Applying thematic synthesis to interpretation and commentary in epidemiological studies: identifying what contributes to successful interventions to promote hand hygiene in patient care

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Objectives: Hand hygiene is considered the most important preventive measure for healthcare associated infections, but adherence is suboptimal. We previously undertook a Cochrane Review which demonstrated that interventions to improve adherence are moderately effective. Impact varied between organisations and sites with the same intervention and implementation approaches. This study seeks to explore these differences.

Methods: A thematic synthesis was applied to the original authors' interpretation and commentary that offered explanations of how hand hygiene interventions exerted their effects and suggested reasons why success varied. The synthesis used a published Cochrane Review followed by three-stage synthesis.

Results: Twenty-one papers were reviewed: eleven randomised, one non-randomised and nine interrupted time series studies. Thirteen descriptive themes were identified. They reflected a range of factors perceived to influence effectiveness. Descriptive themes were synthesised into three analytical themes: *Methodological Explanations for failure or success* (e.g. Hawthorne Effect)*;* and two related themes that address issues with implementing hand hygiene interventions: *Successful implementation needs leadership and cooperation throughout the organisation* (e.g. visible managerial support)*;* and *Understanding the context and aligning the intervention with it*

drives implementation (e.g. embedding the intervention into wider patient safety initiatives).

Conclusions: The analytical themes help to explain the original authors' perceptions of the degree to which interventions were effective and suggested new directions for research: exploring ways to avoid the Hawthorne effect; exploring the impact of components of multimodal interventions; the use of theoretical frameworks for behaviour change; potential to embed interventions into wider patient safety initiatives; adaptations to demonstrate sustainability; and the development of systematic approaches to implementation. Our findings corroborate studies exploring the success or failure of other clinical interventions: context and leadership are important.

275 Words

BACKGROUND

Healthcare-associated infection (HCAI) is spread mainly via health workers' hands. Adherence to hand hygiene protocols is suboptimal and the impact of campaigns to increase adherence to hand hygiene protocols is hard to sustain [1]. The World Health Organization's [1] multimodal hand hygiene promotion strategy recommends system change i.e. the use of alcohol-based handrub at the point of care; written and/or verbal reminders; education; and audit with performance feedback and the promotion of institutional safety climate in relation to hand hygiene. Other components of the hand hygiene intervention [HHI] can be added or modified to customise core recommendations to local need [1]. Initiatives to promote hand hygiene are widely reported but most are uncontrolled before-and-after studies insufficiently robust to generate findings that can be considered sufficiently rigorous to support policy or practice; our recent Cochrane systematic review [second update published in 2017] of the most rigorous interventions [2] demonstrated only modest improvement with variations between organisations and different sites in the same organisation when the same intervention and approach to implementation were applied. Our Cochrane review did not investigate factors that might have contributed to differences in effectiveness. We therefore analysed the original authors' interpretation of and commentary on their findings to explore reasons to explain this variation and identify messages for future research, policy and practice. Two research questions were addressed:

1. What factors identified by thematic synthesis are perceived by the original authors to influence the effectiveness [or lack of effectiveness] of HHIs in different contexts?
2. What are the messages for research, policy and practice?

METHODS

We took an inductive approach to analysis to generate new insights and understandings of the original authors' interpretations for the success or failure of HHIs utilising an adapted approach to thematic synthesis, a method originally developed to bring together and integrate the findings of qualitative studies in healthcare research [3,4].

The adapted thematic synthesis was conducted on the systematic searches and quality appraisal previously conducted for a Cochrane Review of HHIs. The data for analysis and synthesis were the individual study authors' interpretation and commentary offering explanations of how HHIs exerted their effects and the suggested reasons why success varied. The three-stage approach to synthesis remained unchanged from that described by Thomas & Harden [4]. It involved line by line coding of the information contained in primary studies, its organisation and the development of descriptive themes that remained 'close to the [primary] data'. The aim of this rigorous process was to create analytical themes in which the reviewers 'go beyond' the primary studies to provide explanation and identify messages for practice, policy and future research [3, 4].

DJG and JC undertook line by line coding of the original authors' accounts of their studies and their opinions of what contributed to or detracted from the effectiveness of the HHI to generate provisional descriptive themes. These were agreed between other members of the research team [ND, EP]. The resulting descriptive themes were labelled and synthesised into analytical themes. Membership of the full research team included policymakers, clinicians and academics with experience in qualitative and quantitative analysis in order to increase utility of the findings as recommended [3]. DJG, JC, DP, DM, RG, AJ and NW have backgrounds in infection prevention. DJG, DP, RG, AJ and NW have

contributed to policy, including policy relating to hand hygiene. EP's background is in surveillance of infectious diseases. ND is an epidemiologist.

Included publications

Eligibility of papers for the thematic synthesis was based on eligibility to be included in our recently updated Cochrane Review [1] that included 26 papers meeting the stringent quality criteria of the Cochrane Evaluation of Practice and Care Group [5]. This is an adaptation of the standard approach to thematic synthesis described by Thomas and Harden [4]. The approach they recommend would usually be conducted with a smaller purposive sample of qualitative findings. We chose to use a large sample comprised of all the eligible papers from the Cochrane Review, because our analysis is conducted on the original authors' interpretation and commentary of their quantitative findings and not upon standard qualitative findings as generated from a typical qualitative study. It would not have been logical to interpret commentary in HHI studies already deemed to be of poor quality, as the validity of the studies' findings is unknown, and thus explanations for their success or otherwise nonsensical. Existing tools employed to critically appraise qualitative work were not applicable to the types of study we were investigating.

To meet the criteria for thematic synthesis, papers had to contain authors' interpretations and commentary offering explanation of how hand hygiene interventions exerted their effects and suggest reasons why success varied. Before embarking on thematic synthesis, the text of each publication was scrutinised to determine whether this information was provided. Two members of the research team worked together to select the included publications [DJG and ND]. Third party arbitration to resolve divergent opinion was not required.

