI], –65% to –41%) compared with children living in control neighborhoods. Infants living in households that received handwashing promotion and plain soap had 39% fewer days with diarrhea (95% CI, –61% to –16%) vs infants living in control neighborhoods. Severely malnourished children (weight for age z score, <–3.0) younger than 5 years living in households that received handwashing promotion and plain soap had 42% fewer days with diarrhea (95% CI, –69% to –16%) vs severely malnourished children in the control group. Similar reductions in diarrhea were observed among children living in households receiving antibacterial soap.

Conclusion In a setting in which diarrhea is a leading cause of child death, improvement in handwashing in the household reduced the incidence of diarrhea among children at high risk of death from diarrhea.

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NEARLY 2 MILLION CHILDREN die annually from diarrheal disease.[1] A recent meta-analysis concluded that handwashing promotion interventions decrease diarrhea by a mean of 47%.[2] The authors estimate that such interventions could prevent 1 million child deaths per year.[2] However, the systematic meta-analysis and the studies it included summarized the reduction in diarrheal rates among all children or all family members. But all family members are not at equal risk of death from diarrhea. Children younger than 5 years are at much higher risk of death from diarrhea than older children and adults,[1] and infants (younger than 1 year) are at the highest risk of death. Verbal autopsy studies from Egypt,[3] Pakistan,[4] Bangladesh,[5] and Ethiopia[6] report that 43% to 78% of deaths from diarrhea among children younger than 5 years occur in the first year of life.

Infants cannot wash their own hands and therefore cannot interrupt the transfer of pathogens between their hands and their mouth. Infants might benefit from a lower rate of diarrheal pathogen transmission from parents and siblings who wash their hands more

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frequently with soap but the benefit to the infant might be quite different from the overall benefit.

We identified only 2 handwashing intervention trials from developing countries that reported diarrheal rates among infants.[7,8] In 1 study in which the intervention assignment was randomized,[7] the analysis accounted for the cluster design but the measured 24% reduction in diarrheal disease among children younger than 1 year was not significantly different from the control group. A second handwashing promotion study[8] reported a 61% reduction in diarrheal disease among children younger than 1 year but there was only 1 intervention handwashing promotion community and 1 control community. The data were analyzed at the individual level and the repeated measures of each individual were not accounted for in the analysis.[8]

In addition to young age, malnutrition[9-11] and persistent diarrhea[10,12,13] are important risk factors for death from diarrhea. We cannot identify any handwashing intervention trials that evaluated effectiveness among malnourished children or for persistent diarrhea. Thus, the effectiveness of handwashing with soap in preventing diarrhea among the most vulnerable children is unclear.

In Karachi, Pakistan, more than 4 million low-income residents live in squatter settlements where they do not own legal title to the land and municipal infrastructure is limited.[14] A verbal autopsy study from these communities concluded that 41% of all childhood deaths younger than 5 years were due to diarrhea.[15] Seventy-three percent of these diarrheal deaths occurred among infants.[15] We evaluated whether promoting washing hands with soap decreased diarrhea among children at the highest risk of death from diarrhea in Karachi squatter settlements.

METHODS

Setting

The Karachi Soap Health Study was conducted in adjoining multiethnic squatter settlements in central Karachi—Bilal, Hazara, Manzoor, and Mujahid colonies—in collaboration with Health Oriented Preventive Education (HOPE), a nongovernmental organization that operates local health clinics and supports community-based health and development initiatives.

Most residents in these communities have household toilets but the discharge flows into open sewers. After defecation, toilet paper is rarely used. Instead, residents routinely rinse their anus with water from a pitcher. Although handwashing, typically with water alone, is part of ritual preparation for prayer in these communities, thorough washing of hands with soap is less common, even though affordable hand soap is widely available throughout these communities from small neighborhood shops. The water used for drinking and handwashing in these communities is heavily contaminated with fecal organisms.[16] Hands are typically dried on clothing. Clothing is usually laundered after several days of wear.

Study Groups

Field workers identified 42 candidate neighborhoods of 60 to 273 households, separated from one another by a street or market area. Field workers conducted a census of these neighborhoods, and before intervention assignment, identified and obtained informed consent from 1050 households. Eligible households were located in the study area, had at least 2 children younger than 15 years, at least 1 of whom was younger than 5 years, and planned to continue to reside in their homes for the duration of the study.

