An Roinn Sláinte
Department of Health

Infection Prevention and Control (IPC)

National Clinical Guideline No. 30

Annex A: Clinical and cost-effectiveness of healthcare-associated infection interventions: a systematic review

National Patient Safety Office
Oifig Náisiúnta um Shábháilteacht Othar

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

Clinical and cost-effectiveness of healthcare-associated infection interventions: a systematic review

July 2022

About HRB-CICER

In 2016, the Department of Health requested that the Health Research Board (HRB) fund an evidence synthesis service called HRB-CICER (Collaboration in Ireland for Clinical Effectiveness Reviews) to support the activities of the Ministerial appointed National Clinical Effectiveness Committee (NCEC). Following a competitive process, the Health Information and Quality Authority (HIQA) was awarded the contract for the five-year period from 2017 to 2022. The HRB-CICER team comprises a dedicated multidisciplinary research team supported by staff from the Health Technology Assessment (HTA) team in HIQA and the HRB Centre for Primary Care Research at the Royal College of Surgeons in Ireland (RCSI), as well as national and international clinical and methodological experts.

With regard to clinical guidelines, the role of the HRB-CICER team is to independently review evidence and provide scientific support for the development, by guideline development groups, of National Clinical Guidelines for the NCEC. The HRB-CICER team undertakes systematic reviews of the clinical effectiveness and cost-effectiveness of interventions included in the guidelines as well as estimating the budget impact of implementing the guidelines. The HRB-CICER team also works closely with the guideline development groups; provides tailored training sessions; assists in the development of clinical questions and search strategies; performs systematic reviews of international clinical guidelines and supports the assessment of their suitability for adaption to Ireland; and supports the development of evidence-based recommendations informed by the evidence produced by HRB-CICER within the National Clinical Guidelines.

Membership of the evaluation team

Members of the HRB-CICER Evaluation Team were Barrie Tyner, Thomas Plunkett, Michelle O'Neill, Dr Barbara Clyne, Dr Laura Comber, Dr Kieran Walsh, Joan Quigley, Dr Karen Cardwell, Professor Susan M. Smith and Dr Máirín Ryan.

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List of abbreviations that appear in this report

ABHR	Alcohol-based hand rub
ACE	Acute care for the elderly
AMRO	Antimicrobial resistant organisms
B-A	Before-after study
BSI	Blood stream infection
C. difficile	*Clostridioides difficile*
CA$	Canadian dollars
CBA	Cost-benefit analysis
CEA	Cost-effectiveness analysis
C-RCT	Cluster randomised control trial
ED	Emergency department
HAI	Hospital-acquired infection
HCAI	Healthcare-associated infections
HCW	Healthcare worker
HDU	High dependency unit
HH	Hand hygiene
HIQA	Health Information and Quality Authority
HR	Hazard ratio
ICC	Intracluster correlation coefficient
ICER	Incremental cost-effectiveness ratio
ICU	Intensive care unit
IRR	Incidence rate ratio
ITS	Interrupted time series
LTCF	Long-term care facility
MBR	Multi-bed rooms
MDRO	Multi-drug resistant organism
MM	Multimodal
MRSA	Methicillin-resistant *Staphylococcus aureus*
NCEC	National Clinical Effectiveness Committee
nRCT	Non-randomised control trial

OR	Odds ratio
PICOS	Population, intervention, comparator, outcome, study design framework
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life year
RCT	Randomised control trial
RR	Risk ratio (also known as relative risk)
SPR	Single patient room
VRE	Vancomycin-resistant *Enterococcus*
WHO	World Health Organization
WHO Compliant	WHO multimodal strategy including three or more key components
WHO Plus	WHO multimodal strategy including additional components
WTP	Willingness-to-pay

1 Introduction

1.1 Description of the condition

A healthcare-associated infection (HCAI) is any infection that is acquired after contact with healthcare services.[1] It neither present nor incubating at the time of initial contact. HCAI is best described during treatment in a hospital, but can also occur in outpatient clinics, long-term residential care facilities and other healthcare settings. HCAIs that are picked up in hospitals are also known as hospital-acquired infections or nosocomial infections. The prevention and control of HCAI also encompasses the control of acquisition of colonisation with antimicrobial-resistant organisms with the potential to cause serious infection at a later date.

According to a European-wide survey, conducted in May 2017, of HCAI and antimicrobial use in European acute care facilities, that included 60 acute Irish hospitals (46 public and 14 private), the overall prevalence of HCAI in Irish hospitals was estimated to be 6.1% in 2017[2] and 5.2% in the 2012 survey.[3] Overall prevalence of HCAI in 2017 was highest in tertiary hospitals (8.7%) when compared to primary (7.6%), secondary (4.2%), specialist (3.4%) and private hospitals (5.9%).[2] This is likely to be related to the differences in the nature of healthcare services. According to a national survey conducted in 2012 and including 69 long-term care facilities, the estimated prevalence of HCAI in Irish long-term care facilities was 3.7%.[4] Data on the prevalence of HCAI in primary care or outpatient settings in Ireland is unavailable. In 2008 it was estimated the total annual healthcare cost of HCAI in hospitals for the EU 27 was €7 billion per year.[5] The annual healthcare costs associated with HCAI in hospitals in Ireland were estimated in 2011 to be €118 million.[6]

1.2 Description of the intervention

Better control of the transmission of pathogens which can lead to infections is an important part of infection, prevention and control. This requires a broad range of practices that aim to reduce or eliminate the likelihood of the transmission of infection from one person to another, such as directly from a healthcare worker (HCW) to a patient or vice versa, or indirectly by way of a medical device or surface contact. Other measures to prevent HCAI include timing and preparation of procedures, appropriate use of medical devices, appropriate use of antimicrobial agents and attention to nutrition, hydration and overall care

of the person.

A number of standards have been produced to support the prevention and control of HCAI across the Irish healthcare system. These include the 2017 *National Standards for the Prevention and Control of Healthcare-associated Infections in Acute Healthcare Services,*[7] and the 2018 *National Standards for infection prevention and control in community services,*[8] which outline standards specific to community health and social care services, including ambulance services, care delivered in the home, general practices, dental practices, residential services for older people and people with a disability, day care services, and pharmacies.

Two separate interventions for the prevention and control of HCAIs (interventions to improve adherence to hand hygiene recommendations, and the use of all single patient room accommodation in general acute settings) are the focus of this systematic review and are outlined in Section 1.2.1 and Section 1.2.2.

1.2.1 Interventions to improve adherence to hand hygiene recommendations

Hand hygiene (HH) is regarded as one of the most effective means of preventing transmission of organisms in the healthcare setting, as the hands of healthcare workers can be a common source of infection transmission.[9] Hands may become contaminated following contact with intact skin, wounds, mucous membranes or secretions of a patient, and subsequently transmit organisms to other patients they come in contact with. Improving HH removes these contaminants and has been associated with a decrease in the transmission of pathogens.[10]

Interventions aimed at improving HH adherence in healthcare settings fall mainly under the heading of *Implementation Strategies,* as they are designed to change or modify behaviour.[11] The complexity of implementation strategies can vary from single component strategies to five-or-more-component strategies.

One widely used strategy is the World Health Organization (WHO) *Multimodal Hand Hygiene Improvement Strategy (WHO MM),*[12] which consists of five key components:

- **System change** - ensuring necessary infrastructure is available, including access to water, soap and towels and alcohol-based hand rub (ABHR) at the point of care.
- **Education and training** - providing training or educational programmes on the importance

of hand hygiene and the correct procedures for hand rubbing and hand washing for healthcare workers.

- **Evaluation and feedback** - monitoring hand hygiene practices and infrastructure, along with related perceptions and knowledge among healthcare workers, while providing performance and results feedback to staff.

- **Reminders** - prompting or reminding healthcare workers (through printed material, verbal reminders, electronic communications or other methods) about the importance of hand hygiene and appropriate indications and procedures for performing it.

- **Institutional safety climate** - active participation at both institutional and individual levels, creating an environment and perceptions which facilitate awareness-raising about patient safety issues and guarantee the prioritisation of hand hygiene.

The WHO recommend at least three of these components be included in implementation strategies to improve hand hygiene (HH).[13] *My 5 Moments for Hand Hygiene (WHO 5M)* outlines the appropriate situations which require handwashing. The five moments, or indications, of HH are: before touching a patient; before clean or aseptic procedures; after body fluid exposure or risk; after touching a patient; and after touching patient surroundings (see Figure 1). This model is also integrated in various tools included in the WHO MM and is used to train, monitor and report hand hygiene.[14]

The 2015 Irish guideline for hand hygiene in Irish healthcare settings by the Royal College of Physicians of Ireland Clinical Advisory Group recommends that a multimodal hand hygiene improvement strategy, such as that developed by the WHO should be used in all health services.[15] They also recommended hands should be cleaned according the WHO '5 moments of hand hygiene' (Figure 1).

Figure 1 WHO 5 Moments for Hand Hygiene
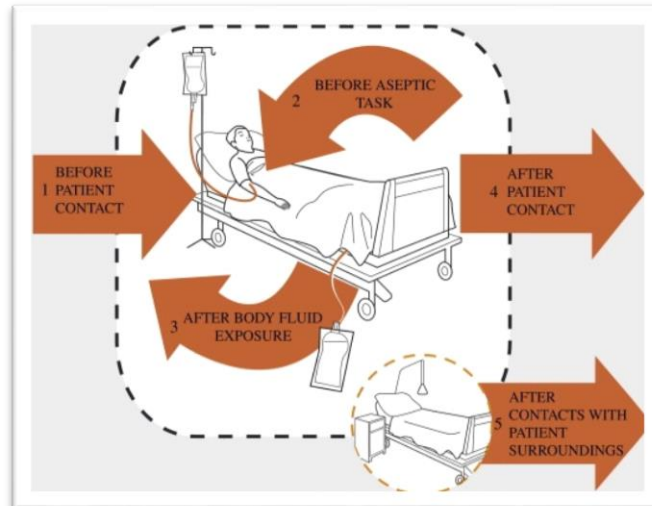
(Reproduced with permission from "WHO Patient Safety 2009, A guide to the implementation of the WHO multimodal hand hygiene improvement strategy, Page 7, Copyright (2009)."[12])

1.2.2 Single patient room accommodation in general acute settings

Single patient room (SPR) accommodation has been suggested as an approach to reducing transmission of HCAIs, based on the principles of isolation and ventilation.[16] By isolating patients in separate rooms (with separate bathrooms), it eliminates the contact between patients who are colonised or infected with infectious organisms and other patients. This reduces opportunities for spreading infectious organisms. With this in mind, the 2008 Infection Prevention and Control Building Guideline for Acute Hospitals in Ireland recommended all newly built hospitals and major renovations should be 100% SPRs with an en suite shower and toilet facility.[17] In 2017 it was estimated that in Irish hospitals, the average proportion of SPRs was 15% in general, 20% in regional, 29% in tertiary-, 23% in specialist- and 52% in private-hospitals.[2] Under construction in 2021, the new national children's hospital at St James's will include 100% SPRs, all with en suite bathrooms.

The systematic review was carried out between 2019 and early 2020. This included agreeing the protocol, conducting searches, assessing the including studies, as well as conducting the analysis and drafting the results section. Due to the COVID-19 pandemic work on the review was paused. In 2022 searches were updated on 13 February and 30 May 2022. Two articles eligible for inclusion were identified from the searches in February, each describing additional analyses of a dataset previously identified in the original search and included in the draft report.[18, 19] The findings of these additional analyses have been included in the discussion.

Figure 2 Median percentage of single patient rooms among the total number of hospital beds, data collected between 2011 and 2012
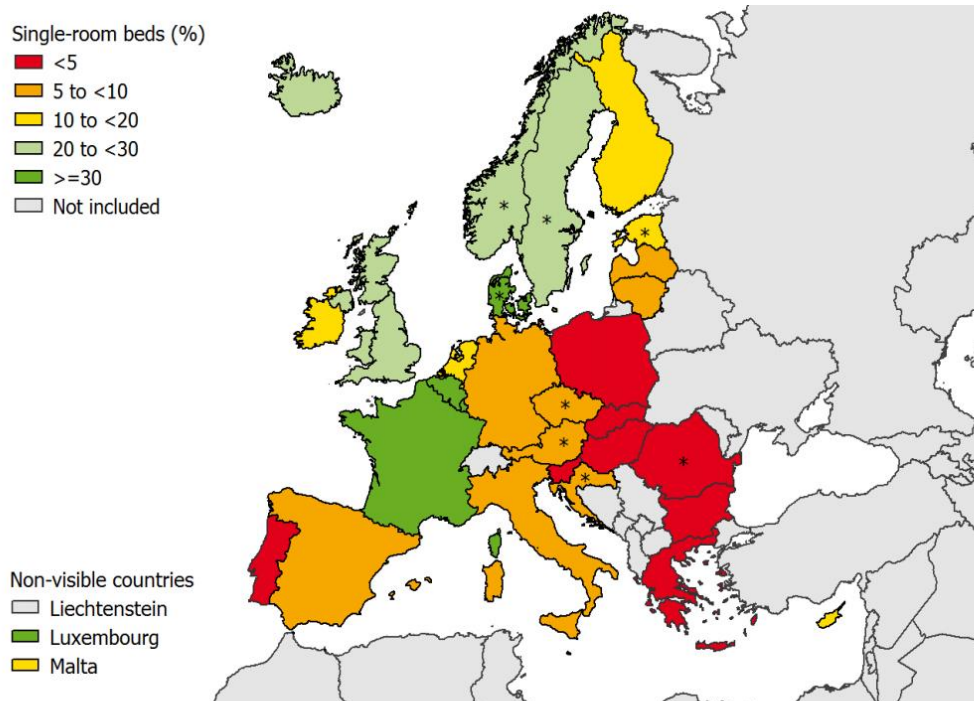
*PPS data representativeness was poor in Austria, Croatia, Czech Republic, Estonia and Romania and very poor in Denmark and Sweden.

(Source of figure: European Centre for Disease Prevention and Control (ECDC). Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012. Stockholm: 2013)

1.3   Purpose of this systematic review

The purpose of this systematic review is to identify and evaluate the clinical and economic evidence relating to the use of interventions to improve hand hygiene and the use of SPRs in the prevention and control of HCAIs, to help inform the recommendations of the NCEC National Clinical Guideline on Healthcare-Associated Infection in Ireland. This systematic review includes two review questions. The first focuses on the effectiveness of strategies to improve adherence to recommendations on hand hygiene. The second focuses on the effectiveness of all single room accommodation at reducing the incidence of HCAI in acute settings. Both review questions aimed to identify and evaluate clinical and cost-effectiveness studies.

2   Methods

The reporting of this systematic review adheres to the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) criteria.[20] The identification and synthesis of economic evidence follows national guidelines for the retrieval and interpretation of economic literature.[21] The proposed methodology for the systematic reviews was outlined in a protocol that was agreed by the Healthcare-Associated Infection (HCAI) Guideline Development Group in July 2019. Each review question was subsequently registered on the PROSPERO database of systematic reviews and meta-analyses.[22]

Link: www.crd.york.ac.uk/prospero

- Review question one: CRD42019142761
- Review question two: CRD42020151883.

2.1   Criteria for considering studies for this review

Review questions were formulated in line with the PICOS (population, intervention, comparator, outcome, study design) framework.[23] These details are provided in Sections 2.1.1 and 2.1.2. Review question one updated the search strategy of the 2017 Cochrane review by Gould et al.[24] with the addition of a new search strategy for economic evidence and a restriction of included study designs to RCTs only (see Table 2.1). Whereas, review question two is a newly developed question.

2.1.1   Review question one- interventions to improve adherence to hand hygiene recommendations

- In relation to healthcare workers in hospitals, nursing homes, long-term care facilities or community healthcare settings, are there specific interventions to promote hand hygiene compared with other interventions to promote hand hygiene that improve hand hygiene adherence among healthcare workers?

The specific objectives were to:

- assess the improvement in hand hygiene adherence in patient care
- determine whether there was a reduction in rates of HCAI
- identify relevant economic evaluations.

Table 2-1 Methods: PICOS for review question one – interventions to improve adherence to hand hygiene recommendations

Population	Included: ■ Healthcare workers (for example, nurses, doctors and other healthcare workers) in any hospital, nursing home, long-term care facility or community healthcare setting, in any country. Excluded: ■ Studies focused on non-healthcare workers (for example, hospital visitors, homecare assistants, catering or cleaning staff).
Intervention	Included: ■ Any intervention intended to improve adherence with hand hygiene using soap and water or alcohol-based products (for example, education, audit with performance feedback, health promotion, or variations in availability and type of products used for hand hygiene). ■ Bundles (multimodal management strategies) as long as the data relating to hand hygiene adherence was presented separately. Excluded: ■ studies based outside clinical settings (for example, simulation or artificial settings) ■ studies looking at surgical hand disinfection in theatre settings and surgical scrubbing.
Comparator	No intervention or another intervention.
Outcome	Primary: ■ Hand hygiene adherence, measured through direct observation (for example use of soap or alcohol-based products, or adherence with hand hygiene measured by an automated monitoring device) or a proxy indicator (for example, increased use of hand hygiene products). Secondary: ■ reduction in HCAI rates (see section 1.1 for definition) ■ reduction in colonisation rates by clinically significant nosocomial pathogens. As per the Cochrane review[24] data on all reported pathogens was included. Any relevant measures of costs and benefits which are applicable to the Irish setting. Excluded: ■ Studies that assessed adherence using self-reported measurements.
Study design	Included: ■ RCTs ■ economic evaluations and systematic reviews (see Section 2.2). Excluded: ■ nRCTs, ITS, before-after studies, cohort studies ■ observational studies.

Search period	For clinical effectiveness studies: 19.10.16 – 08.07.19
	For cost-effectiveness studies 01.07.09 – 08.07.19 (see Table 2-3).

Key: HCAI – healthcare-associated infection; ITS – interrupted time series; nRCT – non randomised control trial; RCT – randomised control trial.

2.1.2 Review question two- effectiveness of single patient rooms in reducing incidence of healthcare-associated infection

■ In acute hospital inpatients, does the use of all single patient room accommodation compared with use of multi-bed rooms or mixed single rooms and multi-bed room accommodation result in reduced incidence of healthcare-associated infection?

The specific objectives are to:

■ evaluate whether single patient room (SPR) accommodation is effective in reducing HCAI rates compared with accommodation consisting of multi-bed rooms or mixed single rooms and multi-bed rooms

■ assess whether the use of SPR accommodation leads to adverse events including physical and or psychological harm compared with accommodation consisting of multi-bed rooms or mixed single rooms and multi-bed rooms

■ evaluate whether SPR accommodation is effective in reducing incidence of colonisation rates by antimicrobial resistant organisms with accommodation consisting of multi-bed rooms or mixed single rooms and multi-bed rooms

■ identify relevant economic evaluations.

Table 2-2 Methods: PICOS for review question two – effectiveness of single patient rooms in reducing HCAI infection rates

Population	Included:
	■ Adult patients based in inpatient wards in acute settings.
	Exclude:
	■ Studies that only included high acuity settings for example ICU, HDU or critical care wards.
Intervention	Included:
	■ SPR accommodation with en suite facilities (for example sink, toilet and shower).

	Excluded: ■ Studies that did not explicitly state the SPRs have en suite facilities ■ Studies that examined the effects of transferring patients who were initially admitted to multi-bed rooms to a SPR after infection or colonization. For example, interventions relating to patients identified as acquiring a HCAI or colonised with an AMRO while in a medical or surgical ward and subsequently transferred to a SPR as part of an infection control measure ■ Studies where it was not possible to identify the effect of SPR alone on the reported outcome(s). For example, bundled interventions that included additional patient decolonization strategies or healthcare worker education programs.
Comparison	■ Multi-bed room accommodation (for example, shared rooms or bays that included patient rooms of two or more) ■ or a mix of multi and SPR accommodation (for example, a ward featuring SPRs and multi-bed rooms).
Outcome(s)	Primary: ■ Reduction in HCAI rates (see section 1.1 for definition) ■ Adverse events (including both physical and psychological harms). Secondary: ■ Reduction in colonisation rates by antimicrobial resistant organisms. Any relevant measures of costs and benefits.
Study design	■ RCTs, nRCTs studies ■ Interrupted time series analysis ■ Controlled and uncontrolled before-after studies ■ Prospective and retrospective cohort studies ■ Health economic studies (see Section 2.2.1).
Search period	For clinical studies 01.07.04 –30.05.22* For cost-effectiveness studies 01.07.09 – 30.05.22 (see Section Table 2-3).*

Key: AMRO – antimicrobial resistant organisms; HCAI – healthcare-associated infection; HDU – high dependency unit; ICU – intensive care unit; nRCT – non randomised control trial; RCT – randomised control trial; SPR – single patient room.

*See section 2.4 for further details on the search dates.

2.1.3   Study design

Review question one included RCTs, nRCTs studies, multi-centre controlled before-and-after studies and ITS studies. However, as per protocol, following the identification of a high number of RCT studies it was decided to restrict the review to RCT studies only.

For review question two, a wide range of study designs were included (Table 2-2) where the

unit of analysis was at ward level or higher. While randomised control trials (RCTs) are considered the gold standard when evaluating causal effects of healthcare interventions, quasi-experimental designs such as interrupted time series (ITS) can provide accurate estimates for health service interventions when conducted appropriately, which is especially relevant when randomisation is not practical.[25] This can be achieved when multiple point estimates are recorded at regular intervals pre- and post-intervention. Data from ITS can be analysed to account for any existing underlying trends, such as ongoing infection prevention and control (IPC) effects or community prevalence. Before-after studies compare only one point estimate pre-intervention with one estimate post-intervention, and so cannot account for underlying trends.

2.2 Health economic studies

2.2.1 Types of studies

This systematic review aimed to identify health economic studies including economic evaluations (cost-effectiveness analyses, cost-utility analyses, cost-minimisation analyses and cost-benefit analyses), costing studies, comparative resource use studies and systematic reviews.

Where sufficient full economic evaluations (cost-effectiveness analyses or cost-utility analyses) were identified, other (lower quality) costing studies were not considered during critical appraisal, data extraction and synthesis of the literature.

Where an existing high-quality systematic review was identified, this was used and updated as appropriate. This reflects a pragmatic approach to support guideline development, consistent with the hierarchy of evidence, wherein duplication of effort is minimised.

2.2.2 Types of outcomes

The following is a non-exhaustive list of economic outcome measures considered applicable to this review.

Economic evaluations

Cost-utility and or cost-effectiveness analysis:

- Incremental cost-effectiveness ratio (ICER).

- Cost per unit of effect (such as cost per life year gained) or effects per unit cost (for example, life years gained per Euro spent).

- Quality-adjusted life years (QALYs), disability-adjusted life years, or health/life years equivalent.

- Incremental net monetary benefit.

Cost-benefit and or cost-minimisation analysis:

- Net monetary benefit

- Incremental costs.

Other economic outcome measures

Costs and resource use:

- direct (for example, cost of staffing and equipment) and indirect (for example, prescription costs) costs, offsets and savings

- length of hospital stay

- implementation costs (for example, training and education)

- service utilisation costs.

2.3 Exclusion criteria

The following exclusion criteria was applied across both review questions:

- children and young people (aged < 16 years)

- editorials/commentaries/opinion pieces

- abstracts only

- animal studies

- non-English language studies.

2.4 Search methods for identification of studies

For review question one, the database searches for clinical effectiveness literature were conducted consistent with the search strategy developed by Gould et al.[24] and focused on studies published between 19 October 2016 and 8 July 2019 (databases listed in Table 2-3).

In addition to database searches, the original review[24] conducted an extensive grey literature search. According to their presented PRISMA flow chart,[24] no studies were identified through these sources. Consequently, for this review, only the grey literature database Opengrey.eu was searched.

For review question two, the searches for clinical evidence were limited to studies published since 2004. This was due to the influential recommendations made in the 2006 guidelines from the Facilities Guidelines Institute and American Institute of Architects Academy of Architecture for Health,[26] informed by a 2004 systematic review, which recommended SPRs. In addition to the databases listed in Table 2-3, the following specific architectural and design publications and organisations were searched:

- Center for Health Design

- Health Environments Research & Design Journal

- American Institute of Architects Academy of Architecture for Health

- Royal Institute of British Architects.

The search for economic evidence for question one and two was conducted in conjunction with the clinical literature search strategies through the addition of an economic filter to each database search string.[27] See Appendix 2 for examples of search strings. A ten year time limit was applied to searches for economic evidence to ensure identified economic literature was applicable to current practice.

For both questions, reference lists of included papers for both reviews were hand searched and forward citations searched via Scopus and Google Scholar to identify additional relevant references.

Table 2-3 Methods: Databases searched by review question

Review question	Databases searched and search dates	
	Clinical effectiveness	Cost-effectiveness
Interventions that improve hand hygiene adherence	Cochrane Central Register of Controlled Trials, MEDLINE (via OVID), Embase, CINAHL (via EBSCO), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform. **Search dates:** 19/10/16 to 08/07/19	Cochrane Central Register of Controlled Trials, MEDLINE (via OVID), Embase, CINAHL (via EBSCO), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, HTA & NHS EED on CRD. **Search dates:** 01/07/09 to 08/07/19

| Single patient rooms in acute settings | Cochrane Central Register of Controlled Trials, MEDLINE (via OVID), Embase, CINAHL (via EBSCO), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, PsycINFO.

Search dates: 01/07/04 to 30/5/2022 | Cochrane Central Register of Controlled Trials, MEDLINE (via OVID), Embase, CINAHL (via EBSCO), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, PsycINFO, HTA & NHS EED on CRD.

Search dates: 01/07/09 to 30/5/2022 |

Key: CINAHL – Cumulative Index to Nursing and Allied Health Literature; CRD – Centre for Reviews and Dissemination – University of York; EBSCO – EBSCO information services; MEDLINE - Medical Literature Analysis and Retrieval System Online; HTA and NHS EED – Health Technology Assessment and National Health Service Economic Evaluation Database; OVID – Ovid Technologies; WHO – World Health Organization.

2.5 Data collection and analysis

2.5.1 Selection of studies

For both questions, potentially eligible papers identified in the search strategy were exported to Endnote (Version X7), where duplicates were identified and removed. Two reviewers independently reviewed the titles and abstracts of the remaining citations, as per the inclusion and exclusion criteria, to determine whether the papers merited a full text review, using Covidence© software. The full texts were obtained and independently evaluated by two members of the team. Any disagreements were resolved by discussion, or when necessary, a third reviewer. Study flow diagrams mapping out the number of records identified, included and excluded in the reviews were maintained.

2.5.2 Data extraction and management

For research question one, data extraction for studies included in the previous review[24] was performed by one reviewer and checked by a second reviewer against the reported data in the previous review. For all newly identified studies, data extraction was performed independently by two reviewers. For both approaches, disagreements were resolved through discussion.

For research question two, data extraction was performed independently by two reviewers, with disagreements resolved through discussion and where necessary a third reviewer.

2.5.3 Assessment of quality (risk of bias) of included studies

Two reviewers independently assessed the methodological quality or risk of bias of included studies, using standardised critical appraisal instruments, with any disagreements resolved through discussion. As different study designs warrant different tools to assess

methodological quality and risk of bias, a number of critical appraisal instruments were used, as appropriate (see Table 2-4).

Table 2-4 Methods: Critical appraisal instruments

Study design	Critical appraisal instrument
RCTs, nRCTs, controlled before-after studies, ITS studies	Cochrane EPOC risk of bias criteria[28]
Cohort studies, uncontrolled before-after studies	Newcastle-Ottawa Scale[29]
Economic evaluations	CHEC-list[30] ISPOR questionnaire – to assess transferability.[31]

Key: CASP – Critical Appraisal Skills Programme; CHEC-list – The Consensus Health Economic Criteria list; EPOC – Effective Practice and Organisation of Care; ISPOR – International Society for Pharmacoeconomics and Outcomes Research; ITS – Interrupted time series; nRCT – non- randomised control trial; RCT – randomised control trial.

2.5.4 Data synthesis

For both review questions, the HIQA *Guidelines for Evaluating the Clinical Effectiveness of Health Technologies in Ireland* were adhered to with regard to data synthesis.[32]

In accordance with national HIQA guidelines,[21] the costs from identified economic evaluations were adjusted and presented in 2018 Irish euro in parentheses alongside the original figures.[33] Cost calculations were undertaken by one reviewer and checked by a second reviewer. Where the cost year was either not clearly reported or was inconsistent in the original publication, the unit cost year was based on the average time difference between publication year and cost year reported in the other relevant studies included within the review.

2.5.4.1 Data synthesis for review question one: interventions to improve adherence to hand hygiene recommendations

Where not reported, risk ratios (RR) and the associated variance in the intervention and control group, were calculated from reported odds ratios (OR) or the number of performed HH opportunities and the total number of observed HH opportunities. Following Cochrane guidance (section 10.3),[34] the generic inverse variance method with a random effects model was used to calculate pooled effect estimates, assess heterogeneity and produce forest plots. A random effects model, which allows for between-study variation when study populations vary considerably, was chosen due to observed heterogeneity between studies. Where a cluster randomised control trial (C-RCT) was not appropriately analysed and reported, an effective sample size (that is, a reduced sample size which takes into account clustering) was

calculated using reported intracluster correlation coefficients (ICC) as follows:

$$\text{Design effect} = 1 + (M - 1) \times ICC$$

Where M is the mean cluster size. Where an ICC was not reported, the average of the reported ICCs from the C-RCTs included in this review was used.[35] For the two C-RCTs that adopted a stepped wedge design, the reported adjusted OR[36] and the adjusted HH adherence rate,[37] which took into account the cluster and temporal effects, was used.

Three of the studies[38-40] compared more than one intervention with a control group. As per the Cochrane guidance,[41] these interventions were assessed for similarities. Where appropriate, similar interventions were pooled,[38] where the interventions were not similar,[39, 40] the control group was split evenly between the intervention groups. Meta-analysis was conducted in Cochrane Review Manager (RevMan; version 5.3).

For the economic literature review, the evidence was compiled and condensed using a narrative synthesis supported by evidence tables. The HIQA guidelines on retrieval and interpretation of economic evaluations of health technologies were adhered to.[42]

2.5.4.2   *Data synthesis for review question two: effectiveness of single patient rooms in reducing healthcare-associated infection*

A meta-analysis was not possible due to differences in how outcomes were measured (heterogeneity). A narrative synthesis, which takes methodological differences between primary studies into account, was completed and an overall picture of the evidence is presented. For the economic literature review, the evidence was compiled and condensed using a narrative synthesis as per question one.

2.6   Assessing the certainty of the body of evidence using the GRADE approach

The certainty of the clinical effectiveness evidence for each primary outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as outlined in the GRADE handbook.[43] Evidence was downgraded by one level for serious (or by two levels for very serious) limitations, depending on the assessments of the risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential publication bias. Where applicable, evidence was upgraded depending on the

assessment of the magnitude of an effect, dose-response gradient and effect of plausible residual confounding. Evidence was graded as high, moderate, low or very low, indicating the confidence in the effect.