[1] *Cochrane Database of Systematic Reviews* 2017, Issue 9. Cochrane Reviews are regularly updated as new evidence emerges and in response to comments and criticisms. The *Cochrane Database of Systematic Reviews* should be consulted for the most recent version of the Review.

Five publications were excluded from those originally included in the Cochrane Review [2]. All were short reports in which the original authors did not express any opinions about why or how the HHIs were effective All the excluded publications concluded that the HHI had increased hand hygiene adherence.

Twenty one publications were included: eleven randomised trials [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16]; one non-randomised trial [17]; and nine interrupted time series [ITS] studies meeting specific criteria adopted by the Cochrane Collaboration [18, 19, 20, 21, 22, 23, 24, 25, 26].

Summary details of the 21 included studies including the study characteristics and contexts are available in Supplementary Table 1 showing study design, journal type, aims, HHI intervention design, method of hand hygiene audit, basis for determining adherence, type of hand hygiene intervention, the study setting, its duration, stakeholder involvement and challenges to recruitment. Supplementary Table 4: contains further information on the characteristics of the included studies. These differ from the Cochrane Review [2] as five studies are excluded from thematic synthesis.

The HHI was considered effective by eleven research teams according to their own interpretation [7, 9, 10, 11, 14, 17, 20, 22, 23, 24 25], moderately effective by a further five [8, 13, 16, 19, 26] and disappointing by three research teams [6, 12, 15, 21] taking into consideration baseline adherence which in one organisation was already good [66%] [15]. In one further study effectiveness was not reported as the effort required to implement the HHI was not considered worthwhile because increase in adherence was modest and did not alter rates of colonisation by meticillin-resistant *Staphylococcus aureus* [MRSA] [12].

RESULTS

Provisional descriptive themes

We identified and labelled 13 provisional descriptive themes [Table 1 and detail in Supplementary Table 2]. We established that there was broad agreement between the different studies in terms of original authors' opinions. Similar descriptive themes were apparent in many of the studies. For example the descriptive theme: *'Concerns about the Hawthorne effect and controlling for bias'* emerged in twelve publications [6, 8, 9, 11, 12, 14, 16, 17, 18, 20, 24] and the descriptive theme: *'Seeking and obtaining organisational support for HHI is important but not always successful'* also appeared in a number of publications. Attempts to obtain organisational support to promote HHIs were made in eleven publications but with variable success [6, 7, 8, 9, 12, 13, 22, 23, 24, 25, 26]. Some divergences of the original authors' opinion were apparent, for example in the descriptive theme: *'HHIs work differently in different clinical settings and with different groups'*. HHIs were reported to work better in some clinical settings than others [6, 16, 26]. Not all the original authors believed that this heterogeneity was problematic however [19].

Table 1. The analytical & Descriptive Themes with examples of supporting evidence extracted from the primary studies

Analytical Themes (AT) & Descriptive Themes (DT)	**Exemplar Quotations from papers** (Author Account & View)
Methodological Explanations for failure or success (AT)	

Concerns about Hawthorne effect and controlling for bias (DT)	"Observers were not blinded to the allocation of homes. HCWs [healthcare workers] being observed might have behaved differently in the presence of outsiders." [8]
Limited scope for improvement as HH rates have already been intensively promoted. (DT)	"The unique and long-standing focus on HH at the University of Geneva Hospitals might have affected the effectiveness of the new interventions." [15]
Challenges of determining which components of bundled HHIs were effective (DT)	"This multifaceted program featured simultaneous implementation of several different interventions making it difficult to ascertain which component had the greatest effect." [23]
The methodological key to sustainability (DT)	"The principal strength of the study is that it met the requirements of systematic reviews calling for large well-designed long-term trials of hand-hygiene interventions which apply behavioural theory to intervention design. The stepped wedge design increases power as wards act as their own control and the extended duration allows assessment of sustainability ." [6]
Theory: Why did it help? (DT)	"the current study has shown that a feedback intervention informed by behavioural science results in moderate significant and sustained increases in hand-hygiene compliance" [6] "Our results are in line with theories from the behavioural sciences where social influence, team effectiveness, role modelling and leadership are considered relevant to successfully changing behaviour." [9]
Successful implementation needs leadership and cooperation from throughout the organisation (AT)	
Leadership for the HHI and high visibility from managers and clinicians supports implementation. (DT)	"The task force was led by the chairman of medicine and included a multidisciplinary group" & "The creation of a highly functional multidisciplinary team composed of physicians, infection control practitioners; and leaders of respiratory therapy, nursing, nutrition, safety and transport played a vital role in increasing the HHCR [hand hygiene compliance rate] and changing the cultural practice of the health care provider." [22]
Patients are unwilling to challenge health workers about hand hygiene (DT)	"the idea of resident participation was not accepted by HCWs [healthcare workers] … They did not like to be reminded to perform HH [hand hygiene] by residents. This is probably because Chinese culture does not generally welcome potential for dispute." [8]
Flexibility of the HHI is important to enable it to fit with the needs of different groups of staff and setting. (DT)	"This program was expected to perform in different facility types with a variety of personnel" & "Program components designed by corporate clinical leaders were based on best practice pulled from experts at the local level, facilitating adoption into patient safety culture." [23]

Understanding the context and aligning the intervention with it drives implementation (DT)	
HHIs need to be embedded into wider patient safety and quality improvement initiatives. (DT)	"the unification of evidence-based practices may improve program effectiveness." [23]
Healthcare workers need to accept the HHI and be included in initiatives to involve behaviour change. (DT)	"An important advantage of our team and leaders-directed strategy was that the participating ward managers believed that the methodology could also be useful to improve team performance on other patient safety issues." [9]
HHIs work differently in different clinical settings and with different groups (DT)	"There was a high significant effect of the intervention in ITUs but not on ACE [acute care of the elderly] wards" & " The effect was stronger on ITUs, where it was easier to implement and where its effectiveness increased with fidelity to intervention" [6] "differences in hand hygiene compliance may exist between different groups" [10]
Need to address specific challenges. (DT)	"Compliance rates differed between specific hand hygiene indications… attention to specific hand hygiene indications… targeted this aspect." [9]
Resources (DT)	"HCWs [healthcare workers] seemed to be overwhelmed because of staff shortages and work loads." [12] "[one] site started with only one observer who decided to stop collaborating after 2 months due to an outbreak … This situation made it impossible to sustain monthly observation." [13]

