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# Gloves, gowns and masks for reducing the transmission of meticillin-resistant Staphylococcus aureus (MRSA) in the hospital setting (Review)

López-Alcalde J, Mateos-Mazón M, Guevara M, Conterno LO, Solà I, Cabir Nunes S, Bonfill Cosp X

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[Intervention Review]

# Gloves, gowns and masks for reducing the transmission of meticillin-resistant Staphylococcus aureus (MRSA) in the hospital setting

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## ABSTRACT

### Background

Meticillin-resistant *Staphylococcus aureus* (MRSA; also known as met**h**icillin-resistant *S aureus*) is a common hospital-acquired pathogen that increases morbidity, mortality, and healthcare costs. Its control continues to be an unresolved issue in many hospitals worldwide. The evidence base for the effects of the use of gloves, gowns or masks as control measures for MRSA is unclear.

### Objectives

To assess the effectiveness of wearing gloves, a gown or a mask when contact is anticipated with a hospitalised patient colonised or infected with MRSA, or with the patient's immediate environment.

### Search methods

We searched the Specialised Registers of three Cochrane Groups (Wounds Group on 5 June 2015; Effective Practice and Organisation of Care (EPOC) Group on 9 July 2013; and Infectious Diseases Group on 5 January 2009); CENTRAL (*The Cochrane Library* 2015, Issue 6); DARE, HTA, NHS EED, and the Methodology Register (*The Cochrane Library* 2015, Issue 6); MEDLINE and MEDLINE In-Process & Other Non-Indexed Citations (1946 to June week 1 2015); EMBASE (1974 to 4 June 2015); Web of Science (WOS) Core Collection (from inception to 7 June 2015); CINAHL (1982 to 5 June 2015); British Nursing Index (1985 to 6 July 2010); and ProQuest Dissertations & Theses Database (1639 to 11 June 2015). We also searched three trials registers (on 6 June 2015), references list of articles, and conference proceedings. We finally contacted relevant individuals for additional studies.

### Selection criteria

Studies assessing the effects on MRSA transmission of the use of gloves, gowns or masks by any person in the hospital setting when contact is anticipated with a hospitalised patient colonised or infected with MRSA, or with the patient's immediate environment. We did not assess adverse effects or economic issues associated with these interventions.

We considered any comparator to be eligible. With regard to study design, only randomised controlled trials (clustered or not) and the following non-randomised experimental studies were eligible: quasi-randomised controlled trials (clustered or not), non-randomised controlled trials (clustered or not), controlled before-and-after studies, controlled cohort before-after studies, interrupted time series studies (controlled or not), and repeated measures studies. We did not exclude any study on the basis of language or date of publication.

**Data collection and analysis**

Two review authors independently decided on eligibility of the studies. Had any study having been included, two review authors would have extracted data (at least for outcome data) and assessed the risk of bias independently. We would have followed the standard methodological procedures suggested by Cochrane and the Cochrane EPOC Group for assessing risk of bias and analysing the data.

**Main results**

We identified no eligible studies for this review, either completed or ongoing.

**Authors' conclusions**

We found no studies assessing the effects of wearing gloves, gowns or masks for contact with MRSA hospitalised patients, or with their immediate environment, on the transmission of MRSA to patients, hospital staff, patients' caregivers or visitors. This absence of evidence should not be interpreted as evidence of no effect for these interventions. The effects of gloves, gowns and masks in these circumstances have yet to be determined by rigorous experimental studies, such as cluster-randomised trials involving multiple wards or hospitals, or interrupted time series studies.

## PLAIN LANGUAGE SUMMARY

**Use of gloves, a gown or a mask for contact with hospitalised patients with *Staphylococcus aureus* resistant to a common antibiotic (MRSA)**

**What is MRSA, and why is it a problem in hospitals?**

MRSA stands for 'meticillin- (or methicillin-) resistant *Staphylococcus aureus'.* This is a common type of bacterium (*Staphylococcus aureus*) that is no longer killed by meticillin (also known as 'methicillin', an antibiotic) or other antibiotics that are frequently used to treat infections. MRSA can live on people without making them ill, and without them showing any symptoms, but is dangerous when it infects people who are unwell.

MRSA is easily transferred from one patient to another in hospitals, where it causes severe infections and can cause death. This transmission occurs mainly through healthcare workers when their hands, clothes, or equipment become contaminated with MRSA during routine care of patients who have MRSA. Later contact of the contaminated hands, clothes or equipment with other patients allows MRSA to spread within the hospital.

**Why might use of gloves, gowns or masks help prevent transmission of MRSA between patients in hospitals?**

It is possible that the use of disposable gloves with or without the use of disposable or washable gowns could prevent transmission of MRSA, as they would protect the healthcare workers' hands and clothes from becoming contaminated with MRSA. The gloves and gowns would be discarded after one patient had been cared for, and clean ones used to visit the next patient. The use of masks might also prevent spread of MRSA through the air.

It is not known whether use of gloves, gowns or masks reduces the spread of MRSA when they are used individually, or whether combining two of the three, or all three, produces better results.

**The aim of this research and what the researchers found**

The researchers aimed to find out whether the use of gloves, a gown or a mask by any person in the hospital (for example, a doctor) getting close to a patient found to have MRSA prevents the transmission of MRSA from this patient to other people in the hospital.

The researchers made a wide search of the medical literature, up to June 2015, but did not find any rigorous studies that addressed this topic.

At present there is no scientific evidence that the wearing of gloves, a gown, or a mask by people getting close to patients with MRSA reduces the transmission of MRSA to other people in the hospital. However, this should not be interpreted as demonstrating that gloves, gowns or masks are not effective; it means that the research that would be required to measure an effect - if there is one - has not been done yet.

# BACKGROUND

## Description of the condition

Meticillin-resistant *Staphylococcus aureus,* commonly known as MRSA, is a bacterium that is resistant to meticillin (better known as 'methicillin', which is its United States Adopted Name) and the rest of the beta-lactam antibiotics (penicillins, cephalosporins and carbapenems). MRSA is a strain of *S aureus* that acquired a gene that confers resistance to these common antibiotics (Hartman 1981; Livermore 2000).

MRSA can colonise or infect people. A colonisation occurs when the micro-organism is present without causing adverse clinical signs or symptoms. On the other hand, an infection implies a localised or systemic condition that results from an adverse reaction to the presence of an infectious agent or its toxins (Garner 1996). The normal bacterial flora of humans often includes *S aureus* (APIC 2010), with the epithelium of the anterior nares (the inside of the nose) being its predominant point of colonisation in adults (Wertheim 2005). Risk factors for MRSA colonisation at hospital admission include: prior healthcare contact (for example, hospitalisation in the past 12 months, or a stay in a nursing home), history of exposure to healthcare-associated pathogens (such as history of MRSA carriage, *Clostridiun difficile* infection, or recent antibiotic use), and co-morbidity (such as congestive heart failure, diabetes or renal failure; McKinnell 2013).

The prevalence of nasal MRSA colonisation varies across populations. For example, in some European countries it is between 0.1% and 0.7%, in the non-institutionalised population (den Heijer 2013), compared with 1.5% in the USA (Gorwitz 2008). At admission of patients to hospital prevalence rises to between 3% and 11% (Troillet 1998; Harbarth 2008; Baker 2010; Morgan 2010), and between 5.8% and 8.3% at patient admission to intensive care units (ICU; Ziakas 2014); and can be up to 15% in healthcare workers (Albrich 2008; Bisaga 2008; Suffoletto 2008; Elie-Turenne 2010). *S aureus* can also colonise the face, throat, hands, axilla (armpit), groin, rectum and perineum (area between the anus and vagina or scrotum; Williams 1963; Mertz 2009). Therefore, as normally only the anterior nares are used as a sampling site for MRSA, the true prevalence of MRSA carriage may be higher.

Since the 1960s, MRSA has been recognised as a source of healthcare-associated infections (HAI; Barrett 1968; Benner 1968). HAIs (formerly known as 'nosocomial infections') are infections that were not present or incubating on admission to a healthcare facility (CDC 2014), and therefore, were acquired in the facility while receiving care. MRSA colonisation in adults is a known risk factor for the development of MRSA infection: 18% to 33% of adult patients colonised with MRSA will develop an MRSA infection, such as pneumonia, or a soft tissue or bloodstream infection (Calfee 2014), and 8.5% of paediatric (child) patients colonised with MRSA will also develop an infection (Calfee 2014). The risk of HAI is even greater in adults who are colonised by MRSA in the hospital, up to 30% of whom will develop an MRSA infection (Huang 2003).

Risk factors for MRSA infection include: MRSA colonisation; advanced age; prolonged hospital stay; previous use of broad-spectrum antimicrobials; a stay in a burn or intensive care unit; severe underlying illness; invasive procedures during hospitalisation (such as insertion of central venous catheters; or surgical wounds), and frequent contact with the healthcare system or healthcare workers (Peacock 1980; Boyce 1981; Ward 1981; Boyce 1983; Boyce 1989; Jernigan 1996; Davis 2004: Calfee 2014). Colonisation pressure (the ratio of MRSA carrier–days to total patient-days) is an independent risk factor for hospital acquisition of MRSA (Merrer 2000; Calfee 2014).

The rates of MRSA in the hospital setting have increased worldwide during the last few decades (Turnidge 2000; Fridkin 2002; Tiemersma 2004; Grundmann 2006). At present, its occurrence is stabilising, or even decreasing in some countries (Burton 2009; Kallen 2010; Wilson 2011; ECDC 2013; Sievert 2013), as are the rates of invasive infections caused by MRSA (Dantes 2013). However, MRSA continues to be one of the commonest antibiotic-resistant pathogens in the hospital setting in many parts of the world. The proportion of *S aureus* isolates resistant to meticillin remains over 25% in many countries, for example, in eastern and southern Europe (ECDC 2013; WHO 2014), and MRSA accounts for 8.5% to 10.7% of HAIs in hospitals in the USA (Sievert 2013; Magill 2014). Although these findings suggest some success in controlling MRSA, many patients continue to be at risk (Calfee 2014), indeed, in the USA there were no significant reductions in healthcare-associated MRSA infections among paediatric populations between 2005 and 2010 (Iwamoto 2013).

MRSA causes skin and wound infections (such as surgical site infections), pneumonia and bloodstream infections (Sievert 2013). Therefore, MRSA infections increase healthcare associated morbidity, mortality and costs significantly (Crowcroft 2002; Cosgrove 2003; Engemann 2003; Cosgrove 2005). Its economic impact includes direct costs (prolonged hospital stay, additional diagnostic procedures and antibiotic use, and costs for containment of outbreaks) and indirect costs (loss of productivity, long-term disability and excess mortality; Gould 2006; Grundmann 2006; Goetghebeur 2007; Gould 2010; WHO 2014). However, it has also been suggested that there is a lack of properly designed and conducted studies to compare the resource use associated with resistant versus nonresistant pathogens (WHO 2014).

## Description of the intervention

Various strategies exist to reduce the transmission of MRSA (Loeb 2003; Gould 2009; APIC 2010; Calfee 2014; Loveday 2014). In practice, multiple interventions are often employed in hospitals (Lee 2011), such as the following.

- Decontamination and disinfection of the environment and equipment.
- Rational antibiotic use.
- Hand hygiene, that is, actions to maintain healthy hands and fingernails, for example, handwashing or hand antisepsis (Public Health Agency of Canada 2012a).
- Identification of carriers through early detection (laboratory surveillance and screening for MRSA, that is, the sampling and culture of sites, such as skin lesions, nose, perineum and throat, that are associated with the carriage of MRSA; Cooper 2003).
- Decolonisation therapy to eradicate MRSA from colonised people.
- Isolation of patients to stop the transmission.

Isolation is the physical segregation of patients colonised or infected with a micro-organism, such as MRSA (or of patients awaiting screening results), for reducing its transmission to other

patients. Isolation strategies can be categorised in descending grades of intensity (Cooper 2003), usually involving the use of disposable gloves, gowns and masks.

- Placement of patients in an isolation unit or isolation ward (either a purpose-built or improvised ward used for the isolation of MRSA patients).
- Nurse cohorting, which implies the physical segregation of a group of patients with MRSA from patients not known to harbour MRSA in a geographically distinct area of the same ward; the MRSA patients are nursed by designated staff who do not nurse non-MRSA patients during the same shifts.
- Isolating patients in a single-room.
- Cohorting without designated staff.
- The use of aprons or gowns, gloves and, in some cases, masks as the only physical barriers to transmission used by healthcare workers when contact with MRSA-colonised or infected patients, or their immediate environment (that is, the patient's room, cubicle or operating room), is anticipated.

Therefore, gloving, gowning and masking are barrier methods of infection control used to restrict the transmission of pathogens in hospitals.

## How the intervention might work

MRSA transmission in hospitals has been well documented using molecular typing techniques (Muto 2003). Hospitalised patients who are colonised or infected with MRSA provide the main reservoir of the pathogen (Thompson 1982; Reboli 1990; Davis 2004; Hidron 2005), and generally MRSA spreads from patient to patient via the transiently contaminated hands, clothing and equipment of healthcare workers (Thompson 1982; Muto 2003; Calfee 2014).

Healthcare workers' hands, clothes or equipment can become contaminated with MRSA as they care routinely for patients (Blok 2003; Snyder 2008). Moreover, MRSA can also survive on objects in the environment and be spread from these to patients, often via healthcare workers (Rutala 1983; Oie 1996; Devine 2001; Srinivasan 2007). Some older studies suggested a role for airborne transmission of *S aureus* (Rammelkamp 1964; Williams 1966; Selkon 1980), and more recent studies also support the possibility that personnel with persistent MRSA nasal colonisation may spread the micro-organism via droplet transmission (see glossary in Appendix 1; Gaynes 1991; Reagan 1991; Boyce 1993; Sheretz 1996; Shiomori 2001; Wilson 2004).

MRSA affects a large proportion of hospitalised patients and is transferable from person-to-person. Moreover, there are studies that point to a positive effect of the use of gloves, gowns and masks in reducing MRSA transmission in both outbreak and non-outbreak situations (Hartstein 1995; Jernigan 1996; Karchmer 2002; Mangini 2007; Johnston 2009). Therefore, it is postulated that the use of gloves, gowns and masks by hospital staff or visitors when in contact with an MRSA patient, or with his/her immediate environment, could prevent the transmission of MRSA (Siegel 2007; Calfee 2014).

The use of gloves during routine hospital procedures has been shown to prevent hand contamination by several organisms (Leclair 1987; Johnson 1990; Olsen 1993; Tenorio 2001), and their appropriate use may be as effective as the isolation of patients in containing multidrug resistant organisms, particularly when isolation is not feasible (Trick 2004; Bearman 2007; NHMRC 2010). Furthermore, gowning by hospital staff can reduce the transient contamination of their clothes (Zachary 2001; Puzniak 2002), and the use of masks by healthcare workers during close contact with MRSA colonised patients may prevent healthcare workers' nasal colonisation with MRSA (Lacey 2001).

## Why it is important to do this review

While some studies point to a positive effect of gloves, gowns and masks in reducing MRSA transmission (Arnow 1982; Safdar 2008), others suggest that gloving and gowning do not decrease HAIs (Yap 2004; Chai 2005; Johnston 2009), or that MRSA can be successfully controlled without some of these barriers (Pan 2005; Grant 2006). A number of systematic reviews assessed the effectiveness of different strategies for controlling micro-organisms in hospitals (Cooper 2003; Aboelela 2006; Loveday 2006; Halcomb 2007; Ranji 2007; Glick 2013, among others), and several Cochrane reviews have focused on the use of barrier precautions (Webster 2003; Tanner 2006; Pammi 2011; Jefferson 2011; Hughes 2013; Lipp 2014; Mischke 2014). However, none of these reviews attempted to disentangle the specific effects of gloving, gowning or masking when contact with MRSA inpatients, or their immediate environment in the hospital, is anticipated.

Professional organisations and national institutions have issued guidelines for MRSA control in the hospital setting (NZMoH 2002; Coia 2006; Grundmann 2006; Rodriguez-Baño 2006; APIC 2010; NHMRC 2010; Lee 2011; Coia 2013; WIP 2012; Calfee 2014), but their recommendations for practice can be inconsistent or inconclusive (Johnston 2009). For example, some guidelines pointed out that the use of a mask for MRSA remains controversial (APIC 2010), and that it represents an area for further research (Irish department of Health 2013). The low quality of the evidence identified may explain the existing reservation for the use of gloves, gowns and masks to prevent transmission of MRSA in the hospital setting (Johnston 2009; Hansen 2010), and the varying ways in which these guidelines are applied in practice (Hails 2003; Gastmeier 2004; Sunenshine 2005; Jarvis 2007; Lee 2011; Zastrow 2011; Pogorzelska 2012; Loveday 2014).

On the other hand, there are some concerns about the potential harms associated with the use of gloves, gowns and masks (Evans 2003; AHRQ 2013; Zahar 2013; Calfee 2014). Contact precautions restrict the patients' autonomy (Santos 2008; Lee 2011; Zastrow 2011), and may be related to increased symptoms of depression and anxiety (Day 2011), and to a decreased patient satisfaction with care (Mehrotra 2013). They could also cause a deterioration of the quality of care due to increased noninfectious adverse events (e.g. falls, pressure ulcers) caused by poorer compliance with hand hygiene or a reduction in visits by medical staff (Girou 2004; Bearman 2007; Morgan 2009; Fuller 2011; Morgan 2011; Karki 2013). In addition, gloves become contaminated and their inappropriate use can result in the transmission of micro-organisms (Public Health Agency of Canada 2012b). However, additional studies are needed to confirm this increase of adverse events (Zastrow 2011; BUGG Study 2013; Calfee 2014).

Finally, as contact precautions require resources that may be limited in hospitals, their cost-effectiveness should also be determined. Moreover, given the difficulties that health professionals have in adhering to preventive measures and precautions, it is essential to identify the most effective measures

for preventing MRSA transmission in order to choose wisely the minimum number of interventions to implement.

Therefore, an accurate determination of the benefits, potential harms and cost-effectiveness of the use of gloves, gowns and masks, alone or in combination, is needed.

## OBJECTIVES

To assess the effectiveness of wearing gloves, a gown or a mask when contact is anticipated with a hospitalised patient colonised or infected with MRSA or with the patient's immediate environment. See Differences between protocol and review for this section.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

This review considered randomised controlled trials (RCTs) and certain non-randomised experimental designs as eligible, irrespective of their language or publication status. In particular, we considered the following study designs to be eligible (Table 1 details the 'study design features' that we assessed to decide on eligibility).

- RCTs.
- Cluster-RCTs (Cl-RCTs).
- Quasi-randomised controlled trials (Q-RCTs).
- Cluster-quasi-randomised controlled trials (ClQ-RCTs).
- Non-randomised controlled trials (NRCTs).
- Cluster non-randomised controlled trials (Cl-NRCTs).
- Controlled before-and-after studies (CBA).
- Controlled cohort before-after studies (CChBA).
- Interrupted time series studies (ITS).
- Controlled interrupted time series studies (CITS).
- Repeated measures studies (RMSs).

Eligible study designs included only experimental designs, as they can minimise some biases usually present in infection control studies (Stone 2007). We defined a study as experimental always that the intervention had been deliberately allocated by the researcher to observe its effects (Shadish 2002). In particular, we considered the following minimum requirements for a study to be defined as experimental: a prospective baseline assessment; a prospective allocation of the intervention; and a prospective outcome assessment.

We excluded observational studies (see glossary in Appendix 1), and outbreak reports (the description of outbreaks and the subsequent interventions adopted for their control; Stone 2007). We also excluded in vitro laboratory-based studies that assessed the efficacy of gloves, gowns or masks impregnated with antiseptic or anti-infective agents to prevent the contamination of the outer surface of the barrier with pathogens.

The RCT is the experimental design that is considered to have the highest level of internal validity (through elimination of selection bias) for assessing the efficacy of an intervention. However, non-randomised studies (NRS) are ubiquitous in the area of interventions for decreasing the spread of antibiotic-resistant pathogens (Harris 2004). Whilst more prone to bias (Deeks 2003), we accepted some types of NRS as eligible. We based this decision on the difficulties of randomising the use of gloves, gowns and masks due to the following circumstances that are present in the context of infection control.

- Ethical concerns: gloves and gowns can be perceived by healthcare workers as effective interventions (Seibert 2014), so it can be difficult to withhold treatment in the control group (Ijaz 2014).
- Logistical difficulties: gloves, gowns, and masks are usually applied as part of complex interventions, which are difficult to implement and evaluate. Moreover, infection control interventions are usually applied in clusters, and the number of clusters available may be low.
- The need to intervene quickly (for example, in outbreak situations).

Therefore, we considered that a disinterested (free from bias and partiality) review that systematically reports the findings and limitations of available NRS could be useful.

See Differences between protocol and review for this section.

#### Types of participants

We considered hospitalised patients to be eligible participants and defined them as those admitted to healthcare facilities that provide board and room for the purpose of observation, care, diagnosis or treatment (MeSH Browser 2014). Therefore, we excluded:

- hospital outpatients: patients admitted to the hospital setting for the purpose of observation, care, diagnosis or treatment without receiving board and room, such as patients attending haemodialysis session; and
- patients attending any other healthcare facilities (as defined by the thesaurus of the US National Library of Medicine; MeSH Browser 2014): 'ambulatory care facilities' or 'hospital outpatient clinics'; 'rehabilitation centres'; and 'residential facilities' (including assisted living facilities, group homes, halfway houses, homes for the aged, nursing homes (Hughes 2013), or orphanages).

See glossary in Appendix 1 for a definition of these terms, and Differences between protocol and review for this section.

#### Types of interventions

##### *Interventions*

The use of gloves, gowns, aprons or masks by any hospital staff (healthcare or non-healthcare professionals) or by any patient's caregiver or visitor for interactions with a patient colonised or infected with MRSA or with potentially contaminated areas in the patient's environment, for example in the patient's room, cubicle or operating room. We considered the use of 'medical gloves'. To be eligible, gloves needed to be disposable and intended for single patient use and then to be discarded. We considered the use of 'gowns', either 'isolation gowns' or 'surgical gowns'. For 'masks', we considered the use of 'procedure masks' and 'surgical masks', as well as 'particulate respirators' (see glossary in Appendix 1 for a definition of all these terms).