3 Review question one: Interventions to improve adherence to hand hygiene recommendations among healthcare workers

The aim of this chapter is to summarise the available evidence on the clinical and cost-effectiveness of interventions to improve adherence to hand hygiene (HH) recommendations. The following research question was addressed:

- In relation to healthcare workers in hospitals, nursing homes, long-term care facilities or community healthcare settings, are there specific interventions to promote hand hygiene compared with other interventions to promote hand hygiene that improve hand hygiene adherence among healthcare workers?

3.1 Search results

The search strategy identified 2,729 potentially relevant records. After removing duplicates, 2,487 records were screened, with 2,288 references excluded based on titles and abstracts. A total of 225 full-text articles were assessed for eligibility, including 26 studies[36, 38, 40, 44-66] from the previous Cochrane review.[24] Of these, 184 articles were excluded according to the inclusion and exclusion criteria, as outlined in Section 2.1.1. A list of excluded studies is available in Appendix 3.

Of the remaining 41 manuscripts, two analysed the same dataset and were considered to be one study.[67, 68] This resulted in 40 unique eligible studies. As per protocol, following the identification of a large number of eligible RCTs of clinical effectiveness (n=17) and cost-effectiveness (n=7), the analysis was restricted to RCTs, as observational studies provide weaker evidence due to the greater risk of bias inherent in these study designs (see Appendix 1: Deviations from protocol). As a result, 16 studies (13 interrupted time series (ITS) analyses and three non-RCTs) were excluded (listed in Appendix 3: Excluded studies). Thus a total of 24 studies were included: 12 from the previous Cochrane review[36, 38, 40, 47-49, 51, 52, 55, 56, 62, 66] and 12 newly identified studies.[37, 39, 67-77]

The PRISMA flow chart outlining this process is depicted in Figure 3.

Figure 3 Review question one: PRISMA flowchart - Interventions to improve adherence to hand hygiene recommendations

Identification

Records included in previous version of the review (*searches up to 18 October 2017*)
n=26

Records identified through database searching (19 October 2017 to 8 July 2019)
n=2,729

Records identified through searching reference lists
n=0

Duplicates removed
n=242

Screening

Records screened
n=2,487

Records excluded
n=2,288

Eligibility

Full-text articles assessed for eligibility
n=225

Excluded articles (n=184):
- Conference abstract (n=71)
- Irrelevant comparator (n=2)
- Irrelevant intervention (n=7)
- Irrelevant outcome (n=6)
- Irrelevant population (n=7)
- Irrelevant setting (n=3)
- Irrelevant study design (n=76)
- Non-English publication (n=5)
- Protocol (n=2)
- Study ongoing or not yet published (n=3)
- Trial Registration (n=2)

Included

Eligible articles n=41*
Unique studies n=40*

Excluded n=16
- ITS (n=13)
- nRCTs (n=3)

Clinical studies included n=17*
- Original review (n=12)
- Newly identified (n=5*)

Economic studies included n=7*
- Original review (n=0)
- Newly identified (n=7)

* von Lengerke et al. (2017)[58] and von Lengerke et al. (2019)[59] analysed the same dataset and was considered to be one study

3.2 Clinical evidence for review question one: Results

3.2.1 Characteristics of included studies

3.2.1.1 Study country

Of the 17 clinical effectiveness studies eligible for inclusion, three were conducted in the US,[49, 62, 70] two in Hong Kong,[38, 66] and one each in Argentina,[36] Canada,[56] China,[51] England,[69] England and Wales,[48] Germany,[67, 68] Indonesia,[39] the Netherlands,[52] Singapore,[47] Spain,[55] and Switzerland.[40] One study was conducted across 11 European countries, including two study sites in Ireland.[37]

3.2.1.2 Study design

All 17 included studies were RCTs. There were two single centre RCTs[51, 70] one multicentre RCT,[47] and 14 cluster-randomised control trials (C-RCTs),[36-40, 48, 49, 52, 55, 56, 62, 66-69] of which 9 were multicentre [36-38, 48, 52, 55, 56, 62, 66] and five were single centre.[39, 40, 49, 67-69] Three of the included C-RCTs were stepped wedge design,[36, 37, 48] one was pair-matched (where randomisation was preceded by pair-matching to ensure the clusters were comparable)[49] and another used a crossover design.[69] Three studies were reported to be pilot studies.[39, 62, 70]

Overall trial duration of the included studies varied from two weeks[69, 70] to 63 months.[40] Post-implementation periods, varied from six months or less in nine studies,[38, 39, 47, 49, 51, 55, 62, 69, 70] six to 12 months in three studies,[36, 56, 66] and longer than 12 months in five studies (see Table 3-2).[37, 40, 48, 52, 67, 68]

Sixteen studies employed direct observation as their primary method of observing HH adherence,[36-40, 48, 49, 51, 52, 55, 56, 62, 66-70] while the remaining study, by Fisher et al.,[47] used an electronic monitoring system. Observation periods and time of day varied in all of the studies employing direct observation.

3.2.1.3 Setting

Fourteen of the included studies were set in hospitals,[36, 37, 39, 40, 47-49, 51, 52, 56, 62, 67-70] two in long-term care facilities for the elderly[38, 66] and one in primary healthcare centres.[55] The number of wards included ranged from 3[47] to 67.[40, 52] While the types of wards included intensive care units (ICUs) only,[36, 37] medical and surgical wards,[69] ICUs and acute care of

the elderly wards,[48] ICUs and hematopoietic stem cell transplantation units,[67, 68] a selection of wards,[39, 40, 47, 49, 52, 56] or all wards.[51, 62] One study recruited four internal medicine physician teams from a single hospital with no details reported on ward types.[70] Studies focusing on long-term care facilities included all areas,[38, 66] as did the study set in primary care centres.[55]

3.2.1.4 Study population

Fifteen studies included multiple professions of healthcare workers (HCWs),[36-40, 47-49, 55, 56, 62, 66-70] while two studies included nurses only.[51, 52] A wide variety of HCWs were represented, with the 14 studies based in a hospital setting including: doctors (n=9),[36, 37, 39, 40, 47, 49, 62, 67, 68, 70] nurses (n=9),[36, 37, 39, 40, 47, 49, 51, 52, 56, 62, 67, 68] certified nursing assistants (n=1),[62] medical students (n=2),[39, 70] nursing students (n=2),[39, 40] physical therapists (n=1),[62] respiratory therapists (n=2),[36, 62] healthcare assistants (n=1),[56] pharmacists (n=2),[36, 49] technicians (such as radiology or laboratory) (n=3),[36, 49, 62] environmental services (n=1),[62] allied health workers (with no further description) (n=2),[47, 56] others (n=3),[37, 40, 62] or simply HCWs (with no details provided) (n=2).[48, 69] One study also included nutritionists, social workers and transporters.[49]

In the two studies set in long-term care facilities for the elderly, the first study listed doctors, registered or enrolled nurses, physical therapists, occupational therapists and healthcare assistants.[38] While the second listed nurses and nursing assistants, and physiotherapists.[66] In the study set in primary care centres, general practitioners, nurses, paediatricians, auxiliary nurses, midwives, dentists and dental hygienists were reported to be included.[55]

3.2.1.5 Interventions aimed at improving hand hygiene adherence to recommendations

Hand Hygiene guidelines

Twelve studies[36-40, 47, 48, 52, 55, 66-69] referred to the WHO guidelines on HH in healthcare.[78] Of the remaining five studies, two [56, 62] referred to guidelines authored by Boyce et al.,[79] one[51] reported the use of guidelines from the Centers for Disease Control and Prevention (CDC)[80-82] and two studies[49, 70] did not reference any guidelines.

Description of interventions identified in the included studies.

Within the 17 included studies, 25 interventions aimed at improving HH adherence were

implemented. Eleven studies considered one intervention,[36, 37, 47, 48, 51, 55, 56, 62, 66, 69, 70] four studies[38, 49, 52, 67, 68] assessed two interventions and two studies[39, 40] assessed three interventions.

Seventeen of the 25 interventions were multiple component interventions (multimodal strategies) and eight were single component interventions (unimodal strategies).

Multimodal strategies

Eight of the 12 studies[36-38, 40, 52, 55, 56, 67, 68] that assessed multimodal strategies cited the WHO multimodal HH improvement strategy.[12] This strategy outlines an evidence-based framework consisting of five key components and recommends that interventions should include at least three of the five key components.[13] It is also recommended that these components be tailored to the specific requirements of the local settings,[12] and consequently can include distinct elements. Four of the included studies[48, 52, 56, 67, 68] tailored the components based on behavioural change theories. One of which[67, 68] used a framework known as the Health Action Process Approach (HAPA)[83] to facilitate the tailoring of their interventions to each type of HCW. This led to the application of 28 different behaviour change techniques for improving adherence.

Three additional components, distinct from the five key components of the WHO multimodal HH improvement strategy,[12] were identified within the included studies. These were incentives, accountability and patient involvement. The eight components and their various elements were:

- **System change (n=12):**
    - ABHR available at point of care or at the entry to patient areas (n=7)
    - supplied pocket-size ABHR bottles to HCWs (n=3)
    - ensured adequate sinks were available (n=1)[56]
    - piloted an end-of-bed table (which incorporated a writing surface, patient charts, alcohol-based hand rub, aprons, gloves, medications locker, and waste bin) (n=1)[69]
    - installed a wireless monitoring system (n=1)[47]
    - introduced gloves (lightly powdered gloves compared with powderless) (n=1).[38]

- **Education and Training (n=13):**
  - videos (n=5)[38, 55, 62, 67, 68, 70]
  - interactive demonstrations (n=5)[38, 40, 51, 55, 62]
  - small group tutorials and workshops (n=4)[37, 51, 67, 68, 70]
  - providing seminars (n=3)[38, 51, 56]
  - online material (n=3)[40, 52, 67, 68]
  - printed material (n=2)[36, 52]
  - active presentations (n=1)[39]
  - role modelling (n=1).[39]

- **Evaluation and feedback (n=11):**
  - group or unit level feedback (n=6)[36, 37, 40, 48, 52, 56]
  - individual level feedback (n=5)[37, 38, 47, 48, 62]
  - comparison between units (n=3).[36, 52, 56]

- **Reminders (n=12):**
  - posters (n=11)[36-38, 40, 49, 52, 55, 56, 62, 66-68]
  - a wireless monitoring system including real-time audible reminders (n=1).[47]

- **Institutional safety climate (n=8):**
  - support from administrative and executive bodies (n=5)[36, 37, 40, 62, 67, 68]
  - collaborative design input from HCWs and or unit managers (n=4)[52, 56, 62, 67, 68]
  - inclusion of HH adherence rates as a quality indicator (n=2)[40, 67, 68]
  - performing executive 'walk-rounds' (n=1).[36]

- **Incentives (n=2):**
  - recognition and rewards programme (n=1)[62]
  - praise and certificates for excellent HH adherence (n=1).[48]

- **Accountability (n=2):**
  - encouraged nurses to address each other's undesirable HH behaviour (n=1)[52]
  - formulated action plans, for those with poor HH adherence, to improve behaviour (n=1).[48]

- **Patient involvement (n=1):**
  - patients supplied with welcome packs (brochure on the importance of HH and a pocket-sized bottle of ABHR) and encouraged to remind HCWs to wash their

hands before touching them, if they had not already visibly done so.[40]

There were 13 interventions that conformed to the WHO recommendations (referred to as WHO Compliant strategies)[36-38, 40, 47, 52, 55, 56, 66-68] and three interventions which were WHO Compliant plus additional components (referred to as WHO Plus strategies).[40, 52, 62] For nine studies[36-38, 47, 48, 55, 56, 62, 66] the comparator was usual care and for three studies[40, 52, 67, 68] it was an alternative WHO Compliant strategy (See Table 3-1).

Unimodal strategies

Five studies examined the effectiveness of seven unimodal strategies.[39, 49, 51, 69, 70] For four studies the comparator was usual care, with one study[69] conducting a pilot study that introduced a system change and three[39, 51, 70] considering educational strategies. One study, by Grant et el.,[49] compared two unimodal strategies based on reminders (Table 3-1).

Table 3-1 Clinical evidence for question one: Included Hand Hygiene intervention components and comparator by study

Author (year)	Key components of the WHO MM strategy					Incentives	Accountability	Involvement of patients	Comparator
	System change	Education & training	Evaluation & feedback	Reminders	Institutional safety climate				
WHO Compliant (3 or more components)									
Fisher (2013)[47]	✓		✓	✓					Usual care
Ho (2012)[38]	✓	✓	✓	✓					Usual care
	✓	✓	✓	✓					Usual care
Martín-Madrazo (2012)[55]	✓	✓		✓					Usual care
Mertz (2010)[56]	✓	✓	✓	✓	✓				Usual care
Rodriguez (2015)[36]	✓	✓	✓	✓	✓				Usual care
Stewardson (2016)[40]	✓	✓	✓	✓	✓				Compared three strategies (see WHO Plus)
Stewardson (2016)[40]	✓	✓	✓	✓	✓				
van der Kooi (2018)[37]	✓	✓	✓	✓	✓				Usual care
Von Lengerke (2017)[67, 68]	✓	✓	✓	✓	✓				Compared two strategies
Von Lengerke (2017)[67, 68]	✓	✓	✓	✓	✓				
Yeung (2011)[66]	✓	✓		✓					Usual care
WHO Plus (5 key components plus additional components)									
Huis (2013)[52]	✓	✓	✓	✓	✓		✓		Compared two strategies
Huis (2013)[52]	✓	✓	✓	✓	✓				
Stevenson (2014)[62]	✓	✓	✓	✓	✓	✓			Usual care
Stewardson (2016)[40]	✓	✓	✓	✓	✓			✓	Compared three strategies (see WHO Compliant)
Multimodal (not WHO Compliant)									
Fuller (2012)[48]			✓			✓	✓		Usual care
Unimodal									
Anderson (2016)[69]	✓								Usual care
Gilmartin (2018)[70]		✓							Usual care
Grant (2011)[49]				✓					Compared two strategies
Grant (2011)[49]				✓					
Huang (2002)[51]		✓							Usual care
Santosaningsih (2019)[39]		✓							Usual care
		✓							Usual care
		✓							Usual care

Key: WHO – World Health Organization

Table 3-2 Clinical evidence for question one: Characteristics of included studies - interventions to improve adherence to hand hygiene recommendations

Author (year) Country Study design	Study period and duration	Setting	Participants (n) and type of wards	Number of observations and method used	Indication for HH	Outcome(s)
Anderson (2016)[69] England crossover C-RCT	2 weeks (2011 to 2012) Intervention: 1 week Control: 1 week	Single centre teaching hospital	HCWs (NR) from 9 acute adult medical and surgical wards at a NHS Trust in London.	996 observations (intervention=412, control=584) Directly by researcher	WHO 5M	▪ HH adherence
Fisher (2013)[47] Singapore RCT	24 weeks (2012s) Phase 1 (baseline): 14 weeks Phase 2: 6 weeks Phase 3: 4 weeks	Multicentre 2 hospitals (1 teaching, 1 general)	HCWs (221) from 3 wards (cardiology, orthopaedic and surgical ICU), including doctors, nurses and allied health staff.	1,017,600 observations (No further details reported) Electronic monitoring system	Entry or exit to patient zone	▪ HH adherence
Fuller (2012)[48] England and Wales stepped-wedge C-RCT	38 months (Oct 2006 to Dec 2009) Different units were added to the intervention at different periods	Multicentre 16 hospitals	HCWs (NR) in 60 wards; 33 wards in intervention arm (11 ICUs and 22 acute care of the elderly wards).	Number of observations not reported. Covertly and directly by ward coordinators	Before and afterpatient contact	▪ HH adherence
Gilmartin (2018)[70] US pilot RCT	2 weeks (Feb to Mar 2016) Baseline: 5 days (excluding weekends) Post intervention: 5 days (excluding weekends)	Single centre teaching hospital	4 physician teaching teams (2 in the intervention group and 2 in the control group) These included physicians (4), residents (4), interns (10) and medical students (14).	1,299 observations (intervention=625, control=674) Covertly and directly by trained researchers and students	Entry and exit of patient room	▪ HH adherence
Grant (2011)[49] US pair-matched C-RCT	4 weeks Baseline: 2 weeks Post intervention: 2 weeks	Single centre hospital	HCWs (NR) from 8 units (paediatric and neonatal ICUs, cardiac and neurological ICUs, cardiology and chest-pain units and general observation and medical teaching units) including nurses, physicians and ancillary staff (technicians, nutritionists, social workers, pharmacists and transporters) (intervention 4 units, control 4 units).	567 observations (intervention=189, control=378) Covertly and directly by independent infection prevention control staff	Before or after patient contact	▪ HH adherence

Author (year) Country Study design	Study period and duration	Setting	Participants (n) and type of wards	Number of observations and method used	Indication for HH	Outcome(s)
Ho (2012)[38] Hong Kong C-RCT	9 months (Nov 2009 to Jul 2010) Baseline: NR Intervention: NR Post intervention: 4 months	Multicentre 18 long-term care facilities for the elderly	HCWs (810) including doctors, registered/enrolled nurses, physical therapists, occupational therapists and healthcare assistants (intervention 2= 6 facilities, control =6 facilities).	11,669 observations (intervention 1 = 3,478, intervention 2 = 3,619, control = 4,572) Directly by trained infection control nurses	WHO 5M	▪ HH adherence ▪ Respiratory infection outbreaks ▪ MRSA infection requiring hospitalisation
Huang (2002)[51] China RCT	4 months (Sept 2000 to Jan 2001) Intervention: baseline Post intervention: 4 months	Single centre general teaching hospital	Nurses (100) randomly selected from all hospital departments.	Each nurse observed once at baseline and at 4 months post intervention Directly by researchers	Before and after patient contact	▪ HH adherence
Huis (2013)[52] The Netherlands C-RCT	14 months (Sept 2008 to Nov 2009) Baseline: NR Intervention: 6 months Post intervention: 6 months	Multicentre 3 hospitals (1 teaching, 2 general)	Nurses (2,733) from 67 wards (intervention=30 wards, control=37 wards).	10,786 observation (intervention=4787, control=5,999) Directly by trained nursing students	WHO 5M and after use of gloves	▪ HH adherence
Martín-Madrazo (2012)[55] Spain C-RCT	12 months (Jan to Dec 2009) Baseline: 3 months Post intervention: 6 months	Multicentre 11 primary healthcare centres	HCWs (170) including general practitioners, nurses, paediatricians, auxiliary nurses, midwives, dentists and dental hygienists (intervention = 5 centres, control = 6 centres).	2,077 (intervention=1,115, control=962) Directly by trained independent staff	WHO 5M	▪ HH adherence
Mertz (2010)[56] Canada C-RCT	15 months (Oct 2006 to May 2008) Baseline: 3 months Intervention: 12 months	Multicentre 3 acute care hospitals	HCW (NR) from 30 wards (9 intensive care, 5 general medical, 3 oncologic and or hematologic, 3 cardiac and or vascular, 3 orthopaedic, 2 rehabilitation, 2 general surgery, 1 neurologic, 1	15,427 observations (intervention=7,901, control=7,526) Directly by trained	WHO 5M and after use of gloves	▪ HH adherence ▪ MRSA colonisati

Author (year) Country Study design	Study period and duration	Setting	Participants (n) and type of wards	Number of observations and method used	Indication for HH	Outcome(s)
			surgery and or trauma and 1 spinal injury unit) including nurses, healthcare assistants and allied health workers (intervention=15 wards, control=15 wards).	research assistants		on
Rodriguez (2015)[36] Argentina stepped-wedge C-RCT	9 months (Aug 2011 to May 2012) Baseline: 11 clusters range (1 to 4 months) Intervention: 11 clusters range (4 to 8 months)	Multicentre 11 general hospitals	HCWs (705) from 11 ICUs including nurses, physicians, respiratory therapists, pharmacists, residents and radiology technicians.	10,429 observations (intervention=6,864, control=3,565) Directly by trained observer	WHO 5M	▪ HH adherence
Santosaningsih (2017)[39] Indonesia pilot C-RCT	24 weeks (May to Oct 2014) Baseline: 8 weeks Intervention: 8 weeks Post intervention: 8 weeks	Single centre teaching hospital	HCWs (NR) including doctors, nurses and students (medical and nursing) from 4 departments (internal medicine, surgery, obstetrics-gynaecology and paediatrics) (1 department in each intervention and control arm).	2,766 observations (intervention 1=733, intervention 2=577, intervention 3=763, control=693) Directly by trained infection prevention control-linked nurses	WHO 5M	▪ HH adherence
Stevenson (2014)[62] US C-RCT feasibility study	9 months (Mar 2003 to Feb 2004) Baseline: 4 months Intervention: 5 months	Multicentre 10 rural hospitals	HCWs (NR) from all wards including doctors, nurses, nurse assistants, respiratory therapists, physical therapists, radiation technicians, lab technicians, environmental services and others (intervention=5 hospitals, control=5 hospitals).	4,527 observations (intervention=2,654, control=1,873) Directly by trained personnel	Before or after patient/ environment al contact	▪ HH adherence
Stewardson (2016)[40] Switzerland C-RCT	63 months (April 2009 to Dec 2014) Baseline: 15 months Intervention: 24 months Post intervention: 24 months	Single centre teaching hospital	HCWs from 67 wards, including nurses, doctors, nursing students and others (intervention 1=24, intervention 2=22, control=21).	12,579 observations (intervention 1=4,549, intervention 2=4,361, control=3,669) Directly by infection prevention control nurses usually assigned to that ward	WHO 5M	▪ HH adherence ▪ HCAI infection ▪ Primary bloodstre am infection

Author (year) Country Study design	Study period and duration	Setting	Participants (n) and type of wards	Number of observations and method used	Indication for HH	Outcome(s)
						▪ MRSA colonisation
van der Kooi (2018)[37] 11 European countries (including 2 sites in Ireland – Galway University and St Vincent's University Hospitals*) stepped-wedge C-RCT	30 months (Jan 2011 to Jun 2013) Baseline: 4 clusters range (6 to 15 months) Intervention: 4 clusters range(15 to 24 months)	Multicentre 4 hospitals	HCWs (NR) including nurse, doctors, auxiliaries and other healthcare professionals from adult ICUs.	16,008 ** observations Direct by trained nurses	WHO 5M	▪ HH adherence
Von Lengerke (2017, 2019)[67, 68] Germany C-RCT	Jun 2013 to Feb 2015 Baseline: 6 months, 2013 Observation: 24 months, 2014 to 2015	Single centre teaching hospital	HCWs (1,087 at the beginning of the study, NR for the remaining study period) including doctors (515) and nurs-es (572) from 10 ICUs and 2 hematopoietic stem cell transplantation units (intervention=6 wards, control=6 wards).	8,552 observations Direct by internally trained observers	WHO 5M	▪ HH adherence ▪ MDRO infection
Yeung (2011)[66] Hong Kong C-RCT	10.5 months (Jan to Oct 2007) Baseline: 3 months Intervention: 2 weeks Post intervention: 7 months	Multicentre 6 long-term care facilities for the elderly	HCWs (180) including nurses (26), and nursing assistants (150) and physiotherapists (4) (intervention=3 facilities, control=3 facilities).	3,300 observations Directly by trained independent nurses	WHO 5M	▪ HH adherence ▪ Infection requiring hospitalisation ▪ Outbreaks of influenza and norovirus infections

Key: ABHR – alcohol-base hand rub; C-RCT – cluster randomised control trial; HCAI – healthcare-associated infection; HCW – healthcare worker; HH – hand hygiene; ICU – intensive care unit; MDRO – multidrug resistant organisms; MRSA - methicillin resistant *Staphylococcus aureus*; NR – not reported; RCT – randomised control trial; WHO 5M – World Health Organization Five Moments of Hand Washing;

*The study included three arms, however only one arm was considered relevant to review, as the number of countries in the relevant arm was not reported, this figure represents all three arms. The study duration, setting and number of observations reflects only the relevant arm.
**Data provided by study authors

3.2.2 Clinical evidence: Primary outcome – hand hygiene adherence

All included studies (n=17) reported HH adherence (see Appendix 4 for all results). Eleven studies[36-40, 52, 55, 56, 66-69] used the WHO 5M[78] as the indication of when to perform HH, with two of these studies also including the indication of 'after the use of gloves'.[52, 56] Of the remaining six studies; three measured adherence before and after patient contact,[48, 49, 51] with one of these studies also including the indication of after contact with the patient's environment;[48] two studies focused on entry and exit of patient rooms or zones;[47, 70] while the remaining study reported "complete" adherence as performing HH before *and* after patient or environmental contact, and "any" adherence as HH before *or* after patient or environmental contact.[62]

A graphical display of 12[36-40, 49, 52, 56, 66-69] of the 17 studies, where HH adherence could be expressed as a risk ratio between the study comparators, is presented in Figure 4.

Figure 4 Clinical evidence for review question one: Risk ratios for interventions to improve adherence to hand hygiene recommendations by study.
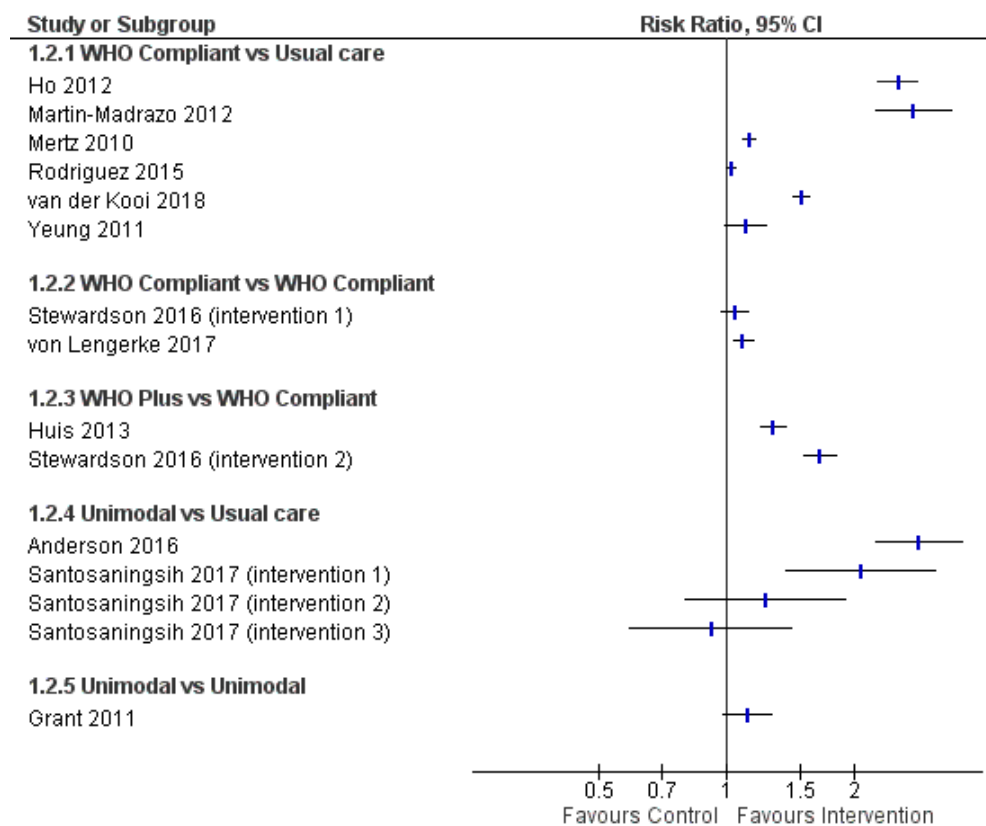
Key: CI – confidence interval

3.2.2.1   Clinical evidence profile – primary outcome: WHO Compliant

WHO Compliant compared with usual care

Seven studies[36-38, 47, 55, 56, 66] implemented eight WHO Compliant strategies and assessed the effectiveness compared with usual care. For one study, the control group included a 2-hour general health talk with a small focus on HH, however, this was still considered to be usual care.[38] Six out of the seven studies reported sufficient data to be included in a meta-analysis.[36-38, 55, 56, 66] Overall, a statistically significant improvement in HH adherence was demonstrated following WHO Compliant strategies compared with usual care in the pooled analysis (RR 1.44, 95% CI: 1.12 to 1.85; p=0.004). However, it must be noted that there was a considerable level of heterogeneity (I^2=98%) among the included studies and thus the pooled estimate must be interpreted with caution. Possible explanations for this heterogeneity include the variation in baseline HH adherence rates (ranging from 8%[55] to 66%[36]), risk of bias concerns relating to contamination in three studies[36, 56, 66] (where the control group adopted some or all elements of the intervention see Section 3.2.4) and variation in the strategies (such as the number and types of components implemented).

Figure 5 Clinical evidence for review question one: Results of meta-analysis for WHO Compliant strategies versus usual care

Study or Subgroup	Weight	Risk Ratio IV, Random, 95% CI
Ho 2012	16.4%	2.55 [1.87, 3.46]
Martin-Madrazo 2012	7.5%	2.96 [1.42, 6.16]
Mertz 2010	20.2%	1.13 [0.96, 1.32]
Rodriguez 2015	21.9%	1.03 [1.00, 1.06]
van der Kooi 2018	21.8%	1.50 [1.44, 1.57]
Yeung 2011	12.2%	1.11 [0.69, 1.78]
Total (95% CI)	**100.0%**	**1.44 [1.12, 1.85]**

Heterogeneity: Tau² = 0.07; Chi² = 234.75, df = 5 (P < 0.00001); I² = 98%
Test for overall effect: Z = 2.89 (P = 0.004)
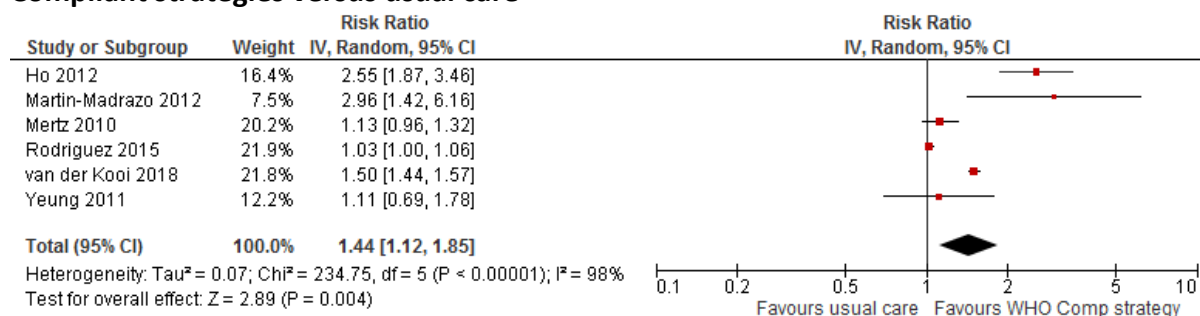
Key: CI – confidence interval; IV – inverse variance; Random - random effects model

Subgroup analysis, was conducted to explore these characteristics further (See Appendix 5). An association with the risk of contamination bias was evident with studies at low risk of contamination bias (n=3) showing a higher estimated pooled RR 2.10 (95% CI: 1.31 to 3.34; p=0.002, I^2=86%) compared to those at unclear or high risk of contamination bias (n=3), where there was little improvement seen in the WHO compliant compared with usual care RR 1.03 (95% CI: 1.00 to 1.06; p=0.04, I^2=0%). A visual inspection was conducted looking at the differences in baseline adherence levels between control and intervention, and number of components included in each strategy, with no trends evident.