Key: HH- Hand Hygiene; HHI- Hand Hygiene Intervention; HHCR- Hand Hygiene Compliance Rate; ITU- Intensive Therapy Unit

Analytical themes

The descriptive themes were synthesised into three analytical themes through discussion and reflection. The themes developed in this way were designed to capture the meaning and content of the findings accurately, discretely and succinctly without recourse to unnecessary extraneous themes. Three major analytic themes emerged: *Methodological explanations for failure or success* of the study; and two related themes that address issues with implementing HHIs: *Successful implementation needs leadership and cooperation from throughout the organisation*; and *Understanding the context and aligning the intervention with it drives implementation*. Table 1 presents the analytical themes and how the descriptive themes map onto them with exemplars supporting evidence extracted from the primary studies. Further detail is available in Supplementary Table 3.

Methodological explanations for failure or success

In twenty of the 21 [95%] publications [6-25] methodological limitations were perceived by the original authors to impinge on their ability to demonstrate the effectiveness of the HHI in their particular study. Concerns about the Hawthorne Effect (increased hand hygiene adherence when health workers become aware that they are watched) [27] were prominent. Other biases affecting the internal validity of studies, which were difficult to eliminate in the study design were also identified. These included cross-contamination with control areas. Four studies [6, 12, 13, 15] identified the problem of showing a meaningful increase in hand hygiene adherence in organisations where adherence was already high. Bundled interventions also posed a problem for researchers wanting to establish which particular elements of a multimodal intervention were responsible for improvements in adherence [23, 24]. Methodological factors were not always cited as limitations by the original authors. A number of unique features were

credited with ability to demonstrate sustained benefit. These included using a stepped wedge design, extended duration of the HHI [6] and feedback of audit findings [13, 15, 18]. A number of these authors also identified having a theoretical underpinning to the HHI as factor contributing to its success [6, 7, 9, 10].

Successful implementation needs leadership and cooperation from throughout the organisation

Leadership was widely cited as essential to the implementation of HHIs [6, 7, 13, 22, 24, 25]. In particular high visibility of managerial and senior clinical staff was important to the necessary change of cultural practices and behaviour [22, 25] and developing a consistent and sustained approach to hand hygiene adherence [13, 22, 24]. Approaches where particular roles were embedded within training and faculty positions also promoted successful implementation [25]. Absence of 'buy-in' from health workers was cited as a reason for poor implementation [6]. The potential role of patients in securing hand hygiene adherence was acknowledged by two authors, but the experience proved problematic as patients were unwilling to challenge healthcare workers [8, 15].

A number of the original authors recognised the importance of having a flexible approach to the HHI to enable it able to fit in with the needs of specific groups of staff and specific clinical settings, often in multiple hospital sites [21, 23, 26]. High staff turnover was recognised as problematic and frequent feedback sessions were employed to ensure that new employees were 'brought up to speed' quickly [16]. In other studies the HHI was designed with local input from clinical staff to ensure 'buy-in' and motivation [26]

Understanding the context and aligning the intervention with it drives implementation

'Buy-in' from staff and organisational support was not the only factor determining the success of HHIs. Equally important was the need to understand the specific context of the HHI and to align it to this context to ensure successful implementation. Strategies that embedded the HHI in existing patient safety and quality improvement initiatives were seen as successful [14, 23, 25], particularly where expertise could be shared with larger units [14]. Allied to this was the need for the HHI to be acceptable to health workers and for them to be included in behaviour change modifications. Interventions that enable managers to address other patient safety issues were identified as helpful [9]. Not involving health workers, disinterest or resistance to the HHI were barriers to implementation [6, 12].

A number of the original authors identified a range of successes or failures with respect to different clinical contexts. Implementation on critical care units was perceived as more successful than uptake in acute elderly care wards [6, 26] perhaps because health workers on critical care units are more aware of the importance of infection prevention [26]. The need to address specific challenges such as differences in hand hygiene adherence between different locations [9] and reducing MRSA acquisition [19, 23] were identified as motivators for change and being able to secure improvements in compliance.

The inability of infection prevention staff to undertake additional tasks related to the HHI was identified as a barrier to improved adherence [12, 13, 16, 25] and there was recognition that successful hand hygiene initiatives require considerable commitment of resources [23]. It was also noted that adherence

varied with the particular daily demands placed on health workers in terms of staff availability and fluctuating patient case-mix [26].

DISCUSSION

We have taken a novel approach to evidence synthesis, adopting the example of interventions to improve adherence to hand hygiene protocols in patient care, we demonstrated that it is possible to apply the principles of evidence synthesis to interpretation and commentary included in epidemiological studies. Combining this approach with the findings of traditional systematic reviews would demonstrate not just whether the intervention is effective but also how it exerts its effects and offer messages for sustainability and transferability to other contexts.

The thematic synthesis identified three major analytical themes relating to explanations of outcomes for the HHIs: *Methodological Explanations for failure or success* and two related themes that address issues associated with implementing HHIs: *Successful implementation needs leadership and cooperation from throughout the organisation*; *and Understanding the context and aligning the intervention with it drives implementation*.

The first theme focused on aspects related to the internal validity of the studies, and methodological explanations mostly related to failure to demonstrate the effectiveness of HHIs. This analytic theme was evident in the majority of papers, reflecting findings from the Cochrane Review [2] and other authors who have identified directions for future hand hygiene research [28]. The Hawthorne effect was most frequently mentioned, followed by other sources of bias. Other reviewers have observed that although hand hygiene is frequently described as a simple preventative measure, HHIs are hard to design and conduct [29]. Some

authors, not meeting the eligibility criteria for our review, have employed the Hawthorne Effect as part of the intervention [45, 46]. In these studies, it was deemed successful and is worth considering explicitly as part of a HHI.