We defined as eligible any 'care bundle' (see Appendix 1) that considered the use of gloves, gowns or masks, or any combination

thereof. Therefore, gloves, masks and gowns could be used in the following ways:

- on their own as a single intervention, for example, the use of gowns alone;
- as a combination, for example, the use of gowns and gloves;
- combined with any other barrier precaution, such as the placement of MRSA patients in isolation units to be attended by staff using gowns, gloves and masks; or
- combined with any other infection control intervention, such as the decolonisation of patients with MRSA.

Only studies in which gloves, gowns or masks were used with patients who had MRSA were eligible. As a consequence we excluded studies that investigated the effects of the following interventions:

- gloves, gowns or masks as 'routine practice' or 'standard precautions', that is, when there is anticipated exposure to a patient's blood, body, fluids, secretions,and excretions (except for sweat), non-intact skin, draining wounds and mucous membranes (Siegel 2006; Johnston 2009). Therefore, we excluded studies assessing gloving, gowning or masking during routine vascular catheter insertion, surgical procedures, and patient care after organ transplantation (Stewart 2006; Tanner 2006; Lipp 2014; Mischke 2014);
- the universal use of gloves, gowns or masks, that is, their use for contacts with all patients (Webster 2003); or
- the pre-emptive use of gloves, gowns or masks, that is, their use for all new admissions or for all patients admitted to a specific unit, until a negative screening culture for the target organism is reported (Siegel 2006).

### *Comparators*

We considered any comparator, provided that it allowed the effects of gloving, gowning or masking (used on their own or in combination) for interactions with patients colonised or infected with MRSA or with their environment to be assessed in their own right. In practical terms, we would have included those studies in which co-interventions were similar in the study groups, as this would allow us to assess the specific impact of the use of gloves, gowns or masks.

We excluded studies that evaluated the effects of MRSA screening programs, isolation of MRSA patients (such as placement in an isolation unit or ward, nurse cohorting or cohorting without designated staff), or campaigns to increase the use barrier precautions, as these do not allow the effects of the use of gloves, gowns or masks to be assessed in their own right. For example, in studies evaluating MRSA screening programmes the observed effects could be attributed to early detection of MRSA carriers (which implies that they do not become a continuous source of MRSA), and not only to the use of gloves, gowns or masks.

See Differences between protocol and review for this section.

## Types of outcome measures

### *Primary outcomes*

#### Outcomes measured in patients

- Healthcare-associated MRSA colonisations (see glossary in Appendix 1). We would have considered this outcome only in the studies reporting an existing screening policy at admission (and throughout the study), as if this is not the case colonisation data would be incomplete owing to failure to detect asymptomatic MRSA-colonised patients (Cooper 2003).
- Healthcare-associated MRSA infections (see glossary in Appendix 1).
- Healthcare-associated MRSA bacteraemias (see glossary in Appendix 1).
- Healthcare-associated MRSA pneumonias (see glossary in Appendix 1).
- Mortality attributable to MRSA.

We would have accepted the study authors' report regarding the methods used to diagnose healthcare-associated MRSA colonisations, infections, bacteraemias or pneumonias and considered any measure of frequency. We would have considered total MRSA colonisations, infections, bacteraemias or pneumonias only if studies did not report healthcare-associated events as outcomes. We would have admitted any definition used for healthcare-associated infections and colonisations, as they are not standardised (Cohen 2008), and any metric for quantifying healthcare acquisition of pathogens, such as incidence rate or incidence density rate.

#### Outcomes measured in hospital staff, patient's caregivers or visitors

- Healthcare-associated MRSA colonisations (only in the articles reporting an existing screening policy during the study).
- Prevalence of carriers of MRSA.

The primary objective of a Cochrane review should be to assess the effects of one or more healthcare interventions on stakeholder-important outcomes, both intended and unintended (MECIR Conduct 2013). Although there are some concerns about the potential harms of the use of gloves, gowns or masks (see Why it is important to do this review), we did not assess them, as we considered that in order to do this adequately we would need to apply different selection criteria for study designs - and include NRS, such as cohort studies, as well - and that it might not be enough to restrict participants to those with demonstrated MRSA. Therefore, this process would have consumed too many of the review team's resources and means that another systematic review that focuses on the unintended effects is warranted.

### *Secondary outcomes*

- MRSA to meticillin-susceptible *S aureus* (MSSA) ratios.
- Length of stay, measured in days (see glossary in Appendix 1).
- Antibiotic use.
- All cause mortality.

We did not exclude any study solely because no outcomes of interest were reported. We did not attempt to assess issues of equity and relevance of evidence to specific populations. See Differences between protocol and review for this section.

## Search methods for identification of studies

### Electronic searches

We searched the following electronic databases for potentially relevant studies.

- The Cochrane Wounds Group Specialised Register (searched 5 June 2015).
- The Cochrane EPOC Group Specialised Register (searched 9 July 2013).
- The Cochrane Infectious Diseases Group Specialised Register (searched 5 January 2009).
- The Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2015, Issue 6).
- The Database of Abstracts of Reviews of Effects (DARE; *The Cochrane Library* 2015, Issue 6).
- The Health Technology Assessment Database (HTA; *The Cochrane Library* 2015, Issue 6).
- The NHS Economic Evaluation Database (NHS EED; *The Cochrane Library* 2015, Issue 6).
- The Methodology Register (*The Cochrane Library* 2015, Issue 6).
- Ovid MEDLINE (1946 to June Week 1 2015).
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations; 1946 to June Week 1 2015).
- Ovid EMBASE (1974 to 4 June 2015).
- Web of Science (WOS) Core Collection: Science Citation Index Expanded (SCI-EXPANDED; 1900 to 7 June 2015); Social Sciences Citation Index (SSCI); 1956 to 7 June 2015; Conference Proceedings Citation Index Science (CPCI-S; 1990 to 7 June 2015).
- EBSCO CINAHL (1982 to 5 June 2015).
- Ovid British Nursing Index (BNI; 1985 to 6 July 2010).
- ProQuest Dissertations & Theses A&I (1639 to 11 June 2015).

See Appendix 2 and Table 2 for a description of the strategy used in each database, the dates searched, and the results.

We used the following search strategy in the Cochrane Central Register of Controlled Trials (CENTRAL):

#1 MeSH descriptor: [Staphylococcus aureus] explode all trees
#2 "staphylococcus aureus":ti,ab,kw
#3 MeSH descriptor: [Staphylococcal Infections] explode all trees
#4 (staphylococ* next infection*):ti,ab,kw
#5 (staphylococ* near/3 (bacteremia or bacteraemia)):ti,ab,kw
#6 {or #1-#5}
#7 MeSH descriptor: [Methicillin Resistance] explode all trees
#8 MeSH descriptor: [Penicillin Resistance] explode all trees
#9 (methicillin* or meticillin* or penicillin* or oxacillin*) next resistan*:ti,ab,kw
#10 (multi next drug next resistan*) or (multi-drug next resistan*):ti,ab,kw
#11 antibiotic next resistan*:ti,ab,kw
#12 {or #7-#11}
#13 #6 and #12
#14 MeSH descriptor: [Methicillin-Resistant Staphylococcus aureus] explode all trees
#15 (mrsa or emrsa or mdro):ti,ab,kw
#16 {or #13-#15}
#17 MeSH descriptor: [Protective Clothing] explode all trees
#18 MeSH descriptor: [Masks] explode all trees
#19 (glove* or gown* or apron* or mask*):ti,ab,kw
#20 ((barrier* or contact or universal or droplet or isolation or airborne) next precaution*):ti,ab,kw
#21 ((contact or patient or ward* or unit*) near/2 isolation):ti,ab,kw
#22 ((isolated next ward*) or (ward near/2 clos*) or (clos* near/2 ward*)):ti,ab,kw
#23 "cohort nursing":ti,ab,kw
#24 (cohort next patient*):ti,ab,kw
#25 MeSH descriptor: [Hand Disinfection] explode all trees
#26 (handwashing or hand washing or hand hygiene):ti,ab,kw
#27 (control next measure*):ti,ab,kw
#28 {or #17-#27}
#29 #16 and #28

We combined EMBASE and CINAHL search strategies with validated methodological filters for the study designs eligible for our review (MEDLINE had no filters applied). EMBASE had the RCT UK Cochrane Centre filter (Lefebvre 2011), and the EPOC filter. CINAHL had the RCT filter (SIGN 2011), and the EPOC filter. See Differences between protocol and review for this section. We searched without any restrictions regarding language or date of publication.

We searched the following clinical trials registries:

- ClinicalTrials.gov (www.clinicaltrials.gov/);
- WHO (World Health Organization) International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/Default.aspx); and
- International Standard Randomised Controlled Trial Number Register (http://controlled-trials.com/isrctn/search.asp).

### Searching other resources

- We checked the reference lists of relevant studies in the subject area (including systematic reviews) for additional relevant papers.
- We contacted relevant individuals for information about further studies.
- We checked the abstracts from the following conference proceedings (seeDifferences between protocol and review).
  - 1st International Conference on Prevention and Infection Control - ICPIC 2011 (www.biomedcentral.com/bmcproc/supplements/5/S6)
  - 2nd International Conference on Prevention and Infection Control - ICPIC 2013 (www.aricjournal.com/supplements/2/S1/all).
  - IDWeek 2012: Epidemiology and Infection Control track (https://idsa.confex.com/idsa/2012/viewsessionpdf.cgi).
  - IDWeek 2013: Epidemiology and Infection Control track (https://idsa.confex.com/idsa/2013/viewsessionpdf.cgi).
  - IDWeek 2014: Epidemiology and Infection Control track (https://idsa.confex.com/idsa/2014/webprogram/start.html).
  - IDSA Annual meeting 2011 (https://idsa.confex.com/idsa/2011/webprogram/start.html).
  - IDSA Annual meeting 2010 (https://idsa.confex.com/idsa/2010/webprogram/start.html).
  - IDSA Annual meeting 2009 (https://idsa.confex.com/idsa/2009/webprogram/start.html).

## Data collection and analysis

### Selection of studies

At least two review authors (JLA and MM, MG, LOC, or SC) screened all titles and abstracts independently to select potentially relevant studies. Where there was any uncertainty based on this information we obtained the full text for further assessment. At least two review authors (JLA and MM, MG, LOC, or SC) assessed the eligibility of the retrieved full text versions independently. We resolved disagreements by discussion between the two authors. If there was no consensus, a third author (IS) was consulted. We were not blinded to the authors' names of the publications, or their institutions, journals or results during the selection process. We did not exclude studies solely on the basis of the reporting of the outcome data, since this might have introduced bias due to selective outcome reporting (O'Connor 2011). We completed a PRISMA flow chart (Figure 1) and a Characteristics of excluded studies table.

**Figure 1. Study flow diagram.**

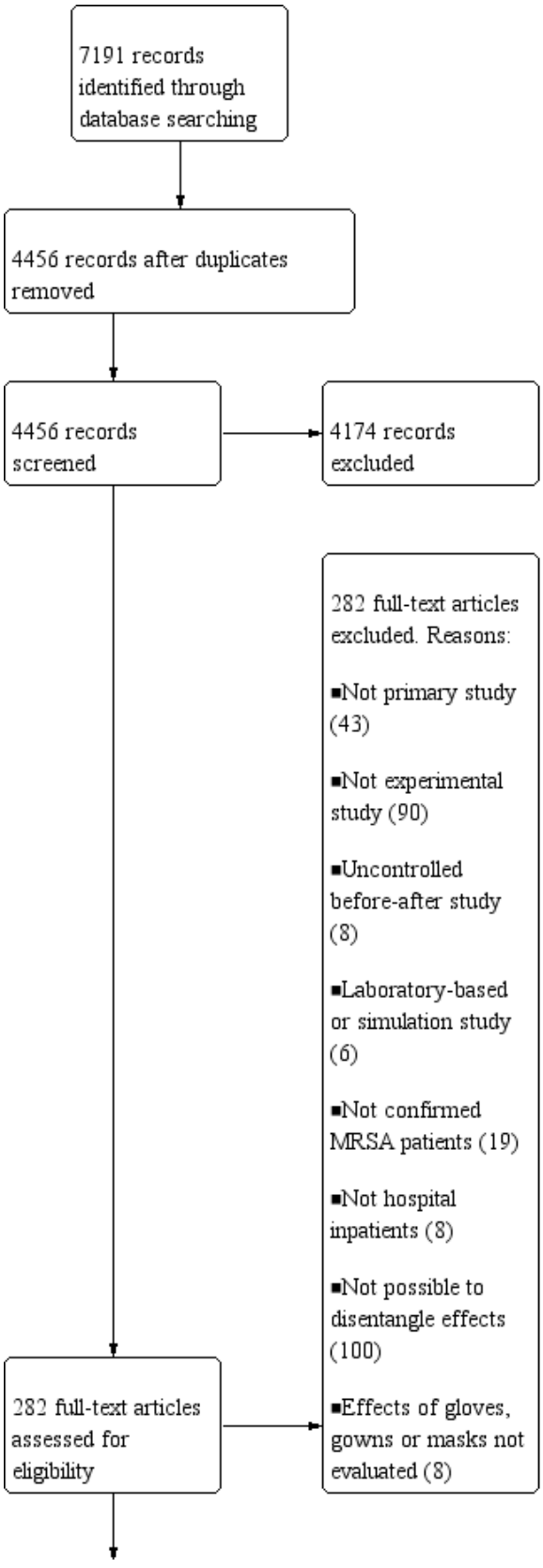
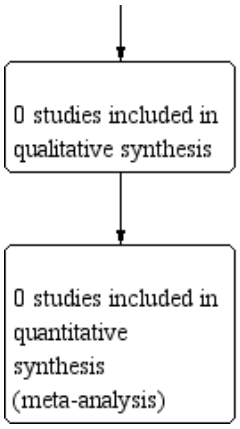


**Figure 1. (Continued)**




If any study meets the inclusion criteria in future updates of this review, we will use the plan outlined below for data extraction and analysis. Moreover, if we find multiple reports of the same included study, we will collate them so that each study - rather than each report - is the unit of interest in the review. See Differences between protocol and review for this section.

### Data extraction and management

We had planned to design a data extraction form and pilot its template for usability. This form would have been adapted from the following templates and tailored to the review question.

- EPOC Data Abstraction form (EPOC 2013b).
- ORION Statement checklist (Stone 2007).
- CONSORT statement (CONsolidated Standards of Reporting Trials) 2010 (Schulz 2010).
- CONSORT extension for non-pharmacological interventions (Boutron 2008).
- CONSORT extension for cluster randomised trials (Campbell 2012).
- Template for intervention description and replication (TIDieR) checklist (Hoffmann 2014).
- *Cochrane Handbook for Systematic Reviews of Interventions*: study design checklist (tables 13.2.a and 13.2.b), following the guidance provided in Box 13.4.a (Reeves 2011), and the templates for collecting information about confounding factors, their comparability at baseline, methods used to adjust for confounding, and effect estimates in non-randomised studies (NRSMG 2011).

For each included study we would have extracted details of participants, setting, methods, intervention and control, outcome data, funding source, and declaration of interests for the primary investigators. We would have collected this information in sufficient detail to populate a table of 'characteristics of included studies'. Moreover, we would have extracted data related to the risk of bias (RoB) and the study results. We would have examined any relevant retraction statements and errata for relevant information regarding each included study.

As infection control interventions usually have several components, we would have created a graphical depiction of the experimental and control interventions using the Pat Plot tool (Perera 2007); once created, a PaT Plot is easy to interpret and would have helped us to establish clear comparisons between different arms of a study (CEBM 2009). For studies with more than two intervention arms, we would have considered only the intervention and control groups that met the eligibility criteria.

At least for outcome data, two review authors would have extracted data independently from reports of each included study. If possible, this dual data extraction would have been applied for the data extraction of all the characteristics of the included studies. We would have resolved any discrepancy in the extraction of the data by consensus. In the case of no consensus, a third review author, or the editorial base of the Cochrane Wounds Group, would have settled the discrepancies. We would have written to authors or organisations to obtain important missing information or clarification, and we would have checked accuracy of numeric data in the review, as suggested by MECIR (MECIR Conduct 2013). See Differences between protocol and review for this section.

### Assessment of risk of bias in included studies

#### *All study designs (clustered or not) except for ITS, CITS and RMS*

We would have assessed the RoB according to the domains proposed by the Cochrane Collaboration's RoB tool and the Cochrane EPOC group (Higgins 2011a; EPOC 2013c).

- Random sequence generation (selection bias).
- Allocation concealment (selection bias). This domain also considers the presence of recruitment bias in cluster-designs.
- Imbalance in baseline characteristics (selection bias), in terms of either the individuals or the clusters (when it is a cluster design). See Appendix 3 for the list of potential confounders to consider. This domain will not be assessed for RCTs allocated at the individual level with an adequate sample size as we will assume that baseline imbalances in these designs are caused by chance.
- Imbalance in baseline outcome measurements (selection bias), when applicable (assessments to be made for each outcome (or class of outcomes); EPOC 2013c).
- Blinding of participants and personnel (performance bias). The *Cochrane Handbook for Systematic Reviews of Interventions* suggests making the assessments for this domain separately for different outcomes (Higgins 2011a; Section 8.5.1), however, we would have assessed this domain for each study as a whole,

as we assumed that the lack of blinding of participants or healthcare providers would distort the actual results of all the review outcomes in a similar manner.

- Blinding of outcome assessment (detection bias). We planned to group the outcomes by the susceptibility of their measurement to the lack of blinding (with assessments to be made for each outcome (or class of outcomes), as follows:
  * high susceptibility: healthcare-associated MRSA colonisations; healthcare-associated MRSA infections; healthcare-associated MRSA bacteraemias; healthcare-associated MRSA pneumonias; mortality attributable to MRSA; prevalence of carriers of MRSA.
  * low susceptibility: MRSA to MSSA ratios; length of stay; antibiotic use; all cause mortality.
- Incomplete outcome data (attrition bias; with assessments to be made for each outcome (or class of outcomes); loss of clusters in cluster-designs will be also assessed).
- Selective reporting (reporting bias).
- Protection against contamination (EPOC 2013c).
- Timing of the assessments of the outcomes (with assessments to be made for each outcome (or class of outcomes).
- Statistical methods taking the clustering into account (only for cluster designs; Higgins 2011b).

See Appendix 4 for details of criteria on which the judgements would have been based. This tool contains also the domains that would have been considered when assessing the RoB of cluster designs.

The following were defined as 'key domains' for the analysis: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data.

***ITS, CITS and RMS***

We would have considered the tool proposed by the Cochrane EPOC group (EPOC 2013c), which has the following domains.

- Was the intervention independent of other changes?
- Was the shape of the intervention effect pre-specified?
- Was the intervention unlikely to affect data collection? (Assessments made for each outcome (or class of outcomes)).
- Blinding of outcome assessment (detection bias; *a*ssessments made for each outcome (or class of outcomes)).
- Incomplete outcome data (attrition bias; assessments made for each outcome (or class of outcomes)).
- Was the study free of selective outcome reporting (reporting bias)?

See Appendix 5 for details of criteria on which the judgements would have been based. All the domains except for 'selective reporting' were defined as 'key domains' for the analysis.

As this systematic review focuses on non-pharmacological interventions, we would have assessed the blinding of participants and personnel and the blinding of outcome assessors following the suggestions of the 'CLEAR NPT checklist' (Boutron 2005). We also planned to assess the quality of reporting of the blinding of patients, 'care providers', 'persons caring for participants' and 'data analyst' as this checklist proposes, but these items would not have been considered for the global rating of the RoB of the study.

We planned to assess most of the domains for each study as a whole (therefore, by a single entry in the RoB tool for each study). However, some domains would have been assessed separately for each individual outcome (and for each time point for the same outcome if several time points are considered). Therefore, we would have assigned a single entry in the RoB tool for each outcome-time point. On the other hand, we planned to limit the number of entries used by grouping outcomes within every study, the same grouping would have been applied to every study in the review. Appendix 6 details how we planned to group the outcomes for the RoB assessment.

At least two review authors would have independently assessed the RoB of each included study (not masked to the study details). Each domain of the RoB tool would have been labelled as 'low RoB' (plausible bias unlikely to seriously alter the results), 'high RoB' (plausible bias that seriously weakens confidence in the results); or 'unclear RoB' (plausible bias that raises some doubt about the results). We planned to obtain the information from the reports but, if there had been not enough information we would have contacted the authors or the organisations for clarification. If clarification had not been obtained, we would have assigned a grading based on the available information and the consensus between the review authors. Disagreements would have been resolved by discussion and consensus, and by consulting a third review author if necessary. We planned to assess inter-rater reliability for the key domains by using the kappa statistic (Higgins 2003), and we planned to report relevant discrepancies in the assessments.

We would have justified judgements of RoB and provided this information in a ‘Risk of bias table’ for each included study; we would have reported the source of information for each RoB judgement, including those based on assumptions made on information provided outside publicly available documents. We would have reported the results of assessments of confounders in an additional table, listing the pre-stated confounders as columns and the studies as rows (Reeves 2011; see Appendix 3 for the list of potential confounders). Two figures would have been also included: a ‘Risk of bias graph’, presenting an overview of our judgements across each RoB domain, and a ‘Risk of bias summary’, to show an overview of judgements for each RoB domain for each study.

We planned to summarize the RoB for each outcome (or class of similar outcomes) in two different manners, 'within each study' and 'across studies' (Higgins 2011a):

| Interpretation | RoB for each outcome across different domains within each study | RoB for each outcome across studies |
|---|---|---|

| | | | |
|---|---|---|---|
| **Low RoB** | Plausible bias unlikely to seriously alter the results | Low risk of bias for all key domains | Most information is from studies at low risk of bias |
| **Unclear RoB** | Plausible bias that raises some doubt about the results | Unclear risk of bias for one or more key domains (and none of them rated as high risk) | Most information is from studies at low or unclear risk of bias |
| **High RoB** | Plausible bias that seriously weakens confidence in the results | High risk of bias for one or more key domains | The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results |

We would have provided a narrative summary of the RoB among the included studies. Summary assessments of RoB for each outcome across studies would have been incorporated into explicit measures of the quality of evidence for each important outcome using the GRADE system (Guyatt 2008). See Differences between protocol and review for this section.

**Measures of treatment effect**

We planned to report the estimate of the effect and its 95% confidence interval (CI) for each study, organised by type of intervention and study design.

***All study designs except for ITS, CITS and RMS***

We planned to present the following estimates of the effect with their associated 95% CI.