The study[47] not included in the meta-analysis performed an adjusted analysis taking into account ward, HCW type and level of HH opportunities (stratified as high, medium and low). The authors reported a statistically significant improvement in HH adherence of 6.4% (95% CI: 2.7–10.0; p<0.005) when entering the patient zone and 8.7% (95% CI: 3.2–14.1; p<0.005) when exiting the patient zone, compared to usual care.

WHO Compliant compared with another WHO compliant

Two studies[40, 67, 68] compared two WHO compliant strategies. The first[67, 68] used behavioural change theories to tailor components specific to HCWs in one arm. This tailored arm demonstrated a 6% (95% CI: 2.4 to 9.5%; p=0.001) increase in improvement compared to the untailored arm at year two but a decrease at year one (-4%, 95% CI:-7.5 to -1.3%; p=0.006). The second study[40] compared two WHO Compliant strategies, with one arm emphasising enhanced feedback. Although enhanced feedback showed an improvement this was not statistically significant (3%, 95% CI: 0 to 7 %; p=0.19).

3.2.2.2 Clinical evidence profile – primary outcome: WHO Plus

WHO Plus compared with usual care

One study[62] compared a WHO Plus strategy that included incentives to usual care. The authors demonstrated a statistically significant increase in HH adherence for both before *and* after patient/environment contact (p=0.001) and before *or* after patient/environment contact (p=0.001), compared to usual care.

WHO Plus compared with WHO compliant

Two studies[40, 52] compared WHO Plus to WHO Compliant strategies. The first[52] included accountability as the additional component and reported a mean difference of 8.91% (95% CI: 0.75 to 17.06%) favouring the WHO Plus strategy. The second study[40] compared a WHO Plus strategy featuring patient involvement and reported an absolute increase in HH adherence of 4% (95% CI: 1 to 8%, p=0.048) compared to a WHO Compliant strategy.

3.2.2.3 Clinical evidence profile – primary outcome: other multimodal strategies

One study[48] implemented a MM strategy not based on the WHO strategy (see Table 3-1). The authors reported results by ward type (acute care of the elderly (ACE) and ICU), with both

demonstrating a statistically significant increase in HH adherence (ACE: OR 1.67, 95% CI: 1.08 to 1.80; p=0.01; ICU: OR 2.09, 95% CI: 1.55 to 2.81; p<0.001), compared with usual care. The authors also reported the increase in HH adherence by baseline ward levels. When baseline adherence was 50%, a 13% increase for the ACE and 18% increase for ICU wards were reported. However, when the baseline adherence was 70% the increase was 10% and 13%, respectively.

3.2.2.4 Clinical evidence profile – primary outcome: unimodal strategy

Unimodal strategy compared with usual care

Four of the included studies compared unimodal strategies to usual care.[39, 51, 69, 70] Three studies examined the effectiveness of education and training based interventions,[39, 51, 70] while the other study examined the effectiveness of a system change intervention.[69]

The three studies that implemented education and training-based interventions all demonstrated improved HH adherence compared with usual care.[39, 51, 70] The first[70] reported an improvement in HH adherence following the intervention by four physician types (ranging from a 4.7% to 24.7% absolute increase). This was statistically significant compared to the control group for three of the four physician types (attending physicians (p=0.035); interns (p=0.007); medical students (p=0.003); and senior residents (p=0.064)). The second study[51] reported improvements that were statistically significant for the intervention group when performing HH before patient contact (RR 1.62 95% CI (1.21 to 2.15, p=0.01)) and after patient contact (RR 1.29 95% CI (1.06 to 1.56, p=0.01)) compared to the control group. The third study[39] examined the effectiveness of three different educational interventions compared with usual care. Baseline adherence rates varied considerably between study arms (interventions: 5.2%, 18.9% and 24.1%, control: 10.1%). The authors reported a statistically significant improvement for the intervention that included role model training (OR 4.08, 95% CI: 1.51 to 11.0; p=0.005) and for the intervention that included active presentations (OR 1.96, 95% CI: 1.18 to 3.27; p=0.01), but not for the intervention that combined role modelling and active presentations.

One study[69] assessed a system change intervention in a C-RCT and reported a statistically significant absolute difference of 26% (p< 0.001) in adherence rate favouring the intervention.

Unimodal strategy compared with unimodal strategy

One study[49] compared two unimodal strategies based on a reminder component: one using a poster based on the consequences of poor HH from a patient perspective and the other using posters with consequences from a HCW's perspective. Baseline adherence rates were similar between study arms (patient perspective: 80.7%, HCW perspective: 80.0%). The authors found that HH adherence was significantly greater with the patient-consequences poster than with the HCW-consequences poster (p=0.05).

3.2.3 Clinical evidence: Secondary outcomes – HCAI and colonisation rates

Five studies reported secondary outcomes.[38, 40, 56, 66-68] Four studies examined the change in HCAI rates,[38, 40, 66-68] with one[66] also looking at the number of outbreaks. Two studies examined colonisation rates for MRSA.[40, 56]

Of the four studies that reported on HCAI rates, two[40, 67, 68] were based in hospital settings and two in long term care facilities (LTCF) for the elderly. The first hospital[40] based study compared a WHO Plus strategy with enhanced feedback, with a WHO compliant strategy. The authors reported statistically significant differences between the strategies for two out of eight HCAIs (bloodstream infections (BSIs) (p=0.02) and clinical isolates of *Clostridioides difficile* (p=0.01)) (see Appendix 4). The authors speculated this was due to low observed infection and colonisation rates at baseline and throughout the study duration. The second hospital-based study[67, 68] compared two different WHO Compliant strategies and reported no statistically significant difference in infection rates for multi-drug resistant organisms (MDRO) after one (p=0.96) or two years (p=0.50) following implementation. As noted by the study authors, this may be due to the small number of observed cases. The two studies[38, 66] based in LTCFs both implemented a WHO Compliant strategy and reported statistically significant decreases in the incidence rates of HCAIs. The first study[38] used historical data from the three years pre-intervention as baseline data (May to September only) and reported a reduction in the risk of respiratory outbreaks (IRR 0.12, 95% CI: 0.01 to 0.93; p=0.04) and MRSA infections requiring hospitalisation (IRR 0.61, 95% CI: 0.38 to 0.97; p=0.04) for the WHO Compliant strategy versus usual care. The second study[66] reported a statistically significant reduction in infections requiring hospitalisation in favour of the WHO Compliant strategy compared to usual care (p=0.004). Data on the number of outbreaks was also collected,

however, no influenza A or norovirus infection outbreaks occurred during the study period.

Two hospital-based studies[40, 56] reported changes in colonisation rates of MRSA. The first compared WHO compliant to usual care,[56] and the second[40] compared two strategies (WHO Compliant strategy with enhanced feedback and a WHO Plus strategy) to a WHO Compliant strategy. Neither study demonstrated a statistically significant difference in colonisation rates.

3.2.4   Methodological quality of included studies

The Cochrane EPOC risk of bias tool[25] was used to appraise the methodological quality of the included RCTs. The results are displayed in Figure 6 and

Figure 7.

Figure 6 Clinical evidence for review question one: Cochrane EPOC risk of bias graph
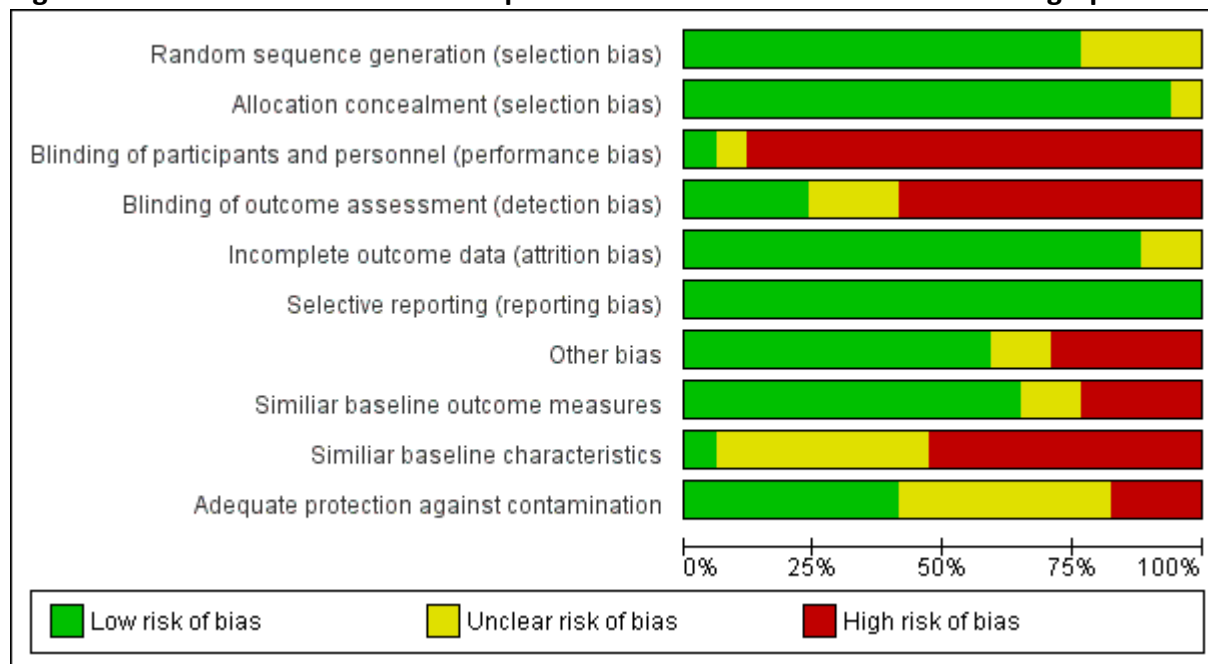
3.2.4.1   Random sequence generation

Thirteen of the studies[36-40, 47, 48, 52, 55, 56, 67-70] described the method of random sequence generation and had low risk of bias. Four studies[49, 51, 62, 66] were unclear for risk of bias as they reported randomisation was performed but did not describe the method used.

3.2.4.2   Allocation concealment

Sixteen studies[36-40, 47-49, 52, 55, 56, 62, 66-70] were at a low risk of bias as allocation was performed

by either team, ward, unit or facility. Huang et al.[51] had an unclear risk of bias as the method of allocation was not reported for all participants from one hospital.

Figure 7 Clinical evidence for review question one: Cochrane EPOC Risk of bias summary

3.2.4.3 *Blinding participants and personnel (performance bias)*

Fifteen studies[36-40, 47-49, 51, 52, 56, 62, 66, 69, 70] were at a high risk of bias due to participants being aware or very likely to be aware of the intervention. Martín-Madrazo et al.[55] had an unclear risk of bias as participants were said to be unaware of the study's aims, outcome and intervention, although posters and ABHR were provided and observers were present. Von

Lengerke et al.[67, 68] was at a low risk of bias as wards were blinded to allocations.

3.2.4.4   Blinding of outcome assessment (detection bias)

Four studies[48, 49, 55, 70] were assessed as having a low risk of detection bias, as the observers were reportedly unaware of the study arm allocation. Three studies were at an unclear risk of bias, two[36, 56] as they did not report any information, and for one,[62] although the observers were blinded, they were recruited from the hospital they were assessing. Ten studies[37-40, 47, 51, 52, 66-69] had a high risk for detection bias due to the visible nature of the interventions or due to observers providing feedback to the participants.

3.2.4.5   Incomplete outcome data (attrition bias)

Fifteen studies were considered at low risk of attrition bias. Eight of these studies[37-39, 49, 51, 56, 67-69] reported no missing outcome data, three[47, 52, 55] reported missing data and performed intention to treat analysis, two[66, 70] reported the loss to follow up was experienced before randomisation and allocation occurred, one[40] reported dropout rates of less than 5% with no observed differences in baseline outcome measures, and one study[36] reported the withdrawal of a hospital unit following randomisation but due to stepped-wedge design was unlikely to bias results. Two studies were at an unclear risk of bias, the first[62] with a 20% dropout in the control arm and baseline outcome measures not reported. The second[48] reported a large dropout rate (45%) following randomisation, with insufficient details on dropouts per group.

3.2.4.6   Selective reporting (reporting bias)

All 17 studies were assessed as at low risk of reporting bias. All reported on all outcomes discussed in their studies. Five studies registered a protocol, two prospectively[40, 52] and three[37, 48, 67, 68] retrospectively.

3.2.4.7   Other bias

Ten studies[36-38, 40, 47, 49, 51, 62, 67, 68, 70] had no other identified risk of bias. Two studies[48, 69] had an unclear risk of bias; the study by Anderson et al.[69] had an unclear risk of funding bias as the university that hosted the study had royalties from the intervention being assessed although the investigators did not; Fuller et al.[48] reported that the intervention finished in some of the study sites before the end of the study. Five studies were considered at a high

risk of other biases, three studies[52, 55, 56] had increased awareness or additional measures (such as the installation of ABHR dispensers) hospital-wide, due to outbreaks occurring during the study period, one study[39] reported preparations for national accreditation took place during the study period which impacted all groups and another study[66] reported high staff turnover where new staff might not have had exposure to the intervention.

3.2.4.8 Similar baseline outcome measures

Eleven studies were at a low risk of bias, nine studies[40, 47, 49, 51, 52, 55, 56, 66-68] reported similar baseline adherence rates, while two studies[36, 48] used a step wedge design resulting in all study units act as both control and intervention group. There was an unclear risk of bias for two studies as baseline adherence rates were not reported.[62, 69] Whereas for four studies,[37-39, 70] there was a high risk of bias due to significant differences in HH adherence at baseline.

3.2.4.9 Similar baseline characteristics

Two studies[37, 55] were assessed as having a low risk of bias. Seven studies were at an unclear risk of bias: four[36, 38, 51, 69] reported characteristics at baseline that demonstrated differences between groups, but it is unclear what effect this had; one study[40] reported the types of units in each group only but stratified units according to similar patient characteristics before randomisation; one study[62] reported that the mean number of beds per hospital included in each group were balanced, with no further details; one study[49] only reported which units were allocated to each group and the ratios of signs to patient beds, but no further details. Eight studies were at a high risk of bias, five studies[47, 48, 52, 56, 70] did not report the characteristics in text or tables and in accordance with the EPOC criteria are at high risk of bias. For three studies[39, 66-68] there were substantial differences between control and intervention groups.

3.2.4.10 Adequate protection against contamination

Seven studies[37, 38, 48, 52, 55, 62, 69] were at low risk of contamination, as the allocation occurred at unit or facility level, with low risk of participants leaving groups. Seven studies were at an unclear risk of contamination bias. One[36] due to every site coordinator knowing that HH had to be improved, another study[66] provided a performance feedback session halfway through the trial on HH adherence to both groups with staff encouraged to increase adherence when monthly infection rates increased, and the remaining five studies[39, 49, 51, 67, 68, 70] due to single

facility settings and reported free movement of staff. Three studies had a high risk of contamination bias. For one study[47] this was due to the intervention having an audible cue which could be heard by the control group. The other two were due to the authors reporting that knowledge of the trial had spread to the control units,[56] with one of the control wards creating and implementing their own HH campaign.[40]

3.2.5 Certainty of the evidence

We assessed the overall certainty of the evidence using the GRADE methodology. Separate narrative summary of findings table were created for the primary outcome (HH adherence rates) for multimodal strategies (Table 3-3) and unimodal strategies (

Table 3-4).

Overall the certainty of the evidence for multimodal strategies was very low to low. This was due to concerns over the risk of bias (including a lack of blinding for participants, lack of blinding for outcome assessment, high risk of contamination bias in which the control groups became aware of the intervention and large dropout rates following randomisation), concerns relating to imprecision and concerns relating to indirectness.

The totality of the evidence suggests that WHO Compliant strategies may improve HH adherence in hospital, long-term care facilities and primary healthcare settings compared to usual care (low certainty of evidence). There was very low certainty of evidence that WHO Plus strategies, that include extra components (incentives, accountability, and patient involvement) in addition to the five key components recommended by the WHO, would result in further improvement in hospital settings. One study assessed a non WHO multimodal strategy, consisting of one recommended key component (evaluation and feedback) and two additional components (incentives and accountability). There was very low certainty evidence suggesting that this strategy would improve HH adherence in hospital settings.

For unimodal strategies there was a very low certainty of evidence due to serious concerns relating to the risk of bias and indirectness as a result of the limited generalizability of study settings.

Table 3-3 Clinical evidence for review question one: Summary of findings table for multimodal interventions compared with alternative or usual care

Patient or population: healthcare workers
Setting: hospital, nursing home, long-term care facility or community healthcare setting
Intervention: strategy intended to improve adherence with hand hygiene

Comparison: no intervention or another intervention
Outcome: hand hygiene adherence

Types of intervention	Impact	№ of observations (studies) Setting	Certainty of the evidence (GRADE)
WHO compliant strategies (3 or more components)	**WHO Compliant versus usual care** 6 C-RCTs included in a meta-analysis RR 1.44 (95% CI: 1.12 to 1.85; p=0.004) in favour of the WHO Compliant strategy compared to usual care. 1 RCT not included in meta-analysis: reported improvement in HH adherence of 6.4% (95% CI: 2.7–10.0; p<0.005) for entering and 8.7% (95% CI: 3.2–14.1; p<0.005) for exiting patient zones, compared to usual care.	1,076,510 6 C-RCTs, 1 RCT 20 hospitals, 24 LTCFs, 11 PHCs	⊕⊕◯◯ LOW a
	WHO Compliant versus WHO Compliant 2 C-RCTs: Improvement of 6% (95% CI 2.4 to 9.5%; p=0.001) was demonstrated in favour of WHO Compliant (tailored arm) compared to WHO Compliant (untailored arm) strategy. No statistically significant improvement was demonstrated when comparing a WHO Compliant (enhance feedback) to the standard WHO Compliant strategy.	14,935 2 C-RCT 2 hospitals	⊕◯◯◯ VERY LOW a, b
WHO compliant strategies with an additional component (all 5 components plus at least one additional component)	**WHO Plus versus usual care** 1 C-RCT: Statistically significant improvement was demonstrated in favour of a WHO Plus (incentives) strategy compared to usual care (p=0.001).	4,527 1 C-RCT 10 hospitals	⊕◯◯◯ VERY LOW a, b
	WHO Plus versus WHO Compliant 2 C-RCTs: Mean difference of 8.91% (95% CI: 0.75 to 17.06%) in favour of WHO Plus (accountability) in one study, and 4% absolute difference (95% CI: 1 to 8%, p=0.048) in favour of a WHO Plus (patient involvement), both studies compared to WHO Compliant.	16,982 2 C-RCTs 4 hospitals	⊕◯◯◯ VERY LOW b, c, d
Multimodal strategies (non-WHO components)	1 C-RCT reported ORs for different ward types of 1.67 (95% CI: 1.08 to 1.80; p=0.01) and 2.09 (95% CI: 1.55 to 2.81; p<0.001) favouring multimodal strategy compared to usual care.	Not available 1 C-RCT 16 hospitals	⊕◯◯◯ VERY LOW b, d

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Downgraded twice for serious risk of bias: lack of blinding for participants and or outcome assessment, and contamination due to control group being exposed to the intervention, b. Downgraded once due once for indirectness due to limited generalizability of

setting, c. Downgraded once for imprecision, d. Downgraded twice for serious risk of bias: lack of blinding for participants and or outcome assessment, and large dropout rate following randomisation.

Key: CI – confidence interval; C-RCT – cluster randomised control trial; HH – hand hygiene; LTCF – long term care facility; OR – odds ratio; PHC - primary healthcare centre; RCT – randomised control trial; RR – risk ratio; WHO – World Health Organisation.

Table 3-4 Clinical evidence for review question one: Summary of findings table for unimodal interventions compared with alternative or usual care

Patient or population: healthcare workers
Setting: hospital setting
Intervention: strategy intended to improve adherence with hand hygiene

Comparison: no intervention or another intervention
Outcome: hand hygiene adherence

Types of intervention	Impact	№ of observations (studies) Setting	Certainty of the evidence (GRADE)
Unimodal strategies (education and training)	1 RCT reported statistically significant improvement in HH adherence following a talk and video on mindfulness and HH adherence, compared to usual care. 1 RCT reported statistically significant increases in HH adherence of 16.3 and 34.7 percentage points in the intervention group before and after patient contact, respectively, with no change or a decrease of 4.1 percentage points in the group that received usual care 1 RCT reported improvement in HH adherence compared to usual care for 2 of 3 interventions, adjusted ORs of 1.96 (95% CI: 1.18 to 3.27; p=0.01) and 4.08 (95% CI: 1.51 to 11.0; p=0.05), while the third intervention was reported as statistically non-significant (with no further details).	4,065* 3 RCTs 3 hospitals	⊕◯◯◯ VERY LOW a, b
Unimodal strategies (reminders)	1 RCT compared two signs and reported an increase in HH adherence for the patient-consequences sign compared to the personal-consequences sign (p=0.05).	567 1 RCT 1 hospital	⊕◯◯◯ VERY LOW b, c, d
Unimodal strategies (system change)	1 RCT reported an absolute difference of 26% in HH adherence following the introduction of a bed-side-table with ABHR and gloves when compared to usual care (p<0.001).	996 1 RCT 1 hospital	⊕◯◯◯ VERY LOW b, c

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Downgraded twice for serious risk of bias: lack of blinding for participants and or outcome assessment; baseline characteristics and or outcomes not reported; and concurrent external campaigns in progress, b. Downgraded once for indirectness due to limited generalizability of setting, c. Downgraded twice for serious risk of bias: lack of blinding for participants and or outcome assessment; baseline characteristics and or outcomes not reported, d. Downgraded once for imprecision due to low number of observations and small effect size.

Key: ABHR – alcohol-based hand rub; RCT – randomised control trial; HH – hand hygiene; LTCF – long term care facility; PHC - primary healthcare centre; OR – odds ratio

* data on observations was not reported in one study

3.3 Economic evidence for review question one: Results

The following section summarises the available evidence on the cost-effectiveness of interventions to improve adherence to hand hygiene recommendations.

3.3.1 Characteristics of included studies

Seven economic evaluations were identified, two from Taiwan,[71, 72] and one each from Australia,[74] the Netherlands,[75] the Republic of Korea,[73] Thailand,[76] and Vietnam.[77] The studies were published between 2011 and 2018. One study conducted a cost-utility analysis (CUA) and a cost-effectiveness analysis (CEA),[76] three studies conducted CEAs,[74, 75, 77] one study conducted a CEA and a cost-benefit analysis (CBA)[72] and two studies conducted CBAs.[71, 73] One study was conducted alongside an RCT (n=2,733),[75] three studies were based on before-after studies,[71-74, 77] and three were modelling studies.[76] Two costing studies and one cost-analysis study were also identified. However, these studies were excluded as per protocol, as more informative studies were identified.

All seven studies included interventions based on the WHO MM[12] (see Section 1.2.1). Four studies included interventions with three or more of the five key components (WHO Compliant),[71, 74, 76, 77] while three included interventions with an additional component (WHO Plus).[72, 73, 75] A summary of the characteristics of the interventions and comparators of the included studies is presented in Table 3.5.

Table 3-5 Economic evidence for review question one: Interventions and comparators included in economic studies

Study (year), country, design	Intervention	Comparator
WHO Compliant		
Chen (2016), Taiwan[71] Alongside B-A study	*System change* – availability of ABHR at point of care *Education* – workshops and training video *Reminders* – posters and leaflets *Feedback* – monthly feedback provided to units *Institutional safety climate* – director, deputy director and ward level ambassador badges encouraging patients and family to remind HCW of HH. Surveys conducted aimed at HCW and the public on the concept of HH and patient-family empowerment.	Pre intervention period included provision of ABHR outside patient rooms and, a hospital wide HH promotion campaign 2 years before the study (no further details reported).
Graves (2016), Australia[74] Alongside B-A study	Australian National Hand Hygiene Initiative, based on WHO MM. Varied across sites but at a minimum included:[84] *System change* - appropriate access to HH facilities; *Education* - training and education *Reminders* – promotion *Feedback* - auditing and feedback of results.	Pre intervention period included existing local efforts to improve HH compliance which ranged from state wide to individual hospitals including a variety of interventions (such as education, monitoring, feedback); 3 of the 8 States/Territories did not have existing campaigns.
Le (2015), Vietnam[77] Alongside B-A study	*System change* - new sinks, ABHR dispensers at the point of care and pocket versions and disposable towel dispensers *Education* - seminars including quiz, in-service workshops on correct technique *Reminders* – posters and flyers *Feedback* – specifics not reported *Institutional safety climate* - HH education provided to patients and their families	Pre intervention period where no other interventions or changes to infection control was reported.
Luangasanatip (2018) Thailand[76] Model based	Theoretical intervention based on Australian National Hand Hygiene Initiative (WHO MM based strategy)[85] – detailed in Graves et al.[74]	Not defined; However, based on findings of another study,[85] reported by Graves et al.[74] as varying between hospitals.
WHO Plus		
Chen (2011), Taiwan[72]	*System change* - ABHR at point of care and affixed to trolleys *Education* - lectures and/or web-based self-learning with exam *Reminders* – posters and verbal reminders by infection control nurses	Pre intervention period included an existing annual HH programme (no further details reported) and hands-free washing facilities with non-medicated liquid soap (not

Study (year), country, design	Intervention	Comparator
Alongside B-A study	*Feedback* - periodic audits and performance feedback provided to units and departments *Institutional safety climate* - use of HH compliance as a quality indicator. Plus *Accountability* - Fine of US$3 for compliance failures for individuals not modifying their behaviour after face-to-face communication; *Incentives*- Reward of US$160 for an outstanding performance (unit and department level).	refilled) and paper towels located in every room of the wards and by every ICU bed. ABHR was not available.
Chun (2016), Republic of Korea[73] Alongside B-A study	*System change* - disposable ABHR at point of care and entry to each room in every ward; *Education* – annual web-based learning program. Additional training for new employees and those with low adherence *Feedback* - immediate individual and monthly for each department *Reminders* - posters, flags and screensavers *Institutional safety climate* - encouraged patients to evaluate the HH performance of HCW using feedback cards. Plus *Incentives* - incentives and certificates awarded quarterly for HCW who complied. Additionally, a central line–associated bloodstream infection intervention was implemented midway through the study intervention period, which included a HH component. However, this was not associated with the study.	Pre intervention period included multiple infection control measures (contact precautions, antibiotic stewardship and environmental cleaning).
Huis (2013), The Netherlands[75] Alongside C-RCT	Same strategy as comparator, with additional emphasis on team and leader-directed strategies based on social theories. Plus *Accountability* - nurses addressing each other in cases of undesirable HH behaviour	*System change* – adequate product availability *Education* – leaflet on HH importance, website *Reminders* – posters, newsletters articles *Feedback* – HH rates provided to ward managers including ward and hospital performance comparisons *Institutional safety climate* – management support.

Key: ABHR – alcohol-based hand rub; B-A – Before-after study; C-RCT – Cluster randomised control trial; HCW – healthcare worker; HH – hand hygiene; ICU – intensive care unit; WHO Compliant – World Health Organization multimodal strategy (three or more key components); WHO Plus – World Health Organization multimodal strategy plus additional components

3.3.2 Economic evidence

In accordance with the methods outlined in Section 2.5.4, all costs are presented as they were in the original studies with the adjusted 2018 Irish euro equivalent presented in parentheses. Where the study's authors did not report the cost year, it was assumed that the unit costs were from four years prior to study publication (based on the average cost year reported in the studies included within this review question). A summary of the characteristics, methods and results of the included studies is presented in Appendix 6.

3.3.2.1 Economic evidence: WHO Compliant compared with usual care

Four studies incorporated interventions based on WHO compliant strategies.[71, 74, 76, 77] One of these studies included both a CUA and CEA,[76] two included CEAs[74, 77] and one included a CBA.[71] In all studies the comparator was the pre-intervention period. One study reported existing infection control programmes were in place but provided no details;[71] one study[74] reported varying interventions in five out of eight States/Territories and no existing campaigns in the remaining three States/Territories; and the remaining studies provided no details.[76, 77] All four studies were conducted from the healthcare payer's perspective, with three studies considering a hospital payer's perspective,[71, 76, 77] and one considering a wider healthcare system (Australian State Government) perspective.[74]

Time horizons ranged from 10 months[77] to lifetime.[74, 76] Discounting was not applicable for two studies (time horizons were one year or less)[71, 77] and applied at a rate of 3% to the future outcomes for the remaining two studies (costs were only modelled for one year in these studies, so discounting was not applicable for costs).[74, 76] All studies considered all HCWs in a hospital setting. Two studies included data from high acuity settings only[76, 77] and two studies[71, 74] included data from all wards.

The annual cost of the interventions varied considerably between studies, ranging from $1,395 (€3,093)[76] for a two ICU programme in Vietnam to $250,000 (€455,372) for a hospital-wide programme in Taiwan.[71] Three studies provided a description of costs, with two[74, 77] including all material costs (such as posters, brochures and ABHR) and one[76] including ABHR only (other material costs assumed to be negligible); two including staff time;[74, 76] one including information and technology, and travel costs;[74] and one including new sinks, handwashing

solution, new dispensers, and staff incentive costs.[77] The fourth study did not provide a breakdown of intervention costs.[71]

The costs saved from avoiding an HCAI varied considerably between studies, ranging from $155 (€343) in Thailand [76] to AU$14,273 (€11,068)[74] per episode avoided. All four studies investigated different types of HCAIs, with one including all recorded HCAIs,[77] one including urinary tract infections, bloodstream infections (BSI) and respiratory tract infections,[71] one including only *Staphylococcus aureus* BSIs,[74] and the remaining study including only MRSA BSIs.[76] The breakdown of costs included in the savings also varied between studies, with one study including only the cost of a hospital bed day (ward and ICU),[74] one including this plus the cost of treatment,[76] one including a total cost of different HCAI types,[71] and the final study providing a detailed breakdown (including accommodation, diet, medicine, materials, and services costs).[77]

Improvements in HH adherence rates were observed or modelled in all studies, ranging from an absolute increase of 11%[71] to 32%[77] with baseline adherence rates ranging from 10%[76] to 62%.[71, 74] Reductions in HCAI rates were observed based on before and after studies, ranging from a reduction of 0.6 per 1,000 admission days[71] to an absolute reduction of 36%.[77]

Two studies determined cost-effectiveness against a willingness to pay (WTP) threshold, both finding the intervention to be cost-effective,[74, 76] with the other two studies finding the intervention to be cost-saving.