Obtaining accurate and valid measurements of hand hygiene adherence is especially difficult not only in relation to the Hawthorne effect but also as a result of observer error, failure to train observers, lack of inter-rater reliability and the challenge of documenting hand hygiene opportunities and events in busy clinical areas [30]. Sustainability and methodological adaptations to achieve internal validity were identified by a number of the original authors. Central to success were HHIs that had sufficient follow-up to demonstrate sustainability and the implementation of techniques to 'refresh the message' in terms of feedback and performance benchmarking.

Theories of behavioural change were identified as helpful by a number of the original authors. It has already been suggested that theoretical frameworks from the behavioural sciences should be used to underpin HHIs [31, 32] but these were employed in only a quarter of the studies. A different theory was applied in each, but all were thought to enhance understanding of hand hygiene behaviour and contribute to improved adherence. In one case, stakeholders suggested that the theoretical framework might help improve performance of other patient safety issues [9].

A number of individual descriptive themes contained in two of the major analytic themes suggested challenges to implementation relating to institutional support and context. These concerns reflected a very broad spectrum of issues rather than a single barrier described in depth. Descriptive themes relating to implementation were less well developed than the themes relating to methodology, unsurprisingly given the focus on internal validity and study design

that exist in evidence-based healthcare and the scant attention paid to issues of context and external validity [33]. The importance of institutional support and context were novel findings not apparent in traditionally conducted systematic literature reviews of HHIs such as our Cochrane review [2] which focused on internal threats to validity.

Leadership from all levels of the organisation, especially from senior management and clinicians, was identified as a key to success. Visibility of senior staff 'walking the walk' [34] and 'buy-in' [35] were especially important. Stakeholder involvement was often lacking or unsuccessful, however. Attempts to engage patients or the public were reported in only two studies although international policymakers recommend including them in initiatives to prevent infection and reduce the risks of antimicrobial resistance [36]. These attempts were viewed as problematic and identified as a barrier to implementing the HHI. None of the studies used a theory of leadership, despite identifying leadership as crucial. New studies would benefit from adopting a defined framework for leadership, such as using 'Leadership and Organizational Change for Implementation' (LOCI) [37], which would enable the leadership components of a HHI to be theoretically driven and individually evaluated separately from bundled components.

Previous work suggests that contextual differences between organisations and clinical settings can affect the uptake of innovation and that initiatives successful in some settings are not always effective in others [38, 39, 40]. As in the HHIs, these variations are attributed to differences in local culture, acceptability to staff and patients, patterns of work and changes in the same organisation over time. In many of the settings where the HHI took place it would have been superimposed onto existing organisational and national policies. Infection prevention 'fatigue' may have undermined impact.

Study design did not appear to affect the type and detail of reporting. We reviewed randomised trials and rigorously undertaken ITS studies. The purpose of randomisation is to remove the effects of confounding variables on trial outcomes [41]. A supposed advantage of ITS studies is ability to take into account the impact of factors that might influence outcomes [42]. We therefore anticipated that trials would contain less interpretation and commentary than ITS studies. Surprisingly, three of the most highly informative studies were randomised trials [6, 8, 9]. Only two of the most highly informative publications were ITS studies [23, 25]. Of the nine ITS studies reviewed, six were not especially rich in interpretation or commentary [18, 19, 21, 22, 24].

The aim of thematic synthesis was to understand the original authors' interpretations and insights into what made a HHI successful or otherwise. Our approach to such 'contextual data' in reports of epidemiological studies is novel and we consider that such an approach combined with traditional systematic reviews (including meta-analysis where possible) may provide additional insight. Our approach has provided new insight into reported factors influencing the success of HHIs. For example, authors of the primary studies placed great emphasis on need to improve approaches to implementation of the HHI, particularly in terms of engaging organisations holistically and leveraging leadership and implementing agile interventions sensitive to the local context and setting.

Advocates of evidence synthesis acknowledge that the effectiveness of evidence synthesis depends on the amount of information provided in primary studies [43]. We confirmed this finding. Some publications contained particularly detailed interpretation and commentary [6, 8, 9, 23, 25], others comparatively little [7, 10, 17, 19]. The value of thematic synthesis is also constrained by the type of

information presented. What the original authors chose to write about and the amount of interpretation and commentary they included influenced our ability to synthesise and integrate the body of research as a whole. This limitation necessarily restricts the extent to which thematic analysis can be applied to data not collected in the usual way in qualitative enquiry. Nevertheless, there were sufficient data in most of the papers eligible for inclusion in thematic synthesis to conduct such analysis.

Messages to inform future research, policy and practice

Thematic synthesis identified key areas for research in relation to methodological rigour and implementation. The original authors expressed greatest concern in relation to the Hawthorne effect and other sources of bias, and indeed methodological shortcomings were sufficient to cause one research team [12] to question the value of the HHI. Such misgivings may have been over emphasised; as HHIs are theoretically effective through breaking the chain of infection and there is evidence from other studies that they can generate positive outcomes [44, 45]. Adaptations to demonstrate sustainability, including having a sufficient follow-up period, are required. Better controlled studies with improved hand hygiene monitoring would increase the credibility of the evidence supporting hand hygiene as the foremost infection prevention strategy. Our findings reiterate messages from Pittet's seminal work in Geneva [44]: organisational support is central to the success of HHIs. Its importance is emphasised in WHO guidelines [1] that also recommend customising HHIs to meet local needs. This requirement calls for greater understanding of how HHIs exert their effects at local level in response to specific needs and challenges and to enhance sustainability and transferability. Details of organisational support and context need to be clearly described in publications of HHIs so that a proper assessment of their external validity and applicability to other settings can be undertaken.

Leadership was identified as a key element of success, but the approach to leadership was neither defined nor theoretically underpinned in the studies. Adapted approaches such as LOCI [37] would enable the role of leadership in the success of HHIs to be clarified and its role in the success or otherwise of HHIs to be evaluated separately. Such an approach may help to provide a clearer specification of HHIs especially where they are bundled, so that the role of different levels of leadership (e.g. frontline managers or middle managers) and styles of leadership (e.g. transformational or transactional) is made clear and their contribution to the success of the HHI is explicit. There is a wider scope for employing systematic approaches to studying the implementation of HHI interventions more widely, such as the Consolidated Framework for Implementation Research (CFIR) [38]. Such an approach would help to guide systematic assessment of the hierarchical contexts that HHIs are situated within and help to systematically identify factors that might influence intervention implementation and effectiveness, potentially increasing the rigour of the research into HHIs and our ability to interpret the findings and generalise from them.