The field workers listed the candidate neighborhoods in order of proximity to their field center. One of the investigators not involved in recruiting neighborhoods or households (S.P.L.) programmed a spreadsheet to generate randomly the integers 1 or 2 with twice the probability of generating a 2 vs a 1. He applied the random numbers sequentially to the list of neighborhoods. Those neighborhoods with a 1 were assigned to control and those with a 2 were assigned to handwashing promotion. Random assignment continued until neighborhoods comprising 600 handwashing promotion households and 306 control households were assigned. Ultimately, 25 neighborhoods were assigned to handwashing promotion and 11 to control (FIGURE 1). Handwashing promotion was assigned at the neighborhood level because a number of the handwashing promotion activities were neighborhood-level activities. Antibacterial vs plain soap was randomly assigned at the household level.

Interventions

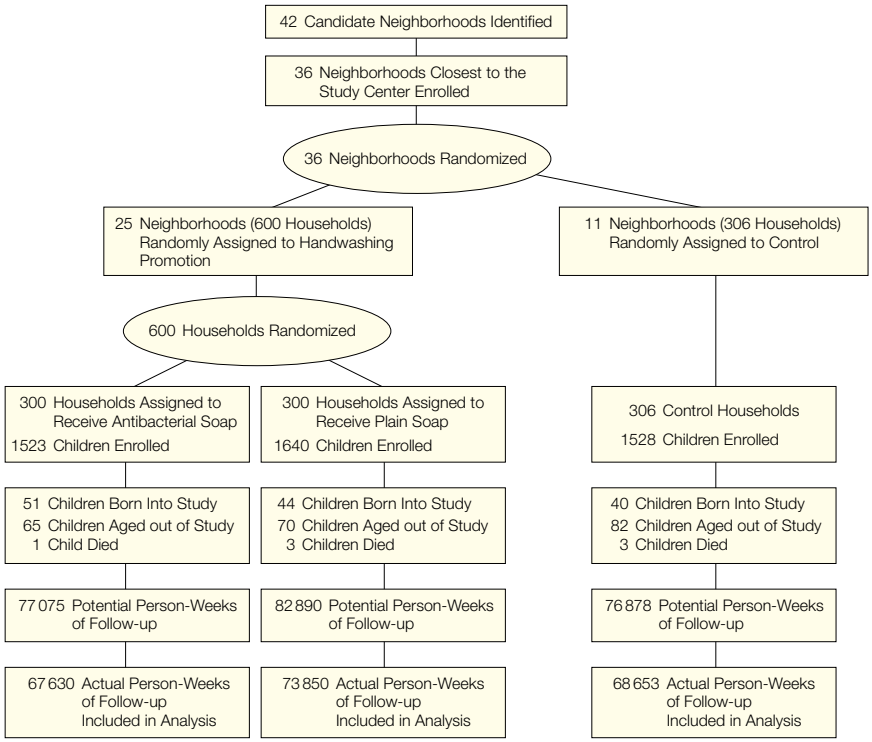
Handwashing Promotion. Field workers conducted neighborhood meetings about handwashing. They used slide shows, videotapes, and pamphlets to illustrate health problems resulting from contaminated hands and to provide specific handwashing instructions. The core handwashing promotion activity was regular, at least weekly, household visits by the field workers. Each field worker spoke the first language of the study households they visited. They described in detail the importance of handwashing. They encouraged participants to wet their hands, lather them completely with soap, and rub them together for 45 seconds. Hands were typically dried on the participants' clothing. Field workers encouraged all persons in intervention households old enough to understand (generally those participants older than 30 months) to wash their hands after defecation and cleaning an infant who had defecated, and before preparing food, eating, and feeding infants. They encouraged adopting regular handwashing habits. Field workers also encouraged participants to bathe once a day with soap and water. Field workers encouraged questions and discussion about handwashing. They resupplied the families with soap as needed. Field workers did not provide educational messages on water treatment, food hygiene, or other strategies to decrease diarrhea.

Soap. The antibacterial soap contained 1.2% triclocarban as an antibacterial agent. The plain soap was identical to the antibacterial soap with the single exception that it did not contain

triclocarban. Both soaps were provided as 90-g white bars without a brand name or symbol and packaged identically in a generic white wrapper. Cases of 96 bars were identified by serial numbers that were matched to households. Neither the field workers nor the families knew whether the family's soap was antibacterial or plain.