The study by Graves et al.[74] reported an incremental cost-effectiveness ratio (ICER) of AU$29,700 (€23,032) per life year gained, which was cost-effective at a WTP threshold of AU$42,000 per life year gained. They also reported specific ICERs for each Australian State/Territory included in their study, these ranged from AU$1,030 (€799) to AU$63 million (€49 million) per life year gained with three out of the six States/Territories cost-effective and three not cost-effective. Luangasanatip et al.[76] reported their intervention to be cost-effective (at a WTP threshold of $4,840 per QALY gained in Thailand) with an estimated ICER of $471 (€1,043) per QALY gained. They also conducted scenario analysis with different baselines and improvements in HH adherence (the base case analysis considered an improvement from 10% to 40%). The scenarios involving a baseline rate of 10% and improvement to either 20% or 60% adherence were cost-effective. However, the scenario involving a baseline adherence of 40%

with an increase to 60% was not cost-effective (ICER of $6,431 (€14,257) per QALY gained; WTP threshold of $4,840 per QALY gained).

Le et al.[77] reported an ICER of $1,074 (€8,664) saved per HCAI prevented in Vietnam. However, as their analysis excluded fixed costs this may be considered an overestimate. Including the fixed costs, the ICER decreases to approximately $1,001 (€8,076) saved per HCAI prevented. Chen at al.,[71] reported a cost-saving of $950,000 (€1,730,413) compared to a total intervention cost of $250,000 (€455,372) in Taiwan, giving a net saving of $700,000 (€1,275,041) over an 18 month period.

3.3.2.2 Economic evidence: WHO Plus compared with usual care

Two studies evaluated WHO Plus strategies compared with usual care.[72, 73] For Chun et al.[73] the additional component was incentives, for Chen et al.[72] it was accountability and incentives. Both studies were conducted alongside before–after studies and both reported that existing infection prevention programmes were in place prior to the introduction of the interventions. However no details on the HH component of these existing programmes were reported.[72, 73] Chen et al.[72] reported the SARS epidemic occurred towards the end of the pre-intervention period (which was accounted for in their analysis) but provided no details on what infection prevention policies were implemented in response. Chun et al.[73] reported that a central line-associated BSI intervention that included a HH component was implemented midway through the intervention period, but they reported that this had no significant effect on infection prevalence.

Chen et al.[72] conducted a CEA and CBA from a hospital payer's perspective and Chun et al.[73] conducted a CBA from a societal perspective. Both were based on a four-year time horizon with a 3% and 5% discount rate, respectively. Both studies were set in a single hospital and included all HCWs.

The annual cost of the interventions were approximately $39,411 (€43,284) in the Republic of Korea and $62,145 (€130,686) per year in Taiwan for Chun et al.[73] and Chen et al.[72] respectively. Both studies included materials costs for the intervention (such as posters, website, leaflets, and ABHR). Chun et al.[73] also included additional staff salaries, the cost of caregiving, and productivity losses due to extended hospitalisation and premature death. Chen et al.[72] included incentive costs and, in a sensitivity analysis, a staff time opportunity cost.

The costs saved due to avoiding one episode of an HCAI were $3,877 (€8,153) in Taiwan for Chen et al.[72] and included the cost of accommodation, materials, and services for MRSA, *Acinetobacter spp.*, and extensively drug-resistant *Acinetobacter baumannii* (XDRAB) infections, and $13,101 (€14,389) in the Republic of Korea for Chun et al.[73] and included direct medical costs for MRSA infections only.

Hand hygiene adherence rates increased in both studies, from a baseline of 43% to 96% for Chen et al.[72] and from 33% to 92% for Chun et al..[73] These were accompanied by decreases of 8.9%[72] and a 33%[73] in HCAI rates, based upon the difference between predicted and observed values.

Both studies reported the intervention to be cost-saving. Chen et al.[72] reported an extra cost of $164 (€344) per HCAI episode prevented, with a resulting saving of $3,877 (€8,153), this resulted in a total net saving of $5,289,364 (€11,123,135) over a 45 month period. Chun et al.[73] reported a total cost of $167,495 (€183,957) and a cost-saving of $851,565 (€935,259), resulting in a net saving of $684,070 (€751,302) over 18 months.

3.3.2.3   *Economic evidence: WHO Plus compared with WHO Compliant*

One study in the Netherlands conducted a CEA of a WHO Plus strategy compared with a WHO Compliant strategy.[75] It was conducted alongside a C-RCT (n=2,733) and included accountability as the additional component. A clinical effectiveness analysis was reported in a separate paper, which is included in the clinical evidence review (see Section 3.2). The study was conducted from a hospital payer's perspective over a one-year time horizon. The study population included nurses only from 67 wards across three hospitals.

Costs relating to both interventions included materials costs and additional staff time (to conduct observations, feedback and to perform additional HH). The WHO Plus intervention had additional personnel costs relating to the salary for a coach and extra time required of managers and role models.

The study reported both the WHO Plus and WHO Compliant strategies improved HH adherence from baseline (19% increased to 52% and 22% increased to 46%, respectively), with a 8.91% mean difference (95% CI: 0.75 to 17.06%) in favour of the WHO Plus. As no HCAI data was collected during the study, estimates of the expected cost saving from the prevention of an

HCAI and the expected reduction in HCAI rates, attributable to each intervention were based on another study.[86] Two scenarios were used – a 15% and a 30% reduction in HCAI rates.

The cost per ward was €12,156 (€12,727) for the WHO plus and €6,659 (€6,972) for the WHO compliant. This resulted in an incremental cost per ward of €5,497 (€5,755) and an ICER of €622 (€651) per extra percentage of HH adherence gained. Also reported were ICERs of €2,074 (€2,171) and €4,125 (€4,319) per extra percentage reduction in HCAI, based on a 30% and 15% reduction in HCAI, respectively. Based on a WTP of €5,000 per percentage reduction in HCAI, the probability that these were cost-effective was estimated at 70% and 90%, respectively.

3.3.3 Methodological quality

A quality assessment of each study included in the systematic review was undertaken using the CHEC list.[87] The outcomes of these assessments are presented in Table 3-6. Based on the evaluation of the methodology quality, one study from Australia was deemed high quality,[74] three were of moderate quality[72, 75, 76] and three were of low quality.[71, 73, 77]

Common methodological limitations included:

- Inadequate details on the comparators were provided in five studies.[71, 73, 74, 76, 77]
- Three studies[71, 75, 77] had insufficient time horizons (one year or less) to account for all relevant costs and outcomes relating to implementing a HH improvement strategy.
- Four studies[71, 72, 76, 77] did not include all relevant costs for each alternative identified (such as campaign costs or staff costs). In one study, it was unclear if all relevant costs were included as a total cost was reported for the campaign with no details on individual items.[73]
- Two studies did not report how all costs were measured or provide detailed costs.[71, 72] In another two studies, it was unclear whether the costs were valued appropriately (one study used data published more than 10 years before their study[75] and the other[73] did not report details on campaign costs).
- Four studies[71, 75-77] did not value outcomes appropriately, making large assumptions to inform HCAI rates or using QALY data originally valued for a high income setting in a low income setting.
- Two studies[71, 73] did not conduct incremental analyses.
- Five studies[71-73, 75, 77] did not subject all important variables to sensitivity analysis.
- Two studies[72, 73] lacked any discussion relating to the generalizability of the results.

- Six studies[71-76] lacked any discussion regarding ethical and distributional issues.

Other limitations which were applicable to individual papers included:

- Discounting not applied to all relevant costs.[73]
- It was unclear if the assumed reduction in HCAI was appropriate for the study setting, given the baseline HH adherence and HCAI rates.[75]

Table 3-6 Economic evidence for review question one: CHEC-list quality assessment

Item	Chen 2011[72]	Chen 2016[71]	Chun 2016[73]	Graves 2016[74]	Huis 2013[75]	Le 2015[77]	Luangasabatip 2018[76]
Is the study population clearly described?	+	+	+	+	+	+	+
Are competing alternatives clearly described?	+	−	−	−	+	−	−
Is a well-defined research question posed in answerable form?	+	+	+	+	+	+	+
Is the economic study design appropriate to the stated objective?	+	+	+	+	+	+	+
Is the chosen time horizon appropriate to include relevant costs and consequences?	+	−	+	+	−	−	+
Is the actual perspective chosen appropriate?	+	+	+	+	+	+	+
Are all important and relevant costs for each alternative identified?	−	−	Unclear	+	+	−	−
Are all costs measured appropriately in physical units?	−	−	+	+	+	+	+
Are costs valued appropriately?	−	−	Unclear	+	Unclear	+	+
Are all important and relevant outcomes for each alternative identified?	+	+	+	+	+	+	+
Are all outcomes measured appropriately?	+	+	+	+	Unclear	+	+
Are outcomes valued appropriately?	+	−	+	+	−	−	−
Is an incremental analysis of costs and outcomes of alternatives performed?	+	−	−	+	+	+	+
Are all future costs and outcomes discounted appropriately?	+	−		+	NA	NA	−
Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	−	−	−	+	−	−	+
Do the conclusions follow from the data reported?	+	+	+	+	+	+	+
Does the study discuss the generalizability of the results to other settings and patient/client groups?	−	+	−	+	+	+	+
Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	+	+	+	+	+	+	+
Are ethical and distributional issues discussed appropriately?	−	−	−	−	−	+	−

+ Yes   Not applicable   − No

3.3.4   Applicability

Applicability (based on relevance and credibility) was assessed using the ISPOR questionnaire.[88] The outcomes of these assessments are presented in Table 3-7. No Irish studies were identified. Of the seven identified studies, four were deemed partially applicable.[72-75] The remaining three[71, 76, 77] were deemed not applicable due to major applicability limitations, such as inappropriate context (low or middle-income country setting and much lower baseline adherence rates), inadequate analysis and reporting, lack of critical data or use of unsuitable data, and inadequate assessment of uncertainty.

The four studies deemed partially applicable contained the following minor limitations:

- All relevant outcomes were not included in two studies.[73, 74]

- None of the four studies reported evidence to suggest sufficient external model validation was conducted,[72-75] and only one study reported on internal verification.[74]

- Two studies used historical data (from 1994-1995[75] and 2005[72]) to inform the cost of HCAI episodes.

- Three studies did not adequately assess the uncertainty of model assumptions (for example, not assessing key parameters).[72, 73, 75]

- An sufficient level of detail regarding the programme cost (for example, only providing a total cost of the campaign) was provide by two studies.[72, 73]

- Two studies reported receiving study funding,[73, 74] with one study providing a statement that the funders had no input into the study.[74] However, given the intervention and possible motivations, this was unlikely to effect the validity of the studies or their applicability to the Irish context.

Table 3-7 Economic evidence for review question one: ISPOR applicability assessment

Item	Chen 2011[72]	Chen 2016[71]	Chun 2016[73]	Graves 2016[74]	Huis 2013[75]	Le 2015[77]	Luangasabatip 2018[76]
Is the population relevant?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Are any critical interventions missing?	No	No	No	No	No	No	No
Are any relevant outcomes missing?	No	Yes	Yes	Yes	No	No	No
Is the context applicable?	Yes	Yes	Yes	Yes	Yes	No	No
Is external validation of the model sufficient?	No	No	No	No	No	No	No
Is internal verification of the model sufficient?	No	No	No	Yes	No	No	No
Does the model have sufficient face validity?	Yes	No	Yes	Yes	Yes	Yes	Yes
Is the design of the model adequate?	Yes	No	Yes	Yes	Yes	Yes	Yes
Are the data used in populating the model suitable?	No	No	Yes	Yes	No	No	Yes
Were the analyses adequate?	No	No	Yes	Yes	Yes	No	Yes
Was there adequate assessment of uncertainty?	No	No	No	Yes	No	No	Yes
Was the reporting adequate?	No	No	No	Yes	Yes	Yes	Yes
Was interpretation fair and balanced?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were there any potential conflicts of interest?	No	No	Yes	Yes	No	Yes	Yes
Were steps taken to address conflicts?	N/A	N/A	No	Yes	N/A	No	No

3.4   Review question one: Discussion and conclusion

3.4.1   Discussion

We identified 24 studies relevant for inclusion in this systematic review of interventions to improve adherence to hand hygiene (HH) recommendations. Seventeen relate to clinical effectiveness and seven relate to economic evidence.

Of the 17 clinical studies, five assessed unimodal interventions and 12 assessed multimodal (MM) interventions. Of the 12 assessing multimodal interventions, eight studies referenced the WHO multimodal hand hygiene improvement strategy.[12]

According to the certainty of the evidence, using the GRADE approach, there is low certainty of evidence that implementing a WHO Compliant strategy (that is, three or more of the five key components) compared to usual care will improve hand hygiene adherence. For WHO Plus strategies (all five components plus at least one additional component) there is very low certainty of evidence that adding additional components can lead to additional improvement. This is due to the limited number of studies examining these strategies and the lack of imprecision around the level of improvement in HH adherence. Our results are in line with those of earlier reviews[89-91] including the review by Gould et al.[24] which was used to inform our search strategy. Compared with this review,[24] restricting inclusion to RCTs only and the identification of five additional studies did not change the overall conclusions but resulted in an increase in the certainty of evidence, from very low to low, for improvement in HH adherence for WHO Compliant strategies compared with usual care.

Five studies assessed unimodal interventions and reported some improvements in HH adherence rates compared with usual care, but due to serious risk of bias and the limited settings included, there was a very low certainty of evidence. A C-RCT,[92] published in October 2019 after our search, of a single-component intervention reported that changing reminder signs weekly or monthly had no effect on HH adherence rates overall compared with hospital units that did not change HH signs throughout the six month intervention period.

The evidence to support the link between an intervention designed to improve HH

adherence and a decrease in HCAI was limited and with mixed results. Four studies examined the effect of interventions on HCAI rates. Two were set in long-term care facilities (LTCFs) and found statistically significant decreases in HCAI rates after implementing a WHO Compliant strategy compared to usual care. Two were set in hospitals, one comparing two different WHO Compliant strategies, finding no statistically significant difference in MDRO infection rates, and one comparing a WHO Plus to a WHO Compliant strategy, finding a statistically significant reduction for primary bloodstream infections and clinical isolates of *Clostridioides difficile*, but not for six other HCAIs assessed. Two studies reported on colonisation rates of methicillin-resistant *Staphylococcus aureus* (MRSA), one set in a hospital (WHO Plus versus WHO Compliant) and one in a group of LTCFs (WHO Compliant versus usual care), with neither study demonstrating any significant difference in rates. However, the lack of any observed differences may be due to low observed infection and colonisation events in the included studies. These findings are in line with a recent overview of systematic reviews[90] which reported that six out of 11 systematic reviews that assessed the effectiveness of HH strategies at reducing HCAI reported either mixed or non-significant effects.

This review identified evidence from a range of countries, settings and healthcare workers, suggesting the findings are generalisable. In Ireland, HIQA reported that a multifaceted approach in line with the WHO MM strategy to improving hand hygiene compliance was seen in all hospitals inspected in 2015.[93] However, they noted that some hospitals were more advanced than others in achieving and sustaining a culture of good HH practices. When considering the results of the review in the Irish context, it is worth considering the impact of baseline HH adherence rates. One of the included studies[48] highlighted that a higher baseline rate is associated with smaller effects, which was further explored in a process evaluation study[94] conducted alongside one of the other studies.[52] This was also explored in our analysis, however no trend was evident, which may be due to the low number of included studies (n=6). Existing high baseline levels as reported in some studies are most likely the result of an on-going strong focus on HH improvement in general. Nevertheless, this is important when understanding the potential impact interventions might have in the Irish context. As Irish hospitals are estimated to have a high adherence rate of 92% (95% CI: 91.2 to 92.3%),[95] these baseline rates are higher than any of the

studies included in this review and are also higher than most of the post-intervention rates in the included studies. Although estimates for Irish LTCFs and primary care centres are not available, they may indeed be lower and thus may derive a greater benefit from the implementation of HH improvement strategies.

Of the seven economic studies, four were partially applicable to the Irish context, three were moderate to high quality. For these three studies, a net economic benefit was demonstrated when implementing a WHO Compliant strategy compared with usual care,[74] a WHO Plus strategy compared with usual care[72] and for a WHO Plus strategy versus a WHO Compliant strategy.[75]

For the first study, an incremental cost-effectiveness ratio (ICER) of €23,032 per life-year gained (cost-effective in the Australian context) was reported in relation to implementing a WHO Compliant strategy compared to usual care.[74] In Ireland there is no official willingness to pay (WTP) threshold for non-pharmaceutical products, however, a WTP threshold of €45,000 per quality-adjusted life year (QALY) is generally employed. Although the Australian study[74] did not add utility weights to convert life years into QALYs, their result would likely be considered cost-effective in the Irish context. However, this result must be interpreted in the context of several factors. It is based on a before-after study design where baseline adherence rates of the included hospitals are unknown. It is sensitivity to the assumption on the reduction in HCAI rates, with a probability of cost-effectiveness of 1% for the two states which saw no improvement in HCAI rates. The second study from Taiwan implemented a WHO Compliant strategy and compared it to usual care,[72] with a net benefit saving of €11 million over four years reported. The final study from the Netherlands[75] compared a WHO Plus to WHO Compliant strategy and reported ICERs of €2,171 and €4,319 per extra percentage reduction in HCAI rate (based on the assumption of a 0.3% or 0.15% reduction in HCAI rate per 1% increase in HH adherence, respectively) and €651 per extra percentage of HH adherence gained. Whether this is cost-effective is unclear, as the results are not directly comparable to interventions for other diseases and therefore cannot be applied to commonly employed WTP thresholds.

Although the results of the economic studies included in this review suggest that strategies

based on WHO compliant and WHO plus strategies are cost-effective, they assume that an increased HH adherence will lead to a decrease in HCAIs rates. The evidence of increased HH adherence rates leading to decreased rates of HCAIs has not been clearly shown in the clinical review and if not realised, may impact of the cost-effectiveness of these strategies in the Irish setting, particularly in a context of high baseline adherence. However as previously noted, to sustain high levels of adherence ongoing HH improvement interventions are likely to be needed.

Studies were conducted in a variety of settings including; hospitals, LTCFs and primary healthcare centres, and included a wide range of healthcare workers. Furthermore, the majority of studies were multicentre studies and included data collected from several European hospitals including Irish hospitals. This suggests the findings of this review are generalisable to the context of the NCEC National Clinical Guideline for HCAI in all healthcare settings. However, heterogeneity in strategies and variations in baseline adherence rates suggests the extent of the effect may be reduced in certain Irish contexts.

3.4.2   Strengths and limitations of this review

Strengths of this systematic review include the comprehensive search strategy based on an earlier review, the addition of economic evidence and the inclusion of meta-analyses.

A limitation of this systematic review would be the restriction to RCTs and therefore, the exclusion of available data. However, limiting the analysis to RCTs removes the inherent biases present in other study designs and has led to a greater certainty in the evidence. In addition, a 2019 systematic review[91] which included 25 non-RCT design studies aligns with the findings of this review, that a WHO Compliant strategy, when implemented correctly, is effective at improving HH adherence.

3.4.3   Future research

Further research should focus on large long term studies with robust designs to investigate whether the improvement in HH adherence rates leads to improvements in HCAI and colonisation rates and whether these effects are prolonged over greater time periods. Additionally, future research could investigate which interventions are more cost-effective in situations of high baseline adherence rates.

3.4.4 Conclusion

The findings from the 17 included clinical studies which looked at interventions to improve hand hygiene adherence in healthcare workers is of very low to low certainty overall. The findings show a consistent trend suggesting that implementation of any intervention will result in some improvement in hand hygiene adherence. Implementing a multimodal approach, especially one informed by the WHO framework, will likely result in improvements compared with usual care. The evidence is less clear on whether including additional components beyond those in the WHO will lead to additional improvements. From the review of economic studies included, implementing the WHO framework is likely to be cost-effective or cost-saving, if improvements in HCAIs can be realised.

4 Review question two: Effectiveness of single patient rooms in reducing the incidence of healthcare-associated infection

This chapter summarises the available evidence on the clinical- and cost-effectiveness of single patient rooms (SPRs) accommodation compared with multi-bed rooms (MBRs) accommodation at reducing the incidence of healthcare-associated infections (HCAIs). The following research question was addressed:

- In acute hospital inpatients, does the use of all SPR accommodation compared with the use of MBRs or mixed SPRs and MBRs accommodation result in reduced incidence of HCAIs?

4.1 Search results

The search strategy identified 3,155 potentially relevant records. After removing duplicates, 2,314 records were screened, with 2,271 references excluded based on titles and abstracts. Of the 43 full-text articles assessed for eligibility, 33 articles were excluded according to the inclusion and exclusion criteria, as outlined in Sections 2.1. A list of excluded studies is available in Appendix 3: Excluded studies.

This resulted in 10 articles identified for inclusion in this review.[96-105] Three articles[100, 101, 103] reported findings relating to the same dataset and are considered as one study in this review. This study is, from here forth, referred to by the earliest publication.[101] Thus, there are eight unique studies in this systematic review. Seven studies investigated clinical-effectiveness,[96, 98, 99, 102, 104, 105] with one of these also investigating the economic impact[101] while one additional study conducted an economic cost-benefit analysis only.[97] The PRISMA flow chart outlining the search process is depicted in Figure 8.

Figure 8 Review question two: PRISMA flowchart – Effectiveness of single patient rooms in reducing incidence of HCAIs

Identification

Records identified through database searching (1 July 2004 to 22 October 2019)
n=3,155

Records identified through searching reference lists
n=0

Duplicates removed
n=841

Screening

Records screened
n=2,314

Records excluded
n=2,271

Eligibility

Full-text articles assessed for eligibility
n=43

Excluded articles (n=33):
- Irrelevant intervention (n=10)
- Irrelevant outcome (n=1)
- Irrelevant publication type (n=16)
- Irrelevant study design (n=6)

Included

Articles included n=10*

Unique studies included n=8

Studies with clinical evidence
n=7

Studies with economic evidence
n=2

* Three articles reported on a single study which investigated both clinical and economic outcomes. See section 4.1 for details.

4.2   Clinical evidence for review question two: Results

4.2.1   Characteristics of included studies

4.2.1.1   Study country

Of the seven clinical effectiveness studies, four were conducted in the UK,[99, 101, 104, 105] and one each in Australia,[98] Canada[102] and Denmark.[96] Three of the UK studies[99, 104, 105] were conducted at different periods in hospitals all within the same health board in Wales. See Table 4-1 for details on the characteristics of the included studies.

4.2.1.2   Study design

Two studies were interrupted time series (ITS) design, accounting for existing temporal trends (see section **Error! Reference source not found.**). One ITS study included two control hospitals and hospital group-level data,[101] while the other did not include a control hospital but included regional level data as a comparison.[102] Three studies were uncontrolled before-after studies.[96, 98, 104] The two remaining studies were cohort studies.[99, 105] The data was prospectively gathered for four of the studies[96, 99, 101, 105] with the remaining three studies[98, 102, 104] using retrospective data gathering methods.

4.2.1.3   Intervention and comparison groups

Five of the studies[96, 98, 101, 102, 104] took place during a hospital move where the old hospital site was used as the control group. Two studies[99, 105] compared a newly built hospital to an existing hospital in the same health board. All intervention settings consisted of 100% SPRs and control settings ranged from 0% to 65% SPR, depending on study and or ward. Four studies were conducted in single centres;[96, 98, 102, 104] two compared two hospitals,[99, 105] and one study compared three hospitals.[101]

4.2.1.4   Study population

The included study populations varied across the studies. Four studies restricted inclusion to target populations at a higher risk of adverse events which resulted in inclusion of patients with dementia,[99, 105] patients 75 years or older[96] and patients from orthopaedic wards only.[98] While three studies included patients from more general and mixed settings, which included all wards;[102] the acute assessment unit, older persons, and surgery

wards;[101] and general medical and care of the elderly wards.[104]

Table 4-1 Clinical evidence for question two: Characteristics of included studies

Author (year) Country Study design	Reported aim of study	Study period and duration	Intervention and comparison groups	Participants and type of wards	Outcome(s)
Interrupted time series analysis studies					
Maben (2015)[101] UK Prospective	To identify the impact of the move to a newly built acute NHS hospital in England with 100% SPRs on patient safety and costs.	36 months (Jan 2010 to Dec 2012) 36 monthly time points, 21 before and 15 after	Move to a new hospital Intervention: New 100% SPR hospital Control: Old 100% MBR hospital, as well as 1 steady state hospital (90% MBR), 1 hospital undergoing renovations (increased proportion of SPRs from 14% to 38%), national level data from the NHS, and trust level data from local NHS Trust.	All patients (n=67,258) from 3 matched wards from each hospital: acute admissions unit, older persons ward, and surgical wards.	HCAIs incidence: ▪ *C. difficile* ▪ MRSA Adverse events: ▪ Falls ▪ Medication errors
McDonald (2019)[102] Canada Retrospective	To examine the outcome of changing from a hospital design of multiple occupancy rooms to 100% SPR on the incidence of HCAI incidence.	63 months (2013 to 2019) 63 monthly time points, 27 before and 36 after.	Move to a new hospital Intervention: New 100% SPR hospital Control: Old 35 to 80% MBR hospital (depending on ward)	General and specialised patients from all wards (n=49,944). Number of wards not reported.	HCAIs incidence: ▪ *C. difficile* ▪ MRSA ▪ VRE HCAI Colonisations: ▪ MRSA ▪ VRE
Uncontrolled Before-after studies					
Blandford (2019) [96] Denmark Prospective	To investigate the risk of delirium among patients ≥ 75 years admitted to a geriatric department in relation to SPR versus MBR.	15 months (Sep 2016 to Dec 2017) Before: 6 months After: 9 months	Move to a new hospital Intervention: New 100% SPR hospital Control: Old 89% MBR hospital.	Patients ≥75 years old from 2 geriatrics wards before (n=461) and 2 after (n=553).	Adverse events: ▪ Risk of delirium ▪ Time to recovery from a patient's first delirium episode
Davis (2019)[98] Australia	To evaluate the impact of a new inpatient single-room	15 months (date not reported)	Hospital move Intervention: New 100% SPR	All patients from orthopaedic ward (819 patients before and 750 patients across 28 SPRs after).	HCAIs Incidence: ▪ MRSA Adverse events:

Author (year) Country Study design	Reported aim of study	Study period and duration	Intervention and comparison groups	Participants and type of wards	Outcome(s)
Retrospective	orthopaedic ward on patient outcomes.	Before: 6 months Washout: 3 months After: 6 months	hospital Control: Old 100% MBR hospital.	Number of wards before move not reported.	▪ Pressure ulcer ▪ Falls ▪ Unwitnessed falls ▪ Medical calls
Singh (2015)[104] UK Retrospective	To compare the outcome of inpatient falls occurring in units with 100% SPR and MBR wards.	36 months (May 2010 to Apr 2013) Before: 18 months After: 18 months	Move to a new hospital Intervention: New 100% SPR hospital Control: Old mostly MBR hospital building (% not reported).	Patients from 2 wards from before (123 beds and 61,330 bed days) and after move (144 beds and 59,340 bed days): general medical and care of the elderly wards.	Adverse events: ▪ Falls ▪ Mortality ▪ Hip fractures
Cohort studies					
Knight (2016)[99] UK Prospective	To investigate the incidence and outcome of inpatient falls prospectively in patients with dementia treated in SPR compared with MBR.	2 months (May and June 2015) Intervention: 2 months Control: 2 months	Hospital comparison Intervention: New 100% SPR hospital Control: Older 100% MBR hospital from the same health board.	50 consecutive patients per hospital with known dementia admitted with acute illness from any ward. Number of wards not reported.	Adverse events: ▪ Falls ▪ Injuries ▪ Hip fractures ▪ Mortality (inpatient, 30 day)
Young (2017)[105] UK Prospective	To profile and compare the clinical outcomes of acutely unwell patients with dementia admitted to 2 different hospital environments (SPR versus MBR).	3 months (May to July 2016) Intervention: 3 months Control: 3 months	Hospital comparison Intervention: New 100% SPR local general hospital Control: Older 100% MBR district general hospital from the same health board.	50 older patients per hospital with diagnosed dementia admitted for acute illness.	Adverse events: ▪ Falls ▪ Mortality ▪ Fractures

Key: *C. difficile - Clostridioides difficile*; ITS - interrupted time series; MBR - multi-bed room; MRSA - methicillin-resistant *Staphylococcus aureus*; SPR - single patient room; VRE - vancomycin-resistant *enterococcus*.

4.2.2 Clinical evidence: Primary outcome – reduction in HCAI

Three studies investigated the impact of SPRs on the incidence rate of HCAIs.[98, 101, 102] These can be seen in Table 4-2 .