Finally feasibility studies are widely advocated to inform study design and methods, refine interventions, maximise acceptability to stakeholders and promote implementation [32]. Many of the perceived methodological failings and implementation failures described above could have been avoided or reduced if more thorough preparatory work had been undertaken, accompanied by process evaluation. A quarter of the research teams reported feasibility studies but in two cases they did not prevent problems related to lack of acceptability and none adequately addressed the methodological challenges later identified by the original authors.

Study limitations

Systematic reviews of evidence synthesis cannot generate meaningful findings unless searches are rigorously undertaken and the included studies are robust [43]. Our included publications met rigorous Cochrane requirements but our second updated Cochrane review [2] demonstrated that although they were the best available, certainty of the evidence was only moderate or low, with implications for validity. It is possible that more recent HHIs meeting the Cochrane criteria have now been published. They were not considered in this thematic synthesis. The value of thematic synthesis was further constrained by the amount and quality of interpretation and commentary included in the primary studies.

CONCLUSIONS

In this evidence synthesis we identified three themes offering explanations of the original authors' interpretations for the success or lack success of HHIs: methodological limitations affecting the internal validity of studies, implementation, external validity, organisational support and the need for HHIs to align with the existing context in the settings where implementation was attempted. New directions for research emerged: exploration of ways to avoid the Hawthorne effect; exploring the impact of individual components of bundled HHIs; the use of theoretical frameworks to underpin behaviour change and HHIs; the potential to embed the HHI into a wider patient safety and quality initiative; adaptations to demonstrate the sustainability of HHIs; and the development of a systematic approach to implementation. They need to be answered before policy and practice to increase hand hygiene adherence can advance.

3,699 words in text

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Supplementary Table 1: Characteristics & Contexts of The Studies

Publication	RCT	Cluster RCT	Stepped-wedge RCT	NRCT	ITS	MDT	Specialist IPC Journal	Non-specialist journal	Aim: Impact HHI on HH	Aim: feasibility New Tech for HH	Aim: explore new theory underpinning HHI	Design: underpinned by WHO	Design: influenced by WHO	Design: theoretical underpinning	Design: feasibility	HH Monitoring: Product consumption	HH Monitoring: Direct HH Observation	HH Monitoring: ATP	HH Monitoring: Video surveillance	Adherence: Five moments or similar	Adherence: Direct Obs before/after	Adherence: Microbiological outcomes	HHI: Performance feedback	HHI: Video monitoring	HHI: Cues	HHI: Education	HHI: Bundles
Whitby et al 2009 [26]					X	X	X					X				X	X										X
Mertz et al 2010 [12]		X				X	X		X			X		X			X			X		X					X
Armellino et al 2011 [18]					X	X	X			X			X						X				X	X			
Grant and Hoffman 2011 [7]		X						X	X				X				X								X		
Yeung et al 2011 [16]		X				X	X		X			X					X					X					X
Fuller et al 2012 [6]			X			X		X	X				X	X	X	X	X						X				
Ho et al 2012 [8]		X				X	X		X			X			X		X					X					X
Martin-Madrazo et al 2012 [11]		X				X	X		X			X			X		X										X
Higgins and Hannan 2013 [20]					X	X	X		X				X					X								X		
Huis et al 2013 [9]		X				X		X	X								X										X
Perlin et al 2013 [23]					X	X		X				X				X	X					X						X
Talbot et al 2013 [24]					X	X	X		X				X				X						X					
Derde et al 2014 [19]					X		X					X					X			X		X					X
Lee et al 2013 [21]					X			X				X					X					X					X
Stevenson et al 2014 [14]	X					X	X		X			X					X					X					X
Midturi et al 2015 [22]					X	X	X		X			X	X				X			X							X
Rodriguez et al 2015 [13]			X					X	X			X			X		X										X
Diegel-Vacek et al 2016 [17]				X		X	X	X			X						X								X		
King et al 2016 [10]	X					X		X	X					X			X								X		
Rosenbluth et al [25]					X	X		X	X			X	X				X										X
Stewardson et al [15]		X				X	X		X				X		X		X			X		X	X				

Supplementary Table 1: Characteristics & Contexts of The Studies (Cont.)

Publication	Settings: long-term care	Settings: Primary care	Settings: general ward or CCU	Settings: Multiple facilities	Setting: Part of wider IPC initiative	Setting: Nurse collected data	Setting: All staff collected data	Duration: Short term (weeks)	Duration: Medium term (< 1 yr)	Duration: Long term (> 1 yr)	Stakeholder: In-house staff	Stakeholder: Snr Manager support	Stakeholder: Ward managers	Stakeholder: Senior clinicians	Stakeholder: in-house IPC team	Stakeholder: Patients views	Recruitment difficulties
Whitby et al 2009 [26]			X				X				X		X				
Mertz et al 2010 [12]			X	X			X						X				
Armellino et al 2011 [18]	X						X		X					X			
Grant and Hoffman 2011 [7]			X				X	X									
Yeung et al 2011 [16]	X					X											X
Fuller et al 2012 [6]			X				X			X			X				X
Ho et al 2012 [8]			X				X		X		X				X	?	
Martin-Madrazo et al 2012 [11]		X					X	X									
Higgins and Hannan 2013 [20]			X				X										
Huis et al 2013 [9]			X	X		X							X				
Perlin et al 2013 [23]			X	X	X		X			X		X					
Talbot et al 2013 [24]			X				X			X				X			
Derde et al 2014 [19]			X		X		X										
Lee et al 2013 [21]			X		X		X										
Stevenson et al 2014 [14]			X				X								X		
Midturi et al 2015 [22]			X				X			X		X					
Rodriguez et al 2015 [13]			X				X					X			X		X
Diegel-Vacek et al 2016 [17]			X				X										
King et al 2016 [10]			X				X										
Rosenbluth et al [25]			X				X			X				X		X	
Stewardson et al [15]			X				X			X	X	X	X		X	X	

Supplementary Table 2: Provisional descriptive themes

'Concerns about the Hawthorne effect and controlling for bias' emerged in twelve publications [6, 8, 9, 11, 12, 14, 16, 17, 18 19, 20, 24]. In eight publications it was suggested that observing hand hygiene in the control group might have caused a Hawthorne effect, reducing the difference between control and test group outcomes [9, 10, 12, 15, 16, 17, 19]. In three publications it was suggested that installing extra hand hygiene dispensers in control wards might have the same effect [11, 12, 20]. Four authors expressed concerns about contamination between test and control groups within the same organisation [9, 12, 13, 15].