- **Risk ratio (RR):** for dichotomous data, such as prevalence of carriers of MRSA.
- **Odds ratio (OR):** for counts of rare events and rates, such as incidence density rate of HAIs.
- **Mean difference (MD):** for continuous data, such as length of stay (or standardised mean difference (SMD) if the continuous data require standardisation across studies).

***ITS, CITS and RMS***

We planned to present, if possible, the results for each outcome as changes along two dimensions (EPOC 2013d).

- **Change in level:** reflecting the immediate effect of the intervention, measured as the difference between the fitted value for the first post intervention data point (one month after the intervention) minus the predicted outcome one month after the intervention based on the pre-intervention slope only.
- **Change in slope:** reflecting the long-term effect of the intervention, this is the change in the trend from pre- to post-intervention.

The preferred analysis method for ITS and RMS is either a regression analysis with time trends before and after the intervention, which adjusted for autocorrelation and any periodic changes, or auto regressive integrated moving average (ARIMA) analysis (EPOC 2013d). We planned not to include, and therefore, not re-analyse, ITS studies or RMS that had an inappropriate analysis of results.

***Adjustment of the estimates of the effects***

This review considered randomised and non-randomised studies as eligible. Susceptibility to selection bias (understood as mean differences in the baseline characteristics of individuals in different intervention groups) is widely regarded as the principal difference between randomised and non-randomised studies. NRS are more prone to confounding (that is, selection bias that gives rise to imbalances between intervention and control groups on prognostic factors because the distributions of the factors differ between groups, and the factors are associated with outcome(s); Reeves 2011).

Randomisation with adequate allocation concealment reduces the possibility of selection bias, so that differences in characteristics between groups can be attributed to chance (Reeves 2011). Therefore, for studies described by the study authors as 'randomised' we would have used unadjusted effect estimates, that is, crude estimates that have not been corrected for the effects of confounding factors. We planned to assess the effects of this decision through Sensitivity analysis (see Differences between protocol and review).

As a result of the need to control for confounding as best as possible in NRS, we would have preferred to use adjusted estimates from these studies, that is, estimates that have been corrected for the effects of confounding factors. If the study report did not provide the adjusted effect estimate, we would have attempted to obtain it by following the guidance provided by the Cochrane EPOC Group (EPOC 2013d). If the study report presented alternative adjusted estimates for the same outcome, by preference we would have used the estimate that was identified as the primary adjusted model (Reeves 2011). We would have assessed the effects of this decision through Sensitivity analysis.

***Summary effect measures derived from the meta-analyses***

For each comparison and outcome, a meta-analysis would have generated a summary effect estimate with its corresponding 95% CI. The results of each meta-analysis would have been re-expressed to easily interpretable statistics in the standard Cochrane 'Summary of findings' table, generated with the GRADEprofiler software (GRADEpro 2014).

- **Dichotomous outcomes and counts of rare events and rates:** we planned to provide both a relative measure (e.g. RR or OR) and measures of absolute risk, all of them with their corresponding CI 95%. By preference, we would have expressed the relative measure as RR, because the OR is the hardest summary statistic to understand and to apply in practice, and many practising clinicians have reported difficulties in using it (Deeks 2011); therefore, if the meta-analysis were based on ORs its global estimate would have been an OR, but we would

have re-expressed it as RR by applying the formula described in section 12.5.4 of the *Cochrane Handbook for Sytematic Reviews of Interventions* (Schünemann 2011). In addition, we planned to re-express the relative measure using absolute effect measures (risk differences). We would have calculated RRs and risk differences from a plausible range of control group event rates from the individual trials.

- **Continuous data:** we planned to provide an absolute measure alone, the MD or SMD, and its 95% CI.

See Differences between protocol and review fro this section.

**Unit of analysis issues**

We had planned to examine the unit of analysis of the studies looking for potential 'unit of analysis errors' (see glossary in Appendix 1).

***Studies with allocation to interventions at the group level***

We expected that many eligible studies would be cluster designs (studies in which the unit of allocation is not a person, but instead is a group of people). If these designs were included, we would have determined whether the data were correctly analysed: comparisons that allocate clusters (for example, groups of professionals or wards) but do not account for clustering during analysis have potential 'unit of analysis errors', resulting in artificially extreme P values (see Appendix 1) and over-narrow confidence intervals (Ukoumunne 1999). For cluster designs, we would have considered data as analysed correctly if:

- the analysis was conducted at the same level as the allocation (i.e. at the 'cluster' level);
- the analysis was conducted at the level of the individual, but appropriate statistical correction for the clustering was performed (such as generalised estimating equations (GEE), mixed models, or multilevel models); or
- the analysis was conducted at the level of the individual, but the sample size was reduced to its 'effective sample size', or the variance was inflated by the design effect.

If the data analysis had been performed incorrectly we would have attempted to perform an 'approximately correct analysis' following the guidance of Section 16.3 of the *Cochrane Handbook for Sytematic Reviews of Interventions* (Higgins 2011b). We planned to contact the authors to obtain relevant data, when necessary. If, finally, these data were not available, the results of the study would have been reported as point estimates of the intervention effect without presentation of any statistical analysis (P values) or confidence intervals and they would have not been included in the meta-analysis (Higgins 2011b).

***Sample size calculation***

We planned to assess whether the unit of allocation had been taken into consideration in the sample size calculation or power calculation. In cluster designs the sample size estimate has to be inflated to take account of the cluster design (Ukoumunne 1999), so we planned to evaluate whether the sample size had been estimated based on the intra-cluster correlation co-efficient (see Appendix 1), however, this would have not been considered for the assessment of the RoB.

***Outcome is an event that may re-occur***

If the outcome of interest would have been an event that may re-occur (such as HAIs), we would have assessed whether the count data had been treated erroneously, that is, as if they were dichotomous data (Deeks 2011).

***Additional analysis issues***

We planned to examine critically the statistical approaches of the included studies.

- We would have assessed whether the statistical approach relating to infection or colonisation outcomes was adequate. For communicable diseases, unless outcomes are independent, the risk to one patient will depend on the status of other patients. For this reason, the use of approaches that assume independence (which include the $Chi^2$ test, Fisher's exact test, linear regression, etc.) can lead to false inferences, and statistical approaches able to account for dependencies in the outcome data should be used instead (Stone 2007). We did not plan to consider our conclusion regarding the statistical approach as part of the global rating of the RoB of the studies.
- For ITS and RMS designs we would also have assessed whether the statistical approach had ignored secular (trend) changes. Analysis of aggregated data of the pre and post intervention phases should be avoided because it does not provide information about trends over time. We had planned to exclude ITS and RMS that did not have a parallel control group that ignored secular changes, and had performed a simple test of the pre versus post intervention periods, from the review without further justification (these studies will be considered as uncontrolled before-and-after studies).

See Differences between protocol and review for this section.

**Dealing with missing data**

***Missing outcome data***

As far as possible, we planned to apply an 'intention-to-treat' analysis for all outcomes, that is, an analysis that fulfils the following principles (Higgins 2011b).

- Participants are kept in the intervention groups to which they were randomised, regardless of the intervention they actually received.
- There is a measurement of outcome data for all participants.
- All randomised participants are included in the analysis.

We planned to contact the primary authors for missing data and clarification of issues. If we could not obtain this information, we would have documented this on the data extraction form and within the text of the review, and we would have performed an 'available case analysis', that is, an analysis that includes data on only those participants whose results are known, and that uses as denominator the total number of people who had data recorded for the particular outcome in question. In the available case analysis the participants would have been analysed according to the group to which they were randomised. If possible, we would have 're-included' avoidable exclusions done by the authors (Higgins 2011b). We planned to perform Sensitivity analysis to assess how sensitive results were to changes in the assumptions made in the available case analysis.

We would have described missing outcomes for the included studies by reporting proportions of allocated participants for whom no outcome data were obtained (with reasons) by outcome and by study group. We planned to explore the impact of the missing outcome data in the overall treatment effect through Sensitivity analysis by excluding studies with high RoB for the domain 'Incomplete outcome data' from the meta-analysis. We would have described in the Discussion the impact of the missing outcome data on the findings of the review.

***Other missing data***

If other relevant data were not directly reported (for example, standard deviation for continuous data), we would have obtained this information by looking carefully in the report for statistics that would allow its calculation. If this was not possible, we would have tried to contact the primary authors. If, finally, we could not obtain the information, we would have recorded this in the data extraction template and we would have imputed this information following the suggestions provided in Higgins 2011c.

See Differences between protocol and review for this section.

**Assessment of heterogeneity**

For each review outcome, we planned to assess heterogeneity of the results across studies qualitatively and quantitatively.

- **Qualitative methods**
  - We would have prepared tables summarising the characteristics of the included studies. This would have allowed us to examine the similarity between the studies for relevant factors.
  - We would have created forest plots of the study results (effect estimates and their CI 95%) to assess the potential disparities of the effect estimates and the degree of overlap among the CIs.
- **Quantitative methods**
  - We would have examined the results of the $Chi^2$ test for statistical heterogeneity (we would have considered a P value of less than 0.10 to be significant).
  - We would have examined the results of the $I^2$ statistic for the quantification of statistical heterogeneity (Higgins 2003). The $I^2$ statistic describes the percentage of total variation across studies that is due to heterogeneity rather than chance. We would have judged the importance of the observed value of the $I^2$ statistic depending on the magnitude and direction of effects and the strength of evidence for heterogeneity (we would have interpreted values of $I^2$ greater than 50% as potentially representing substantial heterogeneity; Deeks 2011).

We recognise that a low number of studies are expected to be included in future updates of this review and that there is considerable uncertainty in tests such as $Chi^2$ test or $I^2$ when there are few studies. Therefore, use of simple thresholds to diagnose heterogeneity will be avoided (Deeks 2011). See Differences between protocol and review for this section.

**Assessment of reporting biases**

We would have attempted to minimise the risk of reporting bias by:

- including both published and unpublished studies;
- extracting data on outcomes from the publication with the most mature data (in the case of studies with multiple publications); and
- not excluding studies solely on the basis of the publication language.

We planned to look for evidence of publication bias for each outcome. In order to do so, we would have assessed the funnel plot of the results of the meta-analysis for each outcome in two different ways: graphically, by visual assessment; and statistically (funnel plots will not give meaningful results if there are fewer than 10 studies in the meta-analysis, or if all the studies are the same size).

Funnel plots can be produced in Review Manager 5.3 (RevMan; RevMan 2014), which takes the results of a meta-analysis and plots the results of each individual study against a measure of the study's size (usually represented by a measure of variance like standard error; Sterne 2011). We would have followed the guide provided by Sterne 2011 for statistical testing for funnel plot asymmetry. Results from tests for funnel plot asymmetry would have been interpreted cautiously: if there had been evidence of small-study effects, that is, when the results of the small studies are consistently different to the larger studies, either more positive or more negative, we would have considered publication bias as only one of a number of possible explanations. If we suspected a small-study effect, we planned to determine its impact on the results by performing a sensitivity analysis: we would have compared the fixed-effect and random-effects meta-analyses (see Sensitivity analysis), as suggested by the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2011). See Differences between protocol and review for this section.

**Data synthesis**

We would have performed the analyses using RevMan 5 (RevMan 2014), the statistical package provided by the Cochrane Collaboration. We would have combined the outcome measures from the individual trials in meta-analyses to provide a pooled effect estimate if there had been at least two studies that were sufficiently similar in terms of clinical setting, participants, intervention, comparison, outcomes and study design.

We would have presented all estimates of treatment effects with their associated 95% CI (see Measures of treatment effect). Estimated intervention effects for different study designs can be expected to be influenced to varying degrees by different sources of bias. As a consequence, results from different study designs should be expected to differ systematically, resulting in increased heterogeneity (Reeves 2011). Therefore, we would have combined the following study designs in different meta-analyses.

- Randomised controlled trials (RCTs) and quasi-randomised controlled trials (Q-RCTs).
- Non-randomised controlled trials (NRCTs).
- Controlled before-and-after studies (CBAs) and controlled cohort before-after studies (CChBAs).
- Interrupted time series studies (ITS) and repeated measures studies (RMS).
- Controlled interrupted time series studies (CITS).

We would have meta-analysed all the included studies independently of their RoB. We acknowledge that such an analysis

may fail to down-weigh studies at a high risk of bias, and hence will lead to an overall intervention that is too precise, as well as being potentially biased (Higgins 2011a). However, we expected a low number of studies to be included, and we planned to explore the impact of this decision by carrying out Sensitivity analysis.

Cluster-designs would have been combined with the corresponding individually allocated trials in the same meta-analysis. However, in the sensitivity analysis we would have considered the possibility of important differences in the effects being evaluated that would depend on the unit of allocation (see Sensitivity analysis).

For comparable studies, we would have displayed their results graphically and looked at sizes and directions of effects to assess heterogeneity qualitatively. In addition, we would have assessed heterogeneity statistically (see Assessment of heterogeneity). If no relevant heterogeneity was detected, we would have pooled data according to a random-effects model, as we considered that it would be very likely that the subjects or interventions in these studies would have differed in ways that would have had an impact on the results, and therefore we should not assume a common effect size (Borenstein 2009). We would have ensured robustness of the model chosen through Sensitivity analysis.

We would have not performed meta-analysis if we had detected relevant heterogeneity or if meta-analysis would have been inappropriate for any other reason. In that case we would have undertaken a narrative analysis of the included studies, providing a descriptive presentation of the results, grouped by intervention, outcome, and study design, with supporting tables. We would have also reported characteristics of the study design(s), the populations, the types of healthcare setting and outcome measures in these tables.

#### *Quality of the body of the evidence*

We would have assessed the quality of the body of the evidence according to the GRADE approach (Schünemann 2011). We would have presented at least one standard 'Summary of findings' table developed using GRADEprofiler (GRADEpro 2014). A 'Summary of findings' table provides key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on all important outcomes for a given comparison.

See Differences between protocol and review for this section.

### Subgroup analysis and investigation of heterogeneity

We would have explored potential sources of heterogeneity by conducting the following subgroup analyses.

- Patients' age: neonate and paediatric versus adult versus elderly.
- Type of patient: medical patients versus surgical patients versus patients in 'high risk units' (i.e. intensive care, neonatal intensive care, burn, or dialysis units; Wenzel 1998).
- Number of wards in which the measures are applied: one versus more than one, versus the whole hospital.
- MRSA outbreak situation versus no MRSA outbreak situation (as defined by the authors of the original article).
- Adjustment of estimates of the effects in meta-analyses of non-randomised studies: studies with adjusted estimates versus studies without adjusted estimates.

If sufficient studies had been available, we would have used a formal statistical test to compare the results of the subgroups. If subgroup analyses had been conducted, we would have followed the subgroup analysis plan specified in the protocol without undue emphasis on particular findings (MECIR Conduct 2013). See Differences between protocol and review for this section.

### Sensitivity analysis

We planned to restrict sensitivity analysis to the review's primary outcomes.

- **Risk of bias**
  - Excluding studies with unclear or high RoB for random sequence generation or allocation concealment.
  - Excluding studies with high RoB (Differences between protocol and review).
  - Excluding studies with high or unclear RoB (Differences between protocol and review).
- **Missing outcome data:** excluding studies with high RoB for the domain 'Incomplete outcome data'.
- **Unit of allocation:** excluding studies allocated at the individual level.
- **Statistical model chosen for meta-analysis:** we would have used a fixed-effect model.
- **Adjustment of the estimates:**
  - In RCTs with unclear or high RoB for randomisation or allocation concealment we would have used adjusted estimates.
  - For NRS we would have considered adjusted estimates from the model with the largest number of confounders defined as important by the review team (see Appendix 3 for list of confounders).
- **Assumptions taken in the 'available case analysis' for dichotomous data:** we would have imputed missing data by considering the 'best case' and 'worst-case' scenarios (Gamble 2005).
  - 'Best-case' scenario: all participants with missing outcomes in the intervention group are assumed to have had good outcomes, and all those with missing outcomes in the control group to have had poor outcomes.
  - 'Worst-case' scenario: the opposite to the 'best-case' scenario above (Higgins 2011b).
- **Study funding:** we would have excluded industry-funded studies from the meta-analysis.

See Differences between protocol and review in this section.

## RESULTS

### Description of studies

See the Characteristics of excluded studies table.

### Results of the search

After removal of duplicates, the search strategy of the electronic databases to June 2015 generated 4456 records. We examined the titles and the abstracts of these records to assess their

potential relevance, and we subsequently retrieved 282 full texts for further examination as they appeared to be potentially eligible (62 articles), or because the title and abstract suggested that the record should be excluded but some key information had to be checked (220 articles). We did not identify any studies that met the eligibility criteria. We identified a total of 1061 records through searching trial registries (duplicates not eliminated), but we found no eligible trials. No additional references were identified after checking the abstracts of relevant conferences, or through personal contact with researchers in the field. See the study flow diagram (Figure 1), which follows the template described in the PRISMA statement (Liberati 2009).

#### Included studies

No eligible studies were found, neither completed nor ongoing, that could be included in this review.

#### Excluded studies

We excluded all the records after full-text assessment of eligibility. The reasons for their exclusion are summarised in the flow diagram (Figure 1). The Characteristics of excluded studies table lists the studies that we considered that a reader of the review might reasonably expect to find in the review, with at least one reason for each exclusion.

### Risk of bias in included studies

No studies met the eligibility criteria, so we could not assess RoB.

### Effects of interventions

We could not determine the effects of the use of gloves, gowns or masks as there were no eligible studies for this review, either completed or ongoing.

## DISCUSSION

### Summary of main results

There were no eligible studies for this review, either completed or ongoing. Consequently, this systematic review could not determine the effects on MRSA transmission of wearing gloves, a gown or a mask for contact with MRSA hospitalised patients or with their immediate environment.

### Overall completeness and applicability of evidence

#### Completeness of the evidence

We identified a large number of potential studies for consideration for the review, but none of them was eligible. The evidence is strikingly incomplete and the effectiveness of the use of gloves, a gown or a mask for hospitalised patients colonised or infected with MRSA remains uncertain. We were surprised by the lack of studies, as the topic area is not immature and the interventions evaluated are commonly used in practice, however, there may be a number of reasons that explain this absence of studies.

Firstly, we considered a narrow population. We specified that trial participants should be hospitalised patients colonised or infected with MRSA, that is, the population considered in both the intervention and control arms of studies must have MRSA. Thus we would have excluded certain studies that the reader might plausibly expect to see amongst the included studies. For example, we excluded those studies assessing the generalised use of gloves and gowns for all patients independent of their MRSA status (BUGG Study 2013), or those assessing the effectiveness of MRSA screening (MOSAR study 2014), as not all participants had MRSA at the time of being recruited.

Secondly, we attempted to disentangle the effects of three particular infection control interventions: gloves, gowns and masks. Therefore, we excluded studies which reported the effect of multiple interventions, which meant we could not elucidate the relative contribution of the review interventions. We expected this, as gloves, gowns and masks are rarely implemented alone in clinical practice (Zastrow 2011), but rather with other interventions as part of care bundles, such as MRSA screening, patient isolation or hand hygiene (usually as part of quality improvement initiatives).

Thirdly, the difficulties associated with the evaluation of complex and non-pharmacological interventions may explain also the scarcity of studies. Gloves, gowns and masks are usually implemented as part of 'complex interventions', that is, interventions with several interacting components. Complex interventions present a number of special problems for evaluators, in addition to the practical and methodological difficulties that any successful evaluation must overcome (MRC 2008). Moreover, the review interventions are non-pharmacological, so the evaluation presents additional methodological challenges, such as the difficulty of blinding participants and care providers, or the unfeasibility of implementing a sham intervention as a comparison group (Boutron 2005; Boutron 2012).

Fourthly, we restricted our review to the strongest feasible study designs given the particular circumstances of infection control studies. For example, we attempted to include only those studies with a prospective baseline assessment, a prospective allocation of the intervention, and a prospective outcome assessment (see Types of studies). Therefore, we excluded studies that used retrospectively gathered data, which are very common in the field of infection prevention. Moreover, we excluded uncontrolled before-and-after designs, which are very common as well, as the validity of their estimates is questionable (Shadish 2002; Cooper 2003; Stone 2007). These studies collect data on one group of participants before the introduction of the intervention and, then, further data after the intervention has been introduced; they finally present MRSA rates as averages in the pre- and post-intervention phases, and use conventional statistical approaches, such as the $Chi^2$ test (see Potential biases in the review process).

#### Applicability of the evidence

In the context of systematic reviews, applicability is the assessment of whether the findings of a review can be applied in a particular context or population (Burford 2013). We cannot assess applicability in this review as we identified no relevant evidence for consideration. However, if future updates include relevant evidence, the applicability of the review findings may be still limited due to the review eligibility criteria.

Firstly, we do not plan to attempt to investigate all relevant outcomes. In particular, we will not assess the harms associated with the use of gloves, gowns or masks. We acknowledge that a Cochrane review should assess the effects of one or more healthcare interventions on outcomes that are important to stakeholders, both intended and unintended (MECIR Conduct

2013). In fact, there are some concerns about the potential harms associated with the use of gloves, gowns or masks (see Why it is important to do this review). However, we consider that the lack of assessment of harms in this review is justified (see Potential biases in the review process).

Secondly, we attempted to disentangle the effectiveness of the use of gloves, gowns, or masks, however, these interventions are commonly used with other interventions. Nonetheless, determining the role of a particular infection control intervention is relevant, as it allows the most effective, safe, and cost-effective interventions to be identified, and provides evidence-based information to implement the minimum interventions needed to reduce transmission of micro-organisms in hospitals (Aboelela 2006). Moreover, quantifying the beneficial effects of the use of gloves, gowns and masks is a critical part of assessing the need for additional or alternative measures (such as MRSA screening) and the uncertainty in estimates of their effectiveness highlights the need for well-designed prospective intervention studies to evaluate their effects with greater precision.