Three studies reported results from analysis on methicillin-resistant *Staphylococcus aureus* (MRSA) infections in SPRs compared to MBRs. Two found no significant difference in the number of infections (SPR versus MBR: 0 of out 750 patients versus 3 out of 819 patients; p=0.25)[98] or in the incidence rate ratio (IRR 0.89, 95% CI: 0.34 to 2.29) when SPR was compared to MBR settings.[102] The third study reported just one MRSA case over the 36 months, which was insufficient for analysis.[101]

Two of the studies reported on *C. difficile* infections.[101, 102] The first study found a significant increase in one SPR ward (older persons ward) and no significant change in the other two SPR wards, when compared to the MRB wards in the old hospital before the hospital move.[101] However, the authors reported the length of stay decreased from 37 to 20 days and the mean Charlson index of diagnoses score decreased significantly in the older person's ward, which suggested a substantial change in case-mix. This was reported as problematic when attributing the changes in *C. difficile* infections to the intervention. Changes in infection rates in two non-equivalent control hospitals were also investigated with no significant change detected in *C. difficile* infections over the study period. While at a national level, there was a 56% reduction in *C. difficile* infections over the same period.[101] The second study found no significant change in infection rates (IRR 0.95, 95% CI: 0.51 to 1.76) between SPR and MRB design.[102]

One study investigated the number of vancomycin-resistant *Enterococcus* (VRE) infections, reporting an immediate reduction in infections after the move to a 100% SPR hospital design (IRR 0.30, 95% CI: 0.12 to 0.75) which did not significantly change again for the 36 months following the move (IRR 0.95, 95% CI: 0.88 to 1.00).[102]

Table 4-2 Clinical evidence for question two: Primary outcome results relating to reduction in HCAI rates

Author (year) Study design	Analysis	Outcome(s)
Davis (2019)[98] Before-after	Unadjusted analysis.	Primary outcome (SPR versus MBR) **MRSA infections:** 0 cases out of 750 patients versus 3 cases out of 819 patients; p=0.25

Author (year) Study design	Analysis	Outcome(s)
study Orthopaedic ward move to new hospital		
Maben (2015)[101] ITS study Move to a new hospital	36 monthly data collection points (20 before and 16 after). Five study groups in total: intervention hospital, new build control hospital, steady state control, national level data from the NHS, and trust level data from local NHS Trust. Interrupted time-series analysis augmented by statistical process control charts using volume-standardised rates to identify special-cause variations = 1) 1 data point outside the confidence limits or 2) 8 or more data points above the centre line. Wards were matched for age, length of stay and the percentage of diagnosis included in the Charlson Comorbidity Index.	Primary outcomes (intervention hospital) **MRSA infections:** Insufficient data - 1 case documented for the entire study period. *C. difficile* **infections:** Increase in older persons ward only (1 of 3 study wards). Demonstrated by a special-cause variation in the time series analysed. Primary outcomes (new build control hospital) **MRSA infections:** Insufficient events for analysis *C. difficile* **infections:** No increase in any ward (0 of 3 study wards). No special-cause variation in time series analysed was demonstrated. Primary outcomes (steady state control hospital) **MRSA infections:** Insufficient events for analysis. *C. difficile* **infections:** No increase in any ward (0 of 3 study wards). No special-cause variation in time series analysed was demonstrated. Primary outcomes (NHS Trust - trust level data) **MRSA infections:** Not reported. *C. difficile* **infections:** Not reported. Primary outcomes (NHS England - national level data) **MRSA infections:** Decrease from 279 cases (before move) to 92 cases (after move). *C. difficile* **infections:** Decreased from 3,489 (before move) to 1,525 (after move), which represents a 56% reduction over the entire study period.
McDonald (2019)[102] ITS study Move to a new hospital	62 data collection points (26 before and 36 after). Poisson regression models with volume-standardised rates per 10,000 patient-days. Results are reported as IRRs comparing consecutive times with 95% CIs. Regional trend data were used to control	Primary outcomes (SPR versus MBR) **MRSA infections:** 1.2 per 10,000 patient-days (0.8 to 1.6) versus 1.2 per 10,000 patient-days (0.8 to 1.8) Trend over 26 months before move: IRR 0.98 (95% CI: 0.94 to 1.03) – not statistically significant Immediate level change following move: IRR 0.89 (95% CI: 0.34 to 2.29) – not statistically significant Trend over 36 months after move: IRR 1.02 (95% CI: 0.97 to 1.07) – not statistically significant *C. difficile* **infections:** 7.0 per 10,000 patient-days (6.1 to 8.0) versus 10.8 per 10,000 patient-days (9.5 to 12.2) Trend over 26 months before move: IRR 0.99 (95% CI: 0.97 to 1.01) – not statistically significant Immediate level change following move: IRR 0.95 (95% CI: 0.51 to 1.76) – not statistically significant

Author (year) Study design	Analysis	Outcome(s)
	for the underlying regional temporal trends for *C. difficile* and VRE. For MRSA, community acquired infection data was used.	Trend over 36 months after move: IRR 1.00 (95% CI: 0.98 to 1.02) – not statistically significant **VRE infections**: 0.4 per 10,000 patient-days (0.2 to 0.7) versus 2.5 per 10,000 patient-days (1.9 to 3.3) Trend over 26 months before move: IRR 1.01 (95% CI: 0.98 to 1.04) – not statistically significant Immediate level change following move: IRR 0.30 (95% CI: 0.12 to 0.75) – statistically significant Trend over 36 months after move: IRR 0.95 (95% CI: 0.88 to 1.00) – not statistically significant

Key: *C. difficile* - *Clostridioides difficile*; IRR - incidence rate ratio; ITS – interrupted time series; MRSA - methicillin-resistant *Staphylococcus aureus*; VRE - vancomycin-resistant enterococci.

4.2.3   Clinical evidence: Primary outcome – adverse events

Six studies investigated the impact of SPRs compared with MBRs on adverse events.[96, 98, 99, 101, 104, 105] Most studies included multiple adverse events and these varied between studies. Outcomes reported were falls (n=5),[98, 99, 101, 104, 105] fractures (n=3),[99, 104, 105] mortality (n=3),[99, 104, 105] pressure injuries (n=2),[98, 101] delirium (n=1),[96] medical deterioration calls (n=1)[98] and medical errors (n=1).[101] See Table 4-3 for all results.

Five studies reported analysis relating to hospital-associated falls,[98, 99, 101, 104, 105] with three of these studies including results relating to fractures.[99, 104, 105] Maben et al.[101] conducted a time series analysis and found an immediate increase in reported falls following the move to SPRs in two of the three study wards (older persons ward and acute assessment unit) when compared with the period before the move. However, this was not sustained with fall rates decreasing to the previous levels after seven to nine months. As noted previously, the older person's ward recorded a decrease in length of stay as well an increase in the proportion of orthopaedic trauma patients (orthopaedics/trauma HRG subgroup) from 4.6% to 24.8%, suggesting a substantial change in the ward case-mix. Additionally, of the two non-equivalent control hospitals, one experienced a decrease, and the other remained the same. While the hospital group-level data showed an increase of 65% during the same time period which was reported to coincide with overall increase in patients at risk of falls accessing services during that period. Singh et al.[104] conducted an adjusted analysis, controlling for age and sex, and reported 10.32 additional falls per 1,000 patient-bed days in the SPR unit compared with the MBR unit (p<0.01). A statistically significant increase in number of falls per faller (2.33 versus 1.66; p<0.001) and hip fractures (0.04 versus 0.15;

p<0.01) were also reported in the SPR unit compared to the MBR unit. Three studies[98, 99, 105] conducted unadjusted analyses, with two of the studies reporting no significant increase in rate of falls,[98, 105] unwitnessed falls,[98] patients that fell[105] or number of fractures[105] when the SPR groups were compared with MBR groups. The remaining study reported the number of patients who sustained an inpatient fall at the two sites was similar (p=0.83), however, there was a significantly higher number of falls per person, 3.4 (± 2.75) in SPR compared with 1.5 (± 0.83) in MBR, p=0.03.[99] Number of days until first fall was not significantly different (p=0.89). The authors also measured the impact of falls, reporting there was no significant difference between the two designs in the number of minor injuries (p=0.65), major injuries (p>0.95) or hip fractures (p>0.95).

Three studies investigated mortality.[99, 104, 105] All three conducted unadjusted analysis and all reported no significant increase in inpatient mortality,[105] 30-day[99, 104] and one-year mortality[99, 104] when SPRs were compared with MBRs.

Two studies reported findings relating to hospital associated pressure injuries.[98, 101] Maben et al.[101] conducted a time series analysis and reported no increase in pressure ulcers in any of the SPR wards compared to MBR wards. While Davis et al.[98] conducted an unadjusted analysis and demonstrated a higher number of pressure injuries in SPR compared to MBR, however this was not statistically significant (2.5% versus 1.6%; p=0.24).

One study by Blandford et al.[96] investigated the risk of delirium among older patients admitted to a geriatric department following a move to SPRs with data collection consisting of six months in MBRs before the move and nine months in SPRs after the move.[96] After adjusting for age, comorbidity, housing conditions, prior diagnosis of dementia, systemic inflammatory response syndrome criteria and main diagnosis, the risk of developing delirium was lower in the SPR wards when compared with MBR wards (HR 0.66, 95% CI: 0.48 to 0.93; p=0.02) while the time to the first instance of delirium was not significantly different (HR 1.06, 95% CI: 0.86 to 1.32; p=0.57).

One study investigated medical errors using time series analysis in three wards.[101] Maben et al. reported an increase in medical errors in one of the study wards in the intervention hospital immediately following the move. However, this increase was temporary and

returned to before move levels after 7 to 9 months. No change in trends of medical errors were demonstrated in any of the control hospitals.

One study reported results from an unadjusted analysis which demonstrated a higher number of medical deterioration calls in the SPR ward when compared with the MBR ward (77 calls from 750 patients versus 178 calls from 819 patients; test for statistical significance not performed).[98]

Table 4-3 Clinical evidence for question two: Primary outcome - adverse events

Author (year)	Analysis	Outcome(s)
Blandford (2019)[96] Prospective cohort study Geriatric department moved to a new hospital	Cox regression model - adjusted for age, comorbidity, housing conditions, prior diagnosis of dementia, systemic inflammatory response syndrome criteria and main diagnosis.	SPR versus MBR **Developing delirium (adjusted)**: aHR = 0.66 (95% CI: 0.48 to 0.93; p=0.02) **Time to first instance of delirium (adjusted)**: aHR = 1.06 (95% CI: 0.86 to 1.32; p=0.57) **Cumulative incidence of delirium in the first 14 days**: 16% versus 29%
Davis (2019)[98] Before-after study Orthopaedic ward move to new hospital	Unadjusted analysis. Tests of statistical significance were conducted for most of the outcomes.	SPR versus MBR **Falls:** 14/750 (1.9%) patients versus 19/819 (2.3%) patients; p=0.60 **Unwitnessed falls:** 9/14 (64%) falls versus 16/19 (84%) falls; p=0.49 **Pressure injuries:** 19/750 (2.5%) patients versus 13/819 (1.6%) patients; p=0.24 **Medical deterioration calls:** 77/750 (10%) versus 178/819 (22%); test for statistical significance not performed.
Knight (2016)[99] Prospective cohort study New general hospital compared to an older existing hospital	Unadjusted analysis. Test of statistical significance were conducted for most of the outcomes.	SPR versus MBR **Total falls:** 53 versus 23; test for statistical significance not performed **Proportion of patients who fell:** 32% versus 30%; p=0.83 **Number of falls per faller:** 3.4 (± 2.75) versus 1.5 (± 0.83); p=0.04 **Proportion of falls with no injury:** 62.2% versus 65.2% **Number of days to first fall:** 12 (SD 18.6) versus 11.4 (SD 12.4); p=0.89 **Minor injury per fall:** 19/53 (35.8%) versus 7/23 (30.4%); p=0.65 **Major injury per fall:** 0 versus 0; p>0.95 **Hip fracture per fall:** 1/53 versus 1/23; p>0.95 **Mortality (inpatient):** 0 versus 0; p>0.95 **Mortality (30 day post discharge):** 0/16 versus 1/15; p=0.33
Maben (2015)[101] ITS study	36 monthly data collection points (20 before and 16 after).	SPR versus MBR (Intervention hospital) **Falls:** Increase in older persons ward and acute assessment unit (2 of 3 study wards). Demonstrated by a special-cause variation in the time series analysed.

Author (year)	Analysis	Outcome(s)
Move to a new hospital with 3 control groups	Interrupted time-series analysis augmented by statistical process control charts using volume-standardised rates to identify special-cause variations = 1) one data point outside the confidence limits or 2) 8 or more data points above the centre line. Wards were matched for age, length of stay and the percentage of diagnosis included in the Charlson Comorbidity Index.	This increase was temporary and returned to before move levels after 7 to 9 months. **Medical errors:** Increase in acute assessment unit (1 of 3 study wards). Demonstrated by a special-cause variation in the time series analysed. This increase was temporary and returned to before move levels after 7 to 9 months. **Pressure ulcers:** Increase in older persons ward only (1 of 3 study wards). Demonstrated by a special-cause variation in the time series analysed.
		Trend over study period (new build control hospital) **Falls:** No increase in any ward (0 of 3 study wards). No special-cause variation demonstrated in time series analysis. **Medical errors:** No increase in any ward (0 of 3 study wards). No special-cause variation demonstrated in time series analysis. **Pressure ulcers:** No increase in any ward (0 of 3 study wards). No special-cause variation demonstrated in time series analysis.
		Trend over study period (steady state control hospital) **Falls:** Decrease in older persons ward and acute assessment unit (2 of 3 study wards). Demonstrated by a special-cause variation in the time series analysis **Medical errors:** No increase in any ward (0 of 3 study wards). No special-cause variation demonstrated in time series analysis. **Pressure ulcers:** No increase in any ward (0 of 3 study wards). No special-cause variation demonstrated in time series analysis.
		Trend over time (NHS Trust - hospital group level data) **Falls (per 1,000 bed-days):** increased by 65% from 4.74 in Apr 2011 (MBR) to 7.84 falls in Sept 2013 (SPR), which coincides with overall increase of patients at risk of falls at Trust-level (correlation = 0.68) **Medical errors:** Not reported **Pressure ulcers:** Not reported
		Trend over study period (NHS England - national level data) **Falls:** Not reported **Medical errors:** Not reported **Pressure ulcers**: Not reported
Singh (2015)[104] Retrospective uncontrolled before-after	Age and sex adjusted mean falls per 1,000 patient-bed days. Other analyses unadjusted. Test of statistical significance were conducted for most of the outcomes.	SPR versus MBR **Falls per 1,000 patient-bed days (adjusted):** 15.83 (95% CI: 14.43 to 17.4) versus 5.51 (95% CI 3.34 to 7.68); p<0.01 **Falls per patient (unadjusted):** 1,244/535 versus 374/224 **Number of falls per faller (adjusted):** 2.33 (± 2.87) versus 1.66 (± 1.46); p<0.001 **Hip fractures (adjusted):** 0.15 (± 1) versus 0.04 (± 0.38); p<0.01 **Mortality (inpatient):** 16.1% (36/224) versus 19.1% (102/535); p=0.35 **Mortality (30 days):** 5.8% (11/188) versus 8.3% (36/433); p=0.29

Author (year)	Analysis	Outcome(s)
		Mortality (1 year): 41.1% versus 47.1%; p=0.12
Young (2017)[105] Prospective cohort study	Unadjusted analysis. Test of statistical significance were conducted for most of the outcomes.	SPR versus MBR **Falls:** 12 versus 8; p=0.18 **Patients who fell:** 6/43 (14%) versus 6/46 (13%); p=0.57 **Fractures:** No fractures occurred in either group **Inpatient mortality:** 4/43 (9%) versus 9/46 (20%); p=0.13

Key: aHR – adjusted hazard ratio; MBR – multi-bed room; NHS – National Health Service UK; SPR – single patient room

4.2.4   Clinical evidence: Secondary outcome – reduction in AMRO colonisation

One study investigated the impact of SPRs on colonisation rates by MRSA and VRE.[102] Statistically significant reductions were demonstrated for MRSA (IRR 0.57, 95% CI: 0.33 to 0.96) and for VRE (IRR 0.25, 95% CI: 0.19 to 0.34) colonisation rates immediately following the move to a new hospital. The rates did not significantly change from the lower level during the 36 months following the move for both MRSA (IRR 1.01, 95% CI: 0.98 to 1.04) and VRE (IRR 1.01, 95% CI: 1.00 to 1.03). See Table 4-4.

Table 4-4 Clinical evidence for question two: Secondary outcomes - HCAI colonisation

Author (year) Study design	Analysis	Outcome(s)
McDonald (2019)[102] ITS study Move to a new hospital	62 data collection points (26 before and 36 after) Poisson regression models with volume-standardised rates per 10,000 patient-days. Results are reported as IRRs comparing consecutive times with 95% CIs. Regional trend data were used to control for the underlying regional temporal trends for VRE infection rates. For MRSA, community acquired infection data was used.	SPR versus MBR **Mean MRSA colonisations per 10,000 patient-days:** 3.5 (95% CI: 2.9 to 4.2) versus 5.9 (95% CI: 4.9 to 7.0) Temporal trends of MRSA colonisation over three time periods: Trend over 26 months before the move: IRR 1.01 (95% CI: 1.00 to 1.03) Trend immediately following the move: IRR 0.57 (95% CI: 0.33 to 0.96) Trend over 36 month period after the move: IRR 1.01 (95% CI: 0.98 to 1.04) SPR versus MBR **Mean VRE colonisation per 10,000 patient-days:** 6.6 (95% CI: 5.7 to 7.5) versus 35.0 (95% CI: 32.6 to 37.6) Temporal trends over three time periods: Trend over 26 months before the move (26 months): IRR 0.99 (95% CI: 0.98 to 1.0) Trend immediately following the move: IRR 0.25 (95% CI: 0.19 to 0.34) Trend over 36 month period after the move: IRR 1.01 (95% CI: 1.00 to 1.03)

Key: IRR - incidence rate ratio; ITS – interrupted time series; MRSA - methicillin-resistant *Staphylococcus*

aureus; VRE - vancomycin-resistant *enterococci*.

4.2.5   Methodological quality of included studies

The Cochrane EPOC risk of bias tool[25] was used to appraise the methodological quality of the included ITS studies and the Newcastle-Ottawa Scale[29] was used for the before-after and cohort studies.

4.2.5.1   Interrupted time series studies

Following the guidelines of the Cochrane EPOC risk of bias tool the two included ITS studies were rated across seven domains (see Figure 9 and Figure 10).[101, 102]

Figure 9 Clinical evidence for review question two: Cochrane EPOC risk of bias summary graph for Interrupted time series studies
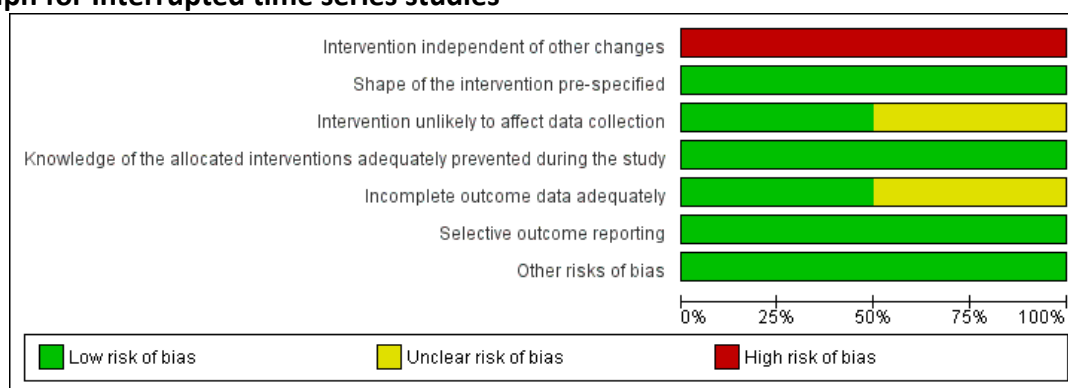
Intervention independent of other changes

Both studies[101, 102] were at a high risk of bias. There were changes in case mix, caseload, ward sizes and staffing levels which could have impacted rates of HCAI and adverse events and these were not controlled for in the analysis. In addition to ongoing quality improvement efforts in the study hospital, such as improving hand hygiene and increasing the number of alcohol rinse dispensers, one of these studies[102] reported introducing new infection prevention policies following the move. This included using hydrogen peroxide vapour during room discharge in local outbreaks of *C. difficile* infection or VRE infection, and contact isolation in SPRs.

Shape of the intervention pre-specified

The two studies were at a low risk of bias as the periods before and after the move were clearly defined.

Intervention unlikely to affect data collection

One study[102] was at a low risk of bias while the other[101] was at an unclear risk of bias due

to a lack of a standard approach to gather incidence data across the four included hospitals and regional surveillance data.

Knowledge of the allocated interventions adequately prevented during the study

Both studies were at a low risk of bias due to the nature of the intervention; knowledge was unlikely to bias the outcome measures.

Incomplete outcome data

One study[101] was at a low risk of bias as the methods used for managing missing data were reported and were deemed appropriate. While for the other study the risk of bias was unclear due to not reporting necessary details to allow an assessment.[102]

Selective outcome reporting

Both studies were at a low risk of bias for selective outcome reporting.

Other bias

No other risks of bias were identified in either study.

Figure 10 Clinical evidence for review question two: Cochrane EPOC risk of bias study specific graph for Interrupted time series studies

4.2.5.2   Cohort and before-after studies

Following the guidelines of the Newcastle-Ottawa Scale quality appraisal tool,[29] we assessed the quality of three cohort studies[96, 99, 105] and two uncontrolled before-after studies[98, 104] across three domains (see Table 4-5 for a summary of risks of bias). Overall, three studies[96, 99, 104] were classified as good quality, one study[98] as fair quality and one study[105] as poor quality.

Selection

There were concerns about four of the five studies relating to the generalisability of the study populations to adult patients based in hospital inpatient wards in acute settings.[96, 98, 99, 105] This was due to the narrow inclusion criteria aimed at targeting elderly patients,[96, 105] patients with dementia[99, 105] or orthopaedic patients.[98] In addition, two studies[98, 104] which evaluated inpatient falls did not measure for prior history of falls which may have introduced selection bias.

Comparability

There were concerns about three studies relating to comparability of the intervention and control groups.[98, 99, 105] One of the studies did not control for comparability at design stage and significant differences existed relating to the place of original residency which may have resulted in selection bias.[105] While three studies did not control for age and either case mix or comorbidity in their analysis.[98, 99, 105]

Outcome

There were concerns about three studies relating to outcome measurement.[96, 98, 99] The first study[98] relied on data collection, which although prospectively gathered, was unblinded. The second study[99] reported a lack of rigorous collection of falls data in the control hospital compared to the intervention hospital. In comparison, the third study[98] did not make any statement or reference to allow assessment of the completeness of data.

Table 4-5 Clinical evidence for review question two: Summary of the Newcastle-Ottawa Scale risk of bias scores for cohort and before-after studies

Study	Selection				Comparability		Outcome			Overall
	Exposed cohort representative	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at beginning	Comparability of cohorts in design phase	Comparability of cohorts in analysis phase^	Assessment of outcome	Follow-up sufficient for outcome to occur	Adequate follow-up	Total stars (Quality)
Blandfort (2019)[96]	Over 75 years	☆	☆	☆	☆	☆	Prospective and not blinded.	☆	☆	7 stars (Good)
Davis (2019)[98]	Orthopaedic patients.	☆	☆	History of falls on admission was not measured.	☆	Did not adjust for age, case mix or comorbidity.	☆	☆	No statement.	5 stars (Fair)
Knight (2016)[99]	Patients with known dementia.	☆	☆	☆	☆	Did not adjust for age, case mix or comorbidity.	Reported a lack of rigorous collection of falls data in MBR group.	☆	☆	6 stars (Good)
Singh (2015)[104]	☆	☆	☆	History of falls on admission was not measured.	☆	☆	☆	☆	☆	8 stars (Good)
Young (2017)[105]	Older patients with diagnosed dementia.	☆	☆	☆	Significant difference at baseline for place of original residence.	Did not adjust for age, case mix or comorbidity.	☆	☆	☆	6 stars (Poor)

^Star given if study controlled for or adjusted for at least age, case mix or comorbidity.

Note: When no star allocated rationale is presented.

Good quality: 3 or 4 stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes.

Fair quality: 2 stars in selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes.

Poor quality: 0 or 1 star(s) in selection, or 0 stars in comparability, or 0 or 1 star(s) in outcomes.

4.2.6   Certainty of the evidence

We assessed the overall certainty of the evidence for question two of the review (*Does the use of all SPR accommodation for acute hospital inpatients compared with use of MBRs or mixed SPRs and MBRs result in reduced incidence of HCAIs?*). A narrative summary of findings table was created for the following primary outcomes: HCAI infection rates (Table 4-6) and adverse events (Table 4-7). According to the GRADE approach, observational studies should initially be graded as low-quality evidence due to the inherent limitations in their study design, while RCTs should be graded as high quality.[106] Both study designs can then be adjusted up or down according to other factors, including risk of bias and imprecision.

Overall the certainty of the evidence is 'very low' owing to a high risk of bias in the various study designs, a high risk of confounding in the observational studies and lack of adjustment and or control at the design and or analysis phase, as well as a high risk of bias due to the intervention not being independent of changes and imprecision.

Table 4-6 Clinical evidence for review question two: Grade summary of findings table for reduction of HCAI in single patient rooms compared with multi-bed rooms

Patient or population: adult patients based in inpatient wards
Setting: acute settings (hospitals)
Intervention: single patient room accommodation with en suite facilities

Comparison: multi-bed room accommodation or a mix of multi-bed and single patient room accommodation
Outcome: healthcare-associated infection

Outcome	Impact	Nº of participants (studies) Setting	Certainty of the evidence (GRADE)
Methicillin-resistant *Staphylococcus aureus* (MRSA) infections	2 studies - no difference: ▪ 0/750 patients vs 3/819 patients; p=0.25 ▪ IRR 0.89, 95% CI: 0.34 to 2.29 1 study lacked sufficient data for analysis with only 1 case documented during study period.	118,771 2 ITS, 1 B-A 5 hospitals	⊕◯◯◯ VERY LOW a, b, c
Clostridioides difficile infections	1 study - an increase in 1 out of 3 wards (older persons ward) compared with no increase in 2 control hospitals. While hospital Trust data for the region demonstrated a reduction of 56% over study period. 1 study - no difference (IRR 0.95, 95% CI: 0.51 to 1.76).	117,202 2 ITS 4 hospitals	⊕◯◯◯ VERY LOW b, c
Vancomycin-resistant *Enterococcus* (VRE) infections	1 study - a decrease (IRR 0.30, 95% CI: 0.12 to 0.75)	49,944 1 ITS 1 hospital	⊕◯◯◯ VERY LOW b

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Downgraded once for serious risk of bias due to lack of adjustment and or control at design and or analysis phase for age and either case mix or comorbidity, b. Downgraded once for serious risk of bias due to intervention not being independent of changes, c. Downgraded once for imprecision

Key: *C. difficile - Clostridioides difficile*; B-A - Before-after study; IRR - incidence rate ratio; ITS – interrupted time series; MRSA - methicillin-resistant *Staphylococcus aureus*; VRE - vancomycin-resistant *enterococci*.

Table 4-7 Clinical evidence for review question two: Grade summary of findings table for reduction of adverse events for single patient rooms compared with multi-bed rooms

Patient or population: adult patients based in inpatient wards
Setting: acute settings
Intervention: single patient room accommodation with en suite facilities

Comparison: multi-bed room accommodation or a mix of multi-bed and single patient accommodation
Outcome: adverse events (psychological and physical harm)

Outcome	Impact	№ of participants (studies) Setting	Certainty of the evidence (GRADE)
Falls	2 studies - no statistically significant difference in falls. 1 study – an increase in 2 of 3 study wards, which was temporary and returned to before-move levels after 7 to 9 months. 1 study - an increase in (adjusting for age and sex) number of falls (15.83 vs. 5.51 per 1,000 patient-days; p<0.01), number of falls in the patients who fell (2.33 vs. 1.66 per 1,000 patient-days; p<0.001), number of hip fractures (0.15 vs. 0.04 per 1,000 patient-days; p<0.01). 1 study – the number of patients who sustained an inpatient fall at the 2 sites was similar (p=0.83), however, there was a significantly higher number of falls per person, 3.4 (± 2.75) in SPR compared with 1.5 (± 0.83) in MBR, p=0.03. Number of days to first fall was not significantly different (12 ± 18.6 days vs 11.4 ± 12.4 days; p=0.89).	69,775 1 ITS, 2 B-A, 2 Cohort 9 hospitals	⊕◯◯◯ VERY LOW a, b, c
Mortality	3 studies - no difference; inpatient mortality (3 studies), 30-day morality (2 studies) or 1-year mortality (1 study).	948 1 B-A, 2 Cohort 5 hospitals	⊕◯◯◯ VERY LOW a
Delirium	1 study - reduction in risk of developing delirium (HR = 0.66, 95% CI: 0.48 to 0.93; p=0.02) with no difference time to 1st instance of delirium (HR=1.06, 95% CI: 0.86 to 1.32; p=0.57).	1,014 1 B-A 1 hospital	⊕◯◯◯ VERY LOW a
Pressure injuries	1 study - an increase in pressure ulcers in 1 of 3 wards. 1 study - no significant difference (19 out of 750 vs. 13 out of 819 patients; p=0.243).	68,827 1 ITS, 1 B-A 4 hospitals	⊕◯◯◯ VERY LOW a, b, c
Medical errors	1 study - an increase in 1 of 3 study wards which was temporary and returned to before-move levels after 7 to 9 months.	67,258 1 ITS 3 hospitals	⊕◯◯◯ VERY LOW a, b, c

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Downgraded once for serious risk of bias due to lack of adjustment and or control at design and or analysis phase for case mix, comorbidity or age, b. Downgraded once for inconsistency, c. Downgraded once for serious risk of bias due to intervention not being independent of changes.

Key: *C. difficile - Clostridioides difficile*; B-A - Before-after study; IRR - incidence rate ratio; ITS – interrupted time series; MRSA - methicillin-resistant *Staphylococcus aureus*; VRE - vancomycin-resistant *enterococci*.

4.3   Economic evidence for review question two: Results

4.3.1   Characteristics of included studies

Two studies were identified that investigated the health economic impact of SPRs compared with MBRs. The first study by Boardman et al. was published in 2011,[97] the second by Maben et al. was first published as a comprehensive report in 2015 (index publication)[101] and later as a journal article in 2016.[100] Boardman et al. conducted a cost-benefit analysis (CBA) over 50 years of a life course of a hospital in Canada, including clinical benefits (adverse events) and hospital level benefits (a patient's willingness to pay for a SPR and shorter waiting times -as a direct result of fewer transfers and reduced noise). The CBA was developed as part of a business case for a proposed new hospital. Maben et al.[101] conducted a cost impact analysis as part of a larger evaluation following a hospital move. The cost impact analysis was informed by available real cost data from a UK before-after study, reported in 4.2, also conducted as part of the evaluation. This cost impact analysis included a model, which extrapolated the costs over a 60-year life cycle of a hospital, but did not include any benefits in the analysis. A summary of the characteristics, methods and results of the included studies is presented in Table 4-8.

Both studies investigated the costs associated with similar-sized 100% SPRs hospitals (approximately 500-bed). Boardman et al.[97] compared this design with a hospital comprising 100% double occupancy rooms. While Maben et al.[101] used two comparators, 50% SPRs and 50% MBRs design for their model-based analysis and 100% MBRs design for the before-after study.

Table 4-8 Economic evidence for review question two: Interventions and comparators included in economic studies

Study (year), country	Population	Intervention	Comparator
Boardman (2011),[97] Canada Cost-benefit analysis	Patients from 537-bed acute care hospital in Vancouver	100% SPR	100% semi-private (double occupancy) rooms
Maben (2015),[101] UK 1) B-A study analysis 2) Model analysis (cost extrapolation over life cycle of the hospital)	1) Patients in AAU, older person and surgical ward in a general 500-bed UK hospital	1)100% SPR (30 bed wards) 2) 100% SPR (28 bed wards)	1) 100% MBR 2) 50% MBR

	2) Patients in a general 500-bed UK hospital		

Key: AAU- Acute assessment unit; SPR – single-patient room, MBR – multi-bed room, B-A – before and after

4.3.2 Economic evidence

Following the methods outlined in Section 2.5.4, all costs are presented as they were in the original studies with the adjusted 2018 Irish euro equivalent presented in parentheses. Mabel et al. did not report the cost year so it was assumed that the unit costs were from three years prior to study publication.[101]

The economic evidence is summarised under the following headings; capital costs (land, construction and maintenance), operational costs (care staff, housekeeping and food service), and cost savings for HCAIs and adverse events prevented. Results are discussed narratively and presented in Table 4-9.

4.3.2.1 Economic evidence: Capital costs

Capital costs, including land, construction and estate-related maintenance costs relating to SPR design, were estimated by both studies to be higher than costs for MBR design. These estimates ranged from 5% for Mabel et al.[101] to 52% for Boardman et al.[97]

Boardman et al.[97] estimated that construction and land costs would be higher for a 100% SPR designed hospital compared to a hospital designed with all double-occupancy rooms. In addition to more space for en suite facilities in the patient bedroom, it was assumed that SPRs also require more corridor space, larger nursing areas and more janitorial facilities per patient bed. To estimate how much higher this would be over a service life of 50 years, the authors assumed that the new hospital design would follow best practices in Canada which recommends about 265 square feet (25 square metres) per patient bed in an SPR. After considering the space requirements of other areas in the hospital, it was estimated that an SPR would require 52% more space than a double-occupancy room (436 vs. 287 square feet (41 vs 27 square metres) per bed). To calculate the associated capital costs associated with an SPR designed hospital, the authors increased all land, construction and maintenance costs of a double occupancy room hospital by 52%.

For Maben et al,[101] the initial capital costs and facilities management costs associated with a 100% SPR hospital compared with a mixed accommodation hospital (50% SPR and 50%

MBR) were assumed to be 5% and 10% higher, respectively, based on data from the original business case made in 2004. This was modelled over an assumed hospital service life of 60 years and was estimated to result in a 0.7% and 1.4% increase in the full life-cycle costs of a hospital.

4.3.2.2   Economic evidence: Operational costs

Operational costs, including staff and cleaning costs, were reported by both studies. Boardman et al.[97] assumed, based on a 52% increase in floor space, the proportion of time spent visiting each patient or patient room by staff would also increase by 52%. This was used to extrapolate costs associated with additional nursing and physician resources and housekeeping (see Table 4-9 for all estimates).

Maben et al.[101] considered the operational costs associated with nurses, midwives and support staff and housekeeping costs. Based on data from the before-after study, staff costs increased in the SPR design by 2.7%. However, due to a planned increase in staff numbers, change in number of beds, the cost of staff time and change in the skills mix of staff, the authors deemed it impossible to attribute this to SPR design alone. Additionally, data from the before-after study demonstrated a 19.6% increase in the number of steps performed per hour by staff following the move to 100% SPR design from a 50% MBR design hospital. Based on administrative data from the relevant hospital Trust, which included data on the bed area, bathrooms and common areas, the total annual costs for cleaning a 500-bed all SPR hospital were estimated to be 18% higher (SPR: £7.88 (€10.41) per bed per day; MBR: £5.44 (€7.18)) when compared to a mixed accommodation hospital (50% SPR and 50% MBR). Based on interviews, it was estimated that it takes around 25 minutes to clean a bed space for an SPR design compared to around 10 minutes in a MBR design.

4.3.2.3   Economic evidence: Cost savings relating to HCAI

Neither study incorporated cost savings related to the effect of the intervention on HCAI rates into their analysis. Boardman et al.[97] conducted a literature review to inform their CBA and concluded there was insufficient evidence to include any impact of HCAIs in their final analysis. Costs associated with reduced *C. difficile*. infection rates were initially considered by Mabel et al.[101] for analysis, but estimates were not considered reliable due to confounding. Costs associated with falls were considered by Mabel et al.[101] but due to insufficient data on

these events, it was not possible to perform a full analysis.

4.3.2.4   Economic evidence: Cost savings relating to adverse events

Boardman et al.[97] did not include any adverse events in their primary analysis. However, adverse events were considered in an additional analysis. This analysis relied heavily on a number of assumptions. Based on a 2002 review,[107] which concluded that a good work environment may reduce medication errors, Boardman et al. calculated that SPRs may reduce the incidence of preventable adverse events by 1%. Additionally, using Canadian national hospital data on adverse events,[108] Boardman et al.[97] estimated that SPRs would avoid 0.002 deaths and 0.008 serious illnesses per bed per year compared to a double-occupancy room. Based on a selection of non-healthcare related articles, the value of a statistical life was valued as CA$4.54 million (€33,867,438) and a value of serious injury avoided was CA$300,000 (€223,794). Using these estimates, Boardman et al. calculated a SPR, in comparison to a double-occupancy room, might save CA$269,146 (€200,777) per bed over the full life cycle of the hospital which would result in a net benefit of $23,340 (€17,411) per bed over the full life cycle. Sensitivity analyses demonstrated that this finding was highly uncertain and may result in either a net cost or a net saving if their assumption on the probability of an adverse event deviated by plus or minus 0.5%. Additional hospital-level benefits were considered by Boardman et al. which related to a patient's willingness to pay extra for an SPR as a result of privacy and noise reduction, and also reduced patient transfers and waiting time (see Table 4-9 for all estimates).

Maben et al.[101] reported an annual cost of £3,483 (€4,600) for three wards (acute assessment unit, older person's ward and surgical ward) associated with additional falls for the SPR design hospital compared with the MBR design hospital, based on their B-A study. However, they reported that due to a number of confounders (such as changes in ward sizes and case-mixes) and insufficient data, there was no clear evidence that this change in cost was directly related to the SPR design.

4.3.2.5   Economic evidence: Overall findings

None of the included studies reported economic results relating to HCAI outcomes. Boardman et al.[97] reported that SPRs when compared with a bed in a double occupancy room, would result in a net benefit of $23,340 (€17,411) per bed over the full hospital life cycle based on

adverse events avoided. Sensitivity analyses reported by the authors demonstrated that this finding was highly uncertain and may result in either a net cost or net saving if their assumption on the probability of an adverse event deviated by plus or minus 0.5%. The second study[101] set out to assess the impact of SPR design following a move from a traditional NHS Trust hospital with 50% MBRs to a new 100% SPR design hospital. However, due to a number of confounders (such as staffing levels, approaches to catering which was centralised in the old hospital and decentralised in the new hospital, changes in ward sizes and case-mix) or insufficient data, the authors reported were unable to attribute any observed differences to the SPR design.

Table 4-9 Economic evidence for review question two: Results relating to capital costs, operational costs and cost savings

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results	Analysis of uncertainty
Boardman (2011),[97] Canada	**Population:** Patients from 537-bed acute care hospital **Intervention:** 100% SPR **Comparator:** 100% double occupancy rooms	**Analysis type:** CBA **Perspective:** Societal **Time horizon:** 50 years **Discount rate:** 3.5%	**Cost year & currency:** 2008 Canadian $ **Cost components:** SPR require additional 52% space compared with MBR (436 vs. 287 sq. ft. per bed). Land (extra $86.23 per buildable sq. ft.), construction (extra $442 per sq. ft.), maintenance (extra 1% of construction costs per year), housekeeping and operating (extra $2,461 per bed per year), staffing: nurses (extra $3,726 per bed year), doctors (extra $165 per bed year). **Clinical outcomes:** HCAIs (considered, but not included). Adverse events including deaths (valued at $4.54 million per life) and serious illness avoided (valued at $300,000 per serious illness). **Other hospital level outcomes:** Patient willingness to pay for a SPR versus double-occupancy room (extra $45 per day),	**Costs over the full life cycle:** Land: extra $10,714 per bed Construction: extra $65,858 per bed Maintenance: extra $15,447 per bed Housekeeping and operating: extra $57,736 per bed Nurses: extra $92,181 per bed Doctors: extra $3,870 per bed **Total additional cost per bed over the full life cycle was $245,806** **Clinical outcomes:** HCAI Not included. Adverse events The number of adverse events avoided per bed per year was assumed to be 0.002 deaths and 0.008 serious illnesses. This was estimated to result in a saving of approximately $11,475 per bed per year or $269,146 per bed over the full life cycle. **Net benefit in relation to clinical outcomes:** Saving $23,340 per bed over the full life cycle. **Additional hospital-level benefits:** Patients' willingness to pay for a SPR: $308,207 Reduced patient transfers: $6,314 Reduced waiting time: $1,011 **Total hospital level benefits per bed**: $315,532	**Probability of an adverse event is 0.5% lower:** Saving of $134,573 over the full life cycle. Compared to the baseline (net benefit $23,340 per bed), this would be less cost effective with a net cost of $111,233 per bed over the full life cycle. **Probability of an adverse event is 0.5% higher:** Saving of $403,719 over the full life cycle. Compared to the baseline (net benefit $23,340 per bed), this would be more cost-effective with a net saving of $157,913 per bed over the full life cycle. **Scenario analysis for other hospital level benefits:** Increased construction costs by 20%: $53,602 Increased floor space for SPR: $30,000

			reduced transfers (saving $269 per bed per year; 8.68 fewer transfers per bed per year), reduced waiting times (saving $43 per bed per year; 0.16 days per bed per year), noise, privacy.	**Net benefit in relation to hospital level benefits:** Saving $69,726 per bed over the full life cycle **Value for patient:** Decreasing noise: $17,570 per bed over the full life cycle	
Maben (2015)[101] UK Before-after study	**Population:** All patients in 3 wards (acute assessment unit, older person's ward and surgical ward) in a general 500-bed hospital **Intervention:** 100% SPR (30 bed wards) **Comparator:** 100% MBR	**Analysis type:** Cost impact study **Perspective:** Payer (NHS) **Time horizon:** 19 months before and after move **Discount rate:** None	**Cost year & currency:** £ (no year reported) **Costs:** Staffing: additional nursing WTE, walking time (considered, but not included) **Clinical outcomes:** HCAIs and falls	**Annual difference in operational costs per bed (nursing staff only):** Acute assessment unit: cost £2,712 more Older person's ward: cost £7,248 more Surgical ward: cost £792 more Total difference per bed per year: £5,328 more **Annual difference in costs per bed as a result of HCAIs (*C. difficile* only):** Acute assessment unit: cost £3,108 more Older person's ward: cost £275,388 more Surgical ward: save £802,644 Total difference per bed per year: £530,364 savings **Annual difference in costs per bed as a result of adverse outcomes (falls only):** Acute assessment unit: cost £835 more Older person's ward: cost £6,736 more Surgical ward: save £4,088 Total annual difference as a result of falls for the 3 study wards: £3,483 more	None.
Maben (2015)[101] UK Life cycle	**Population:** All patients in a general 500-bed hospital **Intervention:**	**Time horizon:** 60 years **Discount rate:** 3.5% for first 30 years; 3%	**Costs:** Building and maintenance costs (assumed 5% to 10% more), cleaning (SPR: £7.88 per bed per day; MBR: £5.44), catering (considered, but not included)	**Capital costs** Building: increase of 0.7% of the full life-cycle costs of the site Maintenance: increase of 1.4% of the full life-cycle costs of the site Cleaning: Increase of 18% for annual costs (£222,650)*	None

analysis	100% SPR	for next 30 years	**Clinical outcomes:** None	**Clinical outcomes:** HCAI Not included. Adverse events Not included.	
	Comparator: 50% SPR 50% MBR				

Key: HCAI – healthcare-associated infection; MBR – multi-bed room; NHS – National Health Service; SPR – single patient room; WTE - whole time equivalent; WTP - willingness to pay threshold

* Annual costs relating to cleaning was incorrectly calculated in the article and reported as 53% higher in Maben et al.[101] study (Table 59 in Maben report). This was recalculated for this review.

4.3.3 Methodological quality

A quality assessment of each study included in the systematic review was undertaken using the Consensus Health Economic Criteria (CHEC) list[87] and the outcomes are presented in Table 4-10. Based on the evaluation of the methodological quality of the two studies, Boardman et al.[97] was considered to be of moderate quality and Maben et al.[101] of low quality.

Limitations common to both included:

- Costs not being valued appropriately. Specifically in one study,[97] costs were based on questionable assumptions (particularly relating to how construction and land costs, maintenance and operational costs, including housekeeping, nursing and physician costs, which were estimated to be 52% higher for a SPR hospital when compared to a double occupancy room hospital, as 52% additional floor space was estimated to be required). Reduced waiting times, transfers and adverse events results were shown to be highly sensitive to assumptions made. Additionally, all assumptions were based on sources predating 2004. The other study[101] also used sources from varying years including construction costs from a 2004 business case for a new hospital and did not report the cost year or adequate details of costs for assessment, such as construction, maintenance and refurbishment costs.

- Not conducting adequate sensitivity analyses.[97, 101]

- Not discussing ethical and distributional issues.[97, 101]

In addition to these limitations, Boardman et al.[97] received funding from the hospital group for their study but did not outline any steps taken to address this potential conflict of interest. Maben et al.[101] did not clearly describe the population, appropriately measure costs, use a sufficient time horizon, or discount future costs or outcomes, in one of their analyses, or use a suitable economic design, include all relevant costs, perform an incremental analysis of all costs and outcomes, appropriately discuss the generalizability of their findings, or make conclusions consistent with all the findings of their report, for both analyses.

Table 4-10 Economic evidence for review question two: CHEC-list quality assessment

Item	Boardman (2011)[97]	Maben (2015)[101]
Is the study population clearly described?	+	−
Are competing alternatives clearly described?	+	+
Is a well-defined research question posed in answerable form?	+	+
Is the economic study design appropriate to the stated objective?	+	−
Is the chosen time horizon appropriate to include relevant costs and consequences?	+	−
Is the actual perspective chosen appropriate?	+	+
Are all important and relevant costs for each alternative identified?	+	−
Are all costs measured appropriately in physical units?	+	−
Are costs valued appropriately?	−	−
Are all important and relevant outcomes for each alternative identified?	+	+
Are all outcomes measured appropriately?	+	+
Are outcomes valued appropriately?	+	+
Is an incremental analysis of costs and outcomes of alternatives performed?	+	−
Are all future costs and outcomes discounted appropriately?	+	−
Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	−	−
Do the conclusions follow from the data reported?	+	−
Does the study discuss the generalizability of the results to other settings and patient/client groups?	+	−
Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	−	+
Are ethical and distributional issues discussed appropriately?	−	−

4.3.4 Applicability

Applicability (based on relevance and credibility) was assessed using the ISPOR Questionnaire to Assess Relevance and Credibility of Modelling Studies,[88] the outcomes of this assessment are presented in Table 4-11. No Irish studies were identified. Following assessment using the ISPOR questionnaire the two included studies were deemed not applicable to the Irish context.[97, 101] In addition to the methodological limitations mentioned in Section 4.3.3, Boardman et al.[97] only assessed double occupancy rooms as a comparator. Maben et al.[101] did not perform or report adequately on their analyses (to allow the cost impact for all variables to be determined), and reported results in a potentially biased manner.

Table 4-11 Applicability of included health economic studies assessed using ISPOR questionnaire

Item	Boardman (2011) [97]	Maben (2015)
Is the population relevant?	Yes	Yes
Are any critical interventions missing?	Yes	No
Are any relevant outcomes missing?	No	No
Is the context applicable?	No	Yes
Is external validation of the model sufficient?	N/A	N/A
Is internal verification of the model sufficient?	N/A	N/A
Does the model have sufficient face validity?	Yes	Yes
Is the design of the model adequate?	Yes	Yes
Are the data used in populating the model suitable?	No	Yes
Were the analyses adequate?	Yes	No
Was there adequate assessment of uncertainty?	No	No
Was the reporting adequate?	Yes	No
Was interpretation fair and balanced?	Yes	No
Were there any potential conflicts of interest?	Yes	No
Were steps taken to address conflicts?	No	N/A

4.4 Discussion and conclusion

4.4.1 Discussion

Single patient room (SPR) have been suggested as an approach to reduce transmission of healthcare-associated infections (HCAIs), based on the principles of isolation and ventilation.[16] By isolating patients in separate en suite rooms, it can eliminate the direct contact between infected and susceptible patients, thereby reducing the spread and development of new infections. A review published in 2004 by Chaudhury al.[16] underpinned recommendations made by the American Institute of Architects published by the Facility Guidelines Institute including a maximum limit of one patient per room for new hospital builds unless there is a demonstrable need for a two-bed design by the licensing authority.[109] Since then a number of national guidelines have been published including the 2008 Infection Prevention and Control Building Guideline for Acute Hospitals in Ireland which recommended SPRs for all newly built acute hospitals.[17] There is strong consensus and a supporting evidence base in favour of isolating infected patients in SPRs as an infection prevention control (IPC) measure and mostly favourable evidence for SPR accommodation in high acuity settings compared to multi-bed room (MBR) design.[110, 111] But for other acute settings, it is unclear how effective 100% SPR accommodation at ward or hospital level is compared with 100% MBR accommodation in reducing HCAI rates. This review aimed to review the existing literature on the effectiveness of SPR at reducing HCAI and adverse events.

We identified eight studies relevant for inclusion in this systematic review of effectiveness of SPRs in reducing the incidence of healthcare-associated infection. Findings relevant to clinical-effectiveness were reported in seven of the studies.[96, 98, 99, 101, 102, 104, 105] While findings relevant to cost impact were reported in two studies.[97, 101]

The GRADE approach was used to assess the certainty of the evidence for all primary outcomes of interest. For the totality of evidence, there is very low certainty of evidence that SPR design reduces or increases infection rates for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Clostridioides difficile* (*C. difficile*) but may decrease the infection rates for vancomycin-resistant *Enterococci* (VRE). There is very low certainty of evidence that SPR design, when compared to MBR design, reduces or increases mortality rates, may possibly increase the risk of falls, may reduce the risk of delirium and has no significant impact on all

other adverse events investigated (such as pressure ulcers, medical errors, or time to first fall).

Specifically, three studies investigated HCAIs and colonisation rates of antimicrobial resistant organisms (AMROs). Two [98, 102] found no significant change in MRSA rates after moving from a MBR design to a SPR design while a third study[101] reported only one MRSA case over the entire study period of 36 months, which was insufficient for analysis. Two studies investigated *C. difficile* infections, with one study[101] reporting an increase in one of the three SPR wards compared with MBR design wards. However, it is unclear whether this increase can be attributed to the design of the ward due to substantial differences associated with the case mix. The second study[102] found no significant difference in *C. difficile* infection rates following a move to a new 100% SPR hospital. An immediate decrease in VRE infections after the move was demonstrated with no temporal trend for the remainder of the study period (36 months). Additionally, the study[102] investigated changes in AMRO colonisation rates and reported an immediate decrease for VRE and MRSA following the move. These rates did not significantly change from this lower level during the 36 months following the move. It should be noted that the infection, prevention and control policy changed shortly after the move, with hydrogen peroxide vapour for discharge cleaning during local outbreaks of *C. difficile* or VRE infection introduced as standard practice. Although not considered within this review, the effectiveness of this method of discharge cleaning is currently uncertain.[112] It may be that SPR accommodation makes it easier to for vapour cleaning to be scheduled without the consideration of other inpatients, and should be assessed within future reviews on SPR design. Another concern, unrelated to SPR design, is a more sterile environment as a result of the new hospital, which could have also contributed to the maintenance of lower AMRO colonisation rates. These studies further highlight the difficulties in conducting robust research on the effect of all SPR design in reducing HCAI.

Five studies[98, 99, 101, 104, 105] reporting results relating to in-hospital falls. Two of these studies[101, 104] reported an increase in falls in the SPR design group compared with MBR design group. However, one of these studies[101] reported the increase was temporary and after six to nine months rates returned to previous levels. The authors speculated that the increase in falls may have more to do with the initial disruption caused by relocating to a new facility than the SPR design itself. The remaining three studies[98, 99, 105] reported no significant

difference.

Six studies considered additional adverse events.[96, 98, 99, 101, 104, 105] Three studies[99, 104, 105] investigated mortality and all reported no significant difference in mortality. However mortality is very rare. Two studies[98, 101] reported no significant change in hospital acquired pressure injuries. One study[96] investigated delirium and found a significant decrease in risk of developing delirium in patients in the SPR design compared to MBR design while there was no significant difference between the days to first instance of delirium in the patients that did develop delirium in either ward. One study[101] investigated medical errors and reported a temporary increase in one of the three SPR study wards when compared with the MBR wards. Finally, one study[98] collected data relating to medical deterioration calls and reported over double the number of medical deterioration calls registered in the SPR design compared with the MBR design, however, no test for significance was conducted.

As the review was initially completed in April 2020, searches were rerun on 13 February 2022 and again on 30 May 2022 to identify studies that may have been published in the interim. Two relevant articles[18, 19] were identified in the February searches, both of these describe further analyses on a dataset first featured in the Blandfort et al.[96] study, already included in this review.

The first article[18] examined whether relocation to a new ward in a new hospital with all SPR accommodation had affected the incidence of falls. The authors concluded that the risk of falls was not significantly different in MRBs compared to SPRs (HR 0.81, 95% CI 0.46 to 1.42). However, in SPRs, but not in MBRs, there was a higher risk of falls among in-patients that developed delirium than among patients who did not develop delirium (these results were published as a graph only and reported by the authors as statistically significant). This further highlights the complexity of room design and effect on patient safety more generally. The second article[19] reported on a subset of the original dataset[96] which focused on the incidence of HCAIs. After controlling for a range of confounders, as per the original study,[96] the time to first HCAI (composite of all infections grouped together, pneumonia, *C. difficile,* sepsis, and other infections - UTI, wound infection, nephritis and erysipelas) was lower for SPR when compared to the MRB group (HR 0.65, 95% CI 0.45 to 0.95; p = 0.03); this was largely driven by the prevalence of UTIs. It should be noted that the analysis did not control for infection as the cause for admission, which was significantly higher in the SPR group. As

reported by the authors, ongoing infections were likely to be treated with antibiotics which may have acted as a prophylaxis for further infection. Overall, these two additional analyses are consistent with the findings of this review.

Two health economic studies were identified and included in this review.[97, 101] Following appraisal using Consensus on Health Economic Criteria quality assessment tool,[87] one study was considered moderate quality[97] and the other low quality.[101] Both were assessed as not applicable to the Irish context using the ISPOR Questionnaire to Assess Relevance and Credibility of Modelling Studies.[88] Neither study incorporated cost savings related the effect of SPRs on HCAI rates. The first study[97] assumed that SPRs would avoid 0.002 deaths and 0.008 serious illnesses per bed per year. After considering the increased costs associated with a SPR design, it was estimated the net benefit over a 50 year life cycle of a hospital of a SPR compared with a double-occupancy room would be $23,340 (€17,411) per bed. However, due to absence of directly relevant data many assumptions were not considered to be robust. For example, if the assumed probability of an adverse event occurring was 0.5% lower or higher SPRs may result in a net cost or net saving, respectively, over the life cycle of a hospital. The second study[101] set out to assess the impact of SPR design following a move from a traditional NHS Trust hospital with 50% MBRs to a new 100% SPR design hospital. Data collection included a number of costs relating to construction, operating costs including staffing and housekeeping and catering costs as well as HCAI and falls. Although estimates were reported, the authors reported it was impossible to attribute any observed differences to the SPR design due to a number of confounders (such as staffing levels, approaches to catering, changes in ward sizes and case-mix) or insufficient data.

Overall, based on the totality of the evidence, it is not possible to conclude whether SPRs are effective in reducing HCAI rates or reducing the incidence of colonisation rates by AMROs compared to MBR accommodation. It is also not possible to say whether the use of SPRs leads to an increase in adverse events, including physical and or psychological harm. The lack of high-quality evidence to evaluate the impact of SPR design on patient and healthcare outcomes is due to a number of factors. Apart from two study,[101, 102] study designs were limited and consisted of uncontrolled and unadjusted studies to sufficiently account for known confounders, as listed above, as well as being of relatively short in duration to capture these rare events. As a result, the economic evidence is insufficient to evaluate the costs and

benefits associated with SPR designed hospitals compared to hospitals consisting of MBR or a mix of room types.

In terms of generalisability, this review included evidence from a range of countries, settings and patient populations which increases the generalisability. It is important to note that four of the studies[96, 98, 99, 105] employed a restrictive inclusion criteria to target populations who were considered at a higher risk of adverse events, such as older patients,[96] patients with delirium[99, 105] and an orthopaedic ward,[98] which may limit the generalisability to wider patient groups. Also worth noting when assessing the generalisability of these findings to the Irish acute sector is that three of the studies[99, 104, 105] collected data from the same health board in Wales. In addition to the close proximity of Wales to Ireland both countries have a large publicly funded acute service, with a similar proportion of people aged 65 years and over 21% in Wales in 2020[113] compared with 17% in Ireland.[114] This age group makes up 67% of the acute hospital inpatients in Wales, as compared with Ireland where this age group accounts for 54% of the total acute bed days.[115, 116] As a result, the data analysis provided from these studies might be considered generalisable to Ireland.

Ireland is transitioning rapidly from a young population to a population that is more evenly distributed in terms of age. Alongside this transition are global upward trends in AMRO rates.[117] These present both challenges and opportunities for hospitals of the future. Furthermore, since the WHO declared COVID-19 a pandemic of international concern, many hospital systems have been forced to implement innovative approaches to delivering care. This also provides researchers with an opportunity to revisit the question of the impact of SPRs on HCAI. Until evidence from high-quality studies is made available, decisions will continue to be made in the context of high uncertainty.[118]

Previous systematic reviews[111, 119] considered the impact SPR designs have on HCAI rates but mainly included high acuity settings such as ICUs rather than general acute settings. Stiller et al.[111] found reduced HCAI rates, but combined infections with colonisations, which did not account for known confounders and was heavily driven by one ICU based study from 1994. The meta-analysis used crude HCAI rates and included only one non-ICU setting making the findings problematic and impossible to generalise to Irish acute settings. Taylor et al.[119] included 13 studies that looked at HCAI rates, and the findings were mixed. Most of the included studies concentrated on isolation as a precaution, instead of the pros and cons of

admitting all patients in single rooms. For example, one of the included studies explored the effects of isolating patients who screened MRSA-positive only, instead of the effects of isolating all patients on the ward to prevent cross-contamination. Their overall conclusion was that results depend on the hospital design and management as the use of 100% SPRs needs to be reviewed alongside necessary modifications and adjustments to workflows and consideration of specific patient populations. The organisational policies, procedures, and models of care also need to be considered.

The COVID-19 pandemic has put extraordinary pressures on healthcare systems, including the need to separate infected patients identified at admission. In a 2018 study, Darley et al.[120] suggested the main value of SPR accommodation outside of ICU settings, in terms of infection prevention and control (IPC), may potentially lie with the ability to quickly isolate patients infected with norovirus at admission during the winter peak months. In the study, the authors investigated the impact of moving from an older hospital with MRB designed accommodation to a new 75% SPR hospital and found no change in *C. difficile*, MRSA bacteraemia and *E. coli* bacteraemia infection rates (there was insufficient number of MRSA cases for analysis) but did observe a reduction in bed-days lost due to norovirus outbreaks. The increased availability of SPRs allowed for the prompt isolation of admitted patients, effectively limiting the extent of viral dissemination, keeping an acute ward open, with individual room closures within the ward, without resultant cross-infection. Currently, in MRB hospitals the ward is likely to remain closed until the last infected patient is discharged from it. A recent publication by Graves et al.[121] (2021), identified after completion of this review, looked at the cost effectiveness of constructing temporary, single-patient, isolation rooms that can be deployed in a patient care area or ward in the context of COVID-19. The authors reported that the mean expected cost of implementing a temporary isolation room per 100,000 ordinary bed days in an NHS hospital was £1,545,949. The mean expected incremental cost per life-year gained was £5,829. The probability that adoption was cost-effective against a £20,000 threshold per additional life-year gained was 93%, and for a £13,000 threshold the probability was 87%. Multiple scenario analyses were performed and showed that in most scenarios the adoption of temporary isolation rooms is more likely to be cost-effective than not.

It is important to consider SPRs in wider context of IPC programmes which include interventions that have been widely studied and have demonstrated effectiveness in reducing

transmission of HCAI and AMRO in acute settings.[122] In 2017, WHO evidence-based recommendations on the core components of effective IPC programmes, hand hygiene is the corner stone. Other core components include IPC guidelines, education and training, surveillance, monitoring and auditing of IPC practices, hygiene and cleaning practices, and the workload, staffing and bed occupancy. While SPRs may potentially bring some benefit, in terms of IPC if adherence to the core principles of IPC are not optimal then any potential benefit may not translate to lower cross-infection.

Although outside the scope of this review, two of the included studies[98, 101] conducted qualitative research, which included surveys and interviews with patients and staff on the merits and experiences of SPR design compared with MBR. The results showed mixed feelings and preferences for both staff and patients. For staff, there were concerns around the loss of panoptic surveillance of patients, social interaction with colleagues as well as an increase in walking distances and challenges to team communication. The move to SPR also required adapting their working practices significantly, including setting up peripheral nurse workstations to improve the visible monitoring of patients and introducing an acuity system tool to allocate higher risk patients to more visible rooms. In favour of SPRs, staff felt it could be better for patient outcomes as SPRs reduced interruptions and distractions allowing nurses to perform their tasks with more focus. Some patients were supportive of SPRs due to increased privacy, more opportunity to personalise their environment, improved sleep patterns and general comfort especially in relation to having an en suite bathroom. However, the potential for loneliness, boredom, loss of shared experience and absence of distraction and social interaction was highlighted. One study observed a notable decline in the use of dayrooms.[101] These observations were consistent with findings from a recently published review on the patient and nurse experiences of SPR accommodation.[123]

4.4.2 Strengths and limitations of this review

This systematic review was conducted according to the PRISMA reporting guidelines.[20] It is based on a protocol which was registered on PROSPERO in advance of conducting the review to ensure transparency and minimise bias in the review process. Specific review questions were formulated based on the PICO approach and a priori-defined primary and secondary outcomes. In addition, an extensive search of the published and unpublished (grey literature including databases specific to architectural and design publications and organisations) was

conducted using a detailed search strategy and according to the principles of Boolean logic. Nine electronic databases and five grey literature databases were searched. Two reviewers were involved in all stages of the review (screening, data extraction, quality appraisal and assessing the certainty of the evidence using the GRADE approach), reducing bias.

However, the review has some limitations which include the eligibility of English language only studies and the application of a date restriction. However, choosing to search for literature published since 2004 could be considered a strength as internationally guidelines only began recommending SPR design from that date onwards and as a result focused this review on the most opportune time period for high quality studies in this area.[16] Furthermore, as with any systematic review, it is limited by the quality of the studies included, which were poor overall leading a very low overall certainty of the evidence for the review's primary outcomes. The scope of the clinical systematic review was limited to quantitative data only, however, the systematic inclusion of qualitative data could give a better understanding of the patient experience of SPRs. However, we did identify some evidence on patient and staff preferences in the included studies highlighting the importance of these perspectives. Additionally, the economic evidence identified was not informative or applicable to the Irish context. This highlights how difficult this research area is and how making recommendations on SPRs is based on large uncertainty. Given this uncertainty potential benefits, harms and opportunity costs need to be considered in policy and decision making.

4.4.3 Future research

There is a clear lack of high-quality studies assessing the effectiveness of SPR hospital design compared to MBR design. In addition, studies that evaluate the cost-effectiveness are currently absent. To address this lack of evidence, researchers and policymakers need to identify potential new hospital upgrades and construct robust studies that include sufficiently long data collection periods while also monitoring the characteristics of both patients and staff, to adequately account for the inherent dynamic reality of this complex intervention. Analysis needs to be able to account for external and internal underlying trends in infection incidence, and the impact of ongoing infection prevention control interventions. As this research was conducted before the COVID-19 pandemic, there is a need to understand how our experience with COVID-19 impacts the current understanding of patient accommodation,

especially in populations with a high proportion of older patients who are more vulnerable to severe illness if infected while receiving care in hospital.

4.4.4 Conclusion

Based on the overall assessment, there is a lack of evidence to determine the net benefit or risk of SPRs as an intervention to reduce HCAI and adverse events. There may possibly be some benefits in reducing HCAI and protecting against delirium though it is of very low certainty. There also may possibly be some harms in relation to increased falls but the evidence is of very low certainty. Overall, the evidence is limited, inconsistent and of poor quality and hence the balance of benefits and harms cannot be determined and does not permit a firm conclusion. Large scale whole-hospital interventions are challenging to evaluate due to multiple confounding factors including ongoing infection protection and control efforts which are constantly being updated. In addition, due to relatively low incidence rates of HCAIs and adverse events, studies require long duration for data collection, which only compounds the difficulties in isolating the effect SPR design has on clinical outcomes. No cost-effectiveness studies were identified that were applicable to the Irish context.

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Appendix 1: Deviations from protocol

Table A1-1 Deviations from protocol

Review question	Deviation	Reason
Question one- Interventions to improve hand hygiene adherence	Exclusion of non RCTs design from the data extraction and quality appraisal.	As outlined in the protocol if sufficient RCTs were identified then all other study designs would not be considered during the synthesis, but would be included in the data extraction and quality appraisal table. However, due to timeline constraints these studies were not considered for critical appraisal and data extraction and as a result are not presented in the appendix.

Appendix 2: Example of search terms

The searches for question one were conducted consistent with the search strategy developed

for 2017 Cochrane review *Interventions to improve hand hygiene compliance in patient care*

by Gould et al..[24]

Table A2-1 Example of a search string for question one

Embase database		
No.	Search terms	Results
1	doctor*:ti,ab OR physician*:ti,ab OR nurse*:ti,ab OR clinician*:ti,ab OR consultant*:ti,ab OR (healthcare:ti,ab AND assistant*:ti,ab) OR (health:ti,ab AND care:ti,ab AND assistant*:ti,ab) OR (health:ti,ab AND care:ti,ab AND professional*:ti,ab) OR (healthcare:ti,ab AND professional*:ti,ab) OR team*:ti,ab OR (healthcare:ti,ab AND worker*:ti,ab) OR (health:ti,ab AND care:ti,ab AND worker*:ti,ab) OR ((health* NEAR/2 personnel):ti,ab) OR medical:ti,ab OR nursing:ti,ab OR staff:ti,ab	2949703
2	ward*:ti,ab OR centre:ti,ab OR centres:ti,ab OR center:ti,ab OR centers:ti,ab OR department*:ti,ab OR unit:ti,ab OR units:ti,ab OR hospital*:ti,ab	3480625
3	'long term care':ti,ab	23623
4	(residential NEAR/3 (care OR healthcare OR facilit*)):ti,ab	6966
5	'nursing home':ti,ab	26279
6	'health care personnel'/exp/mj	493348
7	'health care facility'/exp/mj	461364
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	5801194
9	'hand washing'/exp/mj	4203
10	handwash*:ti,ab OR ((hand NEAR/1 wash*):ti,ab) OR ((hand NEAR/1 hygiene):ti,ab) OR handrub*:ti,ab OR ((hand NEAR/1 rub*):ti,ab)	11494
11	(hand* NEAR/2 (clean* OR decontaminat* OR disinfect* OR hygiene OR hygienic* OR saniti* OR sterili* OR wash*)):ti,ab	12394
12	(hand* NEAR/3 (alcohol* OR propanol* OR ethanol*)):ti,ab	2212
13	(hand* NEAR/1 scrub*):ti,ab	158
14	(hand* NEAR/2 (aseps* OR aseptic* OR antisep*)):ti,ab	494
15	('antisepsis'/de OR 'disinfection'/de) AND 'hand'/de	343
16	#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	16067
17	'randomized controlled trial'/de	548734
18	'controlled clinical trial'/de	426779
19	'quasi experimental study'/de	5549
20	'pretest posttest control group design'/de	386
21	'time series analysis'/de	22964
22	'experimental design'/de	16877
23	'multicenter study'/de	214173
24	randomis*:ti,ab OR randomiz*:ti,ab OR randomly:ti,ab	1149831
25	groups:ab	2626659
26	trial:ti OR multicentre:ti OR multicenter:ti OR (multi:ti AND centre:ti) OR (multi:ti AND center:ti)	332663
27	intervention*:ti,ab OR effect*:ti,ab OR impact*:ti,ab OR controlled:ti,ab OR ((control NEAR/1 group*):ti,ab) OR ((before NEAR/5 after):ti,ab) OR ((pre NEAR/5 post):ti,ab) OR ((pretest:ti,ab OR ((pre NEAR/1 test):ti,ab)) AND (posttest OR ((post NEAR/1 test):ti,ab))) OR quasiexperiment*:ti,ab OR ((quasi NEAR/1 experiment*):ti,ab) OR ((pseudo NEAR/1 experiment*):ti,ab) OR pseudoexperiment*:ti,ab OR evaluat*:ti,ab OR ((time NEAR/1 series):ti,ab) OR ((time NEAR/1 point):ti,ab) OR ((repeated NEAR/1 measur*):ti,ab)	12683652
28	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	13884322

29	'systematic review':ti OR 'literature review':ti	157942
30	'cochrane database of systematic reviews'/jt	13272
31	'animals'/exp OR 'invertebrate'/exp OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'animal cell'/de OR 'nonhuman'/de	27462635
32	'human'/de OR 'normal human'/de OR 'human cell'/de	20759044
33	#31 NOT (#31 AND #32)	6758705
34	#29 OR #30 OR #33	6928415
35	#28 NOT #34	10668241
36	#8 AND #16 AND #35	6207
37	#36 AND [18-10-2016]/sd AND [embase]/lim	1164

Table A2-2 Example of a search string for question two

Embase database		
No.	Search terms	Results
1	'room design':ab,ti OR 'ward design':ab,ti	358
2	single occupancy':ab,ti OR 'multi* occupancy':ab,ti	176
3	'single room*':ab,ti	777
4	(single NEAR/3 room$):ab,ti	1441
5	'single-occupancy':ab,ti	93
6	(single NEAR/3 bed*):ab,ti	1021
7	(room NEAR/3 bay*):ab,ti	32
8	(side NEAR/3 (room* OR bed*)):ab,ti	1841
9	(privat* OR isolat* OR separat*) NEAR/6 room$	4850
10	single-bedded':ab,ti	17
11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	22665
12	'infection control'/de	83264
13	(infection NEAR/2 control*):ab,ti	35216
14	'infection rate':ab,ti	17348
15	coloni$ation rate*':ab,ti OR 'microbial colonization'/exp	55900
16	'hospital infection'/de	41858
17	(hospital NEAR/2 infect*):ab,ti	15511
18	(healthcare NEAR/2 infect*):ab,ti	5451
19	(nosocomial NEAR/2 infect*):ab,ti	20112
20	(cross NEAR/2 infect*):ti,ab	4091
21	outbreak*:ti,ab	92075
22	methicillin resistant staphylococcus aureus'/de	41481
23	mrsa:ti,ab OR emrsa:ab,ti OR mssa:ab,ti	31128
24	((methicillin NEAR/2 resistan*):ti,ab) AND ((staphylococc* NEAR/2 (infect* OR aureus)):ti,ab)	32017
25	'clostridium difficile'/de	14720
26	'clostridium difficile':ti,ab OR 'c diff*':ti,ab OR 'c. diff':ab,ti	22165
27	'gastroenteritis':ti,ab OR 'norwalk-like viruses':ti,ab OR 'norwalk like viruses':ti,ab OR norovirus*:ti,ab OR 'norwalk like virus*':ti,ab OR 'small round-structured virus*':ti,ab OR 'round-structured virus*':ti,ab OR 'small round structured virus*':ti,ab OR 'diarrhea':ti,ab OR 'nausea':ti,ab OR 'stomach virus':ti,ab OR rotavirus:ti,ab OR 'foodborne diseases':ti,ab	215153

28	carbapenem-resistant enterobacteriaceae'/exp OR 'carbapenemase-producing enterobacteriaceae[text word]' OR 'vancomycin-resistant enterococci'/exp	6645
29	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	516869
30	falls:ti,ab OR fall:ti,ab OR harm:ti,ab OR harms:ti,ab OR ((physical NEAR/2 harm*):ti,ab) OR 'adverse event*':ti,ab OR injury:ti,ab	1250354
31	dignity:ti,ab OR privacy:ti,ab OR dignified:ti,ab OR 'consumer satisfaction'/de OR 'consumer satisfaction'/exp OR ((patient*:ti,ab OR consumer*:ti,ab OR parent*:ti,ab OR famil*:ti,ab OR spouse*:ti,ab) AND adj:ti,ab AND (attitude*:ti,ab OR involvement:ti,ab OR desir*:ti,ab OR perspective*:ti,ab OR activation:ti,ab OR view*:ti,ab OR preference*:ti,ab)) OR 'patient preference'/exp OR preferen*:ti,ab OR 'quality of life[majr]' OR 'quality of life':ti,ab OR 'life quality':ti,ab OR 'qol':ab,it OR 'personal satisfaction[majr]' OR 'personal satisfaction':ti,ab OR 'patient satisfaction[majr]' OR 'patient satisfaction':ti,ab OR 'activities of daily living[majr]' OR 'activities of daily living':ti,ab OR 'quality-adjusted life years[majr]' OR 'quality adjusted life year*':ti,ab OR 'personal autonomy[majr]' OR 'personal autonomy':ti,ab OR 'happiness[majr]' OR happiness:ti,ab OR 'patient preference*':ti,ab OR 'fear of death':ti,ab OR 'self-concept[majr:noexp]' OR 'self concept':ti,ab OR 'family relations[majr:noexp]' OR 'family relation*':ti,ab OR 'religion[majr:noexp]' OR religion:ti,ab OR 'social support':ti,ab OR 'social support[majr]' OR 'positive experience':ti,ab OR 'quality of life'/exp OR qol OR 'psychological' OR 'patient satisfaction'/exp OR dissatisfaction OR 'mqql' OR 'mcgill quality of life questionnaire' OR 'loneliness':ti,ab OR alone:ti,ab b	2492011
32	medication error'/de	17422
33	'medical error'/de	17967
34	'surgical error'/de	1410
35	((medication OR medical) NEAR/2 (error* OR mistake*)):ti,ab	14644
36	((surgical OR operative) NEAR/2 (error* OR mistake*)):ti,ab	1076
37	((anaesthetic OR anesthetic) NEAR/2 (error* OR mistake*)):ti,ab	49
38	surgical infection'	45050
39	((surgical OR operative) NEAR/2 infect*):ti,ab	22441
40	((postsurgical OR postoperative) NEAR/2 infect*):ti,ab	12789
41	(wrong NEAR/2 site):ti,ab	480
42	#32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	103396
43	#29 OR #30 OR #31 OR #42	4167523
44	'randomized controlled trial'/de	548650
45	'controlled clinical trial'/de	426764
46	'quasi experimental study'/de	5543
47	'pretest posttest control group design'/de	386
48	'time series analysis'/de	22950
49	'experimental design'/de	16871
50	'multicenter study'/de	214141
51	randomis*:ti,ab OR randomiz*:ti,ab OR randomly:ti,ab	1149584
52	groups:ab	2626160
53	trial:ti OR multicentre:ti OR multicenter:ti OR (multi:ti AND centre:ti) OR (multi:ti AND center:ti)	332603

54	intervention*:ti,ab OR effect*:ti,ab OR impact*:ti,ab OR controlled:ti,ab OR (control:ti,ab AND group*:ti,ab) OR ((before NEAR/5 after):ti,ab) OR ((pre NEAR/5 post):ti,ab) OR ((pretest:ti,ab OR (pre:ti,ab AND test:ti,ab)) AND (posttest:ti,ab OR (post:ti,ab AND test:ti,ab))) OR quasiexperiment*:ti,ab OR (quasi:ti,ab AND experiment*:ti,ab) OR (pseudo:ti,ab AND experiment*:ti,ab) OR pseudoexperiment*:ti,ab OR evaluat*:ti,ab OR ((time:ti,ab AND series:ti,ab OR time:ti,ab) AND point*:ti,ab) OR (repeated:ti,ab AND measur*:ti,ab)	12977296
55	'cohort analysis'/exp OR 'longitudinal study'/exp OR 'prospective study'/exp OR 'follow up' OR cohort$.tw.	2539501
56	#44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55	14922676
57	'child'/exp OR 'neonatal intensive care unit'/exp OR 'infant'/exp OR 'pediatric'/exp	2725201
58	#11 AND #43 AND #56	1789
59	#58 NOT #57	1570
60	#59 AND [humans]/lim AND [english]/lim AND [embase]/lim	1019
61	new-build*' OR (new* NEAR/2 hospital) OR ((build* OR construction) NEAR/6 hospital) OR 'hospital design'/mj OR 'design factors' OR physical OR environmental OR ward OR facility OR planning OR design*	10071643
62	#60 AND #61	712

Appendix 3: Excluded studies

Table A3-1 Excluded interrupted time series studies and non-RCTs for question one

1.	Armellino D, Hussain E, Schilling ME, Senicola W, Eichorn A, Dlugacz Y, et al. Using high-technology to enforce low-technology safety measures: the use of third-party remote video auditing and real-time feedback in healthcare. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2012;54(1):1-7.
2.	Derde LPG, Cooper BS, Goossens H, Malhotra-Kumar S, Willems RJL, Gniadkowski M, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. The Lancet Infectious diseases. 2014;14(1):31-9.
3.	Diegel-Vacek L, Ryan C. Promoting Hand Hygiene With a Lighting Prompt. Herd. 2016;10(1):65-75.
4.	Finco G, Musu M, Landoni G, Campagna M, Lai A, Cabrini L, et al. Healthcare-associated respiratory infections in intensive care unit can be reduced by a hand hygiene program: A multicenter study. Australian Critical Care. 2018;31(6):340-6.
5.	Higgins A, Hannan MM. Improved hand hygiene technique and compliance in healthcare workers using gaming technology. The Journal of hospital infection. 2013;84(1):32-7.
6.	Lee AS, Cooper BS, Malhotra-Kumar S, Chalfine A, Daikos GL, Fankhauser C, et al. Comparison of strategies to reduce meticillin-resistant Staphylococcus aureus rates in surgical patients: a controlled multicentre intervention trial. BMJ Open. 2013;3(9):e003126.
7.	Midturi JK, Narasimhan A, Barnett T, Sodek J, Schreier W, Barnett J, et al. A successful multifaceted strategy to improve hand hygiene compliance rates. 2015;43(5):533-6.
8.	Moghnieh R, Soboh R, Abdallah D, El-Helou M, Al Hassan S, Ajjour L, et al. Health care workers' compliance to the My 5 Moments for Hand Hygiene: Comparison of 2 interventional methods. 2017;45(1):89-91.
9.	Perlin JB, Hickok JD, Septimus EJ, Moody JA, Englebright JD, Bracken RM. A bundled approach to reduce methicillin-resistant Staphylococcus aureus infections in a system of community hospitals. Journal for Healthcare Quality: official publication of the National Association for Healthcare Quality. 2013;35(3):57-68; quiz
10.	Romero DMP, Reboredo MM, Gomes EP, Coelho CM, Paula MAS, Souza LC, et al. Effects of the implementation of a hand hygiene education program among ICU professionals: an interrupted time-series analysis. Jornal Brasileiro De Pneumologia: Publicacao Oficial Da Sociedade Brasileira De Pneumologia E Tisilogia. 2019;45(5):e20180152.
11.	Rosenbluth G, Garritson S, Green AL, Milev D, Vidyarthi AR, Auerbach AD, et al. Achieving hand hygiene success with a partnership between graduate medical education, hospital leadership, and physicians. American Journal of medical Quality : The Official Journal of the American College of Medical Quality. 2016;31(6):577-83.
12.	Scherer AM, Reisinger HS, Goto M, Goedken CC, Clore GS, Marra AR, et al. Testing a novel audit and feedback method for hand hygiene compliance: A multicenter quality improvement study. Infection Control & Hospital Epidemiology. 2019;40(1):89-94.
13.	Shabot MM, Chassin MR, France AC, Inurria J, Kendrick J, Schmaltz SP. Using the targeted solutions tool to improve hand hygiene compliance is associated with decreased health care-associated infections. Joint Commission Journal on Quality & Patient Safety. 2016;42(1):6-17.
14.	Stella SA, Stace RJ, Knepper BC, Reese SM, Keniston A, Burden M, et al. The effect of eye images and a social norms message on healthcare provider hand hygiene adherence. Infection Control & Hospital Epidemiology. 2019;40(7):748-54.
15.	Talbot TR, Johnson JG, Fergus C, Domenico JH, Schaffner W, Daniels TL, et al. Sustained improvement in hand hygiene adherence: utilizing shared accountability and financial incentives. Infection control and hospital epidemiology. 2013;34(11):1129-36.

| 16. | Vernaz N, Sax H, Pittet D, Bonnabry P, Schrenzel J, Harbarth S. Temporal effects of antibiotic use and hand rub consumption on the incidence of MRSA and Clostridium difficile. The Journal of antimicrobial chemotherapy. 2008;62(3):601-7. |

Table A3-2 Excluded economic studies for question one

1	Lee BY, Wettstein ZS, McGlone SM, Bailey RR, Umscheid CA, Smith KJ, et al. Economic value of norovirus outbreak control measures in healthcare settings. Clinical Microbiology & Infection. 2011;17(4):640-6.
2	Nelson RE, Jones M, Leecaster M, Samore MH, Ray W, Huttner A, et al. An economic analysis of strategies to control Clostridium difficile transmission and infection using an agent-based simulation model. 2016;11(3):e0152248.
3	Page K, Barnett AG, Campbell M, Brain D, Martin E, Fulop N, et al. Costing the Australian National Hand Hygiene Initiative. Journal of hospital infection. 2014;88(3):141-8.

Table A3-3 Excluded clinical studies for question one

Reason for exclusion	Study reference
Conference abstract (n=71)	(124-194)
Intervention following outbreak (n=1)	(195)
Irrelevant comparator (n=2)	(196, 197)
Irrelevant intervention (n=7)	(195, 198-203)
Irrelevant outcome (n=6)	(204-209)
Irrelevant population (n=7)	(53, 210-215)
Irrelevant setting (n=3)	(59, 216, 217)
Irrelevant study design (n=76)	(85, 195, 218-291)
ITS or nRCT (16)	(44-46, 50, 54, 60, 61, 63, 64, 292-298)
Non-English publication (n=5)	(299-303)
Protocol (n=2)	(304, 305)
Study ongoing or not yet published (3)	(306-308)
Trial Registration (n=2)	(309, 310)

Table A3-4 Excluded clinical studies for question two

Reason for exclusion	Study reference
Irrelevant intervention (n=10)	(120, 311-319)
Irrelevant outcome (n=1)	(320)
Irrelevant publication type (16)	(321-336)
Irrelevant study design (n=6)	(16, 337-341)

Appendix 4: Clinical results for question one: interventions to improve adherence to hand hygiene recommendations

Table A4-1 Clinical results for question one: interventions to improve adherence to hand hygiene recommendations

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
WHO Compliant strategies			
Fisher (2013)[47] Multicentre C-RCT	**Intervention – WHO Compliant** *System change* - wireless monitoring system; *Reminders* - real-time audible reminders (phase 2 and 3); *Feedback* - confidential individual weekly written feedback reports (phase 3). **Control –No intervention**	*Primary outcome* Median (IQR) adherence rate <u>Entering patient zone</u> **Intervention:** Baseline: 28% (21 to 37%) Phase 2: 33% (25 to 41%) Phase 3: 28% (16 to 40%) **Control:** Baseline: 28% (21 to 37%) Phase 2: 26% (22 to 32%) Phase 3: 24% (19 to 33%) <u>Exiting patient zone</u> **Intervention:** Baseline: 24% (13 to 38%) Phase 2: 32% (21 to 41%) Phase 3: 29% (16 to 42%) **Control:** Baseline: 27% (12 to 37%) Phase 2: 25% (15 to 34%) Phase 3: 20% (11 to 34%)	*Primary outcome* Univariate analysis between intervention and control group for phase 2 and 3 combined (95% CI). <u>Entering patient zone</u> 2.9% higher in the intervention group (-0.2 to 5.9%); p=0.067 <u>Exiting patient zone</u> 5.8% higher in the intervention group (0.5 to 11.1%); p=0.033
Ho (2012)[38] Multicentre C-RCT	**Intervention 1 – WHO Compliant** *System change* - availability of ABHR for each HCW, availability of lightly powdered gloves; *Education* -video clips, hand analysis demonstration to assure skin safety; *Feedback* - individual; *Reminders* – posters. **Intervention 2 – WHO Compliant** Identical to Intervention 1 but with powderless gloves instead of lightly powdered gloves. **Control – Usual care**	*Primary outcome* Mean HH adherence rate– number of opportunities Statistical significance tests of the difference in adherence from baseline **Intervention 1:** Baseline: 27.0% – 325/1,204 4 months: 60.6% – 662/1,093 Overall change: 33.6%; p<0.001 **Intervention 2:** Baseline: 22.2% – 313/1,410 4 months: 48.6% – 454/935 Overall change: 26.4%; p<0.001	*Primary outcome* RR (95% CI) for HH adherence in the intervention group (intervention 1 and 2 combined) compared to the control (adjusted for clustering effects). 2.55 (2.29 to 2.84); p<0.001 *Secondary outcome 1* IRR (95% CI) of respiratory outbreaks requiring hospitalisation (for both intervention groups) compared to the control.

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
	2-hour general health talk with small focus on HH. Historical data was used as the control for secondary outcomes (Mar to Sept of 2007, 2008 and 2009)	**Control:** Baseline: 19.5% – 326/1,671 4 months: 21.6% – 301/1,393Overall change: 2.1%; p=0.85	0.12 (0.01 to 0.93); p=0.04 *Secondary outcome 2* IRR (95% CI) of MRSA infections requiring hospitalisation (for both intervention groups) compared to the control. 0.61 (0.38 to 0.97); p=0.04
Martín-Madrazo (2012)[55] Multicentre C-RCT	**Intervention – WHO Compliant** *System change* - availability of ABHR; *Educational*- interactive workshops; *Reminders* - posters in waiting rooms, emergency rooms and consultation offices. **Control – Usual care**	*Primary outcome* Mean (95% CI) HH adherence rate **Intervention:** Baseline: 8.0% (4.5 to 10.2) Post intervention: 32.7% (NR) **Control:** Baseline: 8.3% (6.2 to 11.6) Post intervention: 11.9% (NR)	*Primary outcome* Absolute difference in change from baseline between intervention and control. 21.16% increase (95% CI 13.83 to 28.48%); p<0.001 RR (95% CI) for HH adherence in the intervention group compared to the control (adjusted for clustering effects). 2.76 (2.25 to 3.39); p<0.001
Mertz (2010)[56] Multicentre C-RCT	**Intervention group – WHO Compliant** *System change* – ABHR and sink units; *Education* - small group teaching seminars; *Reminders* – posters and pamphlets; *Feedback* - unit-specific feedback displayed on whiteboards and compared to other units, biweekly meetings; *Institutional safety climate* – collaborative goal setting and campaign design by clinical managers and HCWs. **Control group – Usual care**	*Primary outcome* Mean HH adherence rate – number of opportunities (calculated using reported data) **Intervention:** Baseline: 15.8% – 276/1,749 Intervention: 48.2% – 3,808/7,901 **Control:** Baseline: 15.9% – 263/1,651 Intervention: 42.6% – 3,206/7,526 *Secondary outcome* Mean incidence rate of hospital-acquired MRSA colonisation per 1,000 patient days **Intervention:** 0.73 **Control:** 0.66	*Primary outcome* Mean (95% CI) difference in HH between intervention and control group. 6.3% (4.3 to 8.4%); p<0.001 RR (95% CI) for HH adherence in the intervention group compared to the control (adjusted for clustering effects). 1.13 (1.09 to 1.17); p<0.001 *Secondary outcome* Mean difference in rate of colonisation of MRSA. 0.07 per 1,000 patient-days; p=0.92
Rodriguez (2015)[36]	**Intervention – WHO Compliant** *System change* – ABHR availability was	*Primary outcome* Mean HH adherence (range per site) – number	*Primary outcome* OR (95% CI) for HH adherence post intervention

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
Multicentre stepped-wedge C-RCT	monitoring; *Reminders* – in patient rooms and hallways; *Education* - pocket size book on evidence of HH adherence; *Feedback* –group feedback with comparisons to other study sites; *Institution safety climate* - signed letter from leaders and director walk-rounds. **Control – Usual care (Baseline period)**	of opportunities. Number of sites = 11 Control period (Baseline): 66.0% (47.2 to 79.8%) – 2,354/3,565 Intervention period (post intervention): 75.6% (57 to 93.9%) – 5,190/6,864	compared to baseline period. Unadjusted: 1.17 (1.13 to 1.22); p<0.0001 Adjusted for time: 1.08 (1.03 to 1.14); p=0.0001 RR (95% CI) for HH adherence post intervention compared to the baseline period (adjusted for clustering effects). 1.03 (1.00 to 1.06); p=0.08
van der Kooi (2018)[37] Multicentre stepped-wedge C-RCT	**Intervention – WHO Compliant** *System change* – ABHR at bedside; *Education* – sessions, small group and bedside training and presentations; *Feedback* – group and individual; *Reminders* – posters; *Institutional safety climate* – supported by hospital and ICU management. **Control– Usual care (Baseline period)**	*Primary outcome* Mean (95% CI) adherence rate, adjusted for underlying hospital-specific trends including type of HCW and acuity levels - number of opportunities **Baseline**: 36% (34 to 37%) – 1,468/4,089§ **Intervention**: 58% (57 to 59%) – 6,920/11,919§	*Primary outcome* Mean (95% CI) change in adherence rate between baseline and intervention period, adjusted for underlying hospital-specific trends including HCW and acuity levels. 18% (15 to 22%); p<0.0001 RR (95% CI) for an increase in HH in the intervention group compared to the control (adjusted for clustering effects) 1.50 (1.44 to 1.57); p<0.001
Von Lengerke (2017)[67, 68] Single centre C-RCT	**Intervention – WHO Compliant** Same as control with extra emphasis on tailoring components using behaviour change techniques – Comprehensive application consisting of training sessions and feedback discussions psychologically tailored using "Health Action Process Approach (HAPA)" framework. Focus on perceptions of risk, action planning, coping planning and habit building through developing self-regulative strategies. **Control – WHO Compliant** *System change* – ABHR availability; *Education* – training sessions, e-learning tool and video;	*Primary outcome 1* Mean adherence rate – number of opportunities **Intervention:** Baseline: 54% – 1,047/1,938 Year 1: 64% – 1,141/1,783 Year 2: 70% – 839/1,198 **Control:** Baseline: 55% – 984/1,789 Year 1: 68% – 1,244/1,830 Year 2: 64% – 950/1,484 *Primary outcome 2* ABHR volume consumption not reported	*Primary outcome 1* Mean difference (95% CI) in adherence rates of intervention compared to control. Baseline: -1% (-4.1 to 2.3%); p=0.58 Year 1: -4% (-7.5 to -1.3%); p=0.006 Year 2: 6% (2.4 to 9.5%); p=0.001 RR (95% CI) for HH adherence in the intervention group compared to the control (year 2) (adjusted for clustering effects). 1.09 (1.04 to 1.15); p<0.001 *Secondary outcome*

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
	Feedback – not detailed; *Reminders* – WHO posters; *Institutional safety climate* – facility management and administration support. Opportunity for certification.	***Secondary outcome*** Mean incident density of MDROs per 1,000 inpatient-days **Intervention:** Baseline: 0.845 Year 1: 0.585 Year 2: 0.348 **Control:** Baseline: 0.691 Year 1: 0.605 Year 2: 0.669	Mean difference in the incidence densities (95% CI) of MDROs (per 1,000 inpatient-days) between intervention and control. Baseline: 0.154 (-1.069 to 1.376); p=0.79 Year 1: -0.020 (-0.811 to 0.771); p=0.96 Year 2: -0.322 (-1.347 to 0.704); p=0.50
Yeung (2011)[66] Multicentre C-RCT	**Intervention – WHO Compliant** *System change* - availability of pocket sized ABHR; *Education* - 2-hour seminar on HH; *Reminders* -posters and ballpoint pens with messages. **Control – Usual care** Basic life support program which did not include HH or HCAI advice.	***Primary outcome*** HH adherence rate – number of opportunities **Intervention** Baseline: 25.8% – 86/333 Post intervention: 33.3% – 488/1,465 **Control** Baseline: 25.8% – 61/236 Post intervention: 30.0% – 380/1,266 ***Secondary outcome 1*** Change from baseline in incidence (per 1,000 resident-days) of all infections requiring hospitalisation Test of statistical significance of the difference from baseline **Intervention**: -0.77; p=0.002 **Control:** 0.56; p=0.004 ***Secondary outcome 2*** Numbers of outbreaks	***Primary outcome*** RR (95% CI) for HH adherence in the intervention group compared to the control (adjusted for clustering effects). 1.11 (0.99 to 1.24); p=0.07 ***Secondary outcome 1*** Difference between the intervention group and control in the change of infection rates for all infections requiring hospitalisation, assessed by Student *t* test. Between group difference: p=0.004 ***Secondary outcome 2*** There were no outbreaks of influenza or norovirus in either group during the study.
WHO Plus strategies			
Huis (2013)[52] Multicentre C-RCT	**Intervention – WHO Plus** MM strategy same as control but with additional emphasis on team and leaders-directed strategies based on social theories, plus *Accountability* - Nurses addressing each	***Primary outcome*** Mean adherence rate – number of opportunities **Intervention:** Baseline: 20% – 312/1,560	***Primary outcome*** OR for HH adherence in intervention group compared to control (adjusted for ward and timing of measurement), from baseline to post intervention.

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
	other in cases of undesirable HH behaviour. **Control – WHO Compliant** *System change* – adequate product availability; *Education* – leaflet on HH importance, website; *Reminders* – posters, newsletters articles; *Feedback* – ward level to ward manager with ward comparisons; *Institutional safety climate* – management support.	Post intervention: 53% – 832/1,570 Follow up: 53% – 878/1,657 **Control:** Baseline: 23% – 456/1,981 Post intervention: 42% – 820/1,953 Follow up: 46% – 950/2,065	1.64 (95% CI 1.33 to 2.02); p<0.001 Mean difference in overall improvement between the intervention and control group, from baseline to post intervention. 8.91% (95% CI: 0.75 to 17.06%)* from Huis et al 2013[75] RR (95% CI) for HH adherence in the intervention group compared to the control (adjusted for clustering effects). 1.29 (1.21 to 1.39); p<0.001
Stewardson (2016)[40] Single centre C-RCT	**Intervention 1 – WHO Compliant** Same as control with extra emphasis on Enhanced feedback - immediate, individualised and intermittent, aggregated components, with ward-level benchmarking and responsive goal setting. Reports and posters detailing adherence rates produced every 3 months. **Intervention 2 – WHO Plus** Same as control with extra emphasis on Enhanced feedback (as described above) plus *Patient participation* – welcome pack provided to patients consisting of a brochure and an individual pocket-sized bottle of ABHR. Patients were invited to ask HCWs who did not visibly perform hand hygiene before touching them (WHO Moment 1) to do so. **Control – WHO Compliant** *System change* - ABHR available at POC and pocket sized bottles for HCWs; *Education* – VigiGerme, website, VigiBox; *Feedback* – individual and to department	*Primary outcome* Mean (95% CI) HH adherence rate – number of opportunities **Intervention 1** Baseline: 65% (62 to 69) –1,040/1,629 Intervention: 75% (72 to 77) –2,160/2,920 Post intervention: 72% (68 to 75) –1,356/1,956 **Intervention 2** Baseline: 66% (62 to 70) –1,024/1,594 Intervention: 77% (74 to 80) –2,107/2,767 Post intervention: 72% (69 to 76) –1,485/2,100 **Control** Baseline: 66% (62 to 70) – 935/1,430 Intervention: 73% (70 to 77) – 1,631/2,239 Post intervention: 70% (66 to 75) – 631/949 *Secondary outcomes* IRR (95% CI) for compared to baseline. Primary blood stream infection of HCAIs	*Primary outcome* Absolute difference in HH adherence (95% CI) intervention compared to control, from baseline to the intervention period. **Intervention 1:** 3% (0 to 7 %) increase; p=0.19 **Intervention 2:** 4% (1 to 8 %) increase; p=0.048 Absolute difference between intervention 1 and intervention 2 was not significant p=0.46 RR (95% CI) for HH adherence in the intervention group compared to the control (adjusted for clustering effects). Intervention 1: 1.04 (0.97 to 1.12); p= 0.24 Intervention 2: 1.67 (1.53 to 1.82); p<0.001 *Secondary outcomes* Results from a mixed-effects regression model, testing the null hypothesis that the change in outcome rate from the baseline period to the intervention period was the same in all 3 study

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
	heads; *Reminders* – posters, video playing in public areas; *Institutional safety climate* – HH team, support from leadership, HH as a quality indicator.	**Intervention 1:** 1.02 (0.78 to 1.34) **Intervention 2:** 0.71 (0.54 to 0.95) Period prevalence of HCAIs **Intervention 1:** 1.05 (0.78 to 1.40) **Intervention 2:** 0.91 (0.68 to 1.23) **Control:** 1.33 (0.94 to 1.88) Colonisation with MRSA **Intervention 1:** 0.82 (0.67 to 0.99) **Intervention 2:** 0.79 (0.66 to 0.95) **Control:** 0.92 (0.75 to 1.13) Clinical isolates - *Clostridioides difficile* **Intervention 1:** 2.14 (1.39 to 3.31) **Intervention 2:** 2.11 (1.39 to 3.22) **Control:** 1.01 (0.71 to 1.45)	groups. Primary blood stream infection of HCAIs Difference between groups: p=0.02 Period prevalence of HCAIs Difference between groups: p=0.28 Colonisation with MRSA Difference between groups: p=0.56 Clinical isolates - *Clostridioides difficile* Difference between groups: p=0.01 Acquisition of ESBL-PE (MDRO): p=0.36 Secondary bloodstream infection (HCAI): p =0.90 Clinical isolates – MRSA: p=0.11 Clinical isolates - ESBL-PE (E coli): p=0.06 Clinical isolates - ESBL-PE (non-E coli): p=0.75
Stevenson (2014)[62] Multicentre C-RCT feasibility study	**Intervention – WHO Plus** *System change* – availability of ABHR; *Education* – sessions on HH; *Reminders* – posters and written material; *Feedback* – results of active surveillance cultures programme; *Institutional safety climate* - admin support, staff involvement. Plus *Incentives* - recognition and rewards programs. **Control – Usual care**	*Primary outcome* Total number of HH opportunities per group for the entire study period **Intervention:** 2,654 **Control:** 1,873 Estimated average change from baseline for complete adherence (HH before *and* after patient/environmental contact) **Intervention**: 20.1% (7.8 to 35.5%) **Control**: −3.1% (-6.3 to 5.9%) Estimated average change from baseline for any adherence (HH before *or* after patient environmental contact) **Intervention**: 28.4% (17.8 to 38.2%) **Control**: 0.7% (-16.7 to 20.7%)	*Primary outcome* P values were reported to demonstrate statistical difference between intervention and control group. Complete adherence (HH before *and* after patient/environmental contact): Difference: p=0.001 Any adherence (HH before *or* after patient environmental contact): Difference: p=0.001
Multimodal (not WHO)			

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
Fuller (2012)[48] Multicentre stepped-wedge C-RCT	**Intervention – Multimodal** *Feedback* -individual feedback after each observation session including plan for improvement and group feedback at ward meetings; *Incentives* - in the form of praise and certificates; *Accountability* –at individual and group level. **Control – Usual care**	***Primary outcome 1*** Overall HH adherence to WHO 5M Absolute percentages or number of complete opportunities not reported. ***Primary outcome 2*** Overall procurement levels of liquid soap. Absolute usage or number of complete opportunities not reported	***Primary outcome 1*** Estimated odds ratio (95% CI) for increase in HH adherence for the intervention group from baseline compared to the control, by ward type. **ACE:** 1.67 OR (1.08 to 1.80); p=0.01 **ICU:** 2.09 OR (1.55 to 2.81); p<0.001 Absolute change in HH adherence according to baseline levels, per ward type. **ACE:** 13% increase when baseline was 50%. 10% increase when baseline was 70%. **ICU:** 18% increase when baseline was 50%. 13% increase when baseline was 70%. ***Primary outcome 2*** Estimated change (95% CI) of liquid soap. **ACE:** 13% (-1 to 30%); p=0.08 **ICU:** 31% (11 to 55%); p=0.003
Unimodal compared with usual care			
Anderson (2016)[69] Single centre crossover C-RCT	**Intervention – Unimodal** *System change* – introduction of an end-of-hospital-bed table (CareCentre©) incorporating a writing surface, patient charts, ABHR dispenser, aprons, gloves, medications locker and waste bin. **Control – Usual care**	***Primary outcome*** Mean HH adherence rate (95% CI) – number of opportunities **Control:** 14% (9 to 18%) –82/584 **Intervention:** 40% (30 to 50%) –165/412	***Primary outcome*** An absolute difference of 26% in adherence rate between groups. P value was reported to demonstrate statistical difference between intervention and control group: p<0.001 Unadjusted RR (95% CI) for HH adherence in the intervention group compared to the control. 2.85 (2.26 to 3.60); p<0.001
Gilmartin[70] (2018) Single centre	**Intervention – Unimodal** *Education* - facilitated, group-based discussion and video on mindfulness and mindful hand hygiene.	***Primary outcome*** Mean change in HH adherence from baseline (95% CI)	***Primary outcome*** Liner regression model including an interaction term for time (pre or post period) and intervention (intervention vs. control) was used

| Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
pilot RCT	**Control – Usual care**	**Intervention:** Baseline: 72% (for all participants) Attending physicians: 14.1% (-1.1 to 29.5%) Senior resident: 24.7% (5.4 to 44%) Intern: 10% (-2.6 to 22.6%) Medical student: 4.7% (-4.4 to 14%) **Control**: Baseline: 85% (for all participants) Attending physicians: - 5.7% (-15.9 to 4.5%) Senior resident: 0.2% (-15.5 to 15.9%) Intern: 4.2% (-6.4 to 14.9%) Medical student: 7.7% (0.2 to 15.1%)	to test for statistical significant deference between comparators. Attending physicians: p=0.035 Senior resident: p=0.064 Intern: p=0.007 Medical student: p=0.003
Huang (2002)[51] Single centre RCT	**Intervention – Unimodal** *Education* - a lecture, demonstration and discussion on universal nursing precautions. **Control – Usual care**	***Primary outcome*** Proportion of nurses observed washing hands – number of nurses Statistical significance test of the difference in adherence from baseline <u>Before patient contact</u> **Intervention:** Baseline: 51.0% – 25/49 Post intervention: 85.7% – 42/49; p<0.001 **Control:** Baseline: 53.1% – 26/49 Post intervention: 53.1% – 26/49 <u>After patient contact</u> **Intervention:** Baseline: 75.5% – 37/49 Post intervention: 91.8% – 45/49; p<0.05 **Control:** Baseline: 75.5% – 37/49 Post intervention: 71.4% – 35/49	***Primary outcome*** RR (95% CI) for HH adherence in the intervention group compared to the control. <u>Before patient contact</u> 1.62 (1.21 to 2.15); p=0.01 <u>After patient contact</u> 1.29 (1.06 to 1.56); p= 0.012
Santosaningsih (2017)[39] Single centre pilot C-RCT	**Intervention 1 – Unimodal** *Education* – featuring role model training. **Intervention 2 – Unimodal** *Education* – featuring active presentation. **Intervention 3 – Unimodal** *Education* – Combination of intervention 1 and	***Primary outcome*** Mean HH adherence rate – number of opportunities Statistical significance test of the difference in adherence from baseline **Intervention 1** Baseline: 24.1% – 80/332	***Primary outcome*** Estimated OR (95% CI) adjusting for class of care, room type, nurse to patient ratio, moment of HH and HCW, compared to control group. **Intervention 1:** 4.08 (1.51 to 11.0); p=0.005 **Intervention 2:** 1.96 (1.18 to 3.27); p=0.01 **Intervention 3:** p>0.05 (no further details)

Author (year) Study design	Intervention and comparator	Outcome(s)	Measures of difference between comparators
	2. **Control – Usual care**	Post intervention: 43.7% – 107/245; p<0.001 **Intervention 2** Baseline: 18.9% – 83/440 Post intervention 24.9% – 73/293; p=0.05 **Intervention 3** Baseline: 5.2% – 19/364 Post intervention: 18.5% – 74/399; p<0.001 **Control** Baseline: 10.1% – 40/395 Post intervention: 20.5% – 61/298; p<0.001	
Unimodal compared with unimodal			
Grant (2011)[(49)] Single centre pair-matched C-RCT	**Intervention 1 – Unimodal** *Reminders* - signs highlighting patient-consequences of poor HH. **Intervention 2 – Unimodal** *Reminders* - signs highlighting personal-consequences of poor HH**.**	*Primary outcome* Mean HH adherence rate – number of opportunities Statistical significance test of the difference in adherence from baseline **Intervention 1:** Baseline: 80.7% – 163/202 Post intervention: 89.2% – 157/176; p=0.02 **Intervention 2:** Baseline: 80.0% – 96/120 Post intervention: 79.7% – 55/69; p=0.85	*Primary outcome* P values assessing statistical significant difference between intervention groups and control group: p=0.05 Unadjusted RR (95% CI) for HH adherence in the intervention group compared to the control. 1.12 (0.98 to 1.27); p=0.09

Key: ACE – acute care for the elderly; aOR – adjusted odds ratio; CI – confidence; ESBL-PE - extended-spectrum beta-lactamase-producing Enterobacteriaceae; ICU – intensive care unit; IRR – incidence rate ratio; MDRO – multidrug resistant organisms; OR – odds ratio; PP – percentage points; RR – relative risk; WHO Compliant – World Health Organization multimodal strategy (three or more key components); WHO Plus – World Health Organization multimodal strategy plus additional components.

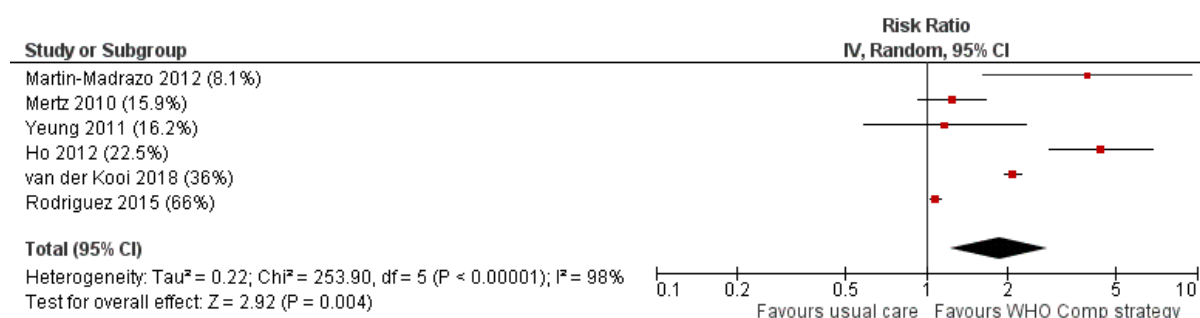**§** additional data provided by study author

Appendix 5: Subgroup and trend analysis for review question one

Figure A5-11 Subgroup analysis grouped by risk of contamination bias
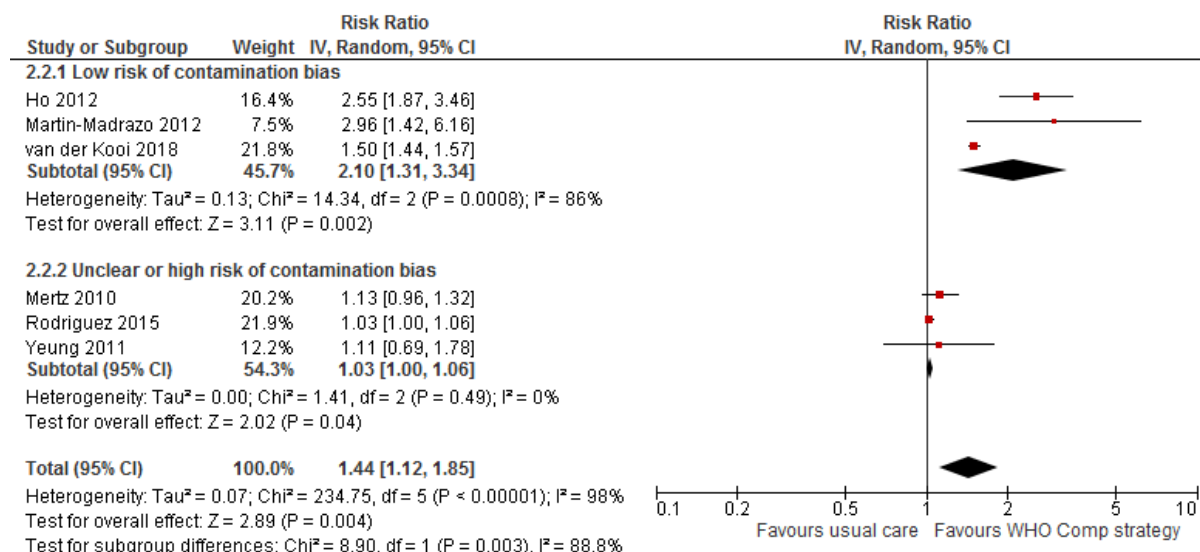
Key: CI – confidence interval; IV – inverse variance; Random – random effects model

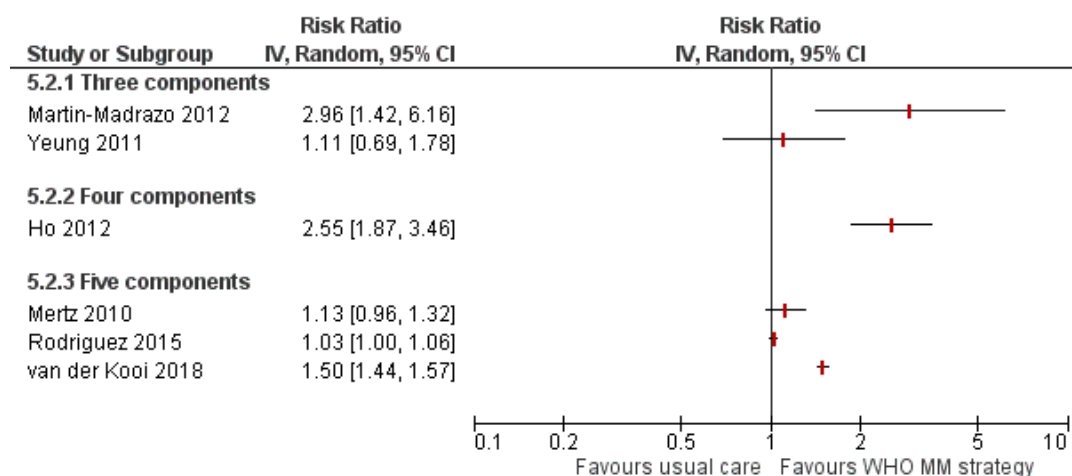**Figure A5-12 Trend analysis ordered by ascending baseline adherence rate**

Key: CI – confidence interval; IV – inverse variance; Random – random effects model

Figure A5-13 Trend analysis ordered by ascending number of components in strategy

Key: CI – confidence interval; IV – inverse variance; Random – random effects model

Appendix 6: Economic evidence for review question one: summary of characteristics, methods and results

Table A6-1 Economic evidence for review question one: summary of characteristics, methods and results of economic evaluation studies

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results (95% CI – unless stated otherwise)	Analysis of uncertainty
WHO Compliant versus usual care					
Chen 2016, Taiwan[71]	**Population:** All HCWs (n=2,463) in a teaching hospital **Intervention:** WHO Compliant **Comparator:** Prior IFC programmes – no further details provided	**Analysis type:** CBA alongside a B-A study **Perspective:** Payer (Hospital perspective) **Time horizon:** 1 year **Discount rate:** Not applicable	**Cost year & currency:** US $ (no year listed) **Cost components:** Costs of intervention: not detailed Cost of HCAI: total cost of each hospital stay including fees for medications, diagnostics, materials, services and diet (UTI: $3,822; RTI: $3,903; BSI $3,384). **Clinical outcomes:** HH adherence, HCAI incidence rate (UTI, RTI and BSI) and length of stay.	**Clinical outcomes:** <u>HH adherence</u> HH adherence improved from 62.3% (56.7 to 68.3%) to 73.3% (68.3 to 83.1%); p<0.001 <u>HCAI events</u> Reduction of 0.6 (3.7 ± 0.4 to 3.1 ± 0.5) HCAIs per 1,000 admission days. Reduction of 256.8 episodes of HCAIs per year. <u>Length of stay</u> Reduction in length of stay: 3,799 admission patient days. **Costs:** Cost of programme: $250,000 Savings per year due to intervention: $950,000. **ICERs:** Not reported.	None
Graves 2016, Australia[74]	**Population:** All HCWs in 50 of the largest acute public hospitals in Australia **Intervention:** Australian National HH Initiative – based on the WHO	**Analysis type:** CEA: Decision analytic model **Perspective:** Payer (Australian State perspective) **Time horizon:**	**Cost year & currency:** 2011 AU $ **Cost components:** Cost of intervention: Annual cost for administering intervention at both national and hospital level, staff time, and consumables.	**Clinical outcomes:** <u>HH adherence</u> Improved from 61.8% to 76.9% <u>Life years gained</u> 96 years gained in total **Costs:** Cost of HCAI: $919 to $14,273** Total annual cost: $2,851,475	Probability each state is cost-effective: ACT: 100% (41% cost saving) NSW: 81% QLD: 100% SA: 26% TAS: 1% WA: 1%

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results (95% CI – unless stated otherwise)	Analysis of uncertainty
	compliant **Comparator:** Varied by state or territory	Costs: 1 year Outcomes: Lifetime **Discount rate:** 3% (outcomes only)	Cost of HCAI: Additional LOS (ward: 1 to 11.4 days; ICU: 1 to 1.6 days). Cost per extra patient bed day (ward: $919 to $1,252; ICU: $3,503 to $4,282) **Clinical outcomes:** HH adherence, HCAI incidence rate (*Staphylococcus aureus*), deaths, life years gained.	**ICERs:** $29,700 per life year gained. State/Territory specific: ACT: $1,030 NSW: $33,353 QLD: $8,988 SA: $64,729 TAS: $10,371,874 WA: $63,332,051	
Le 2015, Vietnam[77]	**Population:** All HCWS (doctors, nurses, technicians, physiotherapists and medical students) in 2 ICU and 15 critical care unit. **Intervention:** WHO compliant **Comparator:** No campaign	**Analysis type:** CEA alongside a B-A study **Perspective:** Payer (hospital perspective) **Time horizon:** 10 months **Discount rate:** Not applicable	**Cost year & currency:** 2011 US $ **Cost components:** Cost of intervention: installing new sinks, new dispensers, printing training materials, pamphlets, posters, personnel and ABHR consumption. Cost of HCAI: bed, food, medication, equipment, pathology and imaging diagnosis charges. **Clinical outcomes:** HH adherence, HCAI incidence rates (nosocomial pneumonia, surgical site infections, UTIs, BSIs, skin infections and others).	**Clinical outcomes:** HH adherence Improved from 25.7% to 57.5% (p<0.001) HCAI Incidence of HCAI decreased by 36% (31.7% to 20.3%; p=0.005) **Costs:** The mean attributable cost of HAI was $1,131 Cost of intervention was $12,570, with variable costs of $5,530 (equating to $6.5 per patient). **ICERs:** Cost-effectiveness was estimated per 100 patients treated and reported as $1,074 saved per HAI prevented.	Sensitivity analyses included varying the incidence of HAIs, varying the mean attributable cost and the intervention costs. Threshold analysis to determine when the intervention would become cost neutral. The intervention remains cost savings up to a HH programme cost of $290 per patient or unless mean attributable cost of a HAI drops below $58. Sensitivity analyses ascertained that the intervention remains cost saving until the

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results (95% CI – unless stated otherwise)	Analysis of uncertainty
					reduction in incidence of HAIs is reduced to 0.6%.
Luangasanatip 2018 Thailand[76]	**Population:** All HCWs in 2 ICUs. Results of adult ICU are only presented. **Intervention:** WHO compliant **Comparator:** No campaign	**Analysis type:** CUA and CEA - decision analytic model **Perspective:** Payer (hospital perspective) **Time horizon:** Costs: 1 year Outcomes: Lifetime **Discount rate:** 3% (outcomes only)	**Cost year & currency:** 2016 US $ **Cost components:** Cost of intervention: ABHR, staff time per bed day. Cost of HCAI: Additional LOS (1.4 to 2.2 days; $5.5 to $47/day) and antibiotic treatment ($143 to $214). **Clinical outcomes:** HH adherence and HCAI incidence rate (MRSA-BSI), deaths averted	**Costs:** Cost of HCAI: $155 to $280** **Baseline scenario:** <u>HH adherence increased from 10% to 40%</u> **MRSA-BSI** avoided per ward: 0.3243 **Deaths** averted per 10,000 bed-days: 0.389 **Incremental cost** per ward: $636.25 **QALY** gained: 1.35 per ward **ICER**: $470.60 per QALY gained **Additional scenarios presented:** <u>HH adherence increased from 10% to 20%</u> **MRSA-BSI** avoided per ward: 0.2326 **Deaths** averted per 10,000 bed-days: 0.2326 **Incremental cost per ward**: $660.46 **QALY** gained: 0.96 per wards **ICER**: $684.77 per QALY gained <u>HH adherence increased from 10% to 60%</u> **MRSA-BSI** avoided per ward: 0.3503 **Deaths** averted per 10,000 bed-days: 0.4211 **Incremental cost** per ward: $629.30 **QALY** gained: 1.46 per ward **ICER**: $430.14 per QALY gained <u>HH adherence increased from 40% to 60%</u> **MRSA-BSI** avoided per ward: 0.0260 **Deaths** averted per 10,000 bed-days: 0.0313 **Incremental cost** per ward: $713.93	Scenario and PSA (Monte Carlo 10,000 iterations) Scenario ICERs ranged from $335 to $3,457 per QALY gained. Factors that tended to increase the cost-effectiveness of the intervention were low baseline compliance, high prevalence of colonization at admission and high rates of transmission. <u>PSA results mean (95% CI)</u> IMNB between $1,453 ($2,919 to $9,586) and $8,580 ($2,709 to $18,321) <u>Cost of intervention (5-fold increase)</u> Incremental cost per ward: $3,600 ICER per QALY: $2,623

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results (95% CI – unless stated otherwise)	Analysis of uncertainty
				QALY gained: 0.11 per ward **ICER**: $6431.80 per QALY gained Paediatric ICU results were similar, albeit with a lower infection rate and lower number of infections avoided due to intervention.	
WHO Plus versus usual care					
Chen (2011), Taiwan[72]	**Population:** Doctors, nurses, other HCWs in 1 teaching hospital **Intervention:** WHO Plus **Comparator:** Existing IPC programmes (no more details reported)	**Analysis type:** CEA and CBA alongside a B-A study **Perspective:** Payer (Hospital perspective) **Time horizon:** 4 years **Discount rate:** 3%	**Cost year & currency:** 2007 US $ **Cost components:** Cost of HCAI, intervention (ABHR products, posters, wall displays, rewards and other expenses); Opportunity costs of personnel were included in sensitivity analysis. **Clinical outcomes:** HH adherence and HCAI rate (MRSA, Acinetobacter, and XDRAB)	**Clinical outcomes:** HH adherence Improved from 43.3% to 95.6% HCAI rate 8.9% reduction in HCAI **Costs:** Incremental cost: $233,044 **ICERs or other comparisons:** $163.60 per episode of HCAI prevented Benefit-cost ratio: 23.7 Net benefit: $5,289,364	OWSA: key parameters - discount rates (0 to 7%), cost of ABHR, campaign expenses, personnel, extra cost per HCAI episode and number of averted HCAIs. ICERs between $89.5 and $468.3 per HAI prevented
Chun 2016, Republic of Korea[73]	**Population:** Doctors, nurses and all other HCWs in a teaching hospital **Intervention:** WHO Plus **Comparator:** Multiple prior IPC measures. CLABSI intervention was implemented midway post	**Analysis type:** CBA alongside a B-A study **Perspective:** Societal **Time horizon:** 4 years **Discount rate:** 5% (Cost of MRSA only)	**Cost year & currency:** 2015 US $ **Cost components:** Cost of intervention: ABHR consumption, HH campaign and salary of 1 employee added to the infection control office Cost of MRSA: additional medical costs and caregiver costs **Clinical outcomes:**	**Clinical outcomes:** HH adherence Improved from 33.2% to 92.2%. HCAI rate Incidence of HA MRSA decreased by 33% (−57 to −7.8%), equating to 5 fewer cases per 100,000 patient days. **Costs:** Total hand sanitizer costs: $21,294 Campaign costs: $8,182 Personnel costs: $138,019 Total costs: $167,495	Not reported

Author (year), country	Population & Interventions	Analysis details	Costs and clinical outcomes	Results (95% CI – unless stated otherwise)	Analysis of uncertainty
	intervention which included a HH component.		HH adherence and HCAI (MRSA only)* incidence rate	Economic burden of 1 case of MRSA: $13,101 Savings from MRSA prevention: $851,565 **ICERs or other comparisons:** Cost-benefit ratio: 5.08 (0.94 to 8.76)	
WHO Plus versus WHO Compliant					
Huis (2013), The Netherlands[75]	**Population:** Nurses (n=2,733) from 67 wards, in three hospitals (2 general and 1 teaching) **Intervention:** WHO Plus **Comparator:** WHO Compliant	**Analysis type:** CEA alongside a C-RCT. **Perspective:** Payer (Hospital perspective) **Time horizon:** 1 year **Discount rate:** Not applicable	**Cost year & currency:** 2009 € **Cost components:** Materials costs (website, leaflets, posters, newsletters, feedback charts and ABHR) and personnel costs (observations, delivery of feedback, extra staff time to perform HH). Intervention contained additional personnel costs (salary for coach, managers and role models). Cost of HCAI: Extended hospital stay, increased medical and nursing care, operations and consumables, microbiology tests and investigations, antibiotics and other drugs. **Clinical outcomes:** HH adherence and HCAI events (based on published studies)	**Clinical outcomes:** HH adherence Mean difference in improvement in HH adherence 8.91% (0.75 to 17.06%) HCAI events 2 scenarios used for HCAI outcome: 15% and 30% reduction. **Costs: (per ward)** Intervention: €12,156 Comparator: €6,659 Incremental: €5,497 (1,962 to €9,032). **ICERs:** €622 (146 to €1,098) per additional percentage of improvement due to the intervention. Scenario 1: 15% reduction in HCAI: €4,125 (€1,016 to €7,234) for an additional percentage reduction in HCAI rates. Scenario 2: 30% reduction in HCAI: €2,074 (€487 to €3,661) for an additional percentage reduction in HCAI rates.	Bootstrap simulation (10,000 replications). 15% reduction: 70% probability of cost-effectiveness at WTP of €5,000 per percentage reduction. 30% reduction: 90% probability of cost-effectiveness at WTP of €5,000 per percentage reduction.

Key: ACT - Australian Capital Territory; B-A - Before-after study; BSI –bloodstream infection; CBA – cost-benefit analysis; CE – cost-effectiveness; CEA – cost-effectiveness analysis; CLABI - central line–associated bloodstream infection; HAI - Hospital-acquired infection; ICER – incremental cost-effectiveness ratio; ICU – intensive care unit; LOS – length of stay; MRSA – methicillin-resistant *Staphylococcus aureus*; XDRAB – extensively drug-resistant Acinetobacter baumannii; NSW - New South Wales; OWSA – one-way sensitivity analysis; QLD – Queensland; RTI – respiratory tract infection; SA - South Australia; TAS – Tasmania; UTI – urinary tract infection; WA - Western Australia; WHO Compliant – World Health Organization multimodal strategy (three or more key

components); WHO Plus – World Health Organization multimodal strategy plus additional components

* Hospital acquired MRSA was defined by a positive blood culture >3 days after admission.
**Not reported. Calculated as multiplying the cost per bed day by the length of stay and adding any additional costs.