'Limited scope for improving adherence in organisations where hand hygiene had already been intensively promoted' was considered problematic in five publications [6, 7, 13, 15, 20].

'*Challenges of determining which components of bundled HHIs were effective'* was identified in six publications [8, 11, 13, 21, 23, 24].

'The methodological key to sustainability' was specifically addressed in 5 papers [6, 7, 13, 15, 18].

'*Theory: why did it help?'* Theoretical frameworks were considered valuable by all the research teams applying them [6, 7, 9, 10, 17].

'*HHIs need to be embedded into wider patient safety and quality initiatives'* Attempts to embed the HHI into wider patient safety culture were made in seven publications [9, 14, 15, 23, 24, 25, 26].

'Health workers need to accept the HHI and be included in initiatives to involve behaviour change' Attempts to make the HHI acceptable to health workers or include them in plans to change behaviour were made in six publications [6, 7, 8, 12, 15, 26].

'HHIs work differently in different clinical settings and with different groups' HHIs were reported to work better in some clinical settings than others in four publications [6, 16, 19, 26]. Derde et al [19], however, did not believe that the heterogeneity evident between intensive care units, hospitals and health services

in the thirteen countries taking part in their trial detracted from effective implementation.

'Flexibility of the HHI is important to enable it to fit with the needs of different groups of staff and settings' Flexibility of the HHI to meet the needs of diverse clinical settings, organisational cultures and different stakeholders and ability to refresh it to meet the needs of newly appointed staff and institutional changes over time were considered central to success in seven publications [14, 16, 20 21, 23, 24, 26].

'*Need to address specific challenges'* Targeting HHIs to meet specific challenges was considered to contribute to successful implementation in five publications: promoting hand hygiene at times when it was most likely to prevent cross-infection [9], targeting the most recalcitrant staff [13] and focusing on organisms that were most problematic [19, 21, 23].

'Patients are unwilling to challenge health workers about hand hygiene' Patient reminders were introduced by two research teams [8, 15]. These proved less effective than anticipated because there had been insufficient consideration of how stakeholders might perceive them. In one of these studies reported from China [8] the authors later concluded that patient reminders might not have been appropriate because questioning behaviour is considered confrontational in Chinese culture. Stewardson et al [15] suggested that challenging professional behaviour proved socially unacceptable despite patients' apparent willingness to engage with this approach when their views were sought in a pre-study survey.

'Leadership for the HHI and high visibility from managers and clinicians supports implementation' Attempts to secure leadership from senior management were apparent in five publications [13, 22, 23, 24, 25]. Support from senior clinicians was sought by four research teams [13, 22, 25, 26]. Visibility of managers and senior clinicians during 'walk-rounds' was considered especially helpful [13, 22, 24]. Support was sought from ward managers in nine reports [6, 8, 9, 13, 22, 23, 24, 25, 26]. Attempts to obtain organisational support to promote HHI were made in eleven publications but with variable success [6, 7, 8, 9, 12, 13, 22, 23, 24, 25, 26]. It was already considered good by another research team [15].

'Resources' were an important issue in ten publications. Heavy workload for clinical staff [6, 12, 13, 14, 16, 26] and for infection prevention teams assisting

with implementation [6, 13, 25] were considered barriers to success. Having access to sufficient resources [e.g. alcohol handrub] was considered important in four publications [12, 13, 23, 25].

Supplementary Table 3: The analytical themes with examples of supporting evidence extracted from the primary studies

Analytical Themes (AT) & Descriptive Themes (DT)	**Quotations (Information) from papers** (Author Account & View)
Methodological explanations for failure or success (AT)	
Concerns about Hawthorne effect and controlling for bias (DT)	"Selection bias was possible because the participating homes might have been more enthusiastic towards HH promotion" [8] "Observers were not blinded to the allocation of homes. HCWs [healthcare workers] being observed might have behaved differently in the presence of outsiders." [8] "A second possible explanation [for positive impact] is that cross-fertilisation [contamination] took place between teams in the same hospital [9] "Our observation were preformed unobtrusively but a possible Hawthorne Effect cannot be ruled out" [9] "In our study the improvement in the control group at six months compared to baseline might be attributed to the introduction of alcohol solution dispensers in all the healthcare centres not just the intervention group"[11] "Exclusion from the intervention groups motivated some wards to develop their own HH interventions." [15] "Staff on the unit were aware of observation … because the investigator was visible … this factor may be a confounder and a limitation." [17]
Limited scope for improvement as HH rates have already been intensively promoted. (DT)	"Participant's sites implemented hand rubs for HH in [sic] 98% [compliance], which shows that some recommendations to facilitate hand hygiene were already in place before the study' [13] "The unique and long standing focus on HH at the University of Geneva Hospitals might have affected the effectiveness of the new interventions" [15]