Control. Field workers provided control households with a regular supply of children's books, notebooks, pens, and pencils to help with their children's education but no products that would be expected to affect diarrhea. Field workers neither encouraged nor discouraged handwashing in control households. Field workers visited control and intervention households with equal frequency to collect health outcome data but the visits were shorter in control households because no health education or encouragement for behavior change was provided.

Figure 1. Intervention Assignment and Completed Follow-up



Field Workers

Field workers recruited from the study or nearby communities were extensively trained in interviewing techniques, data recording, approaches to promote handwashing, and measuring and weighing children. The same field workers promoted handwashing and collected outcome data during their household visits.

Measurements

Trained field workers conducted a preintervention baseline survey of household characteristics. They identified each child (aged <15 years) in the household. Children's dates of birth were confirmed with birth certificates or immunization records. Field workers visited participating households at least weekly for 1 year (April 15, 2002, to April 5, 2003) and asked the mother or other caregiver if the children had diarrhea (≥3 loose stools within 24 hours) in the preceding week, and, if so, for how many days. Typically, field workers visited each household twice during the week to ensure that episodes of diarrhea from both early and late in the week were recalled. Supervisors revisited 40% of homes each week and reviewed the history of diarrhea among family members. The history recorded by the supervisor was compared with the history recorded by the field worker and, if there was a discrepancy, the fieldworker and supervisor revisited the house to clarify the difference.

Field workers weighed participating children younger than 5 years at baseline and every 4 months. Field workers weighed children 3 years or younger by using a hanging scale (Salter, Tonbridge, Kent, England) and children older than 3 years by using a bathroom scale. We calculated weight for age *z* scores to compare the study children's weight with the National Center for Health Statistics standards. The *z* score represents the number of standard deviations that the child's measured weight for age differs from the standard healthy population. We calculated the mean weight for age *z* score from the multiple weighing sessions throughout the study for each child. We classified children as moderately malnourished if their mean weight for age *z* score was less than –2.0 and –3.0 or higher, and severely malnourished if their mean weight for age *z* score was less than –3.0.

Statistics

A primary hypothesis of the Karachi Soap Health Study was that promoting handwashing with antibacterial or plain soap would significantly reduce the amount of diarrheal illness compared with standard habits and practices in the control group. (Other primary hypotheses of the Karachi Soap Health Study address the effectiveness of bathing and handwashing with antibacterial or plain soap in preventing impetigo and acute respiratory illness and will be reported separately.) A primary study outcome was the incidence density of diarrhea (ie, the number of new episodes of diarrhea divided by the at-risk person-weeks of observation). We considered a child at risk for a new episode of diarrhea if he or she reported no diarrhea in the previous week. We also measured disease outcome using longitudi-

nal prevalence because it is more closely associated with growth faltering and child mortality than is diarrhea incidence.[17] We calculated longitudinal prevalence by summing the number of days each child had diarrhea and dividing by the total number of days of observation.

We calculated a sample size of 239 households per intervention group, assuming 1.2 episodes of diarrhea per 100 person-weeks among children younger than 15 years in the control group, 25% lower incidence of diarrhea in each handwashing promotion group vs control, 3.8 children per household, and a doubling of sample size to offset the effect of clustering by neighborhood and repeated measures. We increased the sample size to 300 households per intervention group to assess other health outcomes, which will be reported separately.

Because we assigned soap promotion vs control at the neighborhood level, we analyzed the comparison of outcomes at the neighborhood level. Specifically, within each neighborhood among person-weeks within the subgroup of interest, we identified the total number of new episodes of diarrhea or days of diarrhea and divided it by the total number of person-weeks at risk for children in that neighborhood within the subgroup of interest. We calculated rates by intervention assignment by taking the mean of the appropriate neighborhood rates, weighted by the person-weeks of observation from each neighborhood that contributed to the mean. We calculated rate ratios by dividing the weighted means from intervention neighborhoods by the weighted means from control neighborhoods.[18] We calculated 95% confidence intervals around these rate ratios using Taylor Series approximations to obtain SEs.[19] This approach calculated confidence intervals (CIs) that reflected the different distribution of proportions at the neighborhood level. We report the percentage difference in outcome between intervention and control (ie, rate ratio minus 1). The disease experience of each child, household, and neighborhood was tracked and analyzed with the group they were originally assigned to (ie, intention-to-treat analysis). We considered $P \leq .05$ as statistically significant. We used SAS version 9.0 and JMP version 5.0 (SAS Institute Inc, Cary, NC) to conduct the statistical analysis.

Table 1. Baseline Household Characteristics by Group*

Characteristics	Antibacterial Soap (n = 300)	Plain Soap (n = 300)	Control (n = 306)
Persons per household, mean (SD)	9.3 (4.4)	10.0 (4.8)	9.1 (4.1)
Children aged <5 years per household, mean (SD)	1.7 (1.1)	1.7 (1.1)	1.6 (1.0)
Families per household, mean (SD)	1.3 (0.62)	1.4 (0.76)	1.3 (0.66)
Years family had been living in Karachi, Pakistan, mean (SD)	24.7 (15.1)	25.5 (16.0)	25.5 (15.7)
No. of rooms in house, mean (SD)	2.0 (0.91)	2.0 (0.99)	2.1 (0.94)
Bars of hand soap purchased in preceding 2 weeks, mean (SD)	1.9 (0.75)	2.0 (0.75)	1.9 (0.69)
Households with infants	74 (24)	73 (24)	73 (24)
Children aged <5 years			
With moderate malnutrition†	125 (26)	103 (21)	114 (24)
With severe malnutrition‡	20 (4.1)	24 (4.8)	19 (4.0)
Parent of the youngest child is literate			
Father	176 (59)	171 (57)	196 (64)
Mother	113 (38)	107 (36)	98 (32)
Monthly household US income <$60	137 (46)	131 (44)	152 (50)
Refrigerator ownership	111 (37)	107 (36)	116 (38)
Primary drinking water source			
Municipal supply within the house	34 (11)	35 (12)	30 (10)
Municipal supply at a community tap	42 (14)	59 (20)	45 (15)
Tanker truck	168 (56)	170 (57)	189 (62)
Water bearer	37 (12)	25 (8)	31 (10)
Bore hole	19 (6)	11 (3)	11 (4)
Toilet without flush tank in the home	289 (96)	285 (95)	301 (98)
Handwash station with soap and water observed by study workers	286 (95)	274 (91)	287 (94)
Feces visible where children have access	35 (12)	20 (7)	32 (10)

*Data are No. (%) unless otherwise specified.
†Weight for age *z* score is less than –2.0 and –3.0 or more.
‡Weight for age *z* score is less than –3.0.

Ethics

Community leaders and heads of households provided informed consent. Ill children were assessed by field workers and referred to the appropriate level of health care. The first line of treatment for diarrhea was oral rehydration solution. Ill children referred by field workers were offered clinical services free of charge at HOPE health care facilities located in these communities. The study protocol was approved by the ethics review committee of the Aga Khan University and an institutional review board of the Centers for Disease Control and Prevention.

RESULTS

The 36 neighborhoods in the study included a median 115 households (range, 60-273 households). A median of 21% of households in each neighborhood (range, 6%-39%) met the eligibility criteria for the study. All eligible households chose to enroll. Thus, for the study, a median 26 households participated per neighborhood (range, 9-37; interquartile range, 21-30). Within the 25 neighborhoods randomized to handwashing promotion, 300 households (1523 children) were randomized to receive antibacterial soap and 300 households (1640 children) were randomized to receive plain soap (Figure 1). Eleven neighborhoods, representing 306 households and 1528 children, were randomized to the standard habits and practices control group.

During 51 weeks of follow-up, diarrhea outcome information was collected on 210 133 person-weeks, representing 89% of the study populations' experience (88% in antibacterial soap, 89% in plain soap, and 89% in control households). The most common reason for failure to collect information was that study participants had temporarily left the city to visit relatives. There was a discrepancy between the field worker's record of diarrhea symptoms and the supervisor's record in less than 1% of supervisory visits.

At baseline, households in the 3 intervention groups were of similar size and socioeconomic status, had a comparable number of young children, a similar proportion of whom were malnourished, similar sources of water, sanitary facilities, and reported hand soap purchases (TABLE 1). Mothers reported breastfeeding their children younger than 2 years during 95% of child-weeks of observation in the antibacterial soap group, 95% in the plain soap group, and 94% in the control group. Exclusive breastfeeding was less common. Mothers reported exclusively breastfeeding their infants during 43% of infant-weeks of observation in the antibacterial soap group, 42% in the plain soap group, and 45% in the control group.

During the course of the study, handwashing promotion households received a mean 3.3 bars of the study soap per week; this translates into each household resident using a mean 4.4 g/d of soap.

Compared with children living in control neighborhoods, children living in households that received plain soap and encouragement to wash their hands had a 53% lower incidence of diarrhea (95% CI, –65% to –41%) and a 50% lower longitudinal prevalence of diarrhea (95% CI, –65% to –35%; TABLE 2). The incidence and longitudinal prevalence of diarrhea among households receiving antibacterial soap was similar to households receiving plain soap.

The mean differences in diarrhea rates between handwashing promotion and control neighborhoods were consistent across most of the individual neighborhoods (FIGURE 2). Indeed, the diarrhea incidence in 8 of 11 control neighborhoods was higher than in any of the handwashing promotion neighborhoods.

For the first 8 weeks of the study, the incidence of diarrhea was similar among children living in handwashing promotion neighborhoods compared with children in control neighborhoods. After 8 weeks, the incidence of diarrhea among children living in handwashing promotion neighborhoods was consistently lower than children living in control neighborhoods (FIGURE 3).

Diarrhea was more common among younger children (6.2% longitudinal prevalence among infants and 5.5% among children aged 1-2 years) vs older children (3.3% among children aged 2-5 years and 1.1% among children aged 5-15 years). Infants living in neighborhoods where handwashing was actively promoted and in households that received plain soap had a 39% lower longitudinal prevalence of diarrhea (95% CI, –61% to –16%) vs infants living in control neighborhoods (TABLE 3). Children older than 5 years living in households that received plain soap had a 57% reduction in diarrhea vs children living in control neighborhoods (95% CI, –73% to –41%). The age-specific longitudinal prevalence of diarrhea among households receiving antibacterial soap was similar to households receiving plain soap.

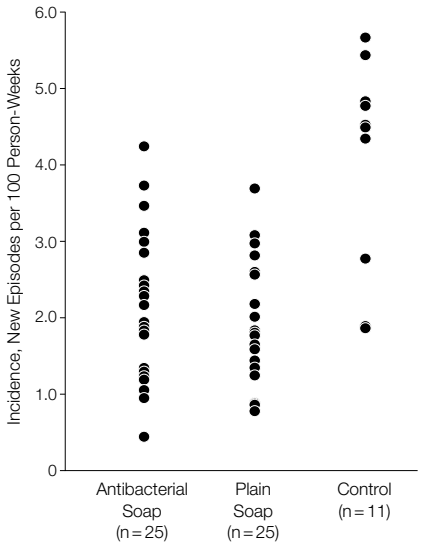
Malnourished children had more diarrhea (5.3% and 4.8% prevalence among children with severe and moderate malnutrition vs 3.7% among children without malnutrition). The effectiveness of soap in preventing diarrhea was independent of childrens' nutritional status. Among children younger than 5 years living in households that received plain soap and handwashing promotion, those who were severely malnourished had a 42% lower longitudinal prevalence of diarrhea (95% CI, –69% to –16%) and those who were moderately malnourished had a 41% lower longitudinal prevalence (95% CI, –65% to –17%) vs children of compa-

Table 2. Primary Diarrhea Outcomes by Group

Diarrhea Outcomes	Antibacterial Soap (n = 300)	Plain Soap (n = 300)	Control (n = 306)
Incidence (197 049 person-weeks at risk)*			
Mean†	2.02	1.91	4.06
% Difference vs control (95% CI)	–50 (–64 to –37)	–53 (–65 to –41)	1.00
Longitudinal prevalence (210 133 person-weeks at risk)‡			
Mean†	1.57	1.46	2.92
% Difference vs control (95% CI)	–46 (–63 to –30)	–50 (–65 to –35)	1.00

Abbreviation: CI, confidence interval.
*Incidence is episodes per 100 person-weeks at risk.
†Mean rates were calculated by taking the mean of the neighborhood rates weighted by the person-weeks at risk from each neighborhood.
‡Prevalence is days with diarrhea divided by days of observation.

Figure 2. Diarrhea Incidence for Each Neighborhood by Intervention Group



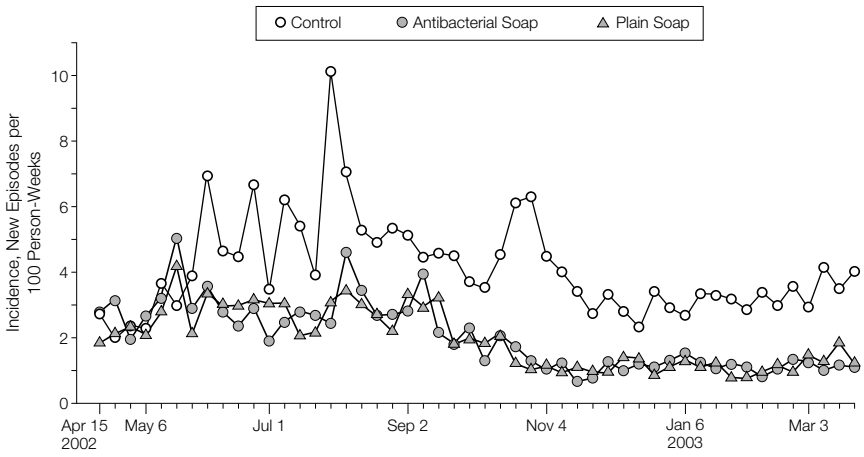
Diarrhea incidence is defined as number of new episodes per 100 person-weeks. All neighborhoods (number indicated in parentheses) are shown for each group but data markers may overlap due to close measurements of diarrhea incidence.

rable age and nutrition status living in control neighborhoods (TABLE 4). The malnutrition-specific longitudinal prevalence of diarrhea among households receiving antibacterial soap was similar to households receiving plain soap.

Compared with control neighborhoods, children living in households that received plain soap and handwashing promotion were 56% less likely to visit a health care practitioner for diarrhea (95% CI, –69% to –43%). Hospitalization for diarrhea was uncommon, occurring in only 0.23% of the observed person-weeks. Children living in households receiving plain soap and handwashing promotion were 26% less likely to be hospitalized for diarrhea but this difference was not statistically significant (95% CI, –100% to 66%). Only 5% of observed episodes of diarrhea were persistent diarrhea (ie, episodes lasting >14 days). Children living in households receiving plain soap and handwashing promotion were 31% less likely to have a persistent episode of diarrhea but this difference was not statistically significant (95% CI, –70% to 8%). The probability of visiting a health care practitioner for diarrhea, being hospitalized for diarrhea, and having a persistent episode of diarrhea was similar among households receiving antibacterial soap vs households receiving plain soap (TABLE 5).

Seven children died during the study. For 3 of the children, 1 from each of the study groups, the mother reported that the child had diarrhea as part of the illness that led to his/her death. These deaths occurred in children aged 33, 36, and 63 months. The diarrhea-specific death rate was 1.6 deaths per 1000 children younger than 5 years per year.

Figure 3. Diarrhea Incidence by Week and Intervention



Diarrhea incidence is defined as number of new episodes per 100 person-weeks.

Table 3. Mean Longitudinal Prevalence of Diarrhea by Age and Group*

Diarrhea Outcomes	Antibacterial Soap (n = 300)	Plain Soap (n = 300)	Control (n = 306)
<1 y (8392 observed person-weeks) Prevalence, %†	5.36	5.16	8.41
% Difference vs control (95% CI)	–36 (–55 to –17)	–39 (–61 to –16)	1.00
≥1 to 2 y (10 578 observed person-weeks) Prevalence, %†	4.24	4.73	7.60
% Difference vs control (95% CI)	–44 (–61 to –27)	–38 (–57 to –19)	1.00
≥2 to 5 y (44 200 observed person-weeks) Prevalence, %†	2.48	2.58	4.91
% Difference vs control (95% CI)	–49 (–69 to –30)	–48 (–67 to –29)	1.00
≥5 to 15 y (146 963 observed person-weeks) Prevalence, %†	0.82	0.73	1.70
% Difference vs control (95% CI)	–52 (–71 to –33)	–57 (–73 to –41)	1.00

Abbreviation: CI, confidence interval.
*Longitudinal prevalence was calculated by taking the mean of the neighborhood longitudinal prevalences by the person-weeks observed for each neighborhood.
†Number of person-days with diarrhea divided by the number of person-days under surveillance.

COMMENT

In these communities in which diarrhea is the leading cause of childhood death, wash water was heavily contaminated with human fecal organisms, and no provisions were made for clean drying of hands, handwashing promotion with soap halved the burden of diarrheal disease. This study addressed many of the methodological concerns raised by previous reviewers of hygiene interventions.[2,20] The intervention was randomly assigned and included a contemporaneous control group. Diarrhea prevalence was similar at the beginning of the study between intervention and control groups. The analysis accounted for the cluster design of the intervention and had sufficient power to evaluate the effectiveness of the intervention in subgroups of children at the highest risk of death from diarrhea. The overall level of reduction in longitudinal prevalence of diarrhea among children in households with handwashing promotion (50% in the plain soap and 46% in the antibacterial soap groups) was remarkably close to the 47% decrease calculated in the recent meta-analysis on the effect of handwashing in preventing diarrhea.[2]

Our study was not designed to evaluate child mortality as an outcome. Only 3 children died from diarrhea during the study, 1 from each group. Our rate of death from diarrhea was 79% lower than the diarrhea-specific death rate for children younger than 5 years previously reported from similar communities.[15] The close surveillance for childhood illness by field workers and rapid referral to appropriate clinical care at no cost to the

family likely contributed to this low death rate.

However, our study did have sufficient power to evaluate the effectiveness of handwashing promotion with soap among children at high risk for death from diarrhea. Important risk factors for diarrhea-specific death in developing countries include age younger than 1 year,[3-6,15] malnutrition,[9-11] and persistent diarrhea.[10,12,13] In our study, infants who were unable to wash their hands had 39% fewer days of diarrhea if they lived in households that received plain soap and encouragement to wash hands compared with control households. This 39% reduction in diarrhea for infants was less than the 57% reduction observed among children aged between 5 and 15 years who are able to regularly wash their own hands.

Handwashing with soap removes transient potentially pathogenic organisms from hands.[21,22] If individuals wash their hands, they are less likely to transmit pathogens from their hands to their mouths. This mechanism benefits the person washing his/her hands and is not available to infants. However, persons washing their hands are also less likely to transfer pathogens from their hands to the hands of others, or to food or the environment that is shared with others. Moreover, parents and siblings who prevent their own episodes of diarrhea are less likely to shed pathogens to the vulnerable infant's environment. Our study findings suggest that household handwashing interrupts transmission of diarrheal pathogens sufficiently to markedly reduce diarrhea among infants.

Moderately or severely malnourished children had as large a reduction in diarrhea from improvement in household handwashing as children without malnutrition. Although some reduction in persistent diarrhea (19%-31%) was observed within households receiving soap and handwashing promotion, persistent diarrhea was uncommon and these reductions were not statistically significant. Nevertheless, the effectiveness of handwashing with soap in reducing the longitudinal prevalence of diarrhea among children at increased risk of death from diarrhea—infants and malnourished children—suggests that handwashing with soap would reduce the risk of death from diarrhea.

We found no significant difference in diarrheal disease among persons living in households receiving antibacterial soap compared with plain soap. This is not surprising because triclocarban is a bacteriostatic agent that inhibits the growth of some gram-positive bacteria but is not effective against gram-negative bacteria, viruses, or parasites that cause infectious diarrhea.[23,24]

There are important limitations to our study. First, study personnel and participants were not blinded to the intervention. It is possible that study participants in the handwashing promotion groups, grateful for the soap, minimized reported episodes of diarrhea in the household, or field workers recorded fewer episodes because of a desire to meet the expectation of study sponsors. However, field workers were formally trained and the importance of accurate recording of reported symptoms was stressed. Unannounced supervisory visits did not identify systematic errors.

Table 4. Mean Longitudinal Prevalence of Diarrhea Among Children Younger Than 5 Years by Nutritional Status and Group*

Nutrition Status	Antibacterial Soap (n = 300)	Plain Soap (n = 300)	Control (n = 306)
No malnutrition† (41 726 person-weeks at risk)			
Diarrhea prevalence, %‡	2.91	2.81	5.32
% Difference vs control (95% CI)	−45 (−65 to −25)	−47 (−66 to −29)	1.00
Moderate malnutrition§ (14 685 person-weeks at risk)			
Diarrhea prevalence, %‡	3.54	4.12	7.01
% Difference vs control (95% CI)	−49 (−66 to −33)	−41 (−65 to −17)	1.00
Severe malnutrition‖ (3916 person-weeks at risk)			
Diarrhea prevalence, %‡	4.11	4.41	7.64
% Difference vs control (95% CI)	−46 (−75 to −18)	−42 (−69 to −16)	1.00

Abbreviation: CI, confidence interval.
*Longitudinal prevalence was calculated for each neighborhood, and the mean of the neighborhood prevalences weighted by the person-weeks at risk within each neighborhood reported.
†Children whose weight for age *z* score is −2.0 or higher.
‡Prevalence is the number of person-days with diarrhea divided by the number of person-days under surveillance.
§Children whose mean weight for age *z* score is less than −2.0 and −3.0 or more.
‖Children whose mean weight for age *z* score is less than −3.0.

Table 5. Severe Diarrhea Outcomes by Group

Diarrhea Outcomes	Antibacterial Soap (n = 300)	Plain Soap (n = 300)	Control (n = 306)
Saw a practitioner for diarrhea (210 133 child-weeks at risk)			
Proportion of child-weeks, %*	2.30	2.14	4.85
% Difference vs control (95% CI)	−53 (−67 to −38)	−56 (−69 to −43)	1.00
Hospitalized for diarrhea (210 055 child-weeks at risk)			
Proportion of child-weeks, %*	0.21	0.20	0.27
% Difference vs control (95% CI)	−24 (−100 to 73)	−26 (−100 to 66)	1.00
Persistent diarrhea† (200 324 child-weeks at risk)			
Mean incidence, episodes per 100 person-weeks‡	0.14	0.12	0.17
% Difference vs control (95% CI)	−19 (−66 to 28)	−31 (−70 to 8)	1.00

Abbreviation: CI, confidence interval.
*The proportion was calculated for each neighborhood, and the mean of the proportions weighted by the person-weeks contributing within each neighborhood reported.
†Episode for more than 14 days.
‡Incidence was calculated by taking the mean of the neighborhood incidence weighted by the person-weeks at risk from each neighborhood.

A second limitation was that our study was not originally undertaken to evaluate the hypothesis that children at the highest risk of death would benefit from handwashing. We observed more diarrhea than we expected. Diarrhea was unusually prevalent in Karachi in the summer of 2002, both as measured within the study as well as by reports from local clinicians. The incidence of diarrhea in the control group was more than 3 times higher than in control groups we had observed in earlier studies in 2000 and 2001, which we used to estimate the sample size. We further increased the sample size to assess other outcomes. Thus, sufficient observations for the analysis of diarrhea among subgroups at high risk of death were recorded. The analysis and reporting of interesting subgroups risks publication bias. However, the reduction in diarrheal disease noted among infants and malnourished children was not statistically borderline. Moreover, there were 2 intervention groups, plain soap and antibacterial soap, and the findings from both suggest a consistent phenomena.

A third limitation was that all of the disease reduction in the intervention communities was not necessarily attributable to improved handwashing. It is possible that regular visits by field workers, the provision of soap, and the successful improvement in hand hygiene led to other behavioral changes in households that reduced diarrheal disease. However, the high soap consumption of families suggests frequent handwashing and field workers were specifically trained to limit behavioral change messages to handwashing promotion. Thus, improved handwashing likely played an important role in reducing the incidence of diarrhea.

Although visiting households weekly to provide free soap and encourage handwashing was effective in reducing diarrhea, this approach is prohibitively expensive for widespread implementation. The next essential step is to develop effective approaches to promote handwashing that cost less and can be used to reach millions of at-risk households. Studies evaluating the durability of behavioral change from handwashing promotion are also important to assess cost-effectiveness. In the interim, existing public health programs should experiment with integrating handwashing promotion into their current activities.

Author Contributions: As principal investigator, Dr Luby had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Luby, Agboatwalla, Altaf, Billhimer, Hoekstra.
Acquisition of data: Agboatwalla, Painter.
Analysis and interpretation of data: Luby, Agboatwalla, Hoekstra.
Drafting of the manuscript: Luby.
Critical revision of the manuscript for important intellectual content: Agboatwalla, Painter, Altaf, Billhimer, Hoekstra.
Statistical expertise: Luby, Hoekstra.
Obtained funding: Luby, Billhimer.
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Supervision: Luby, Agboatwalla.
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Role of the Sponsor: Mr Billhimer, an employee of Procter and Gamble, critically reviewed the study protocol and made technical suggestions. Mr Billhimer arranged for the production and delivery to Karachi, Pakistan, of coded plain and antibacterial soap, and retained the coding of plain vs antibacterial soap. However, Procter and Gamble employees were not involved in data collection or in data analysis but commented on the interpretation of the analysis following oral presentation of the results and in response to drafts of the manuscript. The Centers for Disease Control and Prevention retained the right to publish results without approval from Procter and Gamble.
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