An integrative review of the current evidence on the relationship between hand hygiene interventions and the incidence of health care–associated infections

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Background: The objectives of this integrative review were to critically examine the overall state of the current evidence on the relationship between hand hygiene interventions and the incidence of health care–associated infections (HCAIs) in acute care and long-term care settings, and offer recommendations for future directions in the field based on our findings.
Methods: We searched for original research and reviews of research published between January 1, 1996, and July 31, 2006. Studies were identified through the electronic databases Medline, CINAHL, EMBASE, PUBMED, the Cochrane Library, and through expert consultation. Our comprehensive search strategy included all English articles for which hand hygiene or handwashing-related terms were combined with HCAIs. All studies that investigated a relationship between hand hygiene practices and HCAIs in acute care facilities were considered. These hand hygiene practices included the initiation of multimodal hand hygiene initiatives, the introduction of alcohol sanitizers, the implementation or changes of the infection control practices or infection control policies, and other organizational interventions. Studies only examining hand hygiene compliance, efficacy of alcohol hand gels, plain soap, and antimicrobial soap in reducing bacteria count recovered from hands were excluded.
Results: Of the 1120 articles retrieved, 35 publications, including 4 reviews of research discussed at the outset of this article, met our inclusion criteria. The remaining 31 eligible original studies included 18 (58.07%) before and after studies without control groups, 4 (12.90%) before and after studies with a control group, 3 (9.68%) cohort studies with no control group, 4 (12.90%) cohort studies with a control group, and 2 (6.45%) randomized trials. Over 50% (16 or 31) of the studies were conducted in the U.S. Two independent reviewers conducted independent evaluations of all eligible studies, critiquing and scoring each study using a rating scale for examining the fatal flaws of quasi-experimental and before and after studies.
Conclusions: There is a lack of rigorous evidence linking specific hand hygiene interventions with the prevention of HCAIs. The varied nature of the interventions used and the diverse factors affecting the acquisition of HCAIs make it difficult to show the specific effect of hand hygiene alone. The most frequent methodologies currently used in this research area are before and after observational studies without a control comparison group. Based on these findings, we recommend that researchers used a modified version of Larson's 2005 criteria to guide the design and conduct of future before and after observational studies in this area. We also argue that as we accumulate stronger evidence of which interventions are most effective, we need to develop additional research approaches to study how organizations succeed and fail in fostering the uptake of evidence-based hand hygiene interventions. (Am J Infect Control 2008;36:333-48.)

Health care–associated infections (HCAIs) are one of the most frequent and severe complications of hospitalization and the fourth leading cause of death in Canada.[1] One in 9 patients contract an infection while in a hospital, and an estimated 8000 patients die directly or indirectly each year from HCAIs.[2] According to 1995 US data, ''between 5% and 10% of patients admitted to acute care hospitals acquire 1 or more infections, and the risks have steadily increased during recent decades.''[3]

Although many factors contribute to the development of HCAIs, the consistent practice of adequate hand hygiene, either by washing the hands with soap and water or disinfecting them with an antiseptic solution,[4] is considered to be ''the single most important intervention to prevent nosocomial infections.''[5] However, compliance with hand hygiene among health care professionals remains relatively low. Some of the reasons identified by Pittet for poor compliance include skin irritation, inaccessibility to handwashing

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supplies, lack of adequate hand hygiene facilities, health care workers ''not thinking about it,'' high workloads and inadequate time, busy schedule, time-consuming, hands don't appear soiled, poor location of sinks, and lack of education about hand hygiene in the curricula.[6] Suresh and Cahill have also noted several issues with the structural layout of hospital wards in their ergonomic assessment of 4 hand hygiene resources (sinks, alcohol sanitizer dispensers, gloves, and garbage bins), which are essential to creating a ''user-friendly'' hospital environment for the reliable practice of effective hand hygiene.[7] In turn, the complexities of designing, implementing, and evaluating hand hygiene interventions and other infection control programs are critically shaped by the adequacy of health system resources for infection surveillance and control.[2] Nevertheless, the Canadian Patient Safety Institute has signalled that reducing preventable HCAIs is a priority in modern health care. Other countries around the world, including the United Kingdom, Australia, and Switzerland, are in agreement that a multimodal strategy to hand hygiene is necessary to reduce the occurrence of HCAIs; however, the relative contribution of each intervention is difficult to measure.

To date, 4 reviews of research have examined the evidence of a causal link between hand hygiene and risk of infection. In 1988, Larson[8] reviewed the published literature between 1879 and 1986 and found that the majority of publications were either evaluations of particular products or antiseptics (50.8%) or review articles (29.1%). Approximately 11% of the articles were concerned with behavioral aspects of hand hygiene, and only 14 (3.3%) of the studies reviewed specifically linked hand hygiene with the incidence of infection. Even though there were very few prospective studies assessing the causal link between hand hygiene and the incidence of HCAIs, the collective evidence from this initial review was judged to be consistent with the hypothesis that adequate hand hygiene is associated with a decrease incidence of HCAIs. In a subsequent review of research published between 1977 and 1998, Larson[9] found a temporal relationship between improved hand hygiene and reduced rates of HCAI but noted that the causal link in the majority of these studies was weak.

In a third review, Larson[10] examined the published research for a 1-year period (2004) that assessed the evidence linking hand hygiene interventions with a reduction in HCAIs. Most studies (69.2%) reported a statistically significant reduction in infection rates as a result of the implementation of various infection control interventions. Based on these findings, Larson noted the importance of senior leader and middle management commitment to administrative and system changes that are required to successfully implement and sustain hand hygiene best practices. In a fourth review of research published in 2005, Silvestri et al[11] analyzed the effectiveness of hand hygiene on infection rates in the intensive care unit. Those authors' results argued that hand hygiene alone can only reduce the level of contamination by 40% at most and cannot be expected to eliminate completely the incidence of HCAIs. Silvestri et al recommended that a multicenter, randomized controlled trial on the effect of hand hygiene on all infections was needed to support the statement from the Handwashing Liaison Group that adequate hand hygiene is a practice that can demonstrate big effects.

