Effect of Hand Hygiene on Infectious Disease Risk in the Community Setting: A Meta-Analysis

| Allison E. Aiello, PhD, Rebecca M. Coulborn, BS, Vanessa Perez, MS, and Elaine L. Larson, PhD, RN

To quantify the effect of hand-hygiene interventions on rates of gastrointestinal and respiratory illnesses and to identify interventions that provide the greatest efficacy, we searched 4 electronic databases for hand-hygiene trials published from January 1960 through May 2007 and conducted meta-analyses to generate pooled rate ratios across interventions (N = 30 studies).

Improvements in hand hygiene resulted in reductions in gastrointestinal illness of 31% (95% confidence intervals [CI] = 19%, 42%) and reductions in respiratory illness of 21% (95% CI = 5%, 34%). The most beneficial intervention was hand-hygiene education with use of nonantibacterial soap. Use of antibacterial soap showed little added benefit compared with use of nonantibacterial soap.

Hand hygiene is clearly effective against gastrointestinal and, to a lesser extent, respiratory infections. Studies examining hygiene practices during respiratory illness and interventions targeting aerosol transmission are needed. (*Am J Public Health.* 2008;98:1372–1381. doi:10.2105/AJPH.2007.124610)

Many studies have reported an association between improvements in hand hygiene and reductions in rates of infectious illnesses in the community.[1] Nevertheless, there are still important questions that must be addressed before guidelines regarding the use of specific interventions for reducing rates of infectious illness in the community can be devised. To our knowledge, a comprehensive meta-analysis comparing the relative effectiveness of specific hand-hygiene interventions used in the community has never been conducted. This makes it difficult to make consistent recommendations to consumers regarding the merit and utility of various hand-hygiene regimens for the prevention of common infectious illnesses.

Analysis of the impact of hand-hygiene interventions for reducing infectious illnesses in the community is important for several reasons. First, there has been an explosion in the options and use of hand-hygiene products in the community.[2] Second, hand hygiene is considered an important intervention measure for pandemic public health threats, such as severe acute respiratory syndrome and avian influenza.[3–5] Third, research has suggested that there may be risks, including the emergence of antibiotic-resistant bacteria, associated with the use of some hand-hygiene products such as antibacterial soaps.[6–9]

In this meta-analysis, we assessed the extent to which the published literature has established a benefit of hand-hygiene interventions for the prevention of gastrointestinal and respiratory infectious illnesses. We also identified the specific interventions that provided the greatest potential for reducing these illnesses' symptoms.

METHODS

Search Strategy

We searched the following databases for articles published in any language from January 1960 through May 2007 by using 241 keyword combinations (search terms are available as a supplement to the online version of this article at http://www.ajph.org): PubMed (1960–2007), EMBASE (1980–2007), Scopus for EMBASE (1974–1980), Science Citation Index (Web of Science; 1960–2007), and Cochrane library (1988–2007), which includes the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and the United Kingdom National Health Service Database of Abstracts of Review of Effects.

The search results were surveyed for methodological articles and systematic reviews. In addition, the reference lists in all retrieved review papers were searched for additional related articles, and a manual search was performed with A.E.A.'s reference database.

Selection

A.E.A. and R.M.C. independently evaluated selected studies. When consensus was not reached, discussion and further study evaluation with the other authors was used to resolve data extraction discrepancies. Articles were included in the review if the outcome was (1) a reported or diagnosed gastrointestinal illness (such as shigellosis), (2) a reported or diagnosed respiratory illness (such as influenza), (3) a combination of general gastrointestinal or respiratory symptom(s) of infection (such as diarrhea or runny nose), or (4) gastrointestinal or respiratory infectious symptom-related absences (such as school absence for a "cold"), and if the independent variable(s) was a hand-hygiene intervention, such as hand-hygiene education, soap-use intervention (nonantibacterial or antibacterial soap), or waterless hand sanitizer.

Articles were restricted to intervention trials conducted in the community and employing a randomized or quasi-experimental study design. Quasi-experimental studies were defined as controlled interventions in which treatment was assigned without the use of a randomized experimental protocol.[10,11] These types of studies included crossover studies or interventions with several study arms that were directly assigned by the researcher without randomization.[12–20] In some studies it was not possible to ascertain whether randomization was used, and therefore, these studies were classified as nonrandomized.[21–30]

Articles were excluded if the hand-hygiene intervention was implemented as part of a major public health infrastructure or systems improvement project, such as municipal water supply and waste disposal, or if the setting was a healthcare facility or specialized setting, such as military. Articles that did not provide

Dave Morrison stands in front of one of his trailers outfitted with rows of sinks that are used by firefighters to wash their hands at fire camps in Dorris, California. Photograph by Lee Juillerat. Used with permission of AP Wide World.

an effect estimate (such as a rate ratio [RR], odds ratio, etc.) or did not provide enough data to allow calculation of an RR were also excluded (n=13).[31–43]

To compare rates of infectious illnesses across studies, we grouped the retrieved articles by specific intervention on the basis of 7 possible categories: (1) hand-hygiene education alone, (2) nonantibacterial soap with hand-hygiene education, (3) antibacterial soap with hand-hygiene education, (4) antibacterial soap alone, (5) alcohol-based hand sanitizer alone, (6) alcohol-based hand sanitizer with hand-hygiene education, and (7) non–alcohol-based hand sanitizer containing benzalkonium chloride. In some instances, both the test and control groups received the same training (e.g., nonantibacterial soap with hand-hygiene education in the test group and hand-hygiene education alone in the control group). In these cases, only the unique intervention for the test group was considered as the tested intervention (e.g., nonantibacterial soap).[12,21,44–46]

To be classified as having an educational intervention, the study had to state that education was part of the intervention and that there was some systematic provision of hand-hygiene education to the intervention group but not to the control group. Educational interventions were largely determined by setting. For example, interventions in schools were curriculum based, with unit plans and classroom activities. Teachers and students participated in activities together. Educational interventions in day-care centers were largely directed at staff. Most interventions included infection control and hygiene overviews for staff, such as teaching children or assisting with hand-hygiene practices. Educational interventions in lesser-developed regions often included songs, proverbs, games, community-based trainings, and picture stories or posters.

The outcomes were grouped into 3 categories: (1) gastrointestinal symptoms or infection (e.g., diarrhea, dysentery, shigellosis, vomiting), (2) respiratory symptoms or infection (e.g., cold symptoms, influenza virus), and (3) a combination of outcomes (e.g., any combination of gastrointestinal and respiratory symptoms or related absences). If both primary and secondary episodes were presented, we used only primary episode data. There were 2 instances in which this was not possible. The fully adjusted model for 1 study was presented only for secondary illness episodes[47] and in another study the effect estimate represented a combination of both primary and secondary episodes.[17] The effect estimates used in this meta-analysis applied to episodes of illness rather than duration (e.g., days of illness) with the exception of 1 study that provided only total days with reported symptoms.[48]

Publication Bias

Publication bias was assessed graphically with funnel plots. In addition, the Begg and Mazumdar rank correlation and the Egger test were used in assessing significant publication bias. For the Begg and Mazumdar rank correlation, a 2-tailed P value of less than .10 was considered evidence of publication bias.[49] For the Egger test, a 2-tailed P value of less than .05 was considered evidence of publication bias.[49] The Begg test has previously been shown to be slightly less sensitive to publication bias than the Egger test, and therefore, we used a larger P value cut-off.[49]

Calculation of Effect Estimates

If a study reported RRs and corresponding 95% confidence intervals (CIs), then these estimates were used in the meta-analysis. For studies that did not report RRs or CIs, estimates were calculated with the information provided in the studies. Authors were contacted directly in an attempt to obtain any data that were not reported in their articles.

To validate our calculations of RRs and CIs for studies lacking this information, our formulas were applied to studies that provided RRs and CIs as well as the data required, such as the incidence density, to obtain these estimates. Our recalculation of the data and author correspondence resulted in the identification of 1 error published in a study by Butz et al. (CI updated to 0.55 and 0.93 for our review).[48] (The formulas[50] that were used to calculate RRs and CIs are available as a supplement to the online version of this article at http://www.ajph.org.)

Statistical Analysis

Next, we conducted a meta-analysis of the retrieved studies by using random-effects models with Comprehensive Meta-Analysis Software version 2 (Biostat, Englewood, NJ). At least 2 studies with the same intervention

per outcome were required to calculate the meta-analysis pooled estimates. The relative weights of each study were used to compute overall pooled effect estimates:

$$(1) \qquad [(1/\sigma_i^2)/\sum_i^n \sigma_i^2] \times 100.$$

Forest plots were generated with a mixed-modeling procedure. To assess statistical heterogeneity, we calculated the Cochran Q-statistic and the I^2 statistic for each pooled estimate.[51,52] An I^2 value less than 25% is indicative of homogeneous treatment effects relative to the precision of the individual studies. The Cochran Q-statistic was used to assess significant heterogeneity at P at .05 or below.

To assess potential sources of heterogeneity, we used multilevel random effects models that use the restricted maximum likelihood method (Stata software, version 8.2, StataCorp LP, College Station, TX) to examine age (≤ 5 years vs >5 years), region (developed vs lesser-developed countries as categorized by the World Bank[53]), study duration, and study design components (masking, randomization, and whether the unit of analysis was the same as the unit of randomization or the study statistically controlled for clustered units).

The age categories were based on the age of the individuals who were included in the outcome assessment. For example, if the intervention was at the household level but illness assessments were conducted only among children younger than 5 years, we categorized the study population as 5 years or younger. If all household members contributed to the illness reports, then the average age of the household was used and the study population was classified as older than 5 years. In 2 studies, the outcome was presented by 2 specific age-group categories and is therefore presented separately in the forest plots.[18,54] In addition, we conducted a sensitivity analysis related to study design characteristics by removing 11 studies that lacked masking, lacked randomization, and did not statistically control for clustered units to assess the influence of these studies on the overall effect estimates.[12,14,16–20,22,24,28,55]

Preventive Fraction for Exposure

To calculate the preventive fraction for exposure (PFE), the RRs and corresponding CIs from all studies were used. We calculated the PFE as

$$(2) \qquad PFE = 1 - RR.$$

For example, an RR of 0.80 (95% CI=0.71, 0.90) resulted in a PFE of $1 - 0.80 = 0.20$. The lower CI for the PFE was $1 - 0.90 = 0.10$, and the upper CI for the PFE was $1 - 0.71 = 0.29$. A PFE was calculated only for the hand-hygiene intervention effect estimates that were statistically significant.

RESULTS

Search Strategy

The initial keyword search provided 5378 articles. After exclusion by screening of titles, 718 studies were initially reviewed by abstract or full article. Of these, 602 studies were retrieved for detailed assessment. In addition to intervention studies, 81 review articles were also retrieved, 8 of which were systematic reviews examining the effectiveness of hand hygiene for reducing infection.[1,56–62] (A flowchart of our search process is available as a supplement to the online version of this article at http://www.ajph.org.)

The bibliographies in each of the review articles were searched for pertinent studies that may not have been captured by the initial keyword search, resulting in 1 citation that was not initially identified.[24] A total of 572 articles were excluded on the basis of our review criteria, resulting in 30 intervention studies for meta-analyses.

Publication Bias

Publication bias among all studies by each outcome was first assessed graphically with funnel plots (available as a supplement to the online version of this article at http://www.ajph.org). Of these plots, only studies with gastrointestinal illness outcomes showed a clustering suggestive of publication bias.

For gastrointestinal illness outcomes, there was also statistical evidence of publication bias (Begg rank correlation P=.07; Egger regression P=.006). There was no evidence of publication bias in data for respiratory illness outcomes (Begg rank correlation P=.10; Egger regression P=.37). There was no evidence of publication bias among studies examining combined illnesses (Begg rank correlation P=.28; Egger regression P=.48).

Study Characteristics

There were a few differences in the characteristics of the retrieved studies (Table 1). Overall, a greater proportion of hand-hygiene intervention studies were conducted in developed than in lesser-developed countries (Table 1). Most of the intervention studies took place in child-care centers or schools rather than in community settings and were conducted among younger age groups (≤ 5 years). A higher proportion of the intervention studies focused on gastrointestinal than on respiratory or combined illness outcomes. (A detailed description of each study and the corresponding study characteristics is available as a supplement to the online version of this article at http://www.ajph.org.)

Forest Plots

The forest plots and overall summary RRs for each outcome are shown in Figure 1. There were 24 hand-hygiene intervention effect estimates for gastrointestinal illness outcomes with an overall RR of 0.69 (95% CI=0.58, 0.81; Figure 1a). There were 16 hand-hygiene intervention effect estimates for respiratory illness outcomes with an overall RR of 0.79 (95% CI=0.66, 0.95; Figure 1b). There were 10 hand-hygiene intervention effect estimates for combined illness outcomes with an overall RR of 0.80 (95% CI=0.73, 0.87; Figure 1c).

Heterogeneity by Study Characteristics and Design

Heterogeneity in effect estimates by study characteristics and design features were assessed among all studies (Table 2). Although sources of heterogeneity were not statistically significant for either gastrointestinal or respiratory outcomes, a few of the estimates suggested some influence. For example, there was a larger reduction in gastrointestinal and respiratory illnesses in lesser-developed countries than in more-developed countries and among studies conducted for a shorter duration of time (≤ 100 days vs ≥ 101 days).

In addition, there was a slightly stronger reduction in both gastrointestinal and respiratory outcomes among studies that did

TABLE 1—Summary of Hand-Hygiene Intervention Study Characteristics

Characteristic	% (No.) or Median (Range)	P^a
Country		.07
Developed	67 (20)	
Less developed	33 (10)	
Setting		.14
Child-care center or school	63 (19)	
Households, village, or community	37 (11)	
Age group,[b] y		.29
≤5	59 (19)	
>5	41 (13)	
Illness outcomes		.22
Only gastrointestinal	40 (12)	
Only respiratory	17 (5)	
Only combined outcomes	17 (5)	
Any combination of outcomes[c]	26 (8)	
Sample size[d]	357.5 (18–6080)	

[a]P values were calculated with the χ^2 test for a difference in proportions.
[b]Uhari et al.[54] provided effect estimates for age groups 3 years or younger and older than 3 years. Sircar et al.[18] provided effect estimates for age groups under 5 years and 5 years or older.
[c]Some studies had more than 1 outcome (i.e., gastrointestinal illnesses, respiratory illnesses, or combined illnesses).
[d]Sample size of study population.

not use masking. For combined illness outcomes, a statistically greater reduction was observed among studies with an older age range (>5 years vs ≤5 years) and shorter duration of study (≤100 days vs ≥101 days), and studies that did not present randomization procedures.

Next, we conducted a sensitivity analysis related to study design characteristics by removing 11 studies that lacked randomization procedures, did not apply masking, and used a unit of analysis at a different level from that of the unit of randomization (i.e., ignored clustered data structure).[12,14,16–20,22,24,28,55] Studies lacking randomization, masking, and adjustment for clustering received a score of zero and those that utilized at least 1 of these methodologies received a score of 1. For gastrointestinal illness outcomes, there was little influence on the overall summary RR (overall RR=0.69; 95% CI=0.58, 0.81), versus those with a score of at least 1 (RR=0.74; 95% CI=0.62, 0.90).

For respiratory illness outcomes, removal of studies that received a score of zero slightly increased the overall summary RR and the 95% CI contained the null value

(all studies RR=0.79; 95% CI=0.66, 0.95) versus those with a score of at least 1 (RR=0.83; 95% CI=0.68, 1.02). There was little change in combined illness outcomes after we removed studies that received a score of zero (all studies RR=0.80; 95% CI=0.73, 0.87) versus those with a score of at least 1 (RR=0.82; 95% CI=0.73, 0.91).

Intervention-Specific Rate Ratios for Gastrointestinal Illness

Table 3 presents the single or pooled RRs (where available) for each outcome by specific intervention measure. Nonantibacterial soap combined with hand-hygiene education showed the strongest protective effect against gastrointestinal illnesses (RR=0.61; 95% CI=0.43, 0.88). Similarly, hand-hygiene education showed a strong protective effect against gastrointestinal illnesses (RR=0.69; 95% CI=0.50, 0.95). The pooled estimate of the effect of the use of antibacterial soap with hand-hygiene education compared with no intervention in a control group was similar to the summary estimate of the effect of using nonantibacterial soap with hand-hygiene education, but the CI included the null value

(RR=0.59; 95% CI=0.33, 1.06). Last, the RR was close to null when we compared the effect on gastrointestinal illness rates of using antibacterial soap with using nonantibacterial soap in a control group.