Thirdly, we focus on the effects these barrier precautions have on a single pathogen, MRSA. This review addresses what is called a 'vertical program', in which specific organisms are targeted (for example, active MRSA surveillance plus contact isolation), compared with 'horizontal programs', that is, broad programs that attempt to reduce the rates of all infections due to all pathogens (for example universal contact precautions in high-risk settings; Wenzel 2010). At present there is great debate over whether vertical or horizontal approaches should be used to prevent HAIs (Wenzel 2010; AHRQ 2013). In particular, gloves, gowns and masks are not usually applied to prevent the transmission of just one micro-organism, as target pathogens are MRSA, vancomycin-resistant *Enterococcus* (VRE) species, *Clostridium difficile,* and multidrug-resistant Gram-negative bacilli. This may limit the applicability of the review results, however, focusing on MRSA can be justified by the presence of differential methods of transmission for different bacteria (Siegel 2007), and by the results of some trials that suggest that infection control interventions may have differing effects on specific antibiotic-resistant bacteria (BUGG Study 2013; Climo 2013); for example, the use of gloves and gowns by healthcare workers for all patient contact in the intensive care unit reduced the acquisition of MRSA, but not of VRE (BUGG Study 2013).

Fourthly, we focus on the use of these barrier precautions in hospitals, but it is plausible that the effectiveness of these interventions varies in different types of services within the hospital (for example, medical ICUs may derive the most benefit from barrier precautions; Kypraios 2010), or in other settings, such as nursing homes (Lee 2013). This should be taken into consideration when trying to apply the results of this review to particular settings. It is noteworthy that another Cochrane review that assessed the effects of infection control strategies for preventing the transmission of MRSA in nursing homes for older people also concluded that there is a lack of research in this field (Hughes 2013).

If future updates of this review identify any relevant studies we will follow the guidance of Burford 2013 and address applicability. In particular we will:

- conduct analyses to answer questions relevant for judging applicability (see Subgroup analysis and investigation of heterogeneity);
- collect, and report transparently, information that readers of systematic reviews can use to make judgments about applicability (e.g. population and intervention characteristics as well as characteristics of context and setting);
- appraise applicability for at least one primary target population, setting, and context, for example, future updates of this review will present a 'Summary of findings' table tailored to a specific population and setting, as suggested by the GRADE approach (Schünemann 2011).

## Quality of the evidence

Since we identified no relevant studies for inclusion in this review, we are unable to comment on the quality of the evidence in this field.

## Potential biases in the review process

### Relevance of the review question for key stakeholders

This review did not assess the harms associated with the use of gloves, gowns or masks. This is a limitation as there are concerns about the unintended effects associated with the use of these interventions (see Why it is important to do this review). We did not assess harms for the following reasons:

- rigorous systematic review of harms requires applying methods different to those used for beneficial outcomes. This might require consideration of a variety of study designs (such as, cohort studies, case-control studies or even case reports), the checking of additional sources of information, and the design of highly sensitive searches, as well as assessment of the RoB of the included studies with specific tools (Loke 2011; Golder 2009);
- the participants would need to be defined more widely, for example, not restricted to those with demonstrated MRSA or who attended in the hospital setting.

We encourage the undertaking of a systematic review that will focus on the unintended effects of the use of gloves, gowns and masks, as providing the best available evidence for benefits and harms will make balanced information about the effects of these interventions available.

### Study designs

We considered RCTs and some types of NRS as eligible, although the latter are more prone to bias. However, we consider that the inclusion of NRS is justified (see Types of studies), and we focused on certain NRS that allow the major threats to the validity of inferences drawn from studies of infection control interventions to be minimised. We excluded observational studies and outbreak reports, as well as other study designs. Outbreak reports, which are very common in the infection prevention field, are observational studies that describe a new phenomenon (such as, a new epidemic strain of MRSA) or the resources used to control an outbreak (Sanchez 2010); they are useful for generating hypotheses, but of limited value for assessing the effectiveness of interventions (Grimes 2002; Stone 2007).

The experimental designs defined as eligible for this review minimise the biases usually present in infection control intervention studies including history, secular trends, seasonal effects and regression to the mean (Shadish 2002; Cooper 2003; Stone 2007; Bland 1994; Morton 2003).

### Equity issues

In future updates of this review, if we consider that equity may be an issue, we will attempt to follow the guidance proposed by the Campbell & Cochrane Equity Methods Group (Equity Checklist 2012).

### Search methods for identification of studies

The searches were as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Searches were carefully designed using the expertise of healthcare librarians, and adapted to existing terminology.

## Agreements and disagreements with other studies or reviews

As there are no included studies in this review we were unable to locate any evidence that could be compared with other studies. On the other hand, several systematic reviews have assessed the effectiveness of a variety of strategies for preventing the transmission of micro-organisms in the hospital setting (Aboelela 2006; Ranji 2007; Schlesinger 2009; Backman 2011; AHRQ 2013), some of them focusing on MRSA (Cooper 2003; Loveday 2006; Halcomb 2007; Glick 2013). However, these reviews did not assess the relative effect of gloves, gowns or masks when managing patients colonised or infected with MRSA.

# AUTHORS' CONCLUSIONS

## Implications for practice

We found no studies assessing the effects of wearing gloves, gowns or masks for contact with MRSA hospitalised patients or with their immediate environment on the transmission of MRSA. Thus, we cannot conclude on the impact of these interventions in hospitalised patients (in terms of healthcare-associated MRSA colonisations, infections, bacteraemias, or pneumonias, or mortality attributable to MRSA), or in hospital staff, patients' caregivers or visitors (in terms of healthcare-associated MRSA colonisations or prevalence of carriers of MRSA).

This absence of evidence of an effect for these interventions should not be interpreted as the evidence of no effect; it means that research that would have been eligible for inclusion in this review has not been conducted.

## Implications for research

This is an 'empty review', that is, a review that reports no studies eligible for inclusion. This highlights the need for robust studies to determine the effectiveness of using gloves, a gown, and/or a mask for contact with MRSA hospitalised patients or with their immediate environment. A rigorous evaluation of this topic is relevant as it would allow:

- detection of the effects of these interventions that are impossible to predict with modelling or to disentangle from confounding in observational or non-randomised studies (Ioannidis 2013);
- identification of the most effective, safe, and cost-effective interventions, which will provide evidence-based information to implement the minimum level of interventions needed to reduce transmission of MRSA in hospitals (Aboelela 2006); and
- assessment of the incremental benefit of the addition of these interventions to other interventions (such as universal MRSA decolonisation; BUGG Study 2013; Calfee 2014).

On the basis of the evidence gap identified, this review highlights the need for randomised controlled trials to determine if the use of gloves, a gown, and/or a mask for contact with hospitalised patients colonised or infected with MRSA or with their immediate environment reduces the transmission of MRSA in hospitals. See Table 3 detailing the nature of the further research that would be most desirable according to the 'Evidence-Population(s)-Intervention-Comparison-Outcomes-Time stamp' (EPICOT) format (Brown 2006b).

The most robust method to determine if the use of gloves, gowns or masks prevents the transmission of MRSA in hospitals is the randomised controlled design (Ioannidis 2013; Safdar 2014). In particular, researchers should put more effort into conducting cluster-randomised controlled trials (cluster-RCTs) because they have a number of advantages compared to patient-randomised trials as listed below (Ioannidis 2013; Safdar 2014).

- They can be used to test interventions that are difficult to allocate at an individual level, such as the use of gloves, gowns or masks. In the last few years there has been an increase in cluster-RCTs for testing of interventions to prevent infection (Platt 2010; Ioannidis 2013; Safdar 2014).
- They may be less costly and time-consuming than ordinary randomised controlled trials (RCTs), as they can harness the healthcare system's existing administrative capacities, including quality improvement programs and data collection systems. This simplifies the logistics of implementation and reduces study costs (Smith 2008; Platt 2010; Safdar 2014).
- They control for confounding (Safdar 2014).
- They minimise treatment "contamination" between intervention and control participants (Hayes 2000). In a controlled trial "contamination" is the inadvertent application of the intervention being evaluated to people in the control group; or the inadvertent failure to apply the intervention to people assigned to the intervention group (Higgins 2005)
- They are better for measuring the overall group effect of an intervention (Hayes 2000).
- They are better for judging effectiveness (performance under conditions of actual use), as the interventions are applied at the hospital, practice, or health plan level, which is a better reflection of the way interventions are implemented in usual practice (Platt 2010; Safdar 2014).
- They have broader generalisability due to the following reasons (Platt 2010; Ioannidis 2013; Safdar 2014):
  * patient-randomised trials usually require more standardisation and level of care than occurs in practice;
  * cluster-RCTs minimise the Hawthorne effect, which is the effect (usually positive or beneficial) of being under study upon the persons being studied (Porta 2008);
  * if applied across a variety of healthcare facilities, cluster-RCTs enhance generalisability.

Future cluster-RCTs should be rigorous in design and delivery, with adequate reporting to enable appraisal and interpretation of results.

### Reporting

Researchers should report the studies in a standardised, explicit, informative and transparent manner. In order to do so, the following guidelines should be followed, among others:

- CONSORT statement (CONsolidated Standards of Reporting Trials 2010; Schulz 2010)
- CONSORT extension for cluster randomised trials (Campbell 2012)
- CONSORT extension for non-pharmacological interventions (Boutron 2008)
- ORION Statement (Stone 2007): guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infections
- TIDieR checklist: template for intervention description and replication checklist (Hoffmann 2014)
- SQUIRE: Standards for Quality Improvement Reporting Excellence (Davidoff 2008)
- Reporting guideline for health equity concerns in randomised controlled trials (under development; Welch 2014).

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# REFERENCES

## References to studies excluded from this review

**Agbayani 1981** *{published data only}*

Agbayani M, Rosenfeld W, Evans H, Salazar D, Jhaveri R, Braun J. Evaluation of modified gowning procedures in a neonatal intensive care unit. *American Journal of Diseases of Children* 1981;**135**(7):650-2.

**Alvarez-Lerma 2002** *{published data only}*

Álvarez-Lerma F, Gasulla Guillermo M, Abad Peruga V, Pueyo Pont MJ, Tarrago Eixarch E. Effectiveness of contact isolation in the control of multiresistant bacteria in an intensive care service [Efectividad del aislamiento de contacto en el control de bacterias multirresistentes en un servicio de medicina intensiva.]. *Enfermedades Infecciosas y Microbiologia Clínica* 2002;**20**(2):57-63.

**Assadian 2014** *{published data only}*

Assadian O, Kramer A, Ouriel K, Suchomel M, McLaws ML, Rottman M, et al. Suppression of surgeons' bacterial hand flora during surgical procedures with a new antimicrobial surgical glove. *Surgical Infections* 2014;**15**(1):43-9.

**Batra 2010** *{published data only}*

Batra R, Cooper BS, Whiteley C, Patel AK, Wyncoll D, Edgeworth JD. Efficacy and limitation of a chlorhexidine-based decolonization strategy in preventing transmission of methicillin-resistant Staphylococcus aureus in an intensive care unit. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2010;**50**(2):210-7.

**Bearman 2007** *{published data only}*

Bearman GM, Marra AR, Sessler CN, Smith WR, Rosato A, Laplante JK, et al. A controlled trial of universal gloving versus contact precautions for preventing the transmission of multidrug-resistant organisms. *American Journal of Infection Control* 2007;**35**(10):650-5.

**Bearman 2010** *{published data only}*

Bearman G, Rosato AE, Duane TM, Elam K, Sanogo K, Haner C, et al. Trial of universal gloving with emollient-impregnated gloves to promote skin health and prevent the transmission of multidrug-resistant organisms in a surgical intensive care unit. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2010;**31**(5):491-7.

**Bertrand 2012** *{published data only}*

Bertrand X, Lopez-Lozano JM, Slekovec C, Thouverez M, Hocquet D, Talon D. Temporal effects of infection control practices and the use of antibiotics on the incidence of MRSA. *The Journal of Hospital Infection* 2012;**82**(3):164-9.

**Bischoff 2007** *{published data only}*

Bischoff WE, Tucker BK, Wallis ML, Reboussin BA, Pfaller MA, Hayden FG, et al. Preventing the airborne spread of Staphylococcus aureus by persons with the common cold: effect of surgical scrubs, gowns, and masks. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2007;**28**(10):1148-54.

**Boyce 1998** *{published data only}*

Boyce JM, Chenevert C. Isolation gowns prevent health care workers (HCWs) from contaminating their clothing, and possibly their hands, with methicillin-resistant Staphylococcus aureus (MRSA) and resistant enterococci. *Infection Control and Hospital Epidemiology* 1998;**19**(9):74.

**BUGG Study 2013** *{published data only}*

Croft L, Harris AD, Pineles L, Langenberg P, Shardell M, Simoni-Wastila L, Morgan D. The effect of universal glove and gown use on adverse events in the benefits of universal glove and gown (BUGG) cluster randomized trial. IDWeek, 2014: https://idsa.confex.com/idsa/2014/webprogram/Paper46927.html (accessed 27 June 2015).

* Harris AD, Pineles L, Belton B, Johnson J K, Shardell M, Loeb M, et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. *JAMA* 2013;**310**(15):1571-80.

Harris AD, Pineles L, Belton B, Johnson K, Shardell M, Loeb M, et al. The benefits of universal glove and gown (BUGG) use on the acquisition of antibiotic-resistant bacteria: a cluster randomized trial. IDWeek, 2013: https://idsa.confex.com/idsa/2013/webprogram/Paper42208.html (accessed 3 Sept 2014).

Kett D, Morgan DJ, Pineles L, Zervos MJ, Munoz-Price LS, Harris AD, BUGG Investigators. Compliance with the implementation of an ICU cluster-randomized trial assessing the benefits and potential harms of universal glove and gowning. *Critical Care* 2013;**17**(Suppl 2):54.

**Burden 2011** *{published data only}*

Burden M, Cervantes L, Weed D, Keniston A, Price CS, Albert RK. Newly cleaned physician uniforms and infrequently washed white coats have similar rates of bacterial contamination after an 8-hour workday: a randomized controlled trial. *Journal of Hospital Medicine: an Official Publication of the Society of Hospital Medicine* 2011;**6**(4):177-82.

**Camus 2011** *{published data only}*

Camus C, Bellissant E, Legras A, Renault A, Gacouin A, Lavoue S, et al. Randomized comparison of 2 protocols to prevent acquisition of methicillin-resistant Staphylococcus aureus: results of a 2-center study involving 500 patients. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2011;**32**(11):1064-72.

**Duquette-Petersen 1999** *{published data only}*

Duquette-Petersen L, Francis ME, Dohnalek L, Skinner R, Dudas P. The role of protective clothing in infection prevention in patients undergoing autologous bone marrow transplantation. *Oncology Nursing Forum* 1999;**26**(8):1319-24.

**Ellingson 2011** *{published data only}*

Ellingson K, Muder RR, Jain R, Kleinbaum D, Feng PJ, Cunningham C, et al. Sustained reduction in the clinical incidence of methicillin-resistant Staphylococcus aureus colonization or infection associated with a multifaceted infection control intervention. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2011;**32**(1):1-8.

**Evans 2013** *{published data only}*

Evans ME, Kralovic SM, Simbartl LA, Obrosky DS, Hammond MC, Goldstein B, et al. Prevention of methicillin-resistant Staphylococcus aureus infections in spinal cord injury units. *American Journal of Infection Control* 2013;**41**(5):422-6.

**Eveillard 2001** *{published data only}*

Eveillard M, Eb F, Tramier B, Schmit JL, Lescure FX, Biendo M, et al. Evaluation of the contribution of isolation precautions in prevention and control of multi-resistant bacteria in a teaching hospital. *The Journal of Hospital Infection* 2001;**47**(2):116-24.

**Gandra 2014** *{published data only}*

Gandra S, Barysauskas CM, Mack DA, Barton B, Finberg R, Ellison RT 3rd. Impact of contact precautions on falls, pressure ulcers and transmission of MRSA and VRE in hospitalized patients. *The Journal of Hospital Infection* 2014;**88**(3):170-6.

**Gilmore 1986** *{published data only}*

Gilmore DS, Montgomerie JZ, Graham IE. Category 1, 2, 3 and 4: a procedure-oriented isolation system. *Infection Control* 1986;**7**(5):263-7.

**Gilroy 2009** *{published data only}*

Gilroy SA, Miller Stahl B, Noonan C, Susman R, Johnson L, Kullman M, et al. Reduction of hospital-acquired methicillin-resistant Staphylococcus aureus infection by cohorting patients in a dedicated unit. Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America 2009; Vol. 30, issue 2:203-5.

**Grant 2006** *{published data only}*

Grant J, Ramman-Haddad L, Dendukuri N, Libman MD. The role of gowns in preventing nosocomial transmission of methicillin-resistant Staphylococcus aureus (MRSA): gown use in MRSA control. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2006;**27**(2):191-4.

**Ho 2012** *{published data only}*

Ho ML, Seto WH, Wong LC, Wong TY. Effectiveness of multifaceted hand hygiene interventions in long-term care facilities in Hong Kong: a cluster-randomized controlled trial. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2012;**33**(8):761-7.

**Huang 2011** *{published data only}*

Huang YC, Lien RI, Su LH, Chou YH, Lin TY. Successful control of methicillin-resistant Staphylococcus aureus in endemic neonatal intensive care units - a 7-year campaign. *PloS one* 2011;**6**(8):e23001.

**Jain 2011** *{published data only}*

Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, et al. Veterans Affairs initiative to prevent methicillin-resistant Staphylococcus aureus infections. *The New England Journal of Medicine* 2011;**364**(15):1419-30.

**Kappstein 2009** *{published data only}*

Kappstein I, van der Muhlen K, Meschzan D, Vatou V, Bieg-Habermann S. Prevention of transmission of methicillin-resistant Staphylococcus aureus (MRSA) infection: standard precautions instead of isolation: a 6-year surveillance in a university hospital [Pravention von MRSA-Ubertragungen: Standardhygiene statt Isolierung : 6 Jahre Uberwachung in einem Universitatsklinikum]. *Der Chirurg; Zeitschrift fur alle Gebiete der operativen Medizen* 2009;**80**(1):49-61.

**Kaufman 2014** *{published data only}*

Kaufman DA, Blackman A, Conaway MR, Sinkin RA. Nonsterile glove use in addition to hand hygiene to prevent late-onset infection in preterm infants: randomized clinical trial. *JAMA pediatrics* 2014;**168**(10):909-16.

**Kirkland 2007** *{published data only}*

KirklandK B, Ptak JA, Dugan EA, Smith RH. A voice crying out in the wilderness? Sustained control of healthcare-associated MRSA infection without screening or organism-based isolation [abstract 23]. Presented at the 17th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America;. Baltimore, 2007 April 14-17; Baltimore.

**Klein 1989** *{published data only}*

Klein BS, Perloff WH, Maki DG. Reduction of nosocomial infection during pediatric intensive care by protective isolation. *The New England Journal of Medicine* 1989;**320**(26):1714-21.

**Koss 2001** *{published data only}*

Koss WG, Khalili TM, Lemus JF, Chelly MM, Margulies DR, Shabot MM. Nosocomial pneumonia is not prevented by protective contact isolation in the surgical intensive care unit. *The American Surgeon* 2001;**67**(12):1140-4.

**Lacey 2001** *{published data only}*

Lacey S, Flaxman D, Scales J, Wilson A. The usefulness of masks in preventing transient carriage of epidemic methicillin-resistant Staphylococcus aureus by healthcare workers. *The Journal of Hospital Infection* 2001;**48**(4):308-11.

**Maki 1996** *{published data only}*

Maki DG, Zilz MA, Mccormick R. The effectiveness of using preemptive barrier precautions routinely (protective isolation) in all high-risk patients to prevent nosocomial infection with resistant organisms, especially MRSA, VRE and C. difficile. *Clinical Infectious Diseases* 1996;**23**(4):43.

**Mangini 2007** *{published data only}*

Mangini E, Segal-Maurer S, Burns J, Avicolli A, Urban C, Mariano N, et al. Impact of contact and droplet precautions on the incidence of hospital-acquired methicillin-resistant Staphylococcus aureus infection. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2007;**28**(11):1261-6.

**Marshall 2011** *{published data only}*

Marshall C, McBryde E, Richards M. Do rapid detection and isolation of colonized patients reduce MRSA spread in the intensive care unit?. *BMC Proceedings* 2011;**5**(Suppl 6):O88.

**Marshall 2013** *{published data only}*

Marshall C, Richards M, McBryde E. Do active surveillance and contact precautions reduce MRSA acquisition? A prospective interrupted time series. *PloS one* 2013;**8**(3):e58112.

**Matsumoto 2012** *{published data only}*

Matsumoto K, Shigemi A, Yaji K, Shimodozono Y, Takeda Y, Ikawa K, et al. Reduction in the incidence of MRSA with use of alcohol-based hand rub solutions and gloves. *Journal of Infection and Chemotherapy: Official Journal of the Japan Society of Chemotherapy* 2012;**18**(2):269-71.

**Matsushima 2011** *{published data only}*

Matsushima A, Tasaki O, Tomono K, Ogura H, Kuwagata Y, Sugimoto H, et al. Pre-emptive contact precautions for intubated patients reduced healthcare-associated meticillin-resistant Staphylococcus aureus transmission and infection in an intensive care unit. *The Journal of Hospital Infection* 2011;**78**(2):97-101.

**Moore 2010** *{published data only}*

Moore G, Ali S, FitzGerald G, Muzslay M, Atkinson S, Smith S, et al. Ward assessment of SmartIdeas Project: bringing source isolation to the patient. *The Journal of Hospital Infection* 2010;**76**(2):103-7.

**Morioka 2013** *{published data only}*

Morioka I, Yahata M, Shibata A, Miwa A, Yokota T, Jikimoto T, et al. Impact of pre-emptive contact precautions for outborn neonates on the incidence of healthcare-associated meticillin-resistant Staphylococcus aureus transmission in a Japanese neonatal intensive care unit. *The Journal of Hospital Infection* 2013;**84**(1):66-70.

**MOSAR study 2014** *{published data only}*

Derde LPG, Cooper B, Brun Buisson C, Bonten M. Mastering hospital antibiotic resistance (mosar): a European cluster-randomized trial on reducing acquisition of resistant bacteria in intensive care units. 25th Annual Congress of the European Society of Intensive Care Medicine, ESICM 2012 Lisbon, Portugal. www.esicm.org/flash-conferences/lisbon-2012 (accessed 7 December 2014).

Derde LPG, Cooper BS, Brun-Buisson C, Bonten MJM. Reducing acquisition of resistant bacteria in intensive cares: a European cluster randomised trial. 22nd European Congress of Clinical Microbiology and Infectious Diseases. London, United Kingdom. http://registration.akm.ch/einsicht.php?XNABSTRACT_ID=151880&XNSPRACHE_ID=2&XNKONGRESS_ID=161&XNMASKEN_ID=900 (accessed 7 December 2014).