To build on these previous reviews of research, we searched for original research and reviews of research published between January 1, 1996, and July 31, 2006, to (1) critically examine the overall state of current evidence on the relationship between hand hygiene interventions and the incidence of HCAIs in acute care and long-term care settings and (2) offer recommendations for the design and conduct of future research, research syntheses, and policy in the field.

Our primary goal in conducting this critique was to identify specific organizational hand hygiene interventions that were clearly associated with significant reductions in the incidence of HCAIs in acute care and long-term care settings. We also sought to do as Pawson et al recommend, which is to reconsider how we conduct and learn from organizational intervention research in modern, complex health systems to strengthen practice and improve the outcomes of care.[12]

METHODS

Search strategy

Studies, published between January 1, 1996, and July 31, 2006, were identified through the electronic databases of Medline, CINAHL, EMBASE, PUBMED, The Cochrane Library, and expert consultation. We conducted a comprehensive search strategy that included all English articles with the MESH headings handwashing, the term *hand* combined with related terms such as *disinfection*, *antisepsis*, *disinfectants*, *antiinfective agents*, *local*, *antiviral agents*, *soaps*, *detergents*, *ethanol* or *alcohols* and articles with a title that included the following terms: (*hand$ adj5 wash$*), *handwashing$*, *hand hygiene*, (*hand$ adj5* [*saniti$* or *disinfect$* or *decontaminat$* or *gel$*]). These terms were combined with the terms *cross infection* and *infection control* and other terms such as *nonsocomial*, *nosocomial$*, (*reduc$ adj3 spread$*), *disease transmission*, and (*health care associated* or *health care associated* or *hospital acquired*). Further details of the search strategy are available in Table 1.

Table 1. Search strategy, review period: January 1, 1996- July 31, 2006

Medline	CINAHL	EMBASE	Cochrane Library	PubMed
1. exp handwashing/ 2. (hand$ adj5 wash$).ti. 3. handwashing$.ti. 4. hand hygiene.ti. 5. (hand$ adj5 (saniti$ or disinfect$ or decontaminat$ or gel$)).ti. 6. or/1-5 7. exp hand/ 8. exp Disinfection/ 9. exp Antisepsis/ 10. exp disinfectants/ 11. exp anti-infective agents, local/ or exp antiviral agents/ 12. exp soaps/ or exp detergents/ or exp ethanol/ or exp alcohols/ 13. or/8-12 14. 7 and 13 15. 6 or 14 16. exp Cross Infection/ 17. exp infection control/ 18. nonsocomial.tw. 19. nosocomial$.tw. 20. (reduc$ adj3 spread$).tw. 21. exp Disease Transmission, Professional-to-Patient/ 22. (healthcare associated or health care associated or hospital acquired).tw. 23. or/16-22 24. 15 and 23 25. RANDOMIZED CONTROLLED TRIAL.pt. 26. CONTROLLED CLINICAL TRIAL.pt. 27. RANDOMIZED CONTROLLED TRIALS.sh. 28. RANDOM ALLOCATION.sh. 29. DOUBLE BLIND METHOD.sh. 30. SINGLE BLIND METHOD.sh.	1. handwashing/ 2. (hand$ adj5 wash$4).ti. 3. handwashing$.ti. 4. hand hygiene.ti. 5. (hand$ adj5 (saniti$ or disinfect$ or decontaminat$ or gel$)).ti. 6. or/1-5 7. exp hand/ 8. exp Disinfection/ 9. exp disinfectants/ 10. exp Antiinfective Agents, Local/ or exp antiviral agents/ 11. exp soaps/ or exp detergents/ or exp alcohols/ 12. or/8-11 13. 7 and 12 14. 6 or 13 15. exp Cross Infection/ 16. exp infection control/ 17. nonsocomial.tw. 18. nosocomial$.tw. 19. (reduc$ adj3 spread$).tw. 20. exp Disease Transmission, Professional-to-Patient/ 21. (healthcare associated or health care associated or hospital acquired).tw. 22. or/15-21 23. 14 and 22 24. CLINICAL TRIALS/ 25. RANDOM ASSIGNMENT/ 26. DOUBLE-BLIND STUDIES/ 27. SINGLE-BLIND STUDIES/ 28. (clin$ adj5 trial$).ti,ab. 29. ((singl$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$)).ti,ab. 30. PLACEBOS/ 31. placebo$.ti,ab.	1. hand washing/ 2. handwashing$.ti. 3. (hand$ adj5 wash$).ti. 4. hand hygien$.ti. 5. (hand$ adj5 (saniti$ or disinfect$ or decontaminat$ or gel$)).ti. 6. or/1-5 7. exp HAND/ 8. exp DISINFECTION/ 9. exp Disinfectant Agent/ 10. exp Topical Antiinfective Agent/ or exp antiinfective agent/tp or exp antivirus agent/tp 11. exp soap/ or exp detergent/ or exp alcohol/ 12. or/8-11 13. 7 and 12 14. 6 or 13 15. exp Cross Infection/ 16. exp Infection Control/ 17. nonsocomial$.tw. 18. nosocomial.tw. 19. (reduc$ adj3 spread$).tw. 20. (healthcare associated or health care associated or hospital acquired).tw. 21. exp infection rate/ 22. exp hospital infection/ 23. or/15-22 24. 14 and 23 25. Randomized Controlled Trial/ 26. exp Randomization/ 27. Double Blind Procedure/ 28. Single Blind Procedure/ 29. Clinical Trial/	Search in title, abstract, and keyword: Hand wash* or handwash* or hand hygiene	Search handwashing [mesh] or (hand [mesh] and disinfection [mesh] or antisepsis [mesh] or disinfectants [mesh] or anti-infective agents [mesh] or soaps [mesh] or detergents [mesh] or ethanol [mesh] or alcohols [mesh])) or (handwashing* [ti]) or ((hand [ti] or hands [ti]) and (saniti* [ti] or disinfect* [ti] or decontaminat* [ti] or gel [ti] or gels [ti])) or (handwashing* [ti]) or ((hand [ti] or hands [ti]) and (saniti* [ti] or disinfect* [ti] or decontaminat* [ti] or gel [ti] or gels [ti])) or (hand hygiene [ti]) Limits: Entrez Date from 2006/02/01 to 2006/07/31

