

Effect of handwashing on child health: a randomised controlled trial

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Summary

Background More than 3·5 million children aged less than 5 years die from diarrhoea and acute lower respiratory-tract infection every year. We undertook a randomised controlled trial to assess the effect of handwashing promotion with soap on the incidence of acute respiratory infection, impetigo, and diarrhoea.

Methods In adjoining squatter settlements in Karachi, Pakistan, we randomly assigned 25 neighbourhoods to handwashing promotion; 11 neighbourhoods (306 households) were randomised as controls. In neighbourhoods with handwashing promotion, 300 households each were assigned to antibacterial soap containing 1·2% triclocarban and to plain soap. Fieldworkers visited households weekly for 1 year to encourage handwashing by residents in soap households and to record symptoms in all households. Primary study outcomes were diarrhoea, impetigo, and acute respiratory-tract infections (ie, the number of new episodes of illness per person-weeks at risk). Pneumonia was defined according to the WHO clinical case definition. Analysis was by intention to treat.

Findings Children younger than 5 years in households that received plain soap and handwashing promotion had a 50% lower incidence of pneumonia than controls (95% CI –65% to –34%). Also compared with controls, children younger than 15 years in households with plain soap had a 53% lower incidence of diarrhoea (–65% to –41%) and a 34% lower incidence of impetigo (–52% to –16%). Incidence of disease did not differ significantly between households given plain soap compared with those given antibacterial soap.

Interpretation Handwashing with soap prevents the two clinical syndromes that cause the largest number of childhood deaths globally—namely, diarrhoea and acute lower respiratory infections. Handwashing with daily bathing also prevents impetigo.

Introduction

Every year, more than 3·5 million children aged less than 5 years die from diarrhoea and acute lower respiratory-tract infection.¹ These deaths are concentrated in low-income communities in developing countries.^{2–4} Several studies have shown that regular handwashing with soap reduces the incidence of diarrhoea in children younger than 5 years in communities with a high incidence of diarrhoea,^{5–7} although we are unaware of any reports of the effect of handwashing on acute respiratory-tract infections in settings where pneumonia is a leading cause of death.

In developed countries, the promotion of handwashing has reduced respiratory-tract infections in several settings. Controlled trials of handwashing promotion in child-care centres have reported a 14% reduction in upper respiratory-tract infection in Canada;⁸ a 12% reduction in upper respiratory-tract infection in children aged 24 months or less in Australia;⁹ and a 32% reduction in colds in one US child-care centre in the USA.¹⁰ In a school of children aged 5 to 12 years in the USA, a handwashing promotion programme in selected classrooms was associated with a 21% fall in absences from respiratory illness.¹¹ Another programme at a US Navy training centre that included directives to wash hands five times per day resulted in a 45% reduction in total outpatient visits for respiratory illness.¹²

Impetigo is another condition that is common in low-income countries with high humidity, which affects mothers of young children. A previous study¹³ in Karachi, Pakistan, investigated the effect of antibacterial soap on impetigo. Incidence of impetigo in children living in households receiving antibacterial soap (1·10 episodes per 100 person-weeks) was 23% lower than that in households receiving plain soap ($p=0\cdot28$) and was 43% lower than the standard habit and practice controls ($p=0\cdot02$).

In Karachi, more than 4 million low-income residents live in squatter settlements where they do not legally own the land, and municipal infrastructure is restricted.¹⁴ A study undertaken in these communities concluded that 41% of deaths of children aged less than 5 years were due to diarrhoea and 15% due to acute respiratory-tract infections.¹⁵

We undertook the Karachi Soap Health Study as a randomised controlled trial to measure the broad health benefits brought about by improvement of handwashing and bathing with soap in settings where communicable diseases are leading causes of childhood morbidity and mortality.

Materials and methods

Patients

The study site and intervention for the Karachi Soap Health Study has been described previously.¹⁶ Briefly, the

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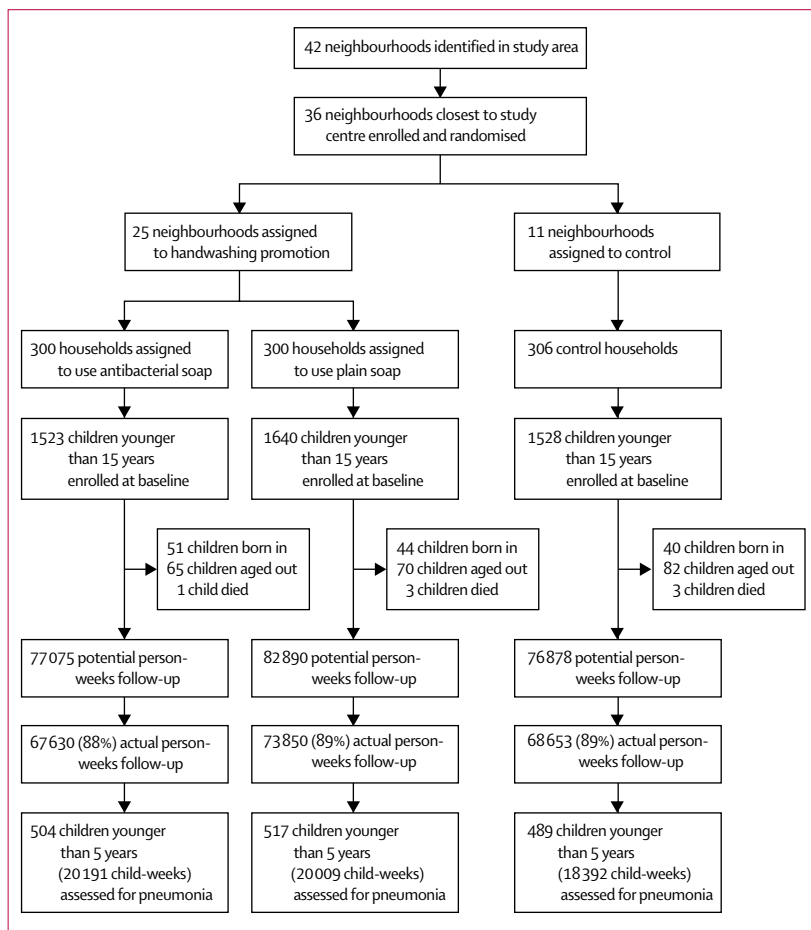


Figure 1: Trial profile

study was undertaken in adjoining multi-ethnic squatter settlements in central Karachi in collaboration with Health Oriented Preventive Education (HOPE), a non-governmental organisation that supports community-based health and development initiatives. Although handwashing, typically with water only, is part of ritual preparation for prayer in these societies, thorough washing of hands with soap is not as common. Affordable hand soap is widely available throughout these communities from small, neighbourhood shops.

Fieldworkers identified 42 candidate neighbourhoods separated by a street or market area. Eligible households were located in a candidate neighbourhood, had at least two children younger than 15 years (at least one of whom was less than 5 years old), and were planning to continue to reside in the same home for the duration of the study. Households that received a soap or water-vessel intervention in any previous study with HOPE were excluded. Fieldworkers undertook a census of these neighbourhoods, and before intervention assignment, they identified and obtained informed consent from 1050 candidate households.

Community leaders and heads of households also provided informed consent. Ill children were referred to the appropriate health care. The study protocol was approved by the ethics review committee of Aga Khan University, and by an institutional review board of the Centers for Disease Control and Prevention.

Procedures

Fieldworkers listed the candidate neighbourhoods in the order of proximity to their field centre. One of the investigators (SL) who did not participate in recruiting neighbourhoods or households programmed a spreadsheet to randomly generate the integers of a 1 or a 2, with a 2 being twice as likely to be generated than a 1. He applied the random numbers sequentially to the list of neighbourhoods. Neighbourhoods with a 1 were assigned to control, and those with a 2 were assigned to handwashing promotion. Random assignment continued until neighbourhoods consisted of at least 600 handwashing promotion households and 300 control households were assigned. Overall, 25 neighbourhoods were assigned to handwashing promotion and 11 to control (figure 1). Handwashing promotion was assigned at the neighbourhood level, because several activities promoting handwashing were undertaken at this level. Antibacterial versus plain soap was randomly assigned at the household level.

During the week before soap was distributed and disease surveillance began, fieldworkers gathered participants from ten to 15 nearby homes for neighbourhood meetings that lasted 30–45 min. They showed slide shows, videotapes, and pamphlets to illustrate health problems resulting from contaminated hands and to provide specific handwashing instructions. They encouraged discussions between participants. For the first 2 months of the intervention, neighbourhood meetings were held for the mothers in every neighbourhood two or three times a week. These were reduced to weekly meetings between 2 and 9 months, and to fortnightly meetings for the last 3 months. For the first 3 months, men also had monthly meetings that covered the same information.

Fieldworkers visited intervention households at least once a week to discuss the importance of handwashing and correct handwashing technique, and to promote regular handwashing habits. They encouraged regular handwashing habits. They encouraged participants to wet their hands, lather them completely with soap, rub them together for 45 s, and rinse the lather off completely. Hands were typically dried on participants' clothing. Fieldworkers encouraged all individuals in intervention households who were old enough to understand (generally those aged more than 30 months) to wash their hands after defaecation, after cleaning an infant who had defaecated, before preparing food, before eating, and before feeding infants. Fieldworkers also encouraged participants to bathe once a day with soap and water. Initially,

fieldworkers provided 2–4 bars of soap per household, depending on size. Throughout the study, soap was regularly replaced during use.

The Procter & Gamble company (Cincinnati, OH, USA) manufactured all the soap for the study. The antibacterial soap (Safeguard Bar Soap) contained 1·2% triclocarban as an antibacterial substance. The plain soap was identical to the antibacterial soap except that it did not contain triclocarban. Both types were provided as 90 g white bars without brand names or symbols. They looked and smelled the same and were packaged identically in generic white wrappers. Cases of 96 bars were identified by serial numbers that were matched to households. Neither the fieldworkers nor the families knew whether soaps were antibacterial or plain.

Fieldworkers provided control families with a regular supply of children's books, notebooks, pens, and pencils to help with their children's education, but they gave no products that would be expected to affect rates of respiratory illness, diarrhoea, or impetigo. Fieldworkers neither encouraged nor discouraged handwashing in control households, and visited both control and intervention households with equal frequency.

Fieldworkers were extensively trained in interviewing techniques, data recording, approaches to promote handwashing, weighing children, and clinical assessment of ill children (including measurement of respiratory rates). They were not trained to assess chest-wall indrawing, because of the difficulty that trained health-care workers have in identifying this symptom reliably.^{17,18} The fieldworkers identified lesions consistent with impetigo in children younger than 15 years old. A study physician then visited all households to confirm the diagnosis of impetigo and referred the family to locally available health-care services. The same fieldworkers promoted handwashing and obtained outcome data during their weekly visits to intervention households. These 22 fieldworkers rotated between neighbourhoods (including both intervention and control) throughout the study.

Trained fieldworkers undertook pre-intervention baseline surveys, and identified children younger than 15 years. Children's dates of birth were confirmed with birth certificates or immunisation records. Fieldworkers visited participating households at least once a week for 1 year (from April 15, 2002, to April 5, 2003) and asked the mother (or other caregiver) whether the child had any symptoms of cough or difficulty breathing in the preceding week. They also asked whether the child had any nasal congestion or coryza (runny nose). If a child was symptomatic with cough or difficult breathing, fieldworkers counted the number of breaths the child took in 60 s timed with a watch.

The primary outcomes for our study were diarrhoea, impetigo, and acute respiratory-tract infections (ie, the number of new episodes of illness per person-weeks at

risk), although we specifically detail respiratory and impetigo findings in this report. Results for diarrhoea have been published elsewhere.¹⁶

We defined pneumonia in children according to the WHO clinical case definition—cough or difficulty breathing with a raised respiratory rate (>60 per min in individuals younger than 60 days old, >50 per min for those aged 60–364 days, and >40 per min for those aged 1–5 years).¹⁹ We did not attempt to assess pneumonia in children aged more than 5 years. An episode of impetigo was defined as a new skin eruption, which was confirmed by the study physician. Only after the diagnosed episode was recorded to have cleared by the community health worker (on one of the weekly visits) could the study participant be a candidate for a new episode of impetigo.

Fieldworkers weighed children aged less than 5 years at baseline and every 4 months. They used a hanging Salter scale for children younger than 3 years and a bathroom scale for those older than 3 years. We calculated weight-for-age Z scores compared with the National Center for Health Statistics standards. Mean weight-for-age Z scores were calculated from the multiple weighing and measuring sessions throughout the study for every child. We classified children as moderately malnourished if their mean Z score was less than -2·0 and -3·0 or greater, and severely malnourished if their score was less than -3·0.

Statistical analysis

Primary hypotheses of the Karachi Soap Health Study were that the promotion of handwashing with antibacterial or plain soap would significantly reduce the frequency of diarrhoea and acute respiratory-tract infection, and that bathing with antibacterial soap would reduce the frequency of impetigo compared with plain soap. Children who did not have the specific syndrome in the preceding week but developed the syndrome were regarded as having a new episode. Only children who did not have the syndrome in the preceding week were defined as at risk for a new episode.

| | Antibacterial soap (n=300) | Plain soap (n=300) | Control (n=306) |
|---|-------------------------------|-----------------------|--------------------|
| Individuals per household | 9·3 (4·1) | 10·0 (4·8) | 9·1 (4·1) |
| Children less than 5 years old per household | 1·7 (0·5) | 1·7 (0·5) | 1·6 (0·4) |
| Rooms in house | 2·0 (0·9) | 2·0 (1·0) | 2·1 (0·9) |
| Bars of hand soap purchased in preceding 2 weeks | 1·9 (0·7) | 2·0 (0·7) | 1·9 (0·7) |
| Households with infants | 71 (24%) | 64 (21%) | 71 (23%) |
| Children less than 5 years old with moderate malnutrition | 125 (26%) | 103 (21%) | 114 (24%) |
| Children less than 5 years old with severe malnutrition | 20 (4%) | 24 (5%) | 19 (4%) |
| Literacy of mother of youngest child in household | 113 (38%) | 107 (36%) | 98 (32%) |
| Monthly household income less than US\$60 | 137 (46%) | 131 (44%) | 152 (50%) |
| Households with natural gas used for cooking fuel | 285 (95%) | 285 (95%) | 298 (97%) |

Data are mean (SD) or number (%).

Table 1: Baseline household characteristics by intervention group

| | Cough or difficulty breathing in children younger than 15 years (n=186 654) | | Congestion or coryza in children younger than 15 years (n=174 483) | | Pneumonia in children younger than 5 years (n=58 592) | |
|--------------------|---|--------------------------------|--|--------------------------------|---|--------------------------------|
| | Mean incidence* | Difference vs control (95% CI) | Mean incidence* | Difference vs control (95% CI) | Mean incidence* | Difference vs control (95% CI) |
| Antibacterial soap | 4.21 | -50% (-65% to -36%) | 7.32 | -51% (-62% to -39%) | 2.42 | -45% (-64% to -26%) |
| Plain soap | 4.16 | -51% (-65% to -37%) | 6.87 | -54% (-63% to -44%) | 2.20 | -50% (-65% to -34%) |
| Control | 8.50 | .. | 14.78 | .. | 4.40 | .. |

*Incidence (of new episodes per 100 person-weeks) calculated with mean of every cluster incidence weighted by person-weeks at risk for that cluster.

Table 2: Primary respiratory outcomes by intervention group

| | Diarrhoea incidence (n=197 049) | | Impetigo incidence (n=200 156) | | |
|--------------------|---------------------------------|--------------------------------|--------------------------------|---|---|
| | Mean incidence* | Difference vs control (95% CI) | Mean incidence* | Difference vs control neighbourhoods (95% CI) | Difference vs plain-soap households (95% CI)† |
| Antibacterial soap | 2.02 | -50% (-64% to -37%) | 0.61 | -36% (-53% to -18%) | -2% (-24% to 20%) |
| Plain soap | 1.91 | -53% (-65% to -41%) | 0.62 | -34% (-52% to -16%) | .. |
| Control | 4.06 | .. | 0.94 | .. | .. |

*Mean incidence (episodes per 100 person-weeks) calculated with mean of neighbourhood rates weighted by person-weeks at risk from every neighbourhood. †Accounts for clustering by household.

Table 3: Primary diarrhoea and impetigo outcomes in children younger than 15 years by intervention group

We calculated a sample size of 220 households per intervention group, assuming the same rates of impetigo as those recorded in the previous Karachi study¹³ (ie, 2.07 episodes of impetigo per 100 person-weeks in the control group, 1.58 episodes per 100 person-weeks in the plain-soap group, and 1.10 episodes per 100 person-weeks in the antibacterial-soap group). We assumed a mean of 3.8 children per household, 95% follow-up, 10% dropout, and a doubling of sample size to offset the effect of clustering by neighbourhood and repeated measures. We increased the sample size to 300 households per group to

provide additional power for subgroup analysis, and to protect against inherent uncertainties in the sample-size assumptions.

Because we assigned soap promotion versus control at the neighbourhood level, we also analysed primary health outcomes at this level. Specifically, within every neighbourhood, we identified the total number of new episodes of illness (in person-weeks in the subgroups of interest) and divided it by the total number of person-weeks at risk for children in that neighbourhood within the subgroup of interest. Incidence rates by intervention assignment (the mean of appropriate neighbourhood incidence rates) were weighted by the number of person-weeks at risk from all neighbourhoods that contributed to the mean. We calculated rate ratios by dividing the mean incidence from intervention neighbourhoods by that from control neighbourhoods. Because we compared antibacterial soap with plain soap at the household level, we also analysed the difference in impetigo incidence between antibacterial and plain soap at this level.

We calculated 95% CIs of rate ratios using Taylor series approximations to obtain standard errors. The difference (%) in outcome between intervention and

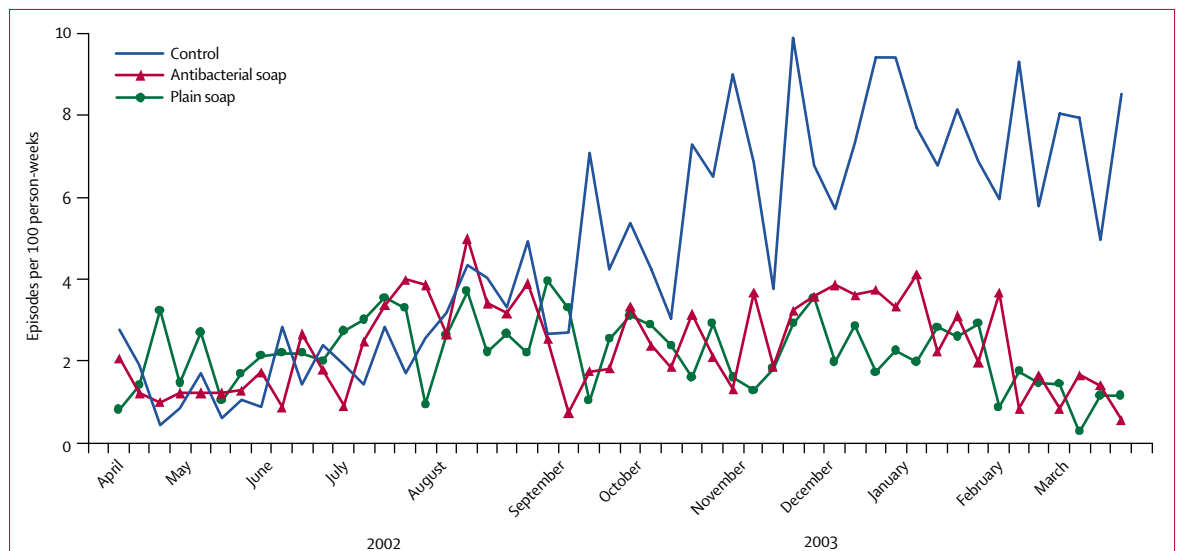


Figure 2: Incidence of pneumonia in children younger than 5 years

control was reported (ie, rate ratio minus one). We regarded differences (%) between groups as significant if 95% CIs excluded 0%.

After the 1 year of planned data collection was completed, Procter & Gamble provided the list identifying which cases of soap were antibacterial or plain for analysis. Disease experiences of every child, household, and neighbourhood was tracked and analysed with the group they were originally assigned to (intention-to-treat analysis).

Role of the funding source

One author (WB) was an employee of the study sponsor (Procter & Gamble). He reviewed and provided feedback on the study protocol, analysis, and manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. The Centers for Disease Control and Prevention retained the right to decide what to submit for publication and to publish results without approval from Procter and Gamble.

Results

The 36 neighbourhoods in the study had a median of 26 participating households per neighbourhood (IQR 21–30). In the 25 neighbourhoods randomly assigned to handwashing promotion, antibacterial soap was randomly allocated to 300 households and plain soap to 300 households. 11 neighbourhoods (306 households) were randomly assigned to undertake standard habits and practices (control). During 51 weeks of follow-up, information was obtained on 210 133 person-weeks, representing 89% of the study populations' experience. Follow-up was similar in the three intervention groups (figure 1). The most common

reason for missing follow-up information was that the family had temporarily left town to visit relatives.

At baseline, households in the three intervention groups were similar (table 1). Households had a mean of 9.5 residents (SD 4.4) and purchased about one bar of hand soap per week. During the study, households assigned to handwashing promotion received a mean of 3.3 bars of study soap per week; thus, every household resident used an average of 4.4 g of soap per day.

Neighbourhoods that received soap and encouragement to wash their hands and bathe had substantially less respiratory disease, impetigo, and diarrhoea than controls (tables 2 and 3; diarrhoea data also reported elsewhere).¹⁶ Children younger than 15 years who lived in households that received plain soap in neighbourhoods where handwashing was promoted, had more than a 50% lower incidence of cough or difficult breathing and of congestion or coryza than did children in control neighbourhoods. Children aged less than 5 years who received plain soap in neighbourhoods where handwashing was promoted had a 50% lower incidence of pneumonia than did children in control neighbourhoods. Incidence of acute respiratory illness in households receiving antibacterial soap was much the same as that in households receiving plain soap (table 2).

Incidence of impetigo was 36% lower in children in households that received antibacterial soap and encouragement to bathe every day than in those in control neighbourhoods but only 2% lower than in children in plain-soap households (table 3). Mean duration of impetigo episodes was 18 days (SD 14) for children in antibacterial-soap households, 18 days (13) for those in plain-soap households, and 22 days (15) for

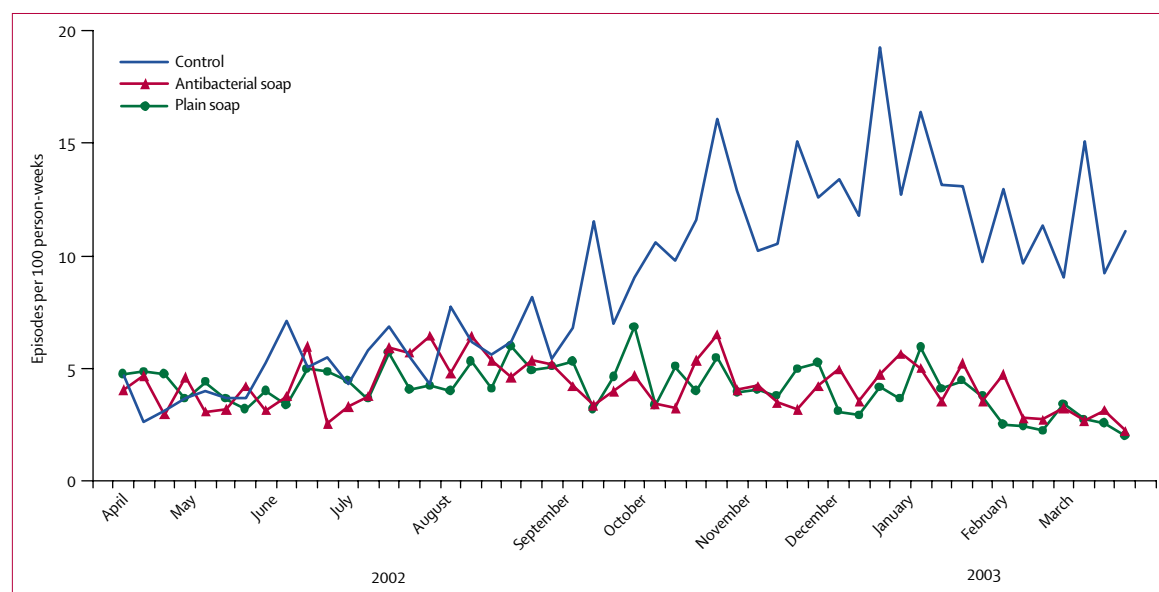


Figure 3: Incidence of cough and difficult breathing in children younger than 15 years

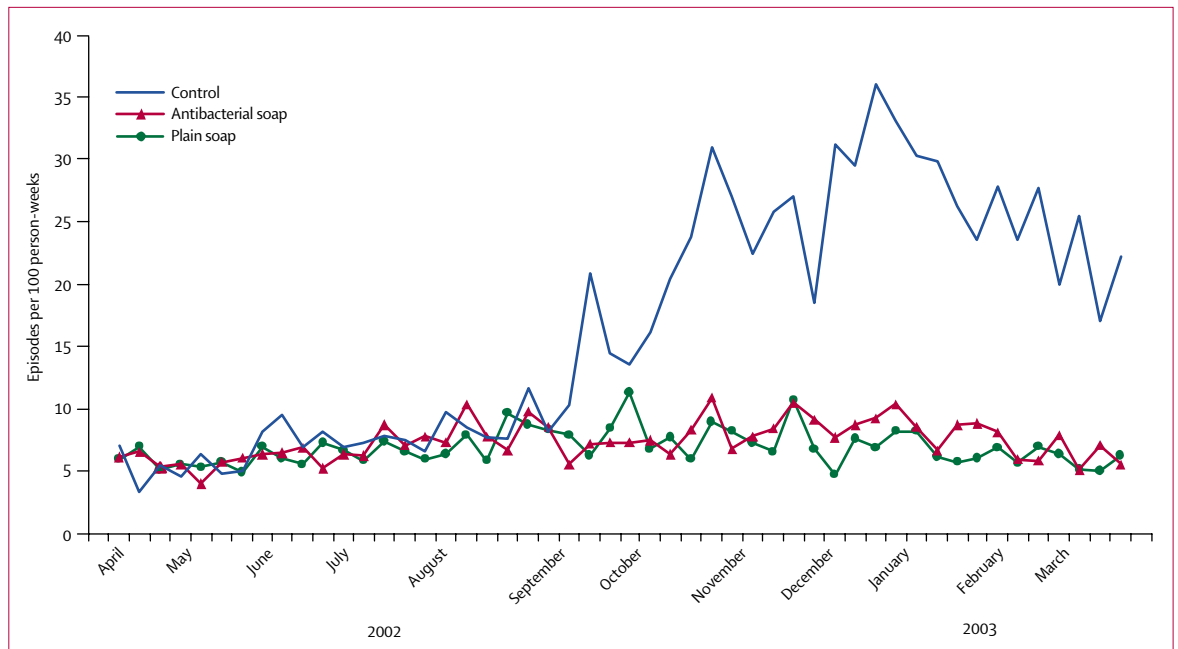


Figure 4: Incidence of congestion and coryza in children younger than 15 years

those in control households. Weekly prevalence of impetigo among children in households that received antibacterial soap and encouragement to bathe daily was 47% lower (–61% to –34%) than those in control neighbourhoods, but only 4% lower than children living in plain-soap households (–28% to 19%).

For the first 6 months of the trial, incidence of pneumonia in children younger than 5 years who lived in neighbourhoods receiving handwashing promotion with soap was only 6% lower (–43% to 32%) than in children in control neighbourhoods (figure 2). However, in the second 6 months, when pneumonia was much more frequent in the control group, incidence of pneumonia was 66% lower (–79% to –53%; figure 2). A similar pattern of illness rates was noted in the incidence of cough or difficulty breathing and congestion or coryza in all ages of participants (figures 3 and 4).

Compared with children aged 2–5 years, children aged less than 1 year had a 1.4 times greater incidence of pneumonia (2.8 vs 2.1 episodes per 100 person-weeks) and children aged 1–2 years had a 3.5 times higher incidence of pneumonia (7.2 vs 2.1 episodes per 100

person-weeks). There was less difference in pneumonia incidence in handwashing-promotion versus control neighbourhoods in children younger than 1 year than the difference seen in children up to the age of 5 years (table 4). Pneumonia incidence in children who received plain soap was nearly 30% lower in those younger than 1 year, more than 50% lower in those aged 1–2 years, and just over 50% lower in those aged 2–5 years, compared with controls. Age-specific incidence of pneumonia was closely similar between households receiving antibacterial versus plain soap (table 4). When data for households that received both types of soap were combined, children younger than 1 year had a 27% lower incidence of pneumonia (–77% to 24%), a 36% lower incidence of cough and difficulty breathing (–59% to –12%), and a 39% lower incidence of congestion and coryza (–56% to –22%) than controls.

Moderately malnourished children had the same risk of pneumonia as non-malnourished children (2.9 vs 2.8 episodes per 100 person-weeks); but severely malnourished children had 1.4 times the incidence of pneumonia of non-malnourished children (4.2 vs 2.9 episodes per 100 person-weeks, $p=0.003$).

| | Individuals aged less than 1 year (n=7679) | | Individuals aged 1–2 years (n=9238) | | Individuals aged 2–5 years (n=41 675) | |
|--------------------|--|--------------------------------|-------------------------------------|--------------------------------|---------------------------------------|--------------------------------|
| | Pneumonia incidence* | Difference vs control (95% CI) | Pneumonia incidence* | Difference vs control (95% CI) | Pneumonia incidence* | Difference vs control (95% CI) |
| Antibacterial soap | 2.65 | –24% (–80% to 32%) | 5.93 | –45% (–69% to –21%) | 1.55 | –51% (–70% to –33%) |
| Plain soap | 2.46 | –29% (–78% to 20%) | 5.04 | –54% (–74% to –33%) | 1.56 | –51% (–68% to –34%) |
| Control | 3.48 | .. | 10.86 | .. | 3.17 | .. |

*Incidence (episodes per 100 person-weeks) calculated with mean incidence of every cluster weighted by person-weeks at risk for that cluster.

Table 4: Mean pneumonia incidence by age and intervention group

| Nutrition status (person-weeks at risk)* | No malnutrition (n=38 830) | | Moderate malnutrition (n=13 604) | | Severe malnutrition (n=3591) | |
|---|----------------------------|-----------------------------------|----------------------------------|-----------------------------------|------------------------------|-----------------------------------|
| | Pneumonia incidence† | Difference vs control (95% CI) | Pneumonia incidence† | Difference vs control (95% CI) | Pneumonia incidence† | Difference vs control (95% CI) |
| Antibacterial soap | 2.42 | -40% (-61% to -20%) | 1.83 | -63% (-80% to -46%) | 4.18 | -27% (-60% to 6%) |
| Plain soap | 2.12 | -48% (-65% to -31%) | 2.24 | -54% (-75% to -34%) | 3.08 | -46% (-74% to -18%) |
| Control | 4.07 | .. | 4.91 | .. | 5.73 | .. |

*Total number of person-weeks at risk is lower than total in table 3, because of missing anthropometry data for 96 children. †Incidence (episodes per 100 person-weeks) calculated with mean incidence of every cluster weighted by person-weeks at risk for that cluster.

Table 5: Mean pneumonia incidence in children younger than 5 years by nutrition status and intervention group

Handwashing with soap was effective against pneumonia in well-nourished and malnourished children (table 5). Compared with controls, pneumonia incidence in households that received plain soap was roughly halved in children irrespective to who was non-malnourished, moderately malnourished, and severely malnourished. Households using antibacterial soap had rates of pneumonia comparable to rates for plain soap, although the fall in rate was not significant in children with severe malnutrition living in households receiving antibacterial soap (table 5).

Discussion

In squatter settlements of Karachi, where diarrhoea and acute respiratory infections are leading causes of death, washing hands with soap reduced both syndromes by half. Incidence of impetigo also fell by almost a third in households encouraged to regularly wash hands and bathe daily. Handwashing was effective in reducing disease incidence in malnourished children, although the reductions in the youngest children were not significant. However, we did not detect any difference in disease incidence between the use of antibacterial and plain soap.

The reduction in incidence of disease was almost certainly due to handwashing with soap only, because interventions were randomly assigned to neighbourhoods, and the participating households had similar characteristics known to affect the incidence of diarrhoea and respiratory disease. Indeed, incidence of respiratory disease did not vary between neighbourhoods for the first several months of the study. The trebling of soap consumption in handwashing promotion households from baseline suggests that handwashing was more regularly practised. Moreover, although this study specifically shows a fall in pneumonia frequency from handwashing, the finding is consistent with data in other settings that have suggested a reduction in respiratory disease from handwashing with soap.⁸⁻¹²

These findings are biologically plausible. At least some of the viruses that usually infect the respiratory tract are readily transmitted from person to person by hand contact.^{20,21} In developing countries, viruses commonly cause pneumonia.^{22,23} Additionally, several viruses that infect the human respiratory tract predispose children to bacterial pneumonia.²⁴⁻²⁶

Soap and the mechanical activity of rubbing hands together enhances the capacity of water to solubilise and to remove dirt and pathogens from hands.^{27,28} This physical removal of pathogens reduces the efficiency of not only pathogen transmission from the hands of an infected person to those of an uninfected person, but also the transmission of infectious organisms from the hands of an uninfected person to the respiratory tract. Triclocarban is effective in vitro against some species of *Streptococcus*, but does not have substantial activity against gram-negative bacteria or viruses.^{29,30} The closely similar effectiveness of antibacterial and plain soap suggests that the physical removal of pathogens from hands and skin with soap and water, rather than the specific antibacterial activity of triclocarban, is the key factor in the prevention of diarrhoea, impetigo, and respiratory infections.

Siblings and other children transmit most respiratory pathogens to young children.³¹⁻³³ Handwashing that interrupts transmission of respiratory pathogens in older siblings and other neighbourhood children not only reduces their own rate of respiratory illness, but also shrinks the pool of people who are transmitting and thus restricts exposure in vulnerable children.

In our study, respiratory infections did not decrease immediately after the introduction of handwashing promotion, but fell substantially after several months. The changing of handwashing habits takes time³⁴ and could need several months for the habit to be taken up by enough family members to interrupt respiratory pathogen transmission. Furthermore, respiratory disease is seasonal in Pakistan; typically more than twice as many cases take place from October to March compared with April to September.^{35,36} Children living in handwashing promotion neighbourhoods avoided the typical winter peak in respiratory disease, suggesting that the transmission of organisms responsible for the winter peak is efficiently interrupted by regular handwashing.

Most childhood respiratory-tract infections are mild and do not lead to childhood death. It is less clear from our data if many severe, life-threatening, lower respiratory-tract infections were prevented. Fieldworkers used the WHO case definition (integrated management of childhood illness [IMCI]) for pneumonia to identify children with lower respiratory-tract infections. They were not trained to recognise lower chest-wall indrawing

or other signs of severe pneumonia that are highly associated with mortality. In clinics, pneumonia is typically over-diagnosed with the IMCI case definition. For example, of 965 Kenyan children who were classified as meeting the IMCI case definition for pneumonia, 38% were judged not to have the disease based on chest radiography and physician diagnosis.³⁷ We would expect the IMCI case definition to identify an increased proportion of false-positive diagnoses of pneumonia in communities, because risk of disease is lower in these individuals than in clinic attendees.

However, the study results suggest that handwashing with soap prevents at least some cases of severe pneumonia. First, some mild upper respiratory-tract infections in children and in their siblings predispose to severe lower respiratory-tract infection.^{24–26,38} Thus, prevention of the mild, upper respiratory-tract infections can also stop severe pneumonia. Second, in the study, handwashing with soap was effective against pneumonia in some children at high risk for death from pneumonia, such as those with severe malnutrition.^{39–41} Incidence of pneumonia was roughly halved in these children if they lived in a household in which handwashing with plain soap was promoted. Of the youngest children—ie, those aged less than 1 year who make up most deaths from acute respiratory infection—handwashing with soap had less of an effect. The reduction in pneumonia (close to 30%) was not significant in these young children from households with handwashing promotion. This non-significance probably indicated restricted statistical power. Indeed, for the other respiratory outcomes that occur more frequently than pneumonia, the reduction in incidence in infants was significant. Infants were not washing their own hands, nor were families encouraged to wash infants' hands. Because the removal of pathogens from older people is the only route of transmission to infants that handwashing would interrupt, a more moderate reduction in disease in infants than in older children is expected. Ultimately, the proportion of severe respiratory illness that is prevented with handwashing needs to be established.

These data, consistent with those of other investigations,^{13,42} suggest that daily bathing with soap lowered the incidence of childhood impetigo. The study showed no added benefit of including triclocarban in soap. This finding differs from previous data¹³ from Karachi suggesting that children in households with triclocarban-containing soap had a 23% lower incidence of impetigo compared with those in households receiving placebo soap. However, the difference in the earlier study was not significant ($p=0.28$). Our present study enrolled nearly four times as many households, and was intentionally designed with sufficient power to detect a 23% difference between triclocarban-containing and placebo soap types. The absence of an effect in a randomised,

placebo-controlled trial that was masked and sufficiently powered, suggests that the addition of triclocarban to soap does not prevent impetigo in this setting and that the 23% difference in the earlier study was due to the chance selection of small, non-representative study groups. Indeed, antibacterial soap did not provide a health advantage over plain soap for any of the health outcomes in our study. Soap companies should consider whether the funds and marketing efforts spent in the addition of antibacterial compounds to soap would be better deployed to improve the lathering and sensory experience of handwashing to make the action more pleasant and to actively promote regular handwashing.

Study personnel and participants were not masked to the intervention. Thus, study participants in the handwashing promotion groups, grateful for the soap, could have kept reported episodes of illness in the household to a minimum, as could have fieldworkers recorded fewer episodes because of a desire, conscious or not, to meet the expectation of the study sponsors. However, fieldworkers were formally trained, and the importance of accurate recording of reported symptoms episodes was stressed. Supervisors, who regularly made unannounced household visits, identified symptoms that were different to those reported by fieldworkers in less than 1% of visits.¹⁶

Our data show that regular handwashing with soap is very effective in preventing diarrhoea¹⁶ and respiratory disease, two of the leading causes of global childhood death. Handwashing with daily bathing also prevents impetigo. Provision of free soap, frequent community meetings, and weekly household handwashing promotion visits to all impoverished households worldwide is prohibitively expensive. Thus, the challenge for the public-health community is to identify cost-effective techniques for handwashing promotion that can reach the hundreds of millions of households at risk.

Contributors

S Luby developed the idea for the study, drafted the study protocol, analysed the data and drafted the manuscript. M Agboatwalla assisted in development of the protocol, designed the handwashing promotion intervention, supervised field implementation of the protocol, assisted in interpretation of the data, and helped revise the manuscript. D Feikin assisted in developing the assessment for acute respiratory-tract infections, and provided published work from previous studies and critical input to place these findings within the broader context of respiratory diseases. J Painter designed the data management strategy, developed the database for data entry and verification, assisted in analysis, interpretation, and revision of the manuscript. A Altaf assisted in developing the protocol addressing human subject issues, assisted in project administration, and reviewed the manuscript. W Billhimer critically reviewed the study protocol, analysis, and manuscript. R M Hoekstra helped develop the analytic strategy, assisted in analysing the data, and had the final say on appropriateness of analytic methods.

Conflict of interest statement

S Luby was supported by the grant from the Procter & Gamble company that funded this study. W Billhimer is an employee of the Procter & Gamble company. The other authors declare that they have no conflict of interest.

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