* Derde LPG, Cooper BS, Goossens H, Malhotra-Kumar S, Willems RJ, 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.

**Moylan 1987** *{published data only}*

Moylan JA, Fitzpatrick KT, Davenport KE. Reducing wound infections. Improved gown and drape barrier performance. *Archives of Surgery (Chicago, Ill. : 1960)* 1987;**122**(2):152-7.

**Muroya 2009** *{published data only}*

Muroya T, Tasaki O, Irisawa T, Shiozaki T, Ogura H, Kuwagata Y, et al. The effect of preemptive contact precaution for intubated patients on the nosocomial infection of MRSA in intensive care unit. Society of Critical Care Medicine's 39TH Critical Care Congress. *Critical Care Medicine* 2009;**37**(12 Suppl):S41.

**Raad 1994** *{published data only}*

Raad II, Hohn DC, Gilbreath BJ, Suleiman N, Hill LA, Bruso PA, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 1994;**15**(4 Pt 1):231-8.

**Reitzel 2009** *{published data only}*

Reitzel RA, Dvorak TL, Hachem RY, Fang X, Jiang Y, Raad I. Efficacy of novel antimicrobial gloves impregnated with antiseptic dyes in preventing the adherence of multidrug-resistant nosocomial pathogens. *American Journal of Infection Control* 2009;**37**(4):294-300.

**Ribner 1986** *{published data only}*

Ribner BS, Landry MN, Gholson GL. Strict versus modified isolation for prevention of nosocomial transmission of methicillin-resistant Staphylococcus aureus. *Infection Control* 1986;**7**(6):317-20.

**Rijnders 2003** *{published data only}*

Rijnders BJ, Van Wijngaerden E, Wilmer A, Peetermans WE. Use of full sterile barrier precautions during insertion of arterial catheters: a randomized trial. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2003;**36**(6):743-8.

**Rodríguez-Baño 2010** *{published data only}*

Rodríguez-Baño J, García L, Ramírez E, Lupion C, Muniain MA, Velasco C, et al. Long-term control of endemic hospital-wide methicillin-resistant Staphylococcus aureus (MRSA): the impact of targeted active surveillance for MRSA in patients and healthcare workers. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2010;**31**(8):786-95.

**Shenoy 2013** *{published data only}*

Shenoy ES, Kim J, Rosenberg ES, Cotter JA, Lee H, Walensky RP, et al. Discontinuation of contact precautions for methicillin-resistant staphylococcus aureus: a randomized controlled trial comparing passive and active screening with culture and polymerase chain reaction. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2013;**57**(2):176-84.

**Slaughter 1996** *{published data only}*

Slaughter S, Hayden MK, Nathan C, Hu TC, Rice T, Van Voorhis J, et al. A comparison of the effect of universal use of gloves and gowns with that of glove use alone on acquisition of vancomycin-resistant enterococci in a medical intensive care unit. *Annals of Internal Medicine* 1996;**125**(6):448-56.

**Slota 2001** *{published data only}*

Slota M, Green M, Farley A, Janosky J, Carcillo J. The role of gown and glove isolation and strict handwashing in the reduction of nosocomial infection in children with solid organ transplantation. *Critical Care Medicine* 2001;**29**(2):405-12.

**Spence 2012** *{published data only}*

Spence MR, Dammel T, Courser S. Contact precautions for methicillin-resistant Staphylococcus aureus colonization: costly and unnecessary?. *American Journal of Infection Control* 2012;**40**(6):535-8.

**STAR ICU Trial 2011** *{published data only}*

Huskins WC, Huckabee CM, O'Grady NP, Murray P, Kopetskie H, Zimmer L, et al. Intervention to reduce transmission of resistant bacteria in intensive care. *The New England Journal of Medicine* 2011;**364**(15):1407-18.

**Trick 2004** *{published data only}*

Trick WE, Weinstein RA, DeMarais PL, Tomaska W, Nathan C, McAllister SK, et al. Comparison of routine glove use and contact-isolation precautions to prevent transmission of multidrug-resistant bacteria in a long-term care facility. *Journal of the American Geriatrics Society* 2004;**52**(12):2003-9.

**Trick 2007** *{published data only}*

Trick WE, Vernon MO, Welbel SF, Demarais P, Hayden MK, Weinstein RA. Multicenter intervention program to increase adherence to hand hygiene recommendations and glove use and to reduce the incidence of antimicrobial resistance. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2007;**28**(1):42-9.

**Williams 2015** *{published data only}*

Williams C, McGraw P, Schneck EE, LaFae A, Jacob JT, Moreno D, et al. Impact of universal gowning and gloving on health care worker clothing contamination. *Infection Control and Hospital Epidemiology* 2015;**36**(4):431-7.

**Yin 2013** *{published data only}*

Yin J, Schweizer ML, Herwaldt LA, Pottinger JM, Perencevich EN. Benefits of universal gloving on hospital-acquired infections in acute care pediatric units. *Pediatrics* 2013;**131**(5):e1515-20.

## Additional references

**Aboelela 2006**

Aboelela SW, Saiman L, Stone P, Lowy FD, Quiros D, Larson E. Effectiveness of barrier precautions and surveillance cultures to control transmission of multidrug-resistant organisms: a systematic review of the literature. *American Journal of Infection Control* 2006;**34**(8):484-94.

**AHRQ 2013**

Agency for Healthcare Research and Quality. Making health care safer II: an updated critical analysis of the evidence for patient safety practices. Available from: www.ahrq.gov/research/findings/evidence-based-reports/ptsafetyuptp.html (accessed 21 July 2014) 2013.

**Albrich 2008**

Albrich WC, Harbarth S. Health-care workers: source, vector, or victim of MRSA?. *The Lancet Infectious Diseases* 2008;**8**(5):289-301.

**APIC 2010**

The Association for Professionals in Infection Control and Epidemiology (APIC). Guide to the elimination of Methicillin-Resistant Staphylococcus aureus (MRSA) transmission in hospital settings, 2nd Edition. http://apic.org/Resource_/EliminationGuideForm/631fcd91-8773-4067-9f85-ab2a5b157eab/File/MRSA-elimination-guide-2010.pdf (accessed 26 May 2014).

**Arnow 1982**

Arnow P, Allyn PA, Nichols EM, Hill DL, Pezzlo M, Bartlett RH. Control of methicillin-resistant Staphylococcus aureus in a burn unit: role of nurse staffing. *The Journal of Trauma* 1982;**22**(11):954-9.

**Backman 2011**

Backman C, Taylor G, Sales A, Marck PB. An integrative review of infection prevention and control programs for multidrug-resistant organisms in acute care hospitals: a socio-ecological perspective. *American Journal of Infection Control* 2011;**39**(5):368-78.

**Baker 2010**

Baker SE, Brecher SM, Robillard E, Strymish J, Lawler E, Gupta K. Extranasal methicillin-resistant Staphylococcus aureus colonization at admission to an acute care Veterans Affairs hospital. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2010;**31**(1):42-6.

**Barrett 1968**

Barrett FF, McGehee RF Jr, Finland M. Methicillin-resistant Staphylococcus aureus at Boston City Hospital. Bacteriologic and epidemiologic observations. *The New England Journal of Medicine* 1968;**279**(9):441-8.

**Benner 1968**

Benner EJ, Kayser FH. Growing clinical significance of methicillin-resistant Staphylococcus aureus. *Lancet* 1968;**2**(7571):741-4.

**Bisaga 2008**

Bisaga A, Paquette K, Sabatini L, Lovell EO. A prevalence study of methicillin-resistant Staphylococcus aureus colonization in emergency department health care workers. *Annals of Emergency Medicine* 2008;**52**(5):525-8.

**Bland 1994**

Bland JM, Altman DG. Some examples of regression towards the mean. *BMJ (Clinical Research Ed.)* 1994;**309**(6957):780.

**Blok 2003**

Blok HE, Troelstra A, Kamp-Hopmans TE, Gigengack-Baars AC, Vandenbroucke-Grauls CM, Weersink AJ, et al. Role of healthcare workers in outbreaks of methicillin-resistant Staphylococcus aureus: a 10-year evaluation from a Dutch university hospital. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2003;**24**(9):679-85.

**Borenstein 2009**

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Fixed-effect versus random-effects models. Introduction to Meta-Analysis. Chichester: John Wiley & Sons, Ltd, 2009:77-86.

**Boutron 2005**

Boutron I, Moher D, Tugwell P, Giraudeauf B, Poiraudeaug S, Nizardh R, et al. A checklist to evaluate a report of a non pharmacological trial (CLEAR NPT) was developed using consensus. *Journal of Clinical Epidemiology* 2005;**58**(12):1233-40.

**Boutron 2008**

Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine* 2008;**148**(4):295-309.

**Boutron 2012**

Boutron I, Moher D, Ravaud P. Randomized clinical trials of nonpharmacological treatments. Boca Raton: CRC Press, 2012.

**Boyce 1981**

Boyce JM, Landry M, Deetz TR, DuPont HL. Epidemiologic studies of an outbreak of nosocomial methicillin-resistant Staphylococcus aureus infections. *Infection Control* 1981;**2**(2):110-6.

**Boyce 1983**

Boyce JM, White RL, Causey WA, Lockwood WR. Burn units as a source of methicillin-resistant Staphylococcus aureus infections. *JAMA* 1983;**249**(20):2803-7.

**Boyce 1989**

Boyce JM. Methicillin-resistant Staphylococcus aureus. Detection, epidemiology, and control measures. *Infectious Disease Clinics of North America* 1989;**3**(4):901-13.

**Boyce 1993**

Boyce JM, Opal SM, Potter-Bynoe G, Medeiros AA. Spread of methicillin-resistant Staphylococcus aureus in a hospital after exposure to a health care worker with chronic sinusitis. *Clinical Infectious Diseases* 1993;**17**(3):496-504.

**Brierley 2012**

Brierley G, Brabyn S, Torgerson D, Watson J. Bias in recruitment to cluster randomized trials: a review of recent publications. *Journal of Evaluation in Clinical Practice* 2012;**18**(4):878-86.

**Brown 2006a**

Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. *BMC Medical Research Methodology* 2006;**6**:54.

**Brown 2006b**

Brown P, Brunnhuber K, Chalkidou K, Chalmers I, Clarke M, Fenton M, et al. How to formulate research recommendations. *BMJ (Clinical Research Ed.)* 2006;**333**(7572):804-6.

**Brown 2008**

Brown C, Hofer T, Johal A, Thomson R, Nicholl J, Franklin BD, et al. An epistemology of patient safety research: a framework for study design and interpretation. Part 2. Study design. *Quality & Safety in Health Care* 2008;**17**(3):163-9.

**Burford 2013**

Burford B, Lewin S, Welch V, Rehfuess E, Waters E. Assessing the applicability of findings in systematic reviews of complex interventions can enhance the utility of reviews for decision making. *Journal of Clinical Epidemiology* 2013;**66**(11):1251-61.

**Burton 2009**

Burton DC, Edwards JR, Horan TC, Jernigan JA, Fridkin SK. Methicillin-resistant Staphylococcus aureus central line-associated bloodstream infections in US intensive care units, 1997-2007. *JAMA* 2009;**301**(7):727-36.

**Calfee 2014**

Calfee DP, Salgado CD, Milstone AM, Harris AD, Kuhar DT, Moody J, et al. Strategies to prevent methicillin-resistant Staphylococcus aureus transmission and infection in acute care hospitals: 2014 update. *Infection Control and Hospital Epidemiology: The Official Journal of the Society of Hospital Epidemiologists of America* 2014;**35**(7):772-96.

**Campbell 2012**

Campbell MK, Piaggio G, Elbourne DR, Altman DG. Consort 2010 statement: extension to cluster randomised trials. *BMJ (Clinical Research Ed.)* 2012;**345**:e5661.

**CDC 2014**

Centers for Disease Control and Prevention (CDC). CDC/NHSN surveillance definitions for specific types of infections. CDC NHSN Patient Safety Component (PSC) Manual, 2014. www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf (accessed 26 May 2014).

**CEBM 2009**

Centre for Evidence Based Medicine. The PaT Plot Tool, 2009. www.cebm.net/index.aspx?o=4200 (accessed 7 June 2014).

**Chai 2005**

Chai LY, Ng TM, Habib AG, Singh K, Kumarasinghe G, Tambyah PA. Paradoxical increase in methicillin-resistant Staphylococcus aureus acquisition rates despite barrier precautions and increased hand washing compliance during an outbreak of severe acute respiratory syndrome. Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America 2005; Vol. 40, issue 4:632-3.

**Climo 2013**

Climo MW, Yokoe DS, Warren DK, Perl TM, Bolon M, Herwaldt LA, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *The New England Journal of Medicine* 2013;**368**(6):533-42.

**Cohen 2008**

Cohen AL, Calfee D, Fridkin SK, Huang SS, Jernigan JA, Lautenbach E, et al. Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC Position paper. *Infection Control and Hospital Epidemiology* 2008;**29**(10):901-13.

**Coia 2006**

Coia JE, Duckworth GJ, Edwards DI, Farrington M, Fry C, Humphreys H, et al. Guidelines for the control and prevention of methicillin-resistant Staphylococcus aureus (MRSA) in healthcare facilities. *Journal of Hospital Infection* 2006;**63 Suppl 1**:1-44.

**Coia 2013**

Coia JE, Ritchie L, Adisesh A, Makison Booth C, Bradley C, Bunyan D, et al. Guidance on the use of respiratory and facial protection equipment. *The Journal of Hospital Infection* 2013;**85**(3):170-82.

**CONSORT glossary 2014**

CONSORT Group. CONSORT glossary. www.consort-statement.org/resources/glossary (accessed 4 Sept 2014).

**Cooper 2003**

Cooper BS, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Medley GF, et al. Systematic review of isolation policies in the hospital management of methicillin-resistant Staphylococcus aureus: a review of the literature with epidemiological and economic modelling. *Health Technology Assessment* 2003;**7**:1-194.

**Cosgrove 2003**

Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible Staphylococcus aureus bacteremia: a meta-analysis. *Clinical Infectious Diseases* 2003;**36**(1):53-9.

**Cosgrove 2005**

Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in Staphylococcus aureus bacteraemia on patient outcomes: mortality, length of stay, and hospital charges. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2005;**26**(2):166-74.

**Crowcroft 2002**

Crowcroft NS, Catchpole M. Mortality for methicillin-resistant Staphylococcus aureus in England and Wales: analysis of death certificates. *BMJ* 2002;**325**(7377):1390-1.

**Dantes 2013**

Dantes R, Mu Y, Belflower R, Aragon D, Dumyati G, Harrison LH, et al. National burden of invasive methicillin-resistant Staphylococcus aureus infections, United States, 2011. *JAMA Internal Medicine* 2013;**173**(21):1970-8.

**Davidoff 2008**

Davidoff F, Batalden P, Stevens D, Ogrinc G, Mooney S. Publication guidelines for quality improvement in health care: evolution of the SQUIRE project. *Quality & Safety in Health Care* 2008;**17 Suppl 1**:i3-9.

**Davis 2004**

Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant Staphylococcus aureus (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2004;**39**(6):776-82.

**Day 2011**

Day HR, Morgan DJ, Himelhoch S, Young A, Perencevich EN. Association between depression and contact precautions in veterans at hospital admission. *American Journal of Infection Control* 2011;**39**(2):163-5.

**Deeks 2003**

Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomised intervention studies. *Health Technology Assessment (Winchester, England)* 2003;**7**(27):iii-x, 1-173.

**Deeks 2011**

Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**den Heijer 2013**

den Heijer CD, van Bijnen EM, Paget WJ, Pringle M, Goossens H, Bruggeman CA, et al. Prevalence and resistance of commensal Staphylococcus aureus, including meticillin-resistant S aureus, in nine European countries: a cross-sectional study. *Lancet Infectious Diseases* 2013;**13**(5):409-15.

**Devine 2001**

Devine J, Cooke RP, Wright EP. Is methicillin-resistant Staphylococcus aureus (MRSA) contamination of ward-based computer terminals a surrogate marker for nosocomial MRSA transmission and handwashing compliance?. *Journal of Hospital Infection* 2001;**48**(1):72-5.

**ECDC 2013**

European Centre for Disease Prevention and Control (ECDC). Annual epidemiological report. Reporting on 2011 surveillance data and 2012 epidemic intelligence data. 2013. www.ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=989 (accessed 26 May 2014).

**Elie-Turenne 2010**

Elie-Turenne MC, Fernandes H, Mediavilla JR, Rosenthal M, Mathema B, Singh A, et al. Prevalence and characteristics of Staphylococcus aureus colonization among healthcare professionals in an urban teaching hospital. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2010;**31**(6):574-80.

**Engemann 2003**

Engemann JJ, Carmeli Y, Cosgrove SE, Fowler VG, Bronstein MZ, Trivette SL, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with Staphylococcus aureus surgical site infection. *Clinical Infectious Diseases* 2003;**36**(5):592-8.

**EPOC 2007**

Cochrane Effective Practice and Organisation of Care Group (EPOC). Which study designs are accepted for inclusion in EPOC reviews? 2007. http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/FAQ%20-%20Included%20Studies%20-%20EPOC%20-%202007-May-01.doc (accessed 1 June 2014).

**EPOC 2009**

Cochrane Effective Practice and Organisation of Care Group (EPOC). The data collection checklist. Ottawa, 2009. http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/datacollectionchecklist.pdf (accessed 31 May 2014).

**EPOC 2013a**

Effective Practice, Organisation of Care (EPOC). EPOC Resources for review authors. What study designs should be included in an EPOC review and what should they be called? Oslo: Norwegian Knowledge Centre for the Health Services; 2013. Available from: http://epocoslo.cochrane.org/epoc-specific-resources-review-authors (accessed 7 June 2014).

**EPOC 2013b**

Effective Practice, Organisation of Care (EPOC). EPOC Resources for review authors. Good practice data extraction form. Oslo: Norwegian Knowledge Centre for the Health Services; 2013. Available at: http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/13a%20Good%20practice%20data%20extraction%20form%202013%2008%2012.doc (accessed 7 June 2014).

**EPOC 2013c**

Effective Practice, Organisation of Care (EPOC). EPOC Resources for review authors. Suggested risk of bias criteria for EPOC reviews. Oslo: Norwegian Knowledge Centre for the Health Services; 2013. Available at: http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/14%20Suggested%20risk%20of%20bias%20criteria%20for%20EPOC%20reviews%202013%2008%2012.pdf (accessed 7 June 2014).

**EPOC 2013d**

Effective Practice, Organisation of Care (EPOC). EPOC Resources for review authors. Analysis in EPOC reviews. Oslo: Norwegian Knowledge Centre for the Health Services; 2013. Available at: http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/19%20Analysis%20in%20EPOC%20reviews%202013%2008%2012.pdf (accessed 13 June 2014).

**Equity Checklist 2012**

Campbell & Cochrane Equity Methods Group. The equity checklist. http://equity.cochrane.org/sites/equity.cochrane.org/files/uploads/EquityChecklist2012.pdf (assessed 15 July 2014).

**Evans 2003**

Evans HL, Shaffer MM, Hughes MG, Smith RL, Chong TW, Raymond DP, et al. Contact isolation in surgical patients: a barrier to care?. *Surgery* 2003;**134**(2):180-8.

**FDA 2008**

US Food, Drug Administration. Guidance for Industry and FDA Staff: Medical Glove Guidance Manual, 2008. www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm150053.htm (accessed 29 May 2014).

**FDA 2014a**

US Food, Drug Administration. Devices@FDA: Patient examination glove. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=880.6250 (accessed 29 May 2014).

**FDA 2014b**

US Food, Drug Administration. Devices@FDA: Surgeon´s glove. www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=878.4460 (accessed 29 May 2014).

**Fridkin 2002**

Fridkin SK, Hill HA, Volkova NV, Edwards JR, Lawton RM, Gaynes RP, et al. Temporal changes in prevalence of antimicrobial resistance in 23 US hospitals. *Emerging Infectious Diseases* 2002;**8**(7):697-701.

**Fuller 2011**

Fuller C, Savage J, Besser S, Hayward A, Cookson B, Cooper B, et al. "The dirty hand in the latex glove": a study of hand hygiene compliance when gloves are worn. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2011;**32**(12):1194-9.

**Gamble 2005**

Gamble C, Hollis S. Uncertainty method improved on best-worst case analysis in a binary meta-analysis. *Journal of Clinical Epidemiology* 2005;**58**(6):579–88.

**Garner 1996**

Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. In: Olmsted RN editor(s). APIC Infection Control and Applied Epidemiology: Principles and Practice. St. Louis: Mosby, 1996:A1-A20.

**Gastmeier 2004**

Gastmeier P, Schwab F, Geffers C, Ruden H. To isolate or not to isolate? Analysis of data from the German Nosocomial Infection Surveillance System regarding the placement of patients with methicillin-resistant Staphylococcus aureus in private rooms in intensive care units. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2004;**25**(2):109-13.

**Gaynes 1991**

Gaynes R, Marosok R, Mowry-Hanley J, Laughlin C, Foley K, Friedman C, et al. Mediastinitis following coronary artery bypass surgery: a 3-year review. *Journal of Infectious Diseases* 1991;**163**(1):117-21.

**Girou 2004**

Girou E, Chai S H, Oppein F, Legrand P, Ducellier D, Cizeau F, et al. Misuse of gloves: the foundation for poor compliance with hand hygiene and potential for microbial transmission?. *The Journal of Hospital Infection* 2004;**57**(2):162-9.

**Glick 2013**

Glick SB, Samson DJ, Huang E, Vats V, Weber S, Aronson N. Screening for methicillin-resistant Staphylococcus aureus (MRSA). Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2013 June. Comparative effectiveness review No. 102. AHRQ Publication No. 13-EHC043-EF.

**Goetghebeur 2007**

Goetghebeur M, Landry PA, Han D, Vicente C. Methicillin-resistant Staphylococcus aureus: a public health issue with economic consequences. *Canadian Journal of Infectious Diseases & Medical Microbiology [Journal Canadien des Maladies Infectieuses et de la Microbiologie Medicale]* 2007;**18**(1):27-34.

**Golder 2009**

Golder S, Loke Y. Search strategies to identify information on adverse effects: a systematic review. *Journal of the Medical Library Association: JMLA* 2009;**97**(2):84-92.