Continued

Table 1. Continued

Medline	CINAHL	EMBASE	Cochrane Library	PubMed
31. CLINICAL TRIAL.pt.	32. STUDY DESIGN/	30. (clin$ adj5 trial$).mp.		
32. exp CLINICAL TRIALS/	33. COMPARATIVE STUDIES/	31. ((singl$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$)).mp.		
33. (clin$ adj5 trial$).ti,ab.	34. exp EVALUATION RESEARCH/	32. exp Placebo/		
34. ((singl$ or doubl$ or trebl$ or tripl$) adj5 (blind$ or mask$)).ti,ab.	35. PROSPECTIVE STUDIES/	33. (placebo$ or random$).mp.		
35. PLACEBOS.sh.	36. (control$ or prospectiv$ or volunteer$). ti,ab.	34. exp Methodology/		
36. placebo$.ti,ab.	37. exp Case Control Studies/	35. exp Comparative Study/		
37. RESEARCH DESIGN.sh.	38. exp Retrospective Design/	36. exp Evaluation/		
38. COMPARATIVE STUDY.sh.	39. exp Experimental Studies/	37. exp Follow Up/		
39. exp EVALUATION STUDIES/	40. (random$ or intervention$ study or intervention$ studies or cohort or quasi-experimental or observational or retrospective). tw.	38. exp Prospective Study/		
40. FOLLOW UP STUDIES.sh.	41. (research or clinical trial or "systematic review").pt.	39. (control$ or prospectiv$ or retrospective or volunteer$).mp.		
41. PROSPECTIVE STUDIES.sh.	42. or/24-41	40. exp Case Control Study/		
42. (control$ or prospectiv$ or retrospective or volunteer$). ti,ab.	43. 23 and 42	41. exp Retrospective Study/		
43. exp Case-Control Studies/	44. limit 43 to yr=1996-2006	42. (random$ or intervention$ study or intervention$ studies or cohort or quasi-experimental or observational).tw.		
44. exp cohort studies/		43. Meta Analysis/		
45. exp Retrospective Studies/		44. exp "Systematic Review"/		
46. exp intervention studies/		45. or/25-44		
47. evaluation studies.pt.		46. 24 and 45		
48. (random$ or intervention$ study or intervention$ studies or cohort or quasi-experimental or observational). tw.		47. limit 46 to yr 1996-2006		
49. meta analysis.pt.				
50. or/25-49				
51. 24 and 50				
52. limit 24 to systematic reviews				
53. 51 or 52				
54. limit 53 to humans				
55. limit 54 to yr 1996-2006				

Inclusion criteria

All studies that investigated a relationship between hand hygiene interventions and HCAIs in acute care and long-term care facilities were considered. Studies that only examined the rate of hand hygiene compliance or the efficacy of alcohol hand gels, plain soap, or antimicrobial soap in reducing bacteria count recovered from hands were excluded. A complete list of the inclusion and exclusion criteria is outlined in Table 2. We defined a hand hygiene intervention (HHI) as any program of hand sanitation that an organization implements to promote compliance with desired standards of hand cleanliness. We defined HCAIs, in accordance

Table 2. Inclusion and exclusion criteria

	Inclusion	Exclusion
Period	January 1, 1996-July 31, 2006 (10 yr)	
	English only	
Population/setting	All health care settings (where care is received in facility, 24-hr coverage by RN care)	All other settings (community, daycare, schools, and others)
	Developed countries only	Developing countries
Intervention	All hand hygiene interventions	Glove use, masks, gowns
		Hospital design/architecture
		Dental products
		Antibiotics or drug therapy
		Artificial nails
		Food handling
		Isolation precautions
		Surveillance
Outcome	All health care-associated infections	
Study design	Experimental studies	Reviews that did not clearly define the parameters of their search strategy, including inclusive dates of the review, databases searched, and search terms used
	Randomized controlled trial	Expert opinion or consensus
	Experimental study without randomization	Editorial letter
	Observational study with control group	Guideline implementation
	Cohort study	Commentary
	Case control study	Outbreak reports
	Observational study without control groups	
	Cross-sectional study	
	Before-and after study	
	Cases series	
	Reviews of research (only if they clearly defined the parameters of their search strategy, including inclusive dates of the review, databases searched, and search terms used)	

with the Centers for Disease Control and Prevention, as infections that occur 72 hours or more after admission that are not in incubation prior to admission.[13] The HHI at issue could be as simple as making cleaning agents and washing facilities readily available or as complex as a multimodal quality improvement program that is designed to increase the rate of hand hygiene compliance through education, incentives, facility design, and other measures within a given care environment. The interventions we reviewed included the initiation of educational programs or campaigns, multimodal hand hygiene initiatives, introduction of alcohol sanitizers, hand hygiene performance improvement, and implementation of changes in the infection control practices.

Of the 1120 papers retrieved, there were 35 studies that met the inclusion criteria. Two reviewers (C.B. and D.Z.) conducted independent evaluations of all eligible studies, critiquing and scoring each study using a rating scale designed to identify the fatal flaws of quasiexperimental and before and after studies (Table 3).[10] Following the initial round of independent reviews, all 3 coauthors discussed the findings and gaps between the scores of the first and second reviewer to ascertain the rationale for any disparate scores between reviewers. Final scores were then determined and assigned to each study based on group consensus.

RESULTS

Characteristics of the studies

Thirty-five publications, including 4 reviews of research discussed at the outset of this article, met our inclusion criteria. The remaining 31 eligible original studies included the following: 18 (58.07%) before and after studies without control groups, 4 (12.90%) before and after studies with a control group, 3 (9.68%) cohort studies with no control group, 4 (12.90%) cohort studies with a control group, and 2 (6.45%) randomized trials.

By type of intervention, the 31 studies were categorized as follows: 7 (22.58%) initiations of a multimodal hand hygiene initiative, 11 (35.48%) introductions of a hand hygiene product, 8 (25.81%) implementations or modifications of infection control practices, 2 (6.45%) implementation of infection control policies, and 3 (9.68%) other interventions (top level administration intervention, electronic monitoring, or survey on

Table 3. Fatal flaws of quasiexperimental and before and after studies[10]

Rating scheme
1. Unblinded intervention or prospective study with 1 or more of the fatal flaws sufficient to weaken confidence in study's conclusions
2. Unblinded intervention or prospective study with 1 or more other flaw, but none is fatal to negate the conclusions
3. Intervention or prospective observational study with no fatal or other flaws not accounted for by study authors
4. Blinded RCT with no fatal or other flaws
Fatal flaws
I. Inadequate sample size
II. Uncontrolled bias or confounding (eg, no evidence of interrater reliability, unclear participant inclusion criteria, data collection unblinded)
III. Unclear operational definitions or description of intervention
IV. Inadequate (or no) statistical analysis
V. Lack of evidence that intervention was actually implemented

current practices). Multiple types of HCAIs (2 or more) were examined in 26 studies (74.28%). Other studies observed the rates of a single infection such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), bloodstream infections, rotavirus, surgical site infections, and *Clostridium difficile*. Most of the studies, 18 of 31 (58.06%), reported a significant reduction in HCAIs (Table 4). Only 5 studies reported a power calculation.

Using Larson's 2005 scoring tool,[10] most of the studies (67.7%) were rated with a score of 1 or 2, indicating that methodologic flaws were found. We assigned a score of 1 to 11 of the studies (35.48%), indicating that there were 1 or more fatal flaws found in the study. Ten of the studies (32.26%) received a score of 2 because they contained 1 or more other (nonfatal) flaw but no fatal flaws. We assigned a score of 3 to 9 intervention or observational studies (29.03%) with no fatal or other flaws. Only 1 of the studies (3.23%) received a score of 4, indicating a randomized study with no fatal or other flaws. The 3 most common flaws identified in the studies were the presence of confounding factors not considered or identified (8 studies), inadequate statistical analysis (6 studies), and inadequate sample size (5 studies). Seven studies (22.58%) had more than 2 fatal flaws. In the next section, we elaborate on our findings for each category of studies by type of intervention.

Category 1. Multimodal hand hygiene initiatives

Seven studies (22.58%) initiated a multimodal hand hygiene initiative to study its impact on the reduction of HCAIs. Six of these studies were before and after studies with no control group,[14-19] and 1 was a cohort study.[20] Of these studies, two[14,18] reported a significant reduction in HCAI rates (P = .04 and P = .003, respectively) and two[15,19] reported no significant reductions in overall HCAI rates. Two studies[14,20] reported a significant reduction (P < .001 and P = .01, respectively) in MRSA rates, and 1 study[17] reported a decrease in MRSA and VRE rates followed by an increased trend in MRSA and VRE rates after year one, but the results were not significant. Finally, a decrease in the rotavirus rate was reported in the results of one other study.[16]

Two of the studies[14,20] had confounding variables, which made it difficult to determine which aspects of the multimodal approach actually accounted for the reduced rates of HCAIs reported. Four of the 7 studies[16-19] had no fatal or other flaws.

Category 2. Hand hygiene products

Eleven studies (35.48%) introduced a hand hygiene product to study its impact on the reduction of HCAIs. In 5 of these studies, one before and after design with no control group[21] and 4 cohort studies with control groups[22-25] compared handwashing with the introduction of an alcohol hand sanitizer. Another before and after study with control group[26] compared the 4% antiseptic solution with the introduction of a 1% antiseptic solution. Three other before and after studies with no control group[27-29] introduced an alcohol hand sanitizer alone. In the remaining 2 studies in this group, one used a randomization design with a comparison group[30] to compare handwashing with the use of gown and glove isolation, and the other study was a randomized equivalence trial[31] comparing alcohol with antiseptic solutions.

Three studies demonstrated a decrease in infection rates with the hand sanitizer.[21,24,25] Two other studies[22,23] reported no significant differences in HCAI rates between handwashing and the introduction of a hand sanitizer. Another study[26] reported a decrease in MRSA rates postintervention.

One study[29] reported a significant reduction in MRSA rates (P = .03), another[27] reported a significant reduction in MRSA (P = .01) and VRE (P < .001) rates, and the results of another study[28] were not statistically significant. One study[30] showed significant reductions in infection rates before and after in each of the groups (P = .008 and P = .008, respectively), and another study[31] showed no significant differences between the 2 protocols (P = .05). In assessing these 11 studies as a whole, 4 had fatal flaws, and all 4 failed to demonstrate adequate statistical analysis (Table 4).