	"We performed a trial on wards already implementing a national hand hygiene campaign" [6] "Our findings are in keeping with data suggesting that the higher the baseline HH adherence rate the greater the relative increase in adherence needed to have an effect on MRSA colonisation" [12]
Challenges of determining which components of bundled HHIs were effective (DT)	"This multifaceted programme featured simultaneous implementation of several different interventions making it difficult to ascertain which component had the greatest effect." [23] "Because other infection prevention initiatives were occurring we cannot attribute causality to the interventions" [24]
The methodological key to sustainability (DT)	"The principal strength of the study is that it met the requirements of systematic reviews calling for large well-designed long-term trials of hand-hygiene interventions which apply behavioural theory to intervention design. The stepped wedge design increases power as wards act as their own control and the extended duration allows assessment of sustainability." [6] "A key limitation of both studies is that they lasted for only 2 weeks. Because the effects of hand-hygiene interventions are often short-lived, an examination of their sustainability is of critical importance." [7] Feedback was presented as a competition or benchmarking, and this seemed to be the strength of the tool." [13] "These findings support the central role of performance feedback in promoting and sustaining hand hygiene behaviour in hospital health-care workers, and suggest that patient participation could be cautiously considered by hospitals seeking additional interventions." [15] "We believe that the feedback was necessary for a sustained effect and that ongoing monitoring and feedback is required to sustain high rates of hand hygiene compliance" [18]
4) Theory: Why did it help? (DT)	"the current study has shown that a feedback intervention informed by behavioural science results in moderate significant and sustained increases in hand-hygiene compliance" [6]

	"Patient consequences rather than personal consequences can encourage hand hygiene among health professionals." [7] "Our results are in line with theories from the behavioural sciences where social influence, team effectiveness, role modelling and leadership are considered relevant to successfully changing behaviour." [9]. "A potential new avenue for intervening to increase hand hygiene behaviour in clinical settings [is] targeting automatic drivers of hand hygiene behaviours." [10]
Successful implementation needs leadership and cooperation from throughout the organisation (AT)	
Leadership for the HHI and high visibility from managers and clinicians supports implementation. (DT)	"The task force was led by the chairman of medicine and included a multidisciplinary group" & "The creation of a highly functional multidisciplinary team composed of physicians, infection control practitioners; and leaders of respiratory therapy, nursing, nutrition, safety and transport played a vital role in increasing the HHCR [hand hygiene compliance rate] and changing the cultural practice of the health care provider." [22] "Physicians champions serve an important role in behaviour change and it is likely that their role was underrepresented in the HHP [HH improvement program]" [25] "The sustained success of this multidimensional HH strategy was the high-level commitment of administrative leadership by leading the task force and making it an institutional priority." [22] "Leadership engagement through a formal accountability structure coupled with institutional financial incentives have encouraged both nursing and physician leadership to pursue a culture of consistent, sustained HH adherence." [24] "Intensive care personnel perceived these factors as contributive to sustain the effect: leaders' commitment shown by executive walkrounds ®, the relationship of the ICP with other personnel able to perform surveillance in the sites. [13] "For each unit the [in-house] patient safety team identified an expert observer with professional training." [7]

	‘’The administrative leadership of our institution created a multidisciplinary `HH task force to increase HH compliance amongst healthcare workers… The task force selected 5 interventions to improve the HHCR, including increasing the number of hand alcohol dispensers in hospital units, using covert observers (secret shoppers) to evaluate compliance of HH, using visual cues of hand dispensers that were empty or nonfunctional, using letters from the chief medical officer to noncompliant HCWs, and using positive recognition and reinforcement of departments with excellence in HHCRs” [22] “Attending physicians from multiple departments were engaged to serve as hand hygiene champions for their units. Several residents and faculty took on roles as physician champions specifically because it was a goal in the resident and fellow quality improvement Incentive Program.” [25] A questionnaire measuring ward culture was filled out by so few [managers] that it was dropped from the protocol [6]
Patients are unwilling to challenge health workers about hand hygiene (DT)	“the idea of resident participation was not accepted by HCWs [healthcare workers] … They did not like to be reminded to perform HH [hand hygiene] by residents. This is probably because Chinese culture does not generally welcome potential for dispute.” [8] “Local cultural and social norms are likely to affect patient participation programmes.” [15]
Flexibility of the HHI is important to enable it to fit with the needs of different groups of staff and setting. (DT)	“Interventions were implemented and assessed under operational conditions in 10 heterogeneous hospitals across Europe and Israel with widely varying infection control practices, staffing, infrastructure and MRSA epidemiology. [21] “The protocol influenced behaviour at the individual level, by enabling healthcare workers to buy-in to the programme and design the components of the intervention. This empowerment may well improve the attitude of individual healthcare workers and their motivation” [26] “This program was expected to perform in different facility types with a variety of personnel” & “Program components designed by corporate clinical leaders were based on best practice pulled from experts at the local level, facilitating adoption into patient safety culture.” [23]

	"Washington and Geneva programmes can improve hand hygiene compliance provided that intermittent reinforcement is continued." [26] "The staff turnover was high … Frequent feedback sessions were necessary to ensure that new staff understood and adhered to hand hygiene practices." [16]
Understanding the context and aligning the intervention with it drives implementation. (AT)	
HHIs need to be embedded into wider patient safety and quality improvement initiatives. (DT)	"Linking small hospitals with larger facilities capable of providing [patient safety] expertise … is a feasible model for future evaluation." [14] "the unification of evidence-based practices may improve program effectiveness." [23] "Engaging residents and fellows through the quality improvement incentive programme was an essential component for success… This prioritization and focused effort helped achieve sustained behavior change, which continued after the incentive was removed" & "Attending physicians from multiple departments were engaged as HH champions for their units" [25]
Healthcare workers need to accept the HHI and be included in initiatives to involve behaviour change. (DT)	"An important advantage of our team and leaders-directed strategy was that the participating ward managers believed that the methodology could also be useful to improve team performance on other patient safety issues." [9] "The main limitation was that the intervention was more difficult to implement than in the exploratory trial … It might increase if the intervention was an integral part of the hospital audit programme, carried out by infection control or ward staff [6]. "62 training visits were made to hospitals. These could be difficult to organise. Representatives from 11 wards, 7 hospitals, never attended training." & "A questionnaire measuring ward culture was filled out by so few nurses that it was dropped from the protocol." [6] "The intervention would have been more successful if the healthcare workers had more time and capacity to implement their own strategies to increase rates of adherence for HH." [12]
HHIs work differently in different clinical settings	"There was a high significant effect of the intervention in ITUs but not on ACE

and with different groups (DT)	[acute care of the elderly] wards" & " The effect was stronger on ITUs, where it was easier to implement and where its effectiveness increased with fidelity to intervention" [6] "differences in hand hygiene compliance may exist between different groups" [10]. "In this context [very acute units already primed to the importance of infection control], hand hygiene becomes an institutional priority for the unit's staff, and it may be this, rather than any specific influence of the hospital executive, which helped provide any institutional support that modified behaviour" & "We have not been able to duplicate the published outcomes of the Geneva intervention except in our IDU, where high compliance with HH already existed." [26]
Need to address specific challenges. (DT)	"Compliance rates differed between specific hand hygiene indications… attention to specific hand hygiene indications… targeted this aspect." [9] "Improved hand hygiene combined with universal chlorhexidine body washing was associated with reduced … reduction of MRSA acquisition." [19] "Implementation of a multifaceted bundle … hand hygiene, disinfection practices and executive involvement was followed by a substantial improvement in MRSA infections." [23] "There was a sustained reduction in [infections] both in the post intervention period and during the follow-up period more than 2 years past program implementation. This suggests that focused attention on MRSA-related infections helped motivate better adherence to infection prevention practices. [23]
Resourcing (DT)	"HCWs [healthcare workers] seemed to be overwhelmed because of staff shortages and work loads." [12] "The frequency of hand hygiene varied dramatically, reflecting day to day changes in staffing and case mix." [26] "The staff may have been too busy to increase hand washing and hand rubbing." [16] "Implementation might increase if the intervention was an integral part of a

	hospital's audit programme, carried out by infection control or ward staff with general responsibilities … with more than one co-ordinator per ward." [6] "This program required a sizeable commitment of resources and executive support" [23] "The infection prevention and control team did not have the resources to increase the frequency of their education sessions." [13] "[one] site started with only one observer who decided to stop collaborating after 2 months due to an outbreak … This situation made it impossible to sustain monthly observation." [25]

Supplementary Table 4: Characteristics of the 21 Included Studies

Characteristics of the studies

The HHIs differed considerably in scope, setting and type [see supplementary data]. Most were undertaken by multidisciplinary teams [6, 8, 18, 17, 9, 10, 11, 12, 14, 15, 16, 20, 22, 23, 24 25] and published in specialist infection prevention journals [8, 11, 12, 14, 15, 16 17 18, 19, 20, 22 24, 26] but some appeared in medical [6, 21], nursing [9], quality improvement [13, 23, 25], health psychology [7, 10] and design journals [17].

Aims and study designs

In 16 publications the primary aim was to determine impact on hand hygiene adherence [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 20, 22, 24, 25]. In one study the primary aim was to feasibility-test the ability of new technology to promote hand hygiene [18]. WHO recommendations were key components of the HHI in 13 studies [8, 9, 11 12, 13, 14 16, 19, 22, 21, 23, 25, 26]. They were cited in the others [6, 7, 15, 18, 20, 22, 24, 25]. A theoretical framework to promote behavioural change was employed by five research teams [6, 7, 9, 10, 12]. In one publication the aim was to explore the potential of a new theory to underpin the HHI [17]. Feasibility studies were reported in five publications [6, 8, 11, 13, 15]. Microbiological outcomes were presented in eight publications, usually MRSA [8, 12, 14, 15, 16, 19, 21, 23].

Monitoring hand hygiene adherence

Uptake of alcohol handrub was the sole audit method in two publications [23, 26]. In one study it was combined with direct observation [6] and in another direct observation was used in conjunction with adenosine triphosphate technology [20]. None of the HHIs employed automated devices to monitor

adherence. In one HHI a video camera was used [18]. In the remaining HHIs direct observation was the sole audit method. Only three research teams assessed adherence in relation to Five Moments [15, 19, 22,] or with a similar tool [12]. In the other publications where direct observation took place, hand hygiene was documented before and after patient contact.

Types of hand hygiene interventions

In three publications the HHI comprised performance feedback [6, 15, 24]. Performance feedback was coupled with video monitoring in another [18]. Cues were employed by three research teams [7, 10, 17]. Diegel-Vacek et al [17] tested the impact of a visual cue [a light switching on at room entry]. Grant and Hoffman [7] evaluated the impact of posters conveying different messages. King et al [10] evaluated the impact of posters [a smiling or stern face] and an olfactory cue [citrus scent]. In one publication the HHI was education [20]. The remaining publications reported multimodal strategies. One reported all WHO components with patient reminders [15]. Five included some but not all components recommended in WHO guidelines [8, 11, 13, 16, 21]. Three included all WHO components [12, 19, 23]. Four HHIs incorporated components also suggested by the WHO but not included in its core components of a HHI [6]: ward leadership [9], financial incentives for doctors [25], creating a multidisciplinary team at senior level with responsibility for implementing the HHI [22] and MRSA surveillance [14]. One publication [26] reported three separate HHIs: one based on the campaign in Geneva [7]; one based on a campaign in Washington [48]; and alcohol handrub with education.

Setting and duration of the intervention

Two HHIs were reported from long-term care facilities [8, 16] and one from primary care [11]. The remainder took place on general wards or critical care units. Eleven HHIs [52%] were implemented in a single centre [7, 10, 14, 15 17,

18, 20, 22, 24, 25, 26]. In two publications the HHI took place in three facilities [9, 12]. One research team introduced the HHI into a large health care system with 166 hospitals and 116 outpatient clinics [23]. Other research teams introduced the HHI in 7 - 18 centres. Hand hygiene was evaluated as part of a wider initiative to prevent infection in three publications [19, 21, 23]. In two studies data were collected from nurses [9, 16]. Huis et al [9] included student nurses. Yeung et al [16] included unqualified healthcare workers. In the remaining publications data were collected from all staff in all clinical areas. Duration of the intervention was less than three months in three cases [7, 10 17], less than a year in six cases [8, 9, 11, 13, 16, 25] and over a year in the others.