**Gorwitz 2008**

Gorwitz RJ, Kruszon-Moran D, McAllister SK, McQuillan G, McDougal LK, Fosheim GE, et al. Changes in the prevalence of nasal colonization with Staphylococcus aureus in the United States, 2001-2004. *The Journal of Infectious Diseases* 2008;**197**(9):1226-34.

**Gould 2006**

Gould IM. Costs of hospital-acquired methicillin-resistant Staphylococcus aureus (MRSA) and its control. *International Journal of Antimicrobial Agents* 2006;**28**(5):379-84.

**Gould 2009**

Gould FK, Brindle R, Chadwick PR, Fraise AP, Hill S, Nathwani D, et al. Guidelines (2008) for the prophylaxis and treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections in the United Kingdom. *The Journal of Antimicrobial Chemotherapy* 2009;**63**(5):849-61.

**Gould 2010**

Gould I, Reilly J, Bunyan D, Walker A. Costs of healthcare associated methicillin-resistant Staphylococcus aureus (MRSA) and its control. *Clinical Microbiology and Infection: the Official Publication of the European Society of Clinical Microbiology and Infectious Diseases* 2010;**16**(12):1721-8.

**GRADEpro 2014 [Computer program]**

McMaster University. GRADEpro. Version 3.2 for Windows. McMaster University, 2014.

**Grimes 2002**

Grimes DA, Schulz KF. Descriptive studies: what they can and cannot do. *Lancet* 2002;**359**(9301):145-9.

**Grundmann 2006**

Grundmann H, Aires-de-Sousa M, Boyce J. Emergence and resurgence of meticillin-resistant Staphylococcus aureus as a public-health threat. *Lancet* 2006;**368**(9538):874-85.

**Guyatt 2008**

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**:924-6.

**Hails 2003**

Hails J, Kwaku F, Wilson AP, Bellingan G, Singer M. Large variation in MRSA policies, procedures and prevalence in English intensive care units: a questionnaire analysis. *Intensive Care Medicine* 2003;**29**(3):481-3.

**Halcomb 2007**

Halcomb EJ, Fernandez R, Griffiths R, Newton RN, Hickman L. The infection control management of MRSA in acute care. *International Journal of Evidence-based Healthcare* 2008;**6**:440–67.

**Hansen 2010**

Hansen S, Schwab F, Asensio A, Carsauw H, Heczko P, Klavs I, et al. Methicillin-resistant Staphylococcus aureus (MRSA) in Europe: which infection control measures are taken?. *Infection* 2010;**38**(3):159-64.

**Harbarth 2008**

Harbarth S, Fankhauser C, Schrenzel J, Christenson J, Gervaz P, Bandiera-Clerc C, et al. Universal screening for methicillin-resistant Staphylococcus aureus at hospital admission and nosocomial infection in surgical patients. *JAMA* 2008;**299**(10):1149-57.

**Harris 2004**

Harris AD, Bradham DD, Baumgarten M, Zuckerman IH, Fink JC, Perencevich EN. The use and interpretation of quasi-experimental studies in infectious diseases. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2004;**38**(11):1586-91.

**Hartling 2010**

Hartling L, Bond K, Harvey K, Santaguida PL, Viswananthan M, Dryden DM. Developing and testing a tool for the classification of study designs in systematic reviews of interventions and exposures, 2010. Agency for Healthcare Research and Quality; Methods Research Report. AHRQ Publication No. 11-EHC-007. Available at http://effectivehealthcare.ahrq.gov/ (accessed 29 May 2014).

**Hartman 1981**

Hartman B, Tomasz A. Altered penicillin-binding proteins in methicillin-resistant strains of Staphylococcus aureus. *Antimicrobial Agents and Chemotherapy* 1981;**19**(5):726-35.

**Hartstein 1995**

Hartstein AI, Denny MA, Morthland VH, LeMonte AM, Pfaller MA. Control of methicillin-resistant Staphylococcus aureus in a hospital and an intensive care unit. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 1995;**16**(7):405-11.

**Hayes 2000**

Hayes RJ, Alexander ND, Bennett S, Cousens SN. Design and analysis issues in cluster-randomized trials of interventions against infectious diseases. *Statistical Methods in Medical Research* 2000;**9**(2):95-116.

**Hidron 2005**

Hidron AI, Kourbatova EV, Halvosa JS, Terrell BJ, McDougal LK, Tenover FC, et al. Risk factors for colonization with methicillin-resistant Staphylococcus aureus (MRSA) in patients admitted to an urban hospital: emergence of community-associated MRSA nasal carriage. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2005;**41**(2):159-66.

**Higgins 2003**

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ (Clinical Research Ed.)* 2003;**327**(7414):557-60.

**Higgins 2005**

Higgins JPT, Green S (editors). Glossary of Cochrane Collaboration Version 4.2.5 [updated in May 2005]. The Cochrane Collaboration, 2005. www.cochrane.org/glossary (accessed 20 May 2014).

**Higgins 2011a**

Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Higgins 2011b**

Higgins JPT, Deeks JJ, Altman DG (editors). Chapter 16: Special topics in statistics. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Higgins 2011c**

Higgins JPT, Deeks JJ (editors). Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Hoffmann 2014**

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ (Clinical Research Ed.)* 2014;**348**:g1687.

**Huang 2003**

Huang SS, Platt R. Risk of methicillin-resistant Staphylococcus aureus infection after previous infection or colonization. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2003;**36**(3):281-5.

**Hughes 2013**

Hughes C, Tunney M, Bradley MC. Infection control strategies for preventing the transmission of meticillin-resistant Staphylococcus aureus (MRSA) in nursing homes for older people. *Cochrane Database of Systematic Reviews* 2013, Issue 11. [DOI: 10.1002/14651858.CD006354.pub4]

**IHI 2006**

Institute for Healthcare Improvement. Raising the bar with bundles: treating patients with an all-or-nothing standard, 2006. www.ihi.org/resources/Pages/Publications/RaisingtheBarwithBundles.aspx (accessed 31 August 2014).

**Ijaz 2014**

Ijaz S, Verbeek JH, Mischke C, Ruotsalainen J. Inclusion of nonrandomized studies in Cochrane systematic reviews was found to be in need of improvement. *Journal of Clinical Epidemiology* 2014;**67**(6):645-53.

**Ioannidis 2004**

Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, et al. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Annals of Internal Medicine* 2004;**141**(10):781-8.

**Ioannidis 2013**

Ioannidis JP, Prasad V. Evaluating health system processes with randomized controlled trials. *JAMA Internal Medicine* 2013;**173**(14):1279-80.

**Irish department of Health 2013**

Irish Department of Health. Prevention and control methicillin-resistant Staphylococcus aureus (MRSA) national clinical guideline. National Clinical Guideline No. 2, 2013. www.dohc.ie/publications/MRSA_Guideline.html (accessed 26 May 2014).

**Iwamoto 2013**

Iwamoto M, Mu Y, Lynfield R, Bulens SN, Nadle J, Aragon D, et al. Trends in invasive methicillin-resistant Staphylococcus aureus infections. *Pediatrics* 2013;**132**(4):e817-24.

**Jarvis 2007**

Jarvis WR, Schlosser J, Chinn RY, Tweeten S, Jackson M. National prevalence of methicillin-resistant Staphylococcus aureus in inpatients at US health care facilities, 2006. *American Journal of Infection Control* 2007;**35**(10):631-7.

**Jefferson 2011**

Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database of Systematic Reviews* 2011, Issue 7. [DOI: 10.1002/14651858.CD006207.pub4]

**Jernigan 1996**

Jernigan JA, Titus MG, Groschel DH, Getchell-White S, Farr BM. Effectiveness of contact isolation during a hospital outbreak of methicillin-resistant Staphylococcus aureus. *American Journal of Epidemiology* 1996;**143**(5):496-504.

**Johnson 1990**

Johnson S, Gerding DN, Olson MM, Weiler MD, Hughes RA, Clabots CR, et al. Prospective, controlled study of vinyl glove use to interrupt Clostridium difficile nosocomial transmission. *The American Journal of Medicine* 1990;**88**(2):137-40.

**Johnston 2009**

Johnston BL, Bryce E. Hospital infection control strategies for vancomycin-resistant Enterococcus, methicillin-resistant Staphylococcus aureus and Clostridium difficile. *Canadian Medical Association Journal* 2009;**180**(6):627-31.

**Kallen 2010**

Kallen AJ, Mu Y, Bulens S, Reingold A, Petit S, Gershman K, et al. Health care-associated invasive MRSA infections, 2005-2008. *JAMA* 2010;**304**(6):641-8.

**Karchmer 2002**

Karchmer TB, Durbin LJ, Simonton BM, Farr BM. Cost-effectiveness of active surveillance cultures and contact/droplet precautions for control of methicillin-resistant Staphylococcus aureus. *The Journal of Hospital Infection* 2002;**51**(2):126-32.

**Karki 2013**

Karki S, Leder K, Cheng A C. Patients under contact precautions have an increased risk of injuries and medication errors: a retrospective cohort study. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2013;**34**(10):1118-20.

**Kypraios 2010**

Kypraios T, O'Neill PD, Huang SS, Rifas-Shiman SL, Cooper BS. Assessing the role of undetected colonization and isolation precautions in reducing methicillin-resistant Staphylococcus aureus transmission in intensive care units. *BMC Infectious Diseases* 2010;**10**:29.

**Leclair 1987**

Leclair JM, Freeman J, Sullivan BF, Crowley CM, Goldmann DA. Prevention of nosocomial respiratory syncytial virus infections through compliance with glove and gown isolation precautions. *The New England Journal of Medicine* 1987;**317**(6):329-34.

**Lee 2011**

Lee AS, Huttner B, Harbarth S. Control of methicillin-resistant Staphylococcus aureus. *Infectious Disease Clinics of North America* 2011;**25**(1):155-79.

**Lee 2013**

Lee BY, Singh A, Bartsch SM, Wong KF, Kim DS, Avery TR, et al. The potential regional impact of contact precaution use in nursing homes to control methicillin-resistant Staphylococcus aureus. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2013;**34**(2):151-60.

**Lefebvre 2011**

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Liberati 2009**

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS medicine* 2009;**6**(7):e1000100.

**Lin 2012**

Lin MY, Bonten MJ. The dilemma of assessment bias in infection control research. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2012;**54**(9):1342-7.

**Lipp 2014**

Lipp A, Edwards P. Disposable surgical face masks for preventing surgical wound infection in clean surgery. *Cochrane Database of Systematic Reviews* 2014, Issue 2. [DOI: 10.1002/14651858.CD002929.pub2]

**Livermore 2000**

Livermore DM. Antibiotic resistance in staphylococci. *International Journal of Antimicrobial Agents* 2000;**16 Suppl 1**:3-10.

**Loeb 2003**

Loeb M, Main C, Walker-Dilks C, Eady A. Antimicrobial drugs for treating methicillin-resistant Staphylococcus aureus colonization. *Cochrane Database of Systematic Reviews* 2003, Issue 4. [DOI: 10.1002/14651858.CD003340]

**Loke 2011**

Loke YK, Price D, Herxheimer A. Chapter 14: Adverse effects. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Loveday 2006**

Loveday HP, Pellowe CM, Jones SR, Pratt RJ. A systematic review of the evidence for interventions for the prevention and control of meticillin-resistant Staphylococcus aureus (1996-2004): report to the Joint MRSA Working Party (Subgroup A). *The Journal of Hospital Infection* 2006;**63 Suppl 1**:S45-70.

**Loveday 2014**

Loveday HP, Wilson JA, Pratt RJ, Golsorkhi M, Tingle A, Bak A, et al. epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *The Journal of Hospital Infection* 2014;**86 Suppl 1**:S1-70.

**Magill 2014**

Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health

care-associated infections. *The New England Journal of Medicine* 2014;**370**(13):1198-208.

**McKinnell 2013**

McKinnell JA, Miller LG, Eells SJ, Cui E, Huang SS. A systematic literature review and meta-analysis of factors associated with methicillin-resistant Staphylococcus aureus colonization at time of hospital or intensive care unit admission. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2013;**34**(10):1077-86.

**MECIR Conduct 2013**

Chandler J, Churchill R, Higgins J, Lasserson T, Tovey D. Methodological standards for the conduct of new Cochrane intervention reviews, 2013. www.editorial-unit.cochrane.org/sites/editorial-unit.cochrane.org/files/uploads/MECIR_conduct_standards%202.3%2002122013.pdf (accessed 7 June 2014).

**Mehrotra 2013**

Mehrotra P, Croft L, Day HR, Perencevich EN, Pineles L, Harris AD, et al. Effects of contact precautions on patient perception of care and satisfaction: a prospective cohort study. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2013;**34**(10):1087-93.

**Merrer 2000**

Merrer J, Santoli F, Appere de Vecchi C, Tran B, De Jonghe B, Outin H. "Colonization pressure" and risk of acquisition of methicillin-resistant Staphylococcus aureus in a medical intensive care unit. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2000;**21**(11):718-23.

**Mertz 2009**

Mertz D, Frei R, Periat N, Zimmerli M, Battegay M, Fluckiger U, et al. Exclusive Staphylococcus aureus throat carriage: at-risk populations. *Archives of Internal Medicine* 2009;**169**(2):172-8.

**MeSH Browser 2014**

US National Library of Medicine. MeSH Browser (2014 MeSH). www.ncbi.nlm.nih.gov/mesh (accessed 28 May 2014).

**Mischke 2014**

Mischke C, Verbeek JH, Saarto A, Lavoie MC, Pahwa M, Ijaz S. Gloves, extra gloves or special types of gloves for preventing percutaneous exposure injuries in healthcare personnel. *Cochrane Database of Systematic Reviews* 2014, Issue 3. [DOI: 10.1002/14651858.CD009573.pub2]

**Morgan 2009**

Morgan DJ, Diekema DJ, Sepkowitz K, Perencevich EN. Adverse outcomes associated with contact precautions: a review of the literature. *American Journal of Infection Control* 2009;**37**(2):85-93.

**Morgan 2010**

Morgan DJ, Day HR, Furuno JP, Young A, Johnson JK, Bradham DD, et al. Improving efficiency in active surveillance for methicillin-resistant Staphylococcus aureus or vancomycin-resistant Enterococcus at hospital admission. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2010;**31**(12):1230-5.

**Morgan 2011**

Morgan DJ, Day HR, Harris AD, Furuno JP, Perencevich EN. The impact of contact isolation on the quality of inpatient hospital care. *PLoS One* 2011;**6**(7):e22190.

**Morton 2003**

Morton V, Torgerson DJ. Effect of regression to the mean on decision making in health care. *BMJ (Clinical Research Ed.)* 2003;**326**(7398):1083-4.

**MRC 2008**

Medical Research Council. Developing and evaluating complex interventions: new guidance, 2008. www.mrc.ac.uk/complexinterventionsguidance (accessed 7 July 2014).

**Muto 2003**

Muto CA, Jernigan JA, Ostrowsky BE, Richet HM, Jarvis WR, Boyce JM, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of Staphylococcus aureus and Enterococcus. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2003;**24**(5):362-86.

**NHMRC 2010**

Commonwealth of Australia. Australian guidelines for the prevention and control of infection in healthcare. www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cd33_complete.pdf (accessed 26 May 2014).

**Noorani 2013**

Noorani HZ, Adams E, Glick S, Weber S, Belinson S, Aronson N. Screening for methicillin-resistant Staphylococcus aureus (MRSA): future research needs. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2013 June. Future research needs paper No. 40. AHRQ Publication No. 13-EHC056-EF.

**NRSMG 2011**

Cochrane Non-Randomised Studies Methods Group. Data extraction for non-randomised studies, 2011. www.cochrane.org/sites/default/files/uploads/data_extraction.doc (accessed 7 May 2014).

**NZMoH 2002**

New Zealand Ministry of Health (NZMoH). Guidelines for the control of methicillin resistant Staphylococcus aureus in New Zealand, 2002. www.health.govt.nz/system/files/documents/publications/mrsa.pdf (accessed 26 May 2014).

**O'Connor 2011**

O'Connor D, Green S, Higgins JPT (editors). Chapter 5: Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S (editors), Cochrane Handbook of Systematic Reviews of Intervention. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Oie 1996**

Oie S, Kamiya A. Survival of methicillin-resistant Staphylococcus aureus (MRSA) on naturally contaminated dry mops. *Journal of Hospital Infection* 1996;**34**(2):145-9.

**Olsen 1993**

Olsen RJ, Lynch P, Coyle MB, Cummings J, Bokete T, Stamm WE. Examination gloves as barriers to hand contamination in clinical practice. *JAMA* 1993;**270**(3):350-3.

**Pammi 2011**

Pammi M, Eddama O, Weisman LE. Patient isolation measures for infants with candida colonization or infection for preventing or reducing transmission of candida in neonatal units. *Cochrane Database of Systematic Reviews* 2011, Issue 11. [DOI: 10.1002/14651858.CD006068.pub3]

**Pan 2005**

Pan A, Carnevale G, Catenazzi P, Colombini P, Crema L, Dolcetti L, et al. Trends in methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections: effect of the MRSA "search and isolate" strategy in a hospital in Italy with hyperendemic MRSA. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2005;**26**(2):127-33.

**Peacock 1980**

Peacock JE Jr, Marsik FJ, Wenzel RP. Methicillin-resistant Staphylococcus aureus: introduction and spread within a hospital. *Annals of Internal Medicine* 1980;**93**(4):526-32.

**Perera 2007**

Perera R, Heneghan C, Yudkin P. Graphical method for depicting randomised trials of complex interventions. *BMJ* 2007;**334**(7585):127-9.

**Platt 2010**

Platt R, Takvorian SU, Septimus E, Hickok J, Moody J, Perlin J, et al. Cluster randomized trials in comparative effectiveness research: randomizing hospitals to test methods for prevention of healthcare-associated infections. *Medical Care* 2010;**48**(6 Suppl):S52-7.

**Pogorzelska 2012**

Pogorzelska M, Stone PW, Larson EL. Wide variation in adoption of screening and infection control interventions for multidrug-resistant organisms: a national study. *American Journal of Infection Control* 2012;**40**(8):696-700.

**Porta 2008**

Porta M, Greenland S, Last JM. A dictionary of Epidemiology. 5th Edition. New York: Oxford University Press, 2008.

**Public Health Agency of Canada 2012a**

Public Health Agency of Canada. Hand hygiene practices in healthcare settings. 2012. www.ipac-canada.org/pdf/2013_PHAC_Hand%20Hygiene-EN.pdf (accessed 8 December 2014).

**Public Health Agency of Canada 2012b**

Public Health Agency of Canada. Routine practices and additional precautions: preventing the transmission of infection in health care. 2012. www.ipac-canada.org/pdf/2013_PHAC_RPAP-EN.pdf (accessed 26 May 2014).

**Puzniak 2002**

Puzniak LA, Leet T, Mayfield J, Kollef M, Mundy LM. To gown or not to gown: the effect on acquisition of vancomycin-resistant enterococci. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2002;**35**(1):18-25.

**Rammelkamp 1964**

Rammelkamp CH, Mortimer EA, Wolinsky E. Transmission of streptococcal and staphylococcal infections. *Annals of Internal Medicine* 1964;**60**:753-8.

**Ranji 2007**

Ranji SR, Shetty K, Posley KA, Lewis R, Sundaram V, Galvin CM, et al. Volumen 6 - Prevention of healthcare-associated infections. Closing the quality gap: a critical analysis of quality improvement strategies. Rockville, MD: Agency for Healthcare Research and Quality, January 2007.

**Reagan 1991**

Reagan DR, Doebbeling BN, Pfaller MA, Sheetz CT, Houston AK, Hollis RJ, et al. Elimination of coincident Staphylococcus aureus nasal and hand carriage with intranasal application of mupirocin calcium ointment. *Annals of Internal Medicine* 1991;**114**(2):101-6.

**Reboli 1990**

Reboli AC, John JF Jr, Platt CG, Cantey JR. Methicillin-resistant Staphylococcus aureus outbreak at a Veterans' Affairs Medical Center: importance of carriage of the organism by hospital personnel. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 1990;**11**(6):291-6.

**Reeves 2011**

Reeves BC, Deeks JJ, Higgins JPT, Wells GA. Chapter 13: Including non-randomised studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**RevMan 2014 [Computer program]**

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

**Rodriguez-Baño 2006**

Rodriguez-Baño J, Millán AB, Domínguez MA, Almirante B, Cercenado E, Padilla B, et al. Control of methicillin-resistant Staphylococcus aureus in Spanish hospitals. A survey from the MRSA 2003 GEIH/GEMARA/REIPI project [Medidas de control de Staphylococcus aureus resistente a meticilina en hospitales españoles. Encuesta del proyecto SARM 2003 GEIH/GEMARA/REIPI.]. *Enfermedades Infecciosas y Microbiología Clínica* 2006;**24**(3):149-56.

**Rutala 1983**

Rutala WA, Katz EB, Sherertz RJ, Sarubbi FA Jr. Environmental study of a methicillin-resistant Staphylococcus aureus epidemic in a burn unit. *Journal of Clinical Microbiology* 1983;**18**(3):683-8.

**Safdar 2008**

Safdar N, Abad C. Educational interventions for prevention of healthcare-associated infection: a systematic review. *Critical Care Medicine* 2008;**36**(3):933-40.

**Safdar 2014**

Safdar N, Anderson DJ, Braun BI, Carling P, Cohen S, Donskey C, et al. The evolving landscape of healthcare-associated infections: recent advances in prevention and a road map for research. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2014;**35**(5):480-93.

**Sanchez 2010**

Sánchez García M, De la Torre MA, Morales G, Peláez B, Tolón MJ, Domingo S, et al. Clinical outbreak of linezolid-resistant Staphylococcus aureus in an intensive care unit. *JAMA* 2010;**303**(22):2260-4.

**Santos 2008**

Santos RP, Mayo TW, Siegel JD. Healthcare epidemiology: active surveillance cultures and contact precautions for control of multidrug-resistant organisms: ethical considerations. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2008;**47**(1):110-6.

**Schlesinger 2009**

Schlesinger A, Paul M, Gafter-Gvili A, Rubinovitch B, Leibovici L. Infection-control interventions for cancer patients after chemotherapy: a systematic review and meta-analysis. *Lancet Infectious Diseases* 2009;**9**(2):97-107.

**Schulz 2010**

Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine* 2010;**8**:18.