The use of alcohol-based hand sanitizer with a hand-hygiene education intervention was associated with a moderate reduction in gastrointestinal illness rates compared with no intervention in a control group, although the CI included the null value (RR=0.77; 95% CI=0.52, 1.13). The pooled RR from 2 studies in which the effect of benzalkonium chloride–based hand sanitizer was examined showed a large reduction in gastrointestinal illness rates but the CI included the null value.
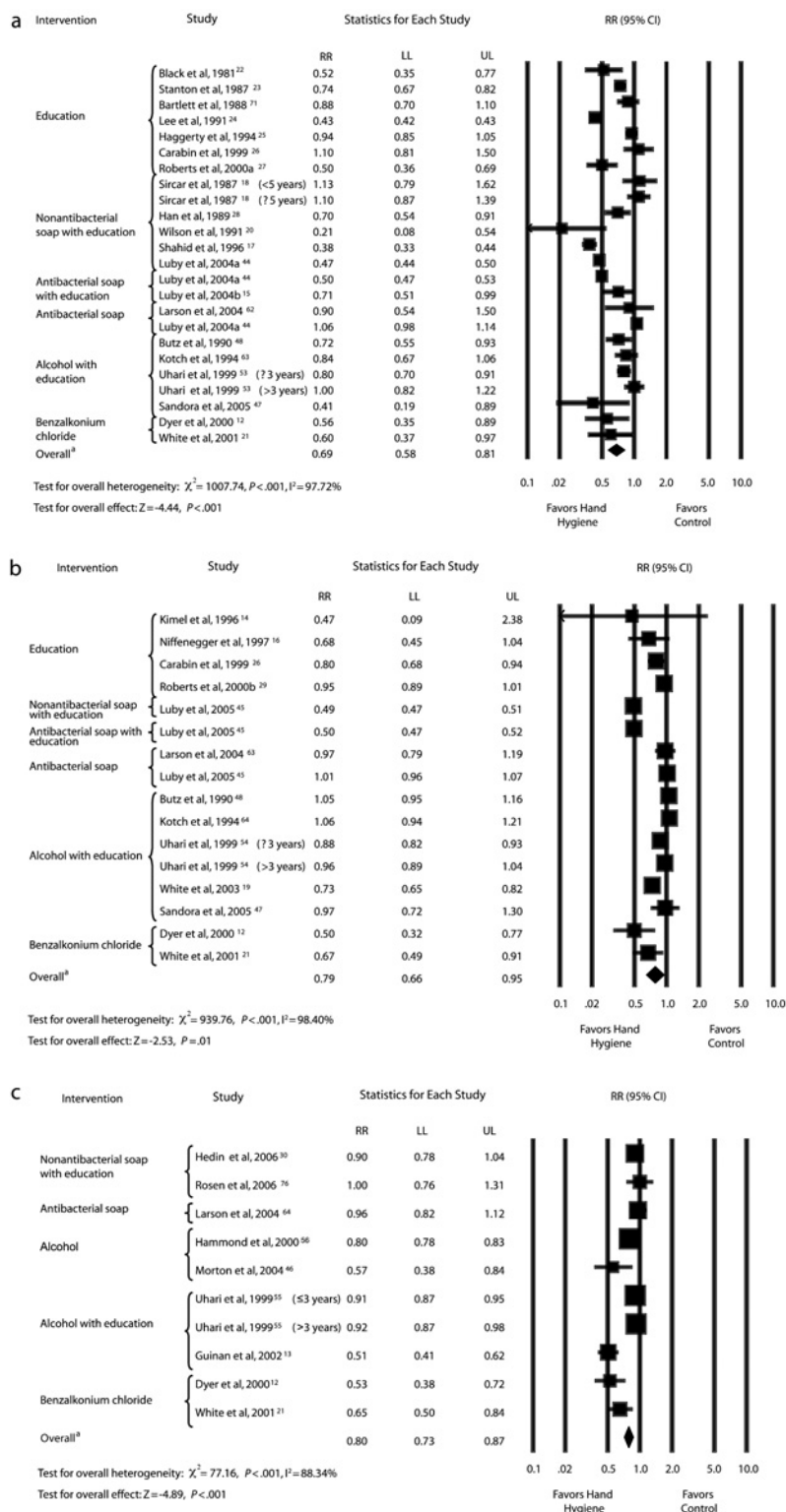
Intervention-Specific Rate Ratios for Respiratory Illness

As with gastrointestinal outcomes, the use of nonantibacterial soap combined with hand-hygiene education showed the strongest protective effect on respiratory illness rates (RR=0.49; 95% CI=0.40, 0.61), but data were available from only 1 study (Table 3).[45] The same study examined the influence of using antibacterial soap with hand-hygiene education on respiratory illness rates compared with no intervention in a control group, and the RR for this was close to that of using nonantibacterial soap with education.[45] The pooled estimate from 4 studies in which hand-hygiene education alone was examined indicated that this intervention was only moderately protective (RR=0.86; 95% CI=0.73, 1.00). The use of antibacterial soap compared with the use of nonantibacterial soap had no effect on respiratory illness rates (RR=1.00; 95% CI=0.84, 1.19; Table 3).

The pooled results of 6 studies in which the effect of using alcohol-based hand sanitizer combined with hand-hygiene education was examined showed that this intervention was weak (Table 3). By contrast, the pooled results of 2 studies in which the effect of using benzalkonium chloride–based hand sanitizer was examined showed a protective effect against respiratory illness outcomes.

Intervention-Specific Rate Ratios for Combined Illness

There were no studies in which the effect of hand-hygiene education alone on combined

a Gastrointestinal illness

Intervention	Study	RR	LL	UL
Education	Black et al, 1981[22]	0.52	0.35	0.77
	Stanton et al, 1987[23]	0.74	0.67	0.82
	Bartlett et al, 1988[71]	0.88	0.70	1.10
	Lee et al, 1991[24]	0.43	0.42	0.43
	Haggerty et al, 1994[25]	0.94	0.85	1.05
	Carabin et al, 1999[26]	1.10	0.81	1.50
	Roberts et al, 2000a[27]	0.50	0.36	0.69
	Sircar et al, 1987[18] (<5 years)	1.13	0.79	1.62
	Sircar et al, 1987[18] (?5 years)	1.10	0.87	1.39
Nonantibacterial soap with education	Han et al, 1989[28]	0.70	0.54	0.91
	Wilson et al, 1991[20]	0.21	0.08	0.54
	Shahid et al, 1996[17]	0.38	0.33	0.44
	Luby et al, 2004a[44]	0.47	0.44	0.50
Antibacterial soap with education	Luby et al, 2004a[44]	0.50	0.47	0.53
	Luby et al, 2004b[15]	0.71	0.51	0.99
Antibacterial soap	Larson et al, 2004[62]	0.90	0.54	1.50
	Luby et al, 2004a[44]	1.06	0.98	1.14
Alcohol with education	Butz et al, 1990[48]	0.72	0.55	0.93
	Kotch et al, 1994[63]	0.84	0.67	1.06
	Uhari et al, 1999[53] (?3 years)	0.80	0.70	0.91
	Uhari et al, 1999[53] (>3 years)	1.00	0.82	1.22
	Sandora et al, 2005[47]	0.41	0.19	0.89
Benzalkonium chloride	Dyer et al, 2000[12]	0.56	0.35	0.89
	White et al, 2001[21]	0.60	0.37	0.97
Overall[a]		0.69	0.58	0.81

RR (95% CI): 0.1 .02 0.5 1.0 2.0 5.0 10.0 — Favors Hand Hygiene / Favors Control

Test for overall heterogeneity: $\chi^2 = 1007.74$, $P<.001$, $I^2=97.72\%$
Test for overall effect: $Z=-4.44$, $P<.001$

b Respiratory illness

Intervention	Study	RR	LL	UL
Education	Kimel et al, 1996[14]	0.47	0.09	2.38
	Niffenegger et al, 1997[16]	0.68	0.45	1.04
	Carabin et al, 1999[26]	0.80	0.68	0.94
	Roberts et al, 2000b[29]	0.95	0.89	1.01
Nonantibacterial soap with education	Luby et al, 2005[45]	0.49	0.47	0.51
Antibacterial soap with education	Luby et al, 2005[45]	0.50	0.47	0.52
Antibacterial soap	Larson et al, 2004[63]	0.97	0.79	1.19
	Luby et al, 2005[45]	1.01	0.96	1.07
Alcohol with education	Butz et al, 1990[48]	1.05	0.95	1.16
	Kotch et al, 1994[64]	1.06	0.94	1.21
	Uhari et al, 1999[54] (?3 years)	0.88	0.82	0.93
	Uhari et al, 1999[54] (>3 years)	0.96	0.89	1.04
	White et al, 2003[19]	0.73	0.65	0.82
	Sandora et al, 2005[47]	0.97	0.72	1.30
Benzalkonium chloride	Dyer et al, 2000[12]	0.50	0.32	0.77
	White et al, 2001[21]	0.67	0.49	0.91
Overall[a]		0.79	0.66	0.95

RR (95% CI): 0.1 .02 0.5 1.0 2.0 5.0 10.0 — Favors Hand Hygiene / Favors Control

Test for overall heterogeneity: $\chi^2 = 939.76$, $P<.001$, $I^2=98.40\%$
Test for overall effect: $Z=-2.53$, $P=.01$

c Combined illnesses

Intervention	Study	RR	LL	UL
Nonantibacterial soap with education	Hedin et al, 2006[30]	0.90	0.78	1.04
	Rosen et al, 2006[76]	1.00	0.76	1.31
Antibacterial soap	Larson et al, 2004[64]	0.96	0.82	1.12
Alcohol	Hammond et al, 2000[56]	0.80	0.78	0.83
	Morton et al, 2004[46]	0.57	0.38	0.84
Alcohol with education	Uhari et al, 1999[55] (≤3 years)	0.91	0.87	0.95
	Uhari et al, 1999[55] (>3 years)	0.92	0.87	0.98
	Guinan et al, 2002[13]	0.51	0.41	0.62
Benzalkonium chloride	Dyer et al, 2000[12]	0.53	0.38	0.72
	White et al, 2001[21]	0.65	0.50	0.84
Overall[a]		0.80	0.73	0.87

RR (95% CI): 0.1 .02 0.5 1.0 2.0 5.0 10.0 — Favors Hand Hygiene / Favors Control

Test for overall heterogeneity: $\chi^2 = 77.16$, $P<.001$, $I^2=88.34\%$
Test for overall effect: $Z=-4.89$, $P<.001$

Note. RR = rate ratio; CI = confidence interval; LL = lower confidence limit; UL = upper confidence limit. Bars with RRs indicate 95% CIs. In studies of antibacterial soap, nonantibacterial soap was provided to the control groups.
[a]Overall weighted summary rate ratio across all studies in the forest plot.

FIGURE 1—Rate ratios for the effect of hand-hygiene interventions on gastrointestinal illness (a), respiratory illness (b), and combined illnesses (c).

illness outcomes was examined (Table 3). The effect of using nonantibacterial soap with hand-hygiene education on combined illness outcomes was weak and not statistically significant (RR=0.94; 95% CI=0.74, 1.18). In addition, there was no difference in combined illness outcomes between intervention groups that received antibacterial soap and those that received nonantibacterial soap.

The pooled RR for the use of alcohol-based hand sanitizer with hand-hygiene education showed a significant reduction in combined illnesses (RR=0.79; 95% CI=0.67, 0.93). Similarly, the pooled RR for alcohol-based hand sanitizer use alone showed a significant reduction in combined illness outcomes, as did the pooled RR for using benzalkonium chloride–based hand sanitizer (Table 3).

Overall Prevention of Illness

For all hand-hygiene interventions combined, the proportion of gastrointestinal illness prevented was 31% (95% CI=19%, 42%). The use of nonantibacterial soap with education prevented 39% (95% CI=12%, 57%) of cases compared with no intervention in a control group. The next-greatest impact was the pooled estimate for the effectiveness of hand-hygiene education alone compared with no intervention; the intervention prevented 31% (95% CI=5%, 50%) of gastrointestinal illnesses.

The overall proportion of respiratory illness prevented by all hand-hygiene interventions combined was 21% (95% CI=5%, 34%). The use of nonantibacterial soap with hand-hygiene education prevented 51% (95% CI=39%, 60%) of respiratory illnesses compared with no intervention in a control group. This estimate was based on a single study by Luby et al. because there were no other intervention studies that assessed the effect of nonantibacterial soap on respiratory illnesses.[45]

The next-greatest impact was the effectiveness of antibacterial soap with hand-hygiene education compared with no intervention in a control group from the same study; this intervention prevented 50% (95% CI=39%, 60%) of cases. Pooled data from 2 studies showed that benzalkonium chloride–based hand sanitizer prevented 40% (95% CI=19%, 55%) of respiratory illnesses. None of the other pooled estimates for interventions

TABLE 2—Heterogeneity in Summary Rate Ratios (RRs) and 95% Confidence Intervals (CIs) Between Study Characteristics

Characteristic	Gastrointestinal Illness (N = 24)			Respiratory Illness (N = 16)			Combined Illnesses (N = 10)		
	No. of Studies	RR[a] (95% CI)	P[b]	No. of Studies	RR[a] (95% CI)	P[b]	No. of Studies	RR[a] (95% CI)	P[b]
Age, y			.46			.93			.03
≤ 5	16	0.72 (0.59, 0.87)		9	0.80 (0.63, 1.01)		3	0.92 (0.77, 1.10)	
> 5	8	0.62 (0.46, 0.85)		7	0.78 (0.58, 1.05)		7	0.73 (0.65, 0.83)	
Country			.52			.11			≤ .99
Developed	12	0.73 (0.58, 0.92)		13	0.85 (0.71, 1.01)		10	0.80 (0.73, 0.87)	
Less developed	12	0.66 (0.53, 0.82)		3	0.63 (0.45, 0.87)		NA	NA	
Study duration, days			.40			.22			< .001
1–100	5	0.54 (0.36, 0.82)		5	0.64 (0.45, 0.92)		5	0.63 (0.54, 0.72)	
101–300	9	0.69 (0.51, 0.92)		5	0.96 (0.71, 1.30)		2	0.83 (0.74, 0.94)	
> 300	10	0.76 (0.58, 0.99)		6	0.76 (0.58, 1.00)		3	0.92 (0.84, 1.02)	
Clustering[c]			.83			.81			.70
No	14	0.68 (0.54, 0.85)		9	0.81 (0.63, 1.03)		6	0.78 (0.70, 0.88)	
Yes	10	0.70 (0.54, 0.92)		7	0.77 (0.60, 0.99)		4	0.81 (0.70, 0.95)	
Randomization[d]			.51			.41			< .001
No	14	0.65 (0.52, 0.82)		7	0.72 (0.53, 0.97)		5	0.70 (0.62, 0.80)	
Yes	10	0.74 (0.56, 0.96)		9	0.84 (0.66, 1.07)		5	0.90 (0.80, 1.02)	
Masking[e]			.65			.36			.74
No	19	0.68 (0.57, 0.81)		12	0.75 (0.61, 0.93)		8	0.79 (0.71, 0.88)	
Yes	5	0.74 (0.52, 1.06)		4	0.91 (0.64, 1.29)		2	0.82 (0.66, 1.02)	

Note. NA = no studies available with the characteristic.
[a]Pooled rate ratios.
[b]*P* values calculated for between-study heterogeneity.
[c]Studies in which the analysis was not conducted at the same unit as the intervention treatment were included in the "No" category.
[d]Studies that utilized a quasi-experimental design or did not give a description of their randomization procedures were included in the "No" category.
[e]Masking included either study participants or study participants and the study investigators and staff.

TABLE 3—Rate Ratios (RRs) and 95% Confidence Intervals (CIs) for the Association Between Specific Hand-Hygiene Interventions and Each Illness Outcome

Intervention	Gastrointestinal Illness (N = 24)		Respiratory Illness (N = 16)		Combined Illnesses (N = 10)	
	No. of Studies	RR[a] (95% CI)	No. of Studies	RR[a] (95% CI)	No. of Studies	RR[a] (95% CI)
Education vs control	7	0.69 (0.50, 0.95)	4	0.86 (0.73, 1.00)	NA	NA
Nonantibacterial soap with education vs control[b,c]	6	0.61 (0.43, 0.88)	1	0.49 (0.40, 0.61)	2	0.94 (0.74, 1.18)
Antibacterial soap with education vs control[b,c]	2	0.59 (0.33, 1.06)	1	0.50 (0.40, 0.61)	NA	NA
Antibacterial soap vs nonantibacterial soap[c]	2	0.99 (0.54, 1.83)	2	1.00 (0.84, 1.19)	1	0.96 (0.71, 1.30)
Alcohol-based hand sanitizer vs control	NA	NA	NA	NA	2	0.74 (0.59, 0.93)
Alcohol-based hand sanitizer with education vs control[b]	5	0.77 (0.52, 1.13)	6	0.93 (0.84, 1.03)	3	0.79 (0.67, 0.93)
Benzalkonium chloride–based hand sanitizer vs control	2	0.58 (0.30, 1.12)	2	0.60 (0.45, 0.81)	2	0.59 (0.45, 0.78)

[a]Pooled or single-study RRs.
[b]Indicates a layered intervention.
[c]Studies that tested more than a single intervention. [44,45]

against respiratory illnesses were associated with strong protective effects (i.e., antibacterial soap compared with nonantibacterial soap; alcohol-based hand sanitizer compared with hand-hygiene education).

For all hand-hygiene interventions combined, the proportion of combined illness prevented was 20% (95% CI=13%, 27%). The use of benzalkonium chloride–based hand sanitizer prevented 41% (95% CI=22%, 55%) of illnesses. Alcohol-based hand sanitizer alone prevented 26% (95% CI=7%, 41%) of illnesses. The proportion of combined illnesses prevented by the use of alcohol-based hand sanitizer combined with hand-hygiene

DISCUSSION

This is the first meta-analysis to show that the effectiveness of hand-hygiene procedures varies depending on both the hygiene intervention method and infectious illness symptoms. The results of our study suggest that the use of nonantibacterial soap with hand-hygiene education interventions is efficacious for preventing both gastrointestinal and respiratory illnesses.

Our review follows several earlier systematic reviews of hand-hygiene interventions, of which only 3 were meta-analyses.[1,56–62] Two of the earlier meta-analyses focused solely on the effect of hand washing with soap and water on gastrointestinal illness in lesser-developed regions of the world.[57,61] The third meta-analysis, by Rabie et al.,[56] examined the effect of various hand-hygiene interventions on respiratory illnesses only.

The percentage reduction in respiratory illnesses associated with the pooled effects of hand hygiene that we observed was similar to the reduction reported by Rabie et al.[56] (21% vs 16%, respectively). Our meta-analysis included several studies that were not included in their study,[14,26,45,47,48,54,55,63,64] and excluded 3 studies included in their study that did not meet our study criteria.[42,65,66] Unlike our study, this earlier meta-analysis provided no information on hygiene intervention–specific pooled estimates and it included a total of only 8 studies, compared with 30 in our study.[56]

Our review indicated that some hand-hygiene interventions were not efficacious against respiratory illnesses, including educational interventions and the use of alcohol-based hand sanitizers. The consistent application of hand hygiene during critical points in the chain of transmission is likely to play a major role in shaping the relative effectiveness of hand-hygiene interventions by disease outcome.

Differences in the frequency and timing of hand-hygiene episodes may account for the stronger reductions in rates of gastrointestinal

illnesses than rates of respiratory illnesses. For example, even with consistent education messages that advocate hand hygiene directly after coughing or sneezing, such practices may not be as consistent or as frequent as hand-hygiene practices directly after defecation.

Very few studies in this review rigorously assessed hand-hygiene practices during the intervention period or monitored the use of products. Future hand-hygiene interventions should seek to incorporate information on the frequency, duration, and triggers for hand-hygiene episodes.

Surprisingly, the use of alcohol-based hand sanitizers combined with hand-hygiene education was not strongly associated with reduced rates of gastrointestinal illnesses or respiratory illnesses. This was unexpected given that alcohol-based antiseptics containing 60% to 80% weight per volume have been shown to be effective against a range of viruses and bacteria, including agents that cause diarrhea or respiratory infections.[67]

The use of benzalkonium chloride, a less-commonly used hand sanitizer, did show significant reductions in respiratory and combined illness outcomes. However, these data were from only 2 studies, 1 of which had several design flaws.[12] Findings from the clinical setting have supported the effectiveness of alcohol-based hand sanitizer for preventing healthcare-associated infections,[68] but it is likely that individuals living in the community have very different hand-hygiene habits from those of staff in the healthcare setting.

Although population-based estimates are not available, a large observational survey sponsored by the American Society for Microbiology has suggested that hand hygiene in the United States is suboptimal.[69] Results from their study of 7836 individuals in 5 major US cities showed that only 67% of participants washed their hands after using a public restroom.[69] Overall, more women (75%) than men (58%) washed their hands, suggesting gender differences in practices.[69] Clearly, consistent and targeted hand hygiene should be advocated in the United States to increase the frequency of use.

Antibacterial Soaps

The reviewed studies provided no evidence to support the use of antibacterial soap as a

more effective alternative to nonantibacterial soap for prevention of either gastrointestinal or respiratory illnesses. By contrast, the use of antibacterial soap with hand-hygiene education did show some efficacy against both gastrointestinal and respiratory illnesses when compared with no intervention in a control group.[15,44,45] These studies were conducted in lesser-developed countries where the control groups had limited access to basic necessities such as clean water and soap.[15,44,45]

On the other hand, intervention studies that enabled a comparison of the use of antibacterial soap with the use of nonantibacterial soap in a control group were conducted in both lesser-developed and developed regions of the world.[44,45,63] The pooled estimates of these studies clearly show that there were no differences in the efficacy of antibacterial versus nonantibacterial soap for reducing gastrointestinal and respiratory illnesses. This is consistent with an earlier qualitative review of some of these studies.[9]

It could be argued that antibacterial soap is targeted at bacteria and that the symptoms assessed in these studies may have been viral rather than bacterial in origin. However, the outcomes assessed in this meta-analysis are the most common infectious illnesses affecting younger children globally.[70] Moreover, antibacterial soaps have been implicated in the laboratory in the emergence of antibiotic-resistant bacteria.[7,9,71] Thus, the ineffectiveness of antibacterial soap compared with nonantibacterial soap observed in this study is concerning.

The Non-Prescription Drug Advisory Committee of the US Food and Drug Administration was convened in October 2005 to discuss the benefits and risks associated with antiseptic products marketed for consumer use such as "antibacterial" hand soap. This meeting resulted in a call for further research regarding the risks and benefits of specific consumer antiseptic products used in the community.

Our findings suggest that there is a need for policy decisions that address the continued use of antimicrobial soaps in the community. This is particularly the case for those products containing triclosan and triclocarban, the ingredients in the antibacterial soaps reviewed in this study that are found in many hand and body soaps.[2]

education was 21% (95% CI=7%, 33%). None of the other interventions were associated with significant prevention of combined illness outcomes (i.e., antibacterial soap compared with nonantibacterial soap; nonantibacterial soap compared with hand-hygiene education).

Sources of Heterogenity

Assessments of heterogeneity indicated that studies of shorter duration and those conducted in lesser-developed countries were more likely to report a greater reduction in rates of both gastrointestinal and respiratory illness. It is possible that participants in studies of shorter duration are more likely to adhere to protocols or enhance normal hand hygiene in response to being a participant than participants in studies of longer duration in which participants may be more likely to revert to their normal hand-hygiene habits. The finding that participants in lesser-developed areas showed a stronger effect against gastrointestinal and respiratory illnesses is not surprising given the differences in the prevalence of common infectious illnesses in developed versus lesser-developed regions.[70]

In terms of heterogeneity stemming from study design, studies that lacked randomization and masking appeared to show a slightly stronger reduction in illnesses. Nevertheless, these differences were not statistically significant for all outcomes, suggesting that these factors did not contribute to a great deal of heterogeneity across studies. A lack of accounting for clustering had no effect on heterogeneity. This might be attributed to the fact that "gastrointestinal illnesses" and "respiratory illnesses" do not represent a single pathogen that could cluster in time and space, but more likely have multiple etiologies.

Use of an outcome that captures a mixture of different pathogen-specific diseases is therefore unlikely to show significant clustering of cases. For example, if some gastrointestinal cases were associated with eating food contaminated with *Shigella* species and other cases were related to fecal–oral spread of *Escherichia coli*, any clustering effects would be reduced by the inclusion of 2 different disease-causing agents in the outcome definition.

There were methodological differences across studies. Often, the definition of symptoms or illnesses varied. Consistent definitions of respiratory infections are needed to further facilitate comparisons across studies. This was of less concern with gastrointestinal illnesses, because most studies used diarrhea as an outcome. Only 3 studies of gastrointestinal illnesses used microbiological analyses to identify the agent associated with symptoms.[17,22,72]

In addition, very few studies directly examined the microflora of the hands. This is important given the complex biology of skin bacteria and the potential importance of this transmission route in the studied disease outcomes.[73,74] None of the respiratory illness studies used microbiological assessments of respiratory pathogens. Clearly, further research on hand hygiene and communicable illnesses should employ an assessment of the microbiological characteristics of the infecting agent.

More-recent studies scored higher on methodological quality.[25,27,29,44,45,47,63,64,75] Additional studies that use formal randomization procedures, masking, and clustering such as the procedures of Larson et al.[63] are needed. However, such studies are extremely costly; it is often difficult to conduct masked studies in many settings; and it may not be logistically feasible to randomize.

Many of the earlier studies did not control for clustered study units, such as schools or classrooms, in which the likelihood of individual infectious outcomes are considered dependent. This could have led to overly narrow CIs and a higher type-1 error rate, but as mentioned previously, this did not have a significant influence on heterogeneity or overall pooled estimates.[76] Nevertheless, future studies should consider more-specific measurement of the outcome and the use of analytic strategies for clustered data such as generalized estimating equations and mixed modeling techniques where appropriate.[76]

Limitations

As with all meta-analytic procedures, we had to make informed decisions on the classification of study interventions and outcome measures. In some cases, classification of the intervention was not clear because of multiple components. Nevertheless, there were very few studies that combined other hygiene-related interventions in addition to the hand-hygiene measures of interest.

For some studies we had to perform calculations to obtain the RRs and 95% CIs using the available data presented. These calculations may not have been as precise as calculations using the actual raw data. We applied our mathematical formulas to studies that provided an RR, 95% CI, and all components

required for deriving these effect estimates; our calculated RRs and 95% CIs using the raw data components were consistent with the reported results of these studies.

For some interventions, such as the use of nonantibacterial and antibacterial soaps, only single studies were available, and therefore, we were unable to generate a pooled estimate for these interventions. In addition, some interventions had only 2 studies available for calculation of pooled estimates. Therefore, intervention-specific single estimates and summary estimates utilizing 2 studies should be interpreted with caution until further research can corroborate these findings.

Heterogeneity was significant in pooled estimates across all studies. We assessed factors such as age, region, and study design characteristics that accounted for some of the heterogeneity. In addition, our intervention-specific pooled estimates provided an assessment across more-similar studies. Head-to-head assessments of more than 1 intervention were conducted in a few studies, but not all, and therefore, conclusions regarding relative efficacy should be made judiciously.

Last, there was evidence of publication bias for gastrointestinal illness outcomes. Therefore, the pooled estimates generated by our meta-analysis of published studies may be exaggerated for this outcome.

Conclusions

The results of our meta-analyses provide the needed data synthesis for formulating consistent community-based hand-hygiene guidelines. First, we confirmed that hand-hygiene interventions are efficacious for preventing gastrointestinal illnesses, in both developed and lesser-developed countries. However, the overall impact of hand hygiene was less efficacious for respiratory illnesses. Overall, there was little evidence for an additional impact of new products, such as alcohol-based hand sanitizers or antibacterial soaps compared with nonantibacterial soaps, for reducing either gastrointestinal or respiratory infectious illness symptoms. Last, there is a need to include microbiological assessments of the agents that may be associated with clinical symptoms of infection so that agent-specific targeted hand-hygiene practices can be evaluated. ■

About the Authors

Allison E. Aiello, Rebecca M. Coulborn, and Vanessa Perez are with the Department of Epidemiology and Center for Social Epidemiology & Population Health, School of Public Health, University of Michigan, Ann Arbor. Elaine L. Larson is with the School of Nursing and the Mailman School of Public Health, Columbia University, New York, NY.

Requests for reprints should be sent to Allison E. Aiello, Assistant Professor of Epidemiology, Department of Epidemiology, Center for Social Epidemiology & Population Health, University of Michigan–School of Public Health, 3659 SPH Tower, 109 Observatory, Ann Arbor, MI 48109-2029 (e-mail: aielloa@umich.edu).

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