Category 3. Infection control practices

Eight studies (25.81%) introduced or modified infection control practices to study their impact on the

Table 4. Studies linking hand hygiene to health care-associated infections by intervention type

				Scoring tool[10]		
Primary author (date)	**Design**	**Intervention**	**Findings**	**Score**	**Fatal flaws**	**Comments**
Category 1. Multimodal hand hygiene initiatives						
Pittet (2000)[14]	Before and after (no control group)	Multimodal	Significant reduction ($P = .04$) 7% decrease in overall nosocomial infection Significant reduction ($P < .001$) 0.01% decrease in MRSA transmission rates	1	II	Uncontrolled bias or confounding factor (reduction in infection rates and MRSA transmission possibly confounded by multiple interventions) Other flaws: Observational bias/possibility of Hawthorne effect
Lam (2004)[15]	Before and after (no control group)	Multimodal	No significant reduction ($P = .14$) 0.51% decrease in HCAI rate	2		Possibility that HCWs behavior changed because they were being observed
Zerr (2005)[16]	Before and after (no control group)	Multimodal	Significant reduction ($P = .01$) 0.37% decrease in rotavirus rate	3		
Aragon (2005)[17]	Before and after (no control group)	Multimodal	6 mo: 17% decrease in MRSA, 13% decrease in VRE 1 yr: increase trend for MRSA and VRE No P value	3		
Won (2004)[18]	Before and after (no control group)	Multimodal	Significant reduction ($P = .003$) 0.44% decrease in HCAI rates; in particular significant reduction ($P = .002$) 0.23% decrease in respiratory tract infections	3		
Hilburn (2003)[19]	Before and after (no control group)	Multimodal	36.1% decrease in infection rates No P value	3		No hand hygiene compliance data provided
Johnson (2005)[20]	Cohort study (no control group)	Multimodal	Significant reduction ($P = .01$) 57% decrease in MRSA bacteremia	1	II	Uncontrolled bias or confounding factor (data collection unblinded) Other flaws: Difficult to determine the merits of each intervention (simultaneous interventions) Reliance on historical controls/possibility of Hawthorne effect Possible that change in MRSA bacteremias were because of natural variability over time Only percentage reductions in MRSA bacteremia and ESBL were provided (and no absolute reductions)

Continued

Table 4. Continued

				Scoring tool[10]		
Primary author (date)	**Design**	**Intervention**	**Findings**	**Score**	**Fatal flaws**	**Comments**
Category 2. Hand hygiene products						
Ng (2004)[21]	Before and after (no control group)	Handwashing	Significant reduction ($P = .048$), 11% fewer MRSA infections in the glove AHS protocol	3		
		vs AHS before gloves	0.87% decrease of late-onset systemic infection			
Larson (2005)[22]	Sequential crossover study (with comparison group)	Antiseptic handwash vs alcohol handrub	No significant differences in neonatal infections (any infections [$P = .88$], bloodstream infections [$P = .94$], CNS infection [$P = .68$], skin infection [$P = .08$], pneumonia [$P = .37$]) between the 2 groups	2		Self reported hand hygiene practices
						Potential investigator bias (because of no blinding of study products)
Mody (2003)[23]	Cohort study (with control group)	alcohol-based handrub vs handwashing only	No differences in HCAI between the 2 units	I	I	Inadequate sample size
			No *P* value		IV	Inadequate statistical analysis (no power calculation—to compare between groups
						Other flaws:)
						Self-reported hand hygiene practices
Marena (2002)[24]	Cohort crossover study (with comparison group)	Plain soap vs chlorhexidine	Decrease in HCAIs	2		Limited sample size and follow-up period
			No *P* value			Possibility that HCWs behavior changed because they were being observed
Fendler (2002)[25]	Cohort study (with control group)	Hand sanitizer vs handwashing	Significant reduction ($P < .05$), 30.4% decrease in infection rates with hand sanitizer	I	II	Uncontrolled bias or confounding factor (different level of acuity between intervention vs control group)
					IV	Inadequate statistical analysis (groups cannot be compared—no power calculation performed and a difference in acuity levels between the groups exists)
Brittain (2004)[26]	Before and after (with control group)	1% antiseptic solution vs 4% antiseptic (control group)	68% lower MRSA infection rates postintervention on orthopedic ward	I	I	Inadequate sample size
			No *P* value		II	Uncontrolled bias or confounding factor (no confirmation of homogeneity between groups)
					IV	Inadequate statistical analysis (groups not comparable—no power calculation performed and—no confirmation of homogeneity between groups)
						Other flaws:

						Compliance with handwashing not monitored
Gordin (2005)[27]	Before and after (no control group)	alcohol-based handrub	Significant reduction ($P = .01$) 21% decrease in MRSA	3		Clear and concise study
			Significant reduction ($P < .001$)			No data on extent of use of product or hand hygiene compliance
			41% decrease in VRE			
			No significant change ($P = .62$) in *C difficile* and rates			
King (2004)[28]	Before and after pilot study (no control group)	Alcohol handrub	No differences	1	I	Inadequate sample size (study underpowered)
			No *P* value		II	Uncontrolled bias or confounding factor (unclear participant inclusion criteria and data collection unblinded)
					III	Unclear operational definitions (unclear definition of outcome)
					IV	No statistical analysis
MacDonald (2004)[29]	Before and after pilot study (no control group)	Alcohol hand gel and performance feedback	Significant reduction ($P = .03$)	2		Unclear whether rates were infection or colonization
			0.9% reduction in MRSA rates			
Slota (2001)[30]	Randomization design (with comparison group)	Handwashing vs gown and glove isolation	Significant reduction ($P = .0008$) in gown and glove isolation group	3		Limited sample size
			2.6% decrease in infection rate			
			Significant reduction ($P = .008$) in handwashing group			
			1.9% decrease in infection rate			
Parienti (2004)[31]	Randomized equivalence trial	Hand rubbing (alcohol) vs hand scrubbing (antiseptic)	No significant differences between the 2 protocols ($P = .05$)	4		First randomized trial to compare hand rubbing with alcohol vs traditional hand scrubbing in the routine surgical setting
			A 0.04% difference between the 2 protocols			No mention of institutional review board approval
Category 3. Infection control practices						
Schelenz (2005)[34]	Before and after (no control group)	Infection control practices	Significant reduction ($P = .003$)	2		Unsure about which intervention was critical for success
			2.14% drop in MRSA nosocomial infection/colonization			
			Significant reduction ($P = .014$)			
			0.89% drop in bloodstream MRSA infection			
Kac (2000)[35]	Before and after (no control group)	Infection control practices	Significant reduction ($P = .02$)	2		Use of historical controls
			6.8% decrease in MRSA infection rates between the pre- and 1994 postintervention			Difficult to determine the merits of each intervention
			Significant reduction ($P = .002$)			
			8.1% decrease in MRSA infection rates between pre- and 1996 postintervention			

Continued

Table 4. Continued

Primary author (date)	Design	Intervention	Findings	Scoring tool[10]		Comments
				Score	Fatal flaws	
Lai (1998)[32]	Before and after (no control group)	Infection control practices	Overall decrease in VRE rates No *P* value	1	IV	Inadequate statistical analysis Other flaws: No hand hygiene intervention described
Schelonka (2005)[36]	Before and after (no control group)	Infection control practices	Significant reduction ($P = .002$) Year 1: 26% reduction in infection rate Significant reduction ($P < .001$) Year 2 and 3: 29% reduction	2		Compliance with all individual practices not measured Impossible to determine role of hand hygiene in this multiintervention study
Zafar (1998)[33]	Before and after (no control group)	Infection control practices	Significant reduction ($P < .05$) 60% decrease in *C difficile*	1	II IV	Uncontrolled bias or confounding factor (data collection unblinded) Inadequate statistical analysis Other flaws: No examination of hand hygiene per se
Kurlat (1998)[37]	Before and after (no control group)	Infection control practices	Significant reduction ($P < .003$) 76% decrease in bacteremia rate	2		Role of HH can not be determined exactly because of multiple interventions, although most of the interventions were aimed at contact using clean hands
Andersen (2005)[38]	Before and after (with *Before* group acting as control)	Infection control practices	Significant reduction ($P = .05$) 12% decrease of bloodstream infections	1	I	Inadequate sample size (study underpowered) Actual sample size was too small: 174 infants instead of 220 required Other flaws: Impossible to have determined the role of hand hygiene even if a statistical significant outcome differences had been noted Adherence to all the interventions was not assessed
Makris (2000)[39]	Before and after (with control group)	Infection control practices	0.24% decrease in overall infections No *P* value No significant reduction ($P = .06$) of upper respiratory infections	1	I II	Inadequate sample size Uncontrolled bias or confounding factor (groups not comparable—no power calculation) Other flaws: Role of hand hygiene cannot be determined
Category 4. Infection control policies						
Stone (1998)[40]	Before and after (no control group)	Infection control policies	Significant reduction ($P < .05$) 1.4% decrease in *C difficile* and Significant reduction ($P < .01$) 2.01% decrease in MRSA	2		Unclear what contribution hand hygiene made over other interventions

Zerr (2005)[41]	Cohort study (no control group)	Infection control policies	Significant reduction ($P < .01$)	1	II	Uncontrolled bias or confounding factor (retrospective data collection)
			Presence of alcohol hand gel was associated with a decreased risk gastrointestinal infections (odd ratio, 0.66)		III	Unclear operational definitions (unclear definition of outcome)
						Outcome could actually be community-acquired infections rather than HAI Other flaws: Survey questions were about the presence of policies and not about a measure of current practice
Category 5. Other interventions						
Swoboda (2004)[42]	Before and after (no control group)	Electronic monitoring	10% reduction of HCAIs in phase II and 40% reduction of HCAIs in phase III No *P* value	3		Sample size not large enough to detect significant change in infection rates
Jusot (2003)[43]	Cohort study (no control group)	Survey on current practices	Overall incidence rate of hospital-acquired diarrhea, 3.6% No *P* value	2		Small sample size Participation was on a voluntary basis Self-assessment questionnaires
Larson (2000)[44]	Before and after (with control group)	Top level administration intervention	Significant reduction ($P = .002$) in VRE rates for intervention hospital (RR, .29)	3		Duration of observation not very long, and VRE rates can vary substantially over time without intervention naturally
			No significant change ($P = .25$) in MRSA rates			

AHS, alcohol hand sanitizer; *ESBL*, extended-spectrum β-lactamase.

reduction of HCAIs. Six studies were before and after studies with no control group,[32-37] and 2 studies[38,39] had a control group.

Two of the studies, 1 with a control group[39] and 1 without a control group,[36] reported a decrease in overall HCAI rates, but it was not possible to determine the role of hand hygiene in any of these studies. One study that used a before group as a control group[38] reported a significant reduction ($P = .05$) of bloodstream infections. In the remaining studies without a comparison control, one[37] reported a significant reduction ($P < .003$) in the bacteremia rate; two[34,36] reported a significant reduction ($P = .003$ and $P = .002$, respectively) in MRSA rates; one[32] reported a decrease in VRE rates; and one[33] reported a significant decrease ($P < .05$) in *C difficile*. In addition to the lack of clarity on the role of hand hygiene in all of these studies, 4 out of 8 studies exhibited at least 1 fatal design flaw (Table 4).

Category 4. Infection control policies

Two studies (6.45%) introduced an infection control policy to study its impact on the reduction of HCAIs. One study,[40] a before and after design with no control group, reported a significant reduction in both *C difficile* ($P < .05$) and MRSA ($P < .01$). The other study,[41] a cross-sectional design with no control group that reported a significant reduction ($P < .01$) in the risk of hospital-associated gastrointestinal infections, demonstrated 2 fatal flaws including an unclear definition of outcome and the presence of confounding factors.

Category 5. Other interventions

Three studies (9.68%) introduced organizational interventions to study their impact on the reduction of HCAIs. In a 2004 before and after study with no control group by Swoboda et al,[42] an electronic monitoring system was implemented to improve hand hygiene and decrease HCAIs, but the results were not statistically significant. In Jusot et al's 2003 cohort study with no control group,[43] neonatal unit staff were surveyed to investigate the relationship between hygienic measures and the overall incidence rate of hospital-acquired diarrhea, but the results were not statistically significant.

In another study, Larson et al[44] used a before and after design with control group to examine the relationship between a top level administration intervention aimed at changing organizational culture and hospital VRE and MRSA rates. No significant change ($P = .25$) in MRSA rates were found, but VRE rates decreased significantly ($P = .002$) for the intervention hospital for the duration of the study, which was over a period of 8 months. The caution with these findings is that VRE rates can naturally vary substantially over time. Nonetheless, the study design ensured that the link between hand hygiene as measured by soap utilization per patient-day and HCAI rates was demonstrably clear. One study[43] received a score of 2, and the other 2 studies[42,44] received a score of 3 (Table 4).

Limitations

The limitations of this integrative review were (1) that the search only included articles that had the term *hand hygiene* or *handwashing* in their title as the focus of the paper because of the large volume of publications available in this area and (2) that the selection of articles was limited to English and to studies conducted in developed countries to allow for better comparison of the results.

DISCUSSION

Overall, the results of the studies, **given the** frequent limitations to their rigor, do not demonstrate a strong relationship between hand hygiene interventions and decreased incidence of HCAIs. Furthermore, the multiple interventions used and the diverse factors related to the presence of HCAIs make it difficult or impossible to isolate the specific effects of hand hygiene or of any other component of the interventions. In addition, there is a paucity of theoretically driven research approaches, which makes it very difficult to weigh the relative merits of the particular HHI tested in each study in relation to the evidence that has accumulated to date. As Sales et al note, researchers need to be able to determine and evaluate the theoretic assumptions that underlie specific interventions if they are to formulate more coherent and sufficient rationale for their choices in strategies, interventions, tools, and study design.[45] Equally, reviewers of research, policy makers, and practitioners all need to understand the theoretic rationale for specific interventions if they are to make informed choices about which intervention might work best for their settings, under which conditions, and at what possible cost.

The most frequent methodologies currently used in this research area are ecologic studies or before and after studies. These types of study designs limit generalizability because there are no way to control for natural variation and random chance. Without an independent control group that is equivalent to the study group in all other respects, it is possible that the observed differences are simply because of random chance or natural variability in the infection rates over the period of observations.

Ultimately, ‘‘the choice of design [is] dependent upon the purpose of the evaluation and the degree of control the researchers have over the delivery of the intervention(s).''[46] Although a randomized controlled trial is the most robust study design, it is challenging to carry it out in this field for several reasons. For example, the use of control groups, in light of expert recommendations about hand hygiene, may raise questions about clinical equipoise. There can also be prohibitive costs associated with conducting a randomized control trial in which the unit of analysis must be at minimum at the level of a hospital unit, and preferably at the hospital level, because of the possibility of communication between units. In addition, the blinding of patients, practitioners, or investigators to a hand hygiene regimen is challenging, with the introduction of bias or confounding factors a real possibility. Furthermore, adequately powered sample sizes are not easy to obtain. When the number of additional factors that influence the comparability of one setting to another are considered, including but not limited to variability in organizational policies, staffing practices, patient characteristics, migrating equipment and facility design, the task of finding valid comparison controls can discourage the most determined researcher.

Characteristics of a well-designed hand hygiene intervention study

Overall, the current studies present inconsistent parameters in their design and thus make it difficult to accurately interpret and compare the research findings in this body of literature. One of our recommendations is to use a modified version of Larson's recommendations for this area of research[10] to establish some common characteristics for future studies. In our estimation, these characteristics should include the following:

- Adequately powered sample size determined in advance to support conclusions;
- use of either (1) a pre- and post-with-comparison control design or (2) a cluster randomized controlled trial such as the recent trial of a multifaceted intervention to reduce antimicrobial prescriptions in nursing homes[47];
- a detailed outline of the features of experimental settings and their control counterparts;
- baseline measurement of HCAIs rates with a minimum number of observations as dictated by proper sample size calculation and at least 6 to 12 months of data;
- clear identification of possible confounding variables;
- identification of a consistent hand hygiene audit tool and observation method;
- clear statement of inclusion and exclusion criteria;
- blinded data collection;
- clear and detailed description of interventions;
- clearly listed operational definitions;
- appropriate and clearly identified statistical analysis;
- evidence that the intervention was actually implemented (ie, quality control);
- common definition of outcomes (ie, HCAIs rates); and
- an explicit theoretic framework for the study that (1) clearly articulates the evidence to date on the relationship between HHIs and HCAIs and that (2) links the assessment of the evidence with sound rationale for the intervention developed and the overall research design.

Even though it is highly unlikely that researchers would consistently meet all of these criteria, the explicit use of this template to guide the design and dissemination of intervention research would enable both scientists and their target audiences to transparently identify and evaluate the limitations of specific studies in relation to chosen study approaches.[45,48,49] As the field progresses, the theoretic and methodologic deficits that repeatedly surface should guide us to generate better intervention theories and more rigorous research designs.

From evidence to uptake: Exploring additional research approaches. Grimshaw et al have already noted that ''some strategies [are] not amenable to randomization'' in health systems research.[50] In the field of ecosystems management, ecologist Crawford ''Buzz'' Holling and Gunderson have extended this observation to argue that 2 forms of science are needed to adequately understand and manage the complex socioecologic systems that characterize today's technologic world.[51-53] In essence, Hollings and others who share a ''two cultures of science'' perspective equally value an analytic ''science of parts'' and an integrative ''systems science of the whole.''[52] In the first analytic line of scientific inquiry, researchers pursue vital questions in ecology, biology, microbiology, and other fields to understand how various elements of the world interact under specific controlled experimental conditions. In the second integrative line of science, researchers ask the following: Now that we better understand how various parts of the world work in an experimental mode, what system conditions are needed for people, communities, and institutions to use evidence about the world to effectively adapt and change? With these latter systems science questions, we are using research to discover how we can translate what we learn from controlled experiments into the effective study and management of an uncontrollable world.

We propose that equal attention to both the analytic and integrative sciences are as important for sound health systems management as they are for effective ecosystems management. If we are right, we need at least 2 research approaches to accelerate the conduct and uptake of research that leads us to reliable, enduring reductions in preventable HCAIs. For example, we know that, in present-day infection control practice, multiple interventions are used to resolve real day-to-day outbreaks as rapidly as we can muster a response. However, we also know that, in our understandable urgency to act without strong levels of evidence, we may be allocating significant resources to interventions that add no or little value or that could even cause unanticipated harms. In a 2-science world, we suspect that an adequate way forward from this state of affairs is distinguished by at least 2 parallel paths of concurrent action. First, in terms of analytic science, we may want to conduct a select number of focused studies that examine specific hand hygiene interventions (such as education, gowns, gloves, cleaning methods, and products) one by one in isolation to determine the relative impact of various interventions on specific HCAIs one at a time. These studies would explore the biologic gradients between hand hygiene and particular HCAIs to establish whether the results are or are not the same for each infection. We should also seek to conduct future studies of complex, multilayered HHIs to determine which synergistic combinations of interventions are most effective and affordable in reducing what HCAIs and under what conditions. Furthermore, as we have already noted, sound HHI studies of any kind should incorporate a clearly articulated and justified theoretic rationale, the use of comparable control groups, and other features of a robust analytic design. In addition, we will need ongoing systematic reviews in the Cochrane tradition of the analytic scientific evidence that accumulates to provide researchers with clear critiques of the evidence and necessary insights into the methodologic challenges with this kind of research.

As we accumulate empirical evidence on which individual and multilayered HHIs are most effective under what controlled experimental conditions, though, we predict that many of the methodologic challenges to conducting rigorous controlled trials of infection control programs such as multifaceted HHIs will prevail. Accordingly, we suggest that there is a pressing need to develop concurrently a parallel, critical path of integrative science for multifaceted HHIs because such programs actually constitute multilayered organizational interventions in complex (and therefore continually confounding) health care systems that are characterized by instability and change.[12] Here, we need to use a range of theoretically driven questions about preventing, minimizing, and managing real outbreaks in a real, inevitably uncontrolled world. In this integrative line of scientific inquiry, our ''systems science'' question would be as follows: What system conditions enable people, communities, and organizations to effectively translate and adapt evidence-informed infection control policies and practices to their specific, local, real worlds of health care?[54] In the case of multifaceted HHIs, we would then study the adaptation of evidence-informed HHI guidelines to determine what helps or hinders us from achieving both ongoing, affordable reductions to a number of HCAIs in a range of health care settings and earlier detection and control of emerging threats.

To reach these goals of integrative science, researchers need to become familiar with a range of mixed methods that enable us to understand health systems change from a variety of qualitative and quantitative vantage points, including but not limited to such research approaches as retrospective, real-time, and planned prospective case studies; institutional ethnography; participatory action research; and other designs.[51] In addition, to ensure that we match the necessary questions about systems change with coherent theories and defensible methods, we agree with safety researchers who urge us to reach beyond a sole focus on evidence-based medicine to a broader and more interdisciplinary view of safety science that encompasses not only the health disciplines but a variety of experts across the social, engineering, economic, political, and ecologic sciences.[55-59] For that matter, ongoing dialogue with experts in many of these fields would arguably strengthen both our analytic and integrative research designs in many areas of health systems research. Furthermore, to synthesize the findings across both categories of science into meaningful guidance for decision makers and practitioners, we will need what Pawson et al call realist reviews of research.[12] In this alternate method of systematic review, the contention is that ''complex policy interventions'' should be informed by syntheses of research across qualitative and quantitative methods that contextualize findings into theoretically driven, principles-based recommendations for local contextualization rather than universal rules of treatment based on effect sizes.[12] According to Pawson et al, a good realist review ''learns from (rather than controls for) real-world phenomena such as diversity, change, idiosyncrasy, adaptation, cross contamination, and programme failure.''[12] In other words, we not only need more good science, but at least 2 kinds of science, and at least two kinds of critical review methods, to synthesize our findings in infection control research into practical knowledge that we can readily use.

CONCLUSION

Even though the number of publications on HHIs is impressively large, the methodologic issues for this area of research remain significant. This integrative review demonstrates that the evidence linking hand hygiene interventions and HCAIs is present, but it is not well quantified. It is clear that we need more robust analytic research designs to obtain better evidence on which HHIs are associated with reduced incidences of what HCAIs in a variety of settings. From our perspective, it is equally clear that, even as we gather this evidence, we also face challenging questions of systems science where we need to integrate evidence on effective HHIs with better knowledge of what drives human, organizational, and health system policy and practice toward evidence-informed, sustainable infection prevention and control.

It is very unlikely that we will ever eliminate infections entirely, even if we achieved 100% compliance with stringent hand hygiene. It is more likely that, for HHIs as well as for other infection control interventions, we may initially see a steep improvement as did Semmelweis,[60] and yet still find that controlling the last 5% of infections requires 90% of our efforts. The development of a more resourceful, evidence-based approach to infection control research and practice therefore remains a very complex yet vital challenge for modern health systems that science will not solve anytime soon. However, if we initiate ongoing dialogue with colleagues across a much wider landscape of expertise than we have previously traveled, we may find that we not only generate better evidence on the relationship between various HHIs and HCAIs but we also create better strategies for translating evidence into wiser resource allocation and the reduction of preventable harms. In the meantime, we can only hope that more and more organizations and practitioners will not let evidence-based medicine act as an erroneous "intellectual hegemony"[51] that substitutes for sound judgment and that, instead of waiting for irrefutable analytic scientific evidence, a rising community of the conscientious will insist that we all consistently and thoroughly wash our hands.

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