**Schünemann 2011**

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

**Seibert 2014**

Seibert DJ, Speroni KG, Oh KM, DeVoe MC, Jacobsen KH. Knowledge, perceptions, and practices of methicillin-resistant Staphylococcus aureus transmission prevention among health care workers in acute-care settings. *American Journal of Infection Control* 2014;**42**(3):254-9. [PUBMED: 24406259]

**Selkon 1980**

Selkon JB, Stokes ER, Ingham HR. The role of an isolation unit in the control of hospital infection with methicillin resistant staphylococci. *Journal of Hospital Infection* 1980;**1**(1):41-6.

**Shadish 2002**

Shadish WR, Cook TD, Campbell DT. Experimental and quasi-experimental designs for generalized causal inference. Boston (MA): Houghton Mifflin, 2002.

**Sheretz 1996**

Sheretz RJ, Reagan DR, Hampton KD, Robertson KL, Streed SA, Hoen HM, et al. A cloud adult: the Staphylococcus aureus-virus interaction revisited. *Annals of Internal Medicine* 1996;**124**(6):539-47.

**Shiomori 2001**

Shiomori T, Miyamoto H, Makishima K. Significance of airborne transmission of methicillin-resistant Staphylococcus aureus in an otolaryngology-head and neck surgery unit. *Archives of Otolaryngology--Head & Neck Surgery* 2001;**127**(6):644-8.

**Siegel 2006**

Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. Management of multidrug-resistant organisms in healthcare settings, 2006. www.cdc.gov/hicpac/pdf/MDRO/MDROGuideline2006.pdf (accessed 29 May 2014).

**Siegel 2007**

Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf (accessed 29 May 2014).

**Sievert 2013**

Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2013;**34**(1):1-14.

**SIGN 2011**

Scottish Intercollegiate Guidelines Network (SIGN). Search filters. Available from: www.sign.ac.uk/guidelines/fulltext/50/index.html (accessed 31 July 2014).

**Smith 2008**

Smith DH, Kramer JM, Perrin N, Platt R, Roblin DW, Lane K, et al. A randomized trial of direct-to-patient communication to enhance adherence to beta-blocker therapy following myocardial infarction. *Archives of Internal Medicine* 2008;**168**(5):477-83; discussion 483; quiz 447.

**Snyder 2008**

Snyder GM, Thom KA, Furuno JP, Perencevich EN, Roghmann MC, Strauss SM, et al. Detection of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci on the gowns and gloves of healthcare workers. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2008;**29**(7):583-9.

**Srinivasan 2007**

Srinivasan M, Uma A, Vinodhkumaradithyaa A, Gomathi S, Thirumalaikolundusubramanian P. The medical overcoat - is it a transmitting agent for bacterial pathogens?. *Japanese Journal of Infectious Diseases* 2007;**60**(2-3):121-2.

**Sterne 2011**

Sterne JAC, Egger M, Moher D (editors). Chapter 10: Addressing reporting biases. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Intervention. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

**Stewart 2006**

Stewart A, Eyers PS, Earnshaw JJ. Prevention of infection in arterial reconstruction. *Cochrane Database of Systematic Reviews* 2006, Issue 3. [DOI: 10.1002/14651858.CD003073.pub2]

**Stone 2007**

Stone SP, Cooper BS, Kibbler CC, Cookson BD, Roberts JA, Medley GF, et al. The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection. *Lancet Infectious Diseases* 2007;**7**(4):282-8.

**Suffoletto 2008**

Suffoletto BP, Cannon EH, Ilkhanipour K, Yealy DM. Prevalence of Staphylococcus aureus nasal colonization in emergency department personnel. *Annals of Emergency Medicine* 2008;**52**(5):529-33.

**Sunenshine 2005**

Sunenshine RH, Liedtke LA, Fridkin SK, Strausbaugh LJ. Management of inpatients colonized or infected with antimicrobial-resistant bacteria in hospitals in the United States. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2005;**26**(2):138-43.

**Tanner 2006**

Tanner J, Parkinson H. Double gloving to reduce surgical cross-infection. *Cochrane Database of Systematic Reviews* 2006, Issue 3. [DOI: 10.1002/14651858.CD003087.pub2]

**Tenorio 2001**

Tenorio AR, Badri SM, Sahgal NB, Hota B, Matushek M, Hayden MK, et al. Effectiveness of gloves in the prevention of hand carriage of vancomycin-resistant enterococcus species by health care workers after patient care. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2001;**32**(5):826-9.

**Thompson 1982**

Thompson RL, Cabezudo I, Wenzel RP. Epidemiology of nosocomial infections caused by methicillin-resistant Staphylococcus aureus. *Annals of Internal Medicine* 1982;**97**(3):309-17.

**Tiemersma 2004**

Tiemersma EW, Monnet DL, Bruinsma N, Skov R, Monen JC, Grundmann H. Methicillin-resistant Staphylococcus aureus in Europe, 1999-2002. *Emerging Infectious Diseases* 2004;**10**(9):1627-34.

**Troillet 1998**

Troillet N, Carmeli Y, Samore MH, Dakos J, Eichelberger K, DeGirolami PC, et al. Carriage of methicillin-resistant Staphylococcus aureus at hospital admission. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 1998;**19**(3):181-5.

**Turnidge 2000**

Turnidge JD, Bell JM. Methicillin-resistant Staphylococcal aureus evolution in Australia over 35 years. *Microbial Drug Resistance (Larchmont, NY)* 2000;**6**(3):223-9.

**Ukoumunne 1999**

Ukoumunne OC, Gulliford MC, Chinn S, Sterne JAC, Burney PGJ. Methods for evaluating area-wide and organisation based interventions in health and health care: a systematic review. *Health Technology Assessment* 1999;**3**(5):1-108.

**Ward 1981**

Ward TT, Winn RE, Hartstein AI, Sewell DL. Observations relating to an inter-hospital outbreak of methicillin-resistant Staphylococcus aureus: role of antimicrobial therapy in infection control. *Infection Control* 1981;**2**(6):453-9.

**Webster 2003**

Webster J, Pritchard MA. Gowning by attendants and visitors in newborn nurseries for prevention of neonatal morbidity and mortality. *Cochrane Database of Systematic Reviews* 2003, Issue 3. [DOI: 10.1002/14651858.CD003670]

**Welch 2014**

Welch V. Operating Grant: improving the relevance of randomized controlled trials for equity-oriented decisions. http://equity.cochrane.org/sites/equity.cochrane.org/files/uploads/CONSORT-equity%20application_sept15_tosubmit%20%282%29.pdf (accessed 25 July 2014).

**Wenzel 1998**

Wenzel RP, Reagan DR, Bertino JS Jr, Baron EJ, Arias K. Methicillin-resistant Staphylococcus aureus outbreak: a consensus panel's definition and management guidelines. *American Journal of Infection Control* 1998;**26**(2):102-10.

**Wenzel 2010**

Wenzel R P, Edmond M B. Infection control: the case for horizontal rather than vertical interventional programs.

*International Journal of Infectious Diseases* 2010;**14 Suppl 4**:S3-5.

**Wertheim 2005**

Wertheim HF, Melles DC, Vos MC, van Leeuwen W, van Belkum A, Verbrugh HA, et al. The role of nasal carriage in Staphylococcus aureus infections. *Lancet Infectious Diseases* 2005;**5**(12):751-62.

**WHO 2004**

World Health Organization. Practical guidelines for infection control in health care facilities. India: World Health Organization, 2004.

**WHO 2014**

World Health Organization (WHO). Antimicrobial resistance: global report on surveillance, 2014. www.who.int/drugresistance/documents/surveillancereport/en/ (accessed 26 May 2014).

**Williams 1963**

Williams RE. Healthy carriage of Staphylococcus aureus: its prevalence and importance. *Bacteriological Reviews* 1963;**27**(1):56-71.

**Williams 1966**

Williams RE. Epidemiology of airborne staphylococcal infection. *Bacteriological Reviews* 1966;**30**(3):660-74.

**Wilson 2004**

Wilson RD, Huang SJ, McLean AS. The correlation between airborne methicillin-resistant Staphylococcus aureus with the presence of MRSA colonized patients in a general intensive care unit. *Anaesthesia and Intensive Care* 2004;**32**(2):202-9.

**Wilson 2011**

Wilson J, Elgohari S, Livermore DM, Cookson B, Johnson A, Lamagni T, et al. Trends among pathogens reported as causing bacteraemia in England, 2004-2008. *Clinical Microbiology and Infection: the Official Publication of the European Society of Clinical Microbiology and Infectious Diseases* 2011;**17**(3):451-8.

**WIP 2012**

Working party on infection prevention. Meticilline-resistente Staphylococcus aureus (MRSA). www.rivm.nl/dsresource?objectid=rivmp:46603&type=org&disposition=inline&ns_nc=1 (accessed 26 May 2014).

**Yap 2004**

Yap FH, Gomersall CD, Fung KS, Ho PL, Ho OM, Lam PK, et al. Increase in methicillin-resistant Staphylococcus aureus acquisition rate and change in pathogen pattern associated with an outbreak of severe acute respiratory syndrome. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 2004;**39**(4):511-6.

**Zachary 2001**

Zachary KC, Bayne PS, Morrison VJ, Ford DS, Silver LC, Hooper DC. Contamination of gowns, gloves, and stethoscopes with vancomycin-resistant enterococci. *Infection Control and Hospital Epidemiology: the Official Journal of the Society of Hospital Epidemiologists of America* 2001;**22**(9):560-4.

**Zahar 2013**

Zahar JR, Garrouste-Orgeas M, Vesin A, Schwebel C, Bonadona A, Philippart F, et al. Impact of contact isolation for multidrug-resistant organisms on the occurrence of medical errors and adverse events. *Intensive Care Medicine* 2013;**39**(12):2153-60.

**Zastrow 2011**

Zastrow RL. Emerging infections: the contact precautions controversy. *The American Journal of Nursing* 2011;**111**(3):47-53.

**Ziakas 2014**

Ziakas PD, Anagnostou T, Mylonakis E. The prevalence and significance of methicillin-resistant Staphylococcus aureus colonization at admission in the general ICU Setting: a meta-analysis of published studies. *Critical Care Medicine* 2014;**42**(2):433-44.

* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Agbayani 1981 | **Participants:** the study considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. |
| Alvarez-Lerma 2002 | **Study design:** the investigator did not allocate the intervention (not an experimental study). |
| Assadian 2014 | **Participants:** RCT that considered the use of gloves for patients with or without confirmed MRSA colonisation or infection. |
| Batra 2010 | **Comparison (ITS):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |

| Study | Reason for exclusion |
|---|---|
| Bearman 2007 | **Study design:** uncontrolled before-after study |
| Bearman 2010 | **Study design:** uncontrolled before-after study |
| Bertrand 2012 | **Study design:** ITS study in which the assessment of outcomes (in the pre- and post-intervention phases), and the administration of the intervention were done retrospectively |
| Bischoff 2007 | **Study design:** simulation study that investigated the impact of barrier precautions on the spread of airborne *S aureus* by volunteers with experimentally induced common cold |
| Boyce 1998 | **Study design:** uncontrolled before-after study |
| BUGG Study 2013 | **Participants:** cluster-RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. The study assessed whether wearing gloves and gowns for all patient contact in the ICU decreased acquisition of MRSA or VRE compared with usual care. Usual care consisted of healthcare workers using gloves and gowns for patients known to have infection or colonisation with antibiotic-resistant bacteria such as VRE and MRSA |
| Burden 2011 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection |
| Camus 2011 | **Comparison (RCT):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Duquette-Petersen 1999 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. The study examined the protective benefit of using gown and shoe covers to prevent infection when caring for patients undergoing transplantation |
| Ellingson 2011 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Evans 2013 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Eveillard 2001 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Gandra 2014 | **Study design**: the investigator did not allocate the intervention (not an experimental study) |
| Gilmore 1986 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Gilroy 2009 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Grant 2006 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Ho 2012 | **Setting:** cluster-RCT that did not consider hospital inpatients |
| Huang 2011 | **Comparison (ITS):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Jain 2011 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients. The study assessed the effects of a 'MRSA bundle' on healthcare–associated MRSA infections |
| Kappstein 2009 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |

| Study | Reason for exclusion |
|---|---|
| Kaufman 2014 | **Participants:** RCT that considered the use of gloves for patients with or without confirmed MRSA colonisation or infection |
| Kirkland 2007 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Klein 1989 | **Participants:** quasi-RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. The study examined whether the use of gowns and gloves reduced nosocomial infections in children who required prolonged intensive care |
| Koss 2001 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. It compared contact isolation with standard 'universal precautions' when caring for intubated patients |
| Lacey 2001 | **Study design:** uncontrolled before-after study |
| Maki 1996 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Mangini 2007 | **Study design:** uncontrolled before-after study |
| Marshall 2011 | **Comparison (ITS):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Marshall 2013 | **Comparison (ITS):** not possible to separate out the effects of gloves, gowns or masks for contact with patients with MRSA. The study compared rapid PCR detection and use of long sleeved gowns and gloves (contact precautions) plus single room isolation or cohorting of MRSA colonised patients with a control group |
| Matsumoto 2012 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Matsushima 2011 | **Comparison**: not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Moore 2010 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Morioka 2013 | **Study design:** uncontrolled before-after study assessing the effects of pre-emptive contact precautions for all transferred outborn neonates while awaiting the results of active surveillance cultures on admission |
| MOSAR study 2014 | **Comparison (cluster-RCT):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients. The study evaluated the impact of different MRSA screening methods, among other interventions |
| Moylan 1987 | **Participants:** the study considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. The study examined whether the wearing of a disposable gown and drape system by the surgical team reduce surgical wound infection |
| Muroya 2009 | **Participants:** considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection |
| Raad 1994 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. It evaluated the effects of barrier precautions during catheter insertion in hospital outpatients |
| Reitzel 2009 | **Study design:** in vitro laboratory-based study that assessed the efficacy of gloves impregnated with antiseptic in preventing contamination on their outer surface |

| Study | Reason for exclusion |
|---|---|
| Ribner 1986 | **Comparison:** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Rijnders 2003 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. It evaluated the effects of barrier precautions during catheter insertion |
| Rodríguez-Baño 2010 | **Comparison (ITS):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Shenoy 2013 | **Comparison (RCT):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients. The study compared two methods of MRSA screening for discontinuation of MRSA contact precautions |
| Slaughter 1996 | **Participants:** non-randomised clinical trial that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection |
| Slota 2001 | **Participants:** RCT that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. It evaluated whether strict handwashing, compared with protective gown and glove isolation, prevents nosocomial infections in children with transplants |
| Spence 2012 | **Study design:** uncontrolled before-after study |
| STAR ICU Trial 2011 | **Comparison (cluster-RCT):** not possible to separate out the effects of gloves, gowns or masks for contact with MRSA patients |
| Trick 2004 | **Setting:** interventions applied in a long-term care facility (not in a hospital setting) |
| Trick 2007 | **Study design:** the investigator did not allocate the intervention (not an experimental study) |
| Williams 2015 | **Participants:** study that considered the use of gloves and gowns for patients with or without confirmed MRSA colonisation or infection |
| Yin 2013 | **Participants:** retrospective cohort study that considered the use of gloves, gowns or masks for patients with or without confirmed MRSA colonisation or infection. It assessed the effects of wearing gloves for all patient contacts in paediatric units during the respiratory Syncytial virus season |

**Abbreviations**
ICU: intensive care unit
ITS: interrupted time series
MRSA: meticillin-resistant *Staphylococcus aureus*
PCR: polymerase chain reaction
RCT: randomised controlled trial
VRE: vancomycin-resistant *Enterococcus*

## ADDITIONAL TABLES

**Table 1. Study designs labels and features**

| Features | Study design labels | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | RCT[1] | Cl-RCT[1] | Q-RCT | ClQ-RCT | NRCT | Cl-NRCT | CBA | CChBA | ITS | CITS | RMS[2] |
| **Allocation unit** | Individual | Group | Individual | Group | Individual | Group | Individual | Group | Group | | NA |
| **Minimum number of allocated units** | NA | At least 2 sites per arm[3] | NA | At least 2 sites per arm[3] | NA | At least 2 sites per arm[3] | NA | At least 2 sites per arm[3] | NA | | NA |
| **Method to assign allocation units to study arms** | Random | Random | Quasi-random | Quasi-random | Non-random | Non-random | Non-random | | Non random:<br>time differences | | Non random:<br>time differences |
| **Assessment of baseline and allocation to intervention** | Prospective | | | | | | Prospective[4] | | | | |
| **Assessment of outcomes** | Prospective | | | | | | Prospective[4]<br>(for both pre- and post-intervention phases) | | | | |
| **Data collection** | NA | | | | | | Contemporaneous in study and control sites during the pre- and post-intervention periods of the study, using identical methods of measurement (EPOC 2009)[5] | | RMS is an ITS study where measurements are made in the same individuals at each time point (EPOC 2013a) | | |
| **Choice of control group** | NA | | | | | | Study and control sites should be comparable with respect to setting of care (EPOC 2009) | | NA | | |
| **Data points** | NA | | | | | | | | At least 3 data points before and 3 after the intervention (EPOC 2013a) | | |

**Table 1. Study designs labels and features** *(Continued)*

| | | |
|---|---|---|
| **Analysis** | NA | Must not ignore secular (trend) changes. For example, a simple t-test of the pre versus post intervention periods must be avoided (EPOC 2013a)[6] |
| **Other** | NA | Clearly defined point in time when the intervention occurred (reported by the researchers) (EPOC 2013a) |

**Abbreviations**

CBA: controlled before-and-after study
CChBA: controlled cohort before-after study

ClQ-RCT: cluster-QRCT

Cl-NRCT: cluster-NRCT

Cl-RCT: cluster-RCT

CITS: controlled ITS
ITS: interrupted time series study

NA: not assessed

NRCT: non-randomised controlled trial

Q-RCT: quasi-RCT

RCT: randomised controlled trial

RMS: repeated measures study

[1]The stepped wedge design applied in RCT and Cl-RCT was also eligible. In this design an intervention is rolled-out sequentially to all the trial participants (either as individuals or clusters of individuals) over a number of time periods. The order in which the different individuals or clusters receive the intervention is determined at random and, by the end of the allocation, all individuals or groups will have received the intervention. Stepped wedge designs incorporate data collection at each point where a new group (step) receives the intervention (Brown 2006a). This is a design increasingly used to assess the effectiveness of patient safety interventions (Brown 2008), as it is particularly relevant where it is predicted that the intervention will do more good than harm and/or where, for logistical, practical or financial reasons, it is impossible to deliver the intervention simultaneously to all participants (Brown 2006a; see Differences between protocol and review).

[2]RMS is an ITS study where measurements are made in the same individuals at each time point. This study design label is not detailed in the *Cochrane Handbook of Systematic Reviews of Interventions* (Reeves 2011), but it is suggested as eligible by the guidance of the EPOC group (EPOC 2013a).

[3]In cluster studies with only one intervention or control site the intervention (or comparison) is completely confounded by study site, which makes it difficult to attribute any observed differences to the intervention rather than to other site-specific variable (EPOC 2013a).

[4]Not specified in the protocol of the review (see Differences between protocol and review). In order a study to be defined as 'experimental', the assessment of baseline, the allocation to intervention, and the assessment of outcomes should be done prospective.

[5]In infection control studies seasonality may be an issue, i.e. if January to June comprises the intervention group and July to December the control group, the 'seasons' could cause a spurious effect (Stone 2007).

[6] For ITS and RMS we will assess if the statistical approach has ignored secular (trend) changes. Analysis of aggregated data of the pre- and post-intervention phases should be avoided because it does not provide information about trends over time (Stone 2007). We excluded ITS studies or RMS without a parallel control group that had ignored secular changes by performing, for example, a simple t test of the pre- versus post-intervention periods (we considered these studies as uncontrolled before and after studies).

**Table 2. Databases searched**

| Database | Interface | Coverage | Date searched | Hits |
|---|---|---|---|---|
| Cochrane Wounds Register | | | 5 June 2015 | 94 |
| Cochrane EPOC Register | | As the EPOC register has not been updated since July 2013, we did not search this source since then. | 9 July 2013 | 54 |
| Cochrane Infectious Diseases Register | | | 5 January 2009 | 8 |
| CENTRAL | *The Cochrane Library* | Issue 6 2015 | 5 June 2015 | 72 |
| DARE; HTA; NHS EED; Methodology Register | | Issue 6 2015 | | |
| MEDLINE | Ovid | 1946 to June Week 1 2015 | 5 June 2015 | 1430 |
| MEDLINE (In-Process & Other Non-Indexed Citations) | Ovid | 1946 to June Week 1 2015 | 5 June 2015 | 105 |
| EMBASE | Ovid | 1974 to 4 June 2015 | 5 June 2015 | 1470 |
| Web of Science (WOS) Core Collection | WOS | SCI-EXPANDED- 1900-7 June 2015; SSCI- 1956-7 June 2015; CPCI-S- 1990-7 June 2015 | 7 June 2015 | 2951 |
| CINAHL | EBSCO | 1982 to 5 June 2015 | 5 June 2014 | 684 |
| BNI | Ovid | 1985 to 6 July 2010 | 6 July 2010[1] | 60 |
| Dissertations & Theses A&I | ProQuest | 1639 to 11 June 2015 | 11 June 2015 | 263 |
| **Total results** | | | | **7191** |
| **Total results without duplicates** | | | | **4456** |
| **Trials registers** | ClinicalTrials.gov | | 6 June 2015 | **308** |
| | WHO International Clinical Trials Registry Platform | | 6 June 2015 | **624** |
| | International Standard Randomised Controlled Trial Number Register | | 31 July 2014[2] | **129** |

[1] Searched 6/07/2010 as we did not have access to this database since then.
[2] Searched 31/07/2014 as this service was under review in 2015 (http://www.isrctn.com/page/mrct)

**Abbreviations**
BNI: British Nursing Index
CENTRAL: The Cochrane Central Register of Controlled Trials
DARE: The Database of Abstracts of Reviews of Effects
EPOC: the Effective Practice and Organisation of Care (Group)
HTA: The Health Technology Assessment Database

NHS EED: The NHS Economic Evaluation Database
WHO: World Health Organization

**Table 3. Research recommendation according to the 'Evidence-Population(s)-Intervention-Comparison-Outcomes-Time stamp' (EPICOT)**

| **Does the use of gloves, a gown, and/or a mask for contact with hospitalised patients colonised or infected with MRSA or with their immediate environment reduce the transmission of MRSA in hospitals?** | | |
|---|---|---|
| | | **Comments** |
| **Evidence** | This systematic review found no eligible studies for inclusion | |
| **Population(s)** | Hospitalised patients.<br>The study may focus in one of the following populations.<br>• Patients in ICUs<br>• Patients in neonatal ICUs<br>• General medical inpatients | • Select the patient population according to the available infrastructure and hospital-specific characteristics (size, staffing for laboratory and nursing, patient population, MRSA prevalence, and information technology support; Calfee 2014) |
| **Intervention** | Any infection control process considering the use of gloves, gowns and/or masks for contact with hospitalised patients colonised or infected with MRSA or with their immediate environment. Therefore, gloves, masks and gowns can be used in one of the following ways.<br>• On their own as a single intervention, for example, the use of gloves alone<br>• In a combination of gloves, gowns and masks, such as the use of gowns and gloves<br>• Combined with any other barrier precaution, such as the placement of MRSA patients in isolation units to be attended by staff using gowns, gloves and masks<br>• Combined with any other infection control intervention, such as the decolonisation of patients with MRSA | • The study should be planned with few interventions to allow the relative contribution of the use of gloves, gowns or masks on outcome measures to be evaluated (Zastrow 2011)<br>• The researchers should provide details of all the interventions and co-interventions undertaken, their compliance and their acceptability (Stone 2007; MRC 2008)<br>• It is strongly recommended that phases are defined by a major change in specific infection control practices (with start and stop dates) and that a summary table with precise details of interventions, how and when were administered in each phase, is presented (Stone 2007)<br>• The report of the study should avoid the use of terms that may not be universally understood, such as 'contact precautions' or 'barrier nursing' without a precise description of the interventions undertaken (Stone 2007)<br>• In order to disentangle the effects of the use of gloves, gowns or masks on outcome measure, all the co-interventions must be similar in all the study groups |
| **Comparison** | Any comparator, provided that it allows the effect of gloving, gowning or masking on MRSA transmission to be evaluated separately | |
| **Outcomes** (Adapted from Noorani 2013) | • **Intermediate outcomes**<br>* MRSA acquisition rate<br>* Mother-to-child transmission rate (for neonates only)<br>• **Health outcomes**<br>* MRSA infection rate<br>* Morbidity (e.g. complications of MRSA infection)<br>* MRSA-attributable mortality<br>* Total mortality | • Outcomes should be measured, collected and reported in an objective, reliable, accurate, and actionable way. This particularly applies to MRSA colonisation/infection outcomes, for which subjective elements in definitions and variations in the timing for the definition of 'hospital-associated' should be avoided (Safdar 2014). Recognised standard definitions and criteria for all specific types of infections should be followed, such as those developed by the Centers for Disease Control and Prevention/National Healthcare Safety Network (Cohen 2008; Calfee 2014; CDC 2014) |

**Table 3. Research recommendation according to the 'Evidence-Population(s)-Intervention-Comparison-Outcomes-Time stamp' (EPICOT)** *(Continued)*

| | | |
|---|---|---|
| | • **Harms, for example**<br>  * Symptoms of depression<br>  * Symptoms of anxiety<br>  * Rate of falls<br>  * Rate of pressure ulcers<br>• **Impact on clinical workflow, for example**<br>  * Frequency of healthcare worker visits<br>  * Staff compliance with infection control procedures, such as hand hygiene<br>• **Satisfaction with care**<br>• **Resource use, such as the following**<br>  * Length of stay<br>  * Antimicrobial use<br>• **Cost analysis** | • If MRSA colonisations are evaluated, there should be an existing screening policy at admission that is applied consistently throughout the study (Cooper 2003)<br>• Blinding of patients, care givers and outcome assessment should be ensured wherever possible to minimise performance, attrition, and detection biases<br>• Blinding in studies of the effects of non-pharmacological interventions, such as gloves, gowns, or masks, is challenging. However, some suggestions about how to overcome this situation are described elsewhere (Brown 2008; Boutron 2008; Lin 2012). For example, assessment of study outcomes should be done through structured observation by external evaluators<br>• Another approach to limit detection bias is to use objective outcomes that are less susceptible to bias, such as total mortality, length of stay, or antimicrobial use (Lin 2012)<br>• As far as possible the data collection should be based on the administrative capacities of the healthcare system to enhance practicality (Safdar 2014)<br>• Relevant harms related to the use of gloves, gowns and masks should be specified beforehand and assessed (Ioannidis 2004); for example, the impact on the clinical workflow should be evaluated, as it may hinder the regular and timely provision of appropriate patient care (Evans 2003) |
| **Time stamp** | Date of literature search: July 2014 | |
| **Study type** | Cluster-randomised controlled trial | Trial that randomises groups (clusters) rather than individuals (see characteristics below) |

## APPENDICES

### Appendix 1. Glossary

| Term | Definition |
|---|---|
| **Aerosolised secretions** | Microscopic particles (less than 5 µm in size) that are the residue of evaporated droplets and are produced when a person coughs, sneezes, shouts, or sings. These particles can remain suspended in the air for prolonged periods of time and can be carried on normal air currents (Siegel 2007) |
| **Ambulatory care facility** | Facility that administers health services to individuals who do not require hospitalisation or institutionalisation (MeSH Browser 2014) |
| **Care bundle** | "A collection of processes needed to effectively and safely care for patients undergoing particular treatments with inherent risks. Several interventions are bundled together and, when combined, significantly improve patient care outcomes" (IHI 2006) |
| **Colonisation** | The presence of micro-organisms (on skin, mucous membranes, in open wounds, or in excretions or secretions) that are not causing adverse clinical signs or symptoms (Garner 1996) |
| **Controlled interrupted time series (CITS) study** | Intrerrupted time series study with a parallel control group |

(Continued)

| | |
|---|---|
| **Cluster non-randomised controlled trial (Cl-NRCT)** | Type of non-randomised study in which the investigator prospectively allocates groups of participants to an intervention or to a control arm (or more) using a process that is clearly not random |
| **Cluster-quasi-randomised controlled trial (ClQ-RCT)** | Type of non-randomised study in which the investigator prospectively allocates groups of participants to an intervention or to a control arm (or more) using a process that attempts, but does not achieve, true randomisation |
| **Cluster-RCT (Cl-RCT)** | RCT in which the investigator prospectively allocates groups of participants (or clusters) to an intervention or to a control arm (or more than one control arm) using a process of random allocation (for example, random number generation or coin flips) |
| **Confidence interval (CI)** | A measure of the uncertainty around the main finding of a statistical analysis. Estimates of unknown quantities, such as the odds ratio comparing an experimental intervention with a control, are usually presented as a point estimate and a 95% confidence interval. This means that if someone were to keep repeating a study in other samples from the same population, 95% of the CIs from those studies would contain the true value of the unknown quantity. Alternatives to 95%, such as 90% and 99% CI, are sometimes used. Wider intervals indicate lower precision; narrow intervals, greater precision (Higgins 2005) |
| **Controlled before-and-after study (CBA)** | Type of non-randomised study in which the participants are allocated at the individual level to the study arms; those in the intervention arm receive an intervention and those in the control arm do not. The effect of the intervention is tested by comparison of the outcomes of participants within the same study arm before and after the intervention is introduced, and then, by comparing outcomes for participants in the control and intervention arms |
| **Controlled cohort before-after study (CChBA)** | Type of non-randomised study in which allocation to the study arms is at the cluster level. The clusters allocated to the intervention arm receive the intervention and those allocated to the control arm do not. The effect of the intervention is tested by assessment of outcomes within the same arm over time both before and after the intervention is introduced, and then, by comparing the control and intervention arms. Note that 'cluster' refers to an entity (e.g. an organisation), not necessarily to a group of participants, and 'arm' refers to one or more clusters (Reeves 2011). Here, the term 'cohort' designates the new sample of individuals that is drawn from each of the clusters at each measurement occasion (Shadish 2002) |
| **Droplets** | Solid or liquid particles suspended in the air, whose motion is governed principally by gravity and whose particle size is greater than 10 µm. Droplets are generated primarily as the result of an infected source coughing, sneezing or talking (Public Health Agency of Canada 2012b) |
| **Estimate of the effect** | The observed relationship between an intervention and an outcome expressed as, for example, a number needed to treat to benefit, odds ratio, risk difference, risk ratio, standardised mean difference, or weighted mean difference. Also called 'treatment effect' (Higgins 2005) |
| **Experimental study** | Study in which an intervention is deliberately introduced by the researcher to observe its effects (Shadish 2002) |
| **Gown** | A impervious material worn to protect the wearer's clothing from possible contamination with micro-organisms and exposure to blood, body fluids/secretions and excretions. The gown should be used only once, for one patient, and discarded or sent for laundering (WHO 2004) |
| **Healthcare-associated colonisation (formerly nosocomial colonisation)** | Colonisation that was not present at the time of admission to the hospital |
| **Healthcare-associated infection (HAI; formerly nosocomial infection)** | Infection that was not present or incubating at the time of admission to the healthcare facility. For most bacterial infections, this means that the infection usually becomes evident 48 hours or more after admission (the typical incubation period). However, because the incubation period varies with the type of pathogen, and to some extent with the patient's underlying condition, each infection must be assessed individually (Garner 1996) |

(Continued)

| | |
|---|---|
| **Healthcare-associated MRSA bacteraemia** | Any MRSA bacteraemia identified more than 48 hours after admission to the setting (for example, ward) where the study is done |
| **Healthcare-associated MRSA colonisations** | MRSA colonisation of any site cultured, identified more than 48 hours after admission to the setting (for example, ward) where the study is done |
| **Healthcare-associated MRSA infections** | Any MRSA infection identified more than 48 hours after admission to the setting (for example, ward) where the study is done |
| **Healthcare-associated MRSA pneumonia** | Any MRSA pneumonia identified more than 48 hours after admission to the setting (for example, ward) where the study is done |
| **Hospital** | Institution with an organised medical staff which provides medical care to patients (MeSH Browser 2014) |
| **Hospital outpatient clinic** | Organised services in a hospital which provide medical care on an outpatient basis (MeSH Browser 2014) |
| **Incidence** | The number of new occurrences of events (for example, infections or colonisations) in a population over a particular period of time. Incidence of MRSA infection or colonisation usually is presented as number of MRSA infections or colonisations per 100 patients |
| **Infection** | Localised or systemic condition that results from an adverse reaction to the presence of an infectious agent(s) or it(s) toxin(s) (Garner 1996). |
| **Interrupted time series (ITS) study** | A study that uses observations at multiple time points before and after an intervention (the 'interruption'). The design attempts to detect whether the intervention has had a significantly greater effect than any underlying trend over time ( EPOC 2013a ) |
| **Intra-cluster correlation coefficient** | The intra-cluster correlation coefficient is the proportion of the total variance of the outcome that can be explained by the variation between clusters (Campbell 2012) |
| **Isolation gown** | Gown, not sold as sterile product, usually intended to protect the wearer clothing/uniform from the transfer of micro-organisms and only small amounts of body fluids |
| **Length of stay** | Number of days spent by a patient in a ward or hospital |
| **Mask** | A term that applies collectively to items used to cover the nose and mouth |
| **Medical gloves** | Disposable medical devices made of natural rubber latex or synthetic material that are intended to be worn on the hands to provide a barrier against potentially infectious materials and other contaminants. Medical gloves in general are used for tasks that do involve contact with patients or body fluids. They must be disposable and intended for simple patient use and then discarded. Medical gloves include patient examination gloves, surgical gloves (FDA 2008), or medical gloves for handling chemotherapy agents |
| **Non-randomised controlled trial (NRCT)** | Type of non-randomised study in which the investigator prospectively allocates each participant to an intervention or to a control group (or more) using a process that is clearly not random (for example, allocation by judgement of the clinician, or by preference of the participant) |
| **Observational study** | A study in which the investigators do not seek to intervene, and simply observe the course of events. Changes or differences in one characteristic (e.g. whether or not people received the intervention of interest) are studied in relation to changes or differences in other characteristic (e.g. whether or not they died), without action by the investigator. There is a greater risk of selection bias than in experimental studies (Higgins 2005) |
| **Outpatient** | Person who receives ambulatory care at an outpatient department or clinic without room and board being provided (MeSH Browser 2014) |

(Continued)

| | |
|---|---|
| **P value** | The probability (ranging from zero to one) that the results observed in a study (or more extreme results) could have occurred by chance, if in reality the null hypothesis was true. In a meta-analysis, the P value for the overall effect assesses the overall statistical significance of the difference between the intervention groups, whilst the P value for the heterogeneity statistic assesses the statistical significance of differences between the effects observed in each study (Higgins 2005) |
| **Particulate respirators** | A personal protective device worn by healthcare personnel to protect them from inhalation exposure to airborne infectious agents that are 5 µm in size or smaller. These include infectious droplet nuclei from patients (for example, *Mycobacterium tuberculosis*), and dust particles that contain infectious particles, such as spores of environmental fungi (for example, *Aspergillus* species). The N95 disposable particulate respirator is the type used most commonly by healthcare personnel (Siegel 2007) |
| **Patient examination gloves** | A disposable device intended for medical purposes that is worn on the examiner's hand or finger to prevent contamination between patient and examiner. They can be powdered internally (to make it easier to put them on) or be powder-free. They are not usually sold as sterile products (FDA 2014a) |
| **Procedure mask** | Type of mask intended for use in general patient care situation |
| **Quasi-randomised controlled trial (Q-RCT)** | Type of non-randomised study in which the investigator prospectively allocates each participant to an intervention or to a control arm using a process that attempts, but does not achieve, true randomisation (for example, alternation of allocation, birth dates or week days) |
| **Randomised controlled trial (RCT)** | Study in which the investigator prospectively allocates each participant to an intervention or to a control arm using a process of random allocation (for example, random number generation or coin flips) |
| **Rate** | The number of new occurrences of events (for example, infections or colonisations) occurring per unit of time. Rate of MRSA infection or colonisation usually is presented as number of MRSA infections or colonisations per 1000 patients-days of hospital stay |
| **Rehabilitation centre** | Facility that provides programs for rehabilitating the mentally or physically disabled individuals (MeSH Browser 2014) |
| **Repeated measures study (RMS)** | An interrupted time series study where measurements are made in the same individuals at each time point ( EPOC 2013a) |
| **Residential facility** | Long-term care facility which provides supervision and assistance in activities of daily living with medical and nursing services when required: assisted living facilities, group homes, halfway houses, homes for the aged, nursing homes or orphanages (MeSH Browser 2014) |
| **Routine practices** | Measures that have been developed for use in the routine care of all patients at all times in all healthcare settings. Routine practices aim to minimise or prevent HAIs in all individuals in the health care setting including patients, healthcare workers, other staff, visitors, contractors, etc. (Public Health Agency of Canada 2012b) |
| **Surgeon's gloves** | A device made of natural or synthetic rubber intended to be worn by operating room personnel to protect a surgical wound from contamination (FDA 2014b) |
| **Surgical gown** | Gown, usually packaged as sterile product or designed to be sterilised, made of fluid-resistant materials to reduce the transfer of body fluids. Some of them are disposable and others are made of fabric that is labelled as washable for multiple use |
| **Surgical mask** | Type of mask worn by operating room personnel during surgical procedures to protect both surgical patients and operating room personnel from transfer of micro-organisms and body fluids |

*(Continued)*

| | |
|---|---|
| **Unit of analysis error** | An error made in statistical analysis when the analysis does not take account of the unit of allocation. In some studies, the unit of allocation is not a person, but is instead a group of people, or parts of a person, such as eyes. Sometimes the data from these studies are analysed as if people had been allocated individually. Using individuals as the unit of analysis when groups of people are allocated can result in overly narrow confidence intervals. In meta-analysis, it can result in studies receiving more weight than is appropriate (Higgins 2005) |

**Abbreviation**

CI: confidence interval

MRSA: meticillin-resistant *Staphylococcus aureus*

## Appendix 2. Additional search strategies

**DARE, HTA, NHS EED, and the Methodology Register (*The Cochrane Library* 2015, Issue 6), searched 5 June 2015**

We used the search string specified as having been used to search CENTRAL, in the Electronic searches section, for the DARE, HTA, NHS EED, and Methodology Register databases.

**The Cochrane Wounds Group Specialised Register, searched 5 June 2015**

((((("Staphylococcus aureus" or "Staphylococcal Infections" or "aureus") near5 resistan*) or MRSA or "methicillin resistance" or "meticillin resistance" or "penicillin resistance" or "methicillin resistant" or "meticillin resistant" or "penicillin resistant" or "methicillin-resistant" or "meticillin-resistant" or "penicillin-resistant") and (glove* or gown* or mask* or barrier* or handwashing or "hand washing" or precaution* or isolation or "infection control" or "control measure" or "control measures" or "ward closure" or "cohort nursing" or "care bundling")) AND (INREGISTER)

**The Cochrane EPOC Group Specialised Register, searched 9 July 2013**

((("Staphylococcus aureus" or "Staphylococcal Infections" or "s aureus") and resistan*) or MRSA or "Methicillin Resistance" or "Penicillin Resistance") and (barrier* or glove* or gown* or mask* or handwashing or "hand washing" or precaution* or isolation or "ward closure" or "cohort nursing" or "care bundling")

**The Cochrane Infectious Diseases Group Specialised Register, searched 5 January 2009**

((("Staphylococcus aureus" or "Staphylococcal Infections" or "s aureus") and resistan*) or MRSA or "Methicillin Resistance" or "Penicillin Resistance") and (barrier* or glove* or gown* or mask* or handwashing or "hand washing" or precaution* or isolation or “infection control” or "ward closure" or "cohort nursing" or "care bundling")

**Ovid MEDLINE (1946 to June Week 1 2015), searched 5 June 2015**

#1 exp Staphylococcus aureus/

#2 staphylococcus aureus.tw.

#3 exp Staphylococcal Infections/

#4 (staphylococ* adj2 infect*).tw.

#5 (staphylococc* adj2 (bacteremia or bacteraemia)).tw.

#6 or/1-5

#7 exp Penicillin Resistance/

#8 (penicillin adj2 resist*).tw.

#9 ((methicillin or meticillin) adj2 resist*).tw.

#10 (oxacillin* adj2 resistan*).tw.

#11 multi-drug resistan*.tw.

#12 (antibiotic* adj2 resistan*).tw.

#13 or/7-12

#14 6 and 13

#15 exp Methicillin-Resistant Staphylococcus aureus/

#16 (mrsa or emrsa or mdro).tw.

#17 or/14-16

#18 exp Protective Clothing/

#19 exp Masks/

#20 (glove* or gown* or apron* or mask*).tw.

#21 ((barrier* or contact or universal or droplet or isolation or airborne) adj precaution*).tw.

#22 ((contact or patient or ward* or unit*) adj2 isolation).tw.

#23 (isolated ward* or (ward adj2 clos*) or (clos* adj2 ward*)).tw.

#24 cohort nursing.tw.

#25 cohort patient*.tw.

#26 exp Hand Disinfection/

#27 (handwashing or hand washing or hand hygiene).tw.

#28 control measure*.tw.

#29 or/18-28

#30 17 and 29

**Ovid MEDLINE (In-Process & Other Non-Indexed Citations), searched 5 June 2015**

Same strategy as Ovid MEDLINE.

**Ovid EMBASE (1974 to 4 June 2015), searched 5 June 2015**

#1 exp Staphylococcus aureus/

#2 staphylococcus aureus.tw.

#3 exp Staphylococcus infection/

#4 (staphylococ* adj2 infect*).tw.

#5 (staphylococc* adj2 (bacteremia or bacteraemia)).tw.

#6 or/1-5

#7 exp penicillin resistance/

#8 (penicillin adj2 resist*).tw.

#9 ((methicillin or meticillin) adj2 resist*).tw.

#10 (oxacillin* adj2 resistan*).tw.

#11 multi-drug resistan*.tw.

#12 (antibiotic* adj2 resistan*).tw.

#13 or/7-12

#14 6 and 13

#15 exp methicillin resistant Staphylococcus aureus/

#16 (mrsa or emrsa or mdro).tw.

#17 or/14-16

#18 exp protective clothing/

#19 exp mask/

#20 (glove* or gown* or apron* or mask*).tw.

#21 ((barrier* or contact or universal or droplet or isolation or airborne) adj precaution*).tw.

#22 ((contact or patient or ward* or unit*) adj2 isolation).tw.

#23 (isolated ward* or (ward adj2 clos*) or (clos* adj2 ward*)).tw.

#24 cohort nursing.tw.

#25 cohort patient*.tw.

#26 exp hand washing/

#27 (handwashing or hand washing or hand hygiene).tw.

#28 control measure*.tw.

#29 or/18-28

#30 17 and 29

#31 Randomized controlled trials/

#32 Single-Blind Method/

#33 Double-Blind Method/

#34 Crossover Procedure/

#35 (random$ or factorial$ or crossover$ or cross over$ or cross-over$ or placebo$ or assign$ or allocat$ or volunteer$).ti,ab.

#36 (doubl$ adj blind$).ti,ab.

#37 (singl$ adj blind$).ti,ab.

#38 or/31-37

#39 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/

#40 human/ or human cell/

#41 and/39-40

#42 39 not 41

#43 38 not 42

#44 30 and 43

#45 Randomized controlled trial/

#46 random$.tw.

#47 experiment$.tw.

#48 (time adj series).tw.

#49 (pre test or pretest or post test or posttest).tw.

#50 impact.tw.

#51 intervention?.tw.

#52 chang$.tw.

#53 evaluat$.tw.

#54 effect?.tw.

#55 compar$.tw.

#56 (controlled adj study).tw.

#57 or/45-56

#58 30 and 57

#59 44 or 58

**Web of Science Core Collection (Science Citation Index Expanded (SCI-EXPANDED) 1900 to 7 June 2015; Social Sciences Citation Index (SSCI) 1956 to 7 June 2015; Conference Proceedings Citation Index - Science (CPCI-S) 1990 to 7 June 2015); searched 7 June 2015**

#1
TOPIC: (Methicillin-resistant Staphylococcus aureus) OR TOPIC: (mrsa) OR TOPIC: (emrsa) OR TOPIC: (mdro) OR TOPIC: ((staphylococcus aureus AND resistant))
Indexes=SCI-EXPANDED, SSCI, CPCI-S Timespan=All years

#2
TOPIC: (glove*) OR TOPIC: (gown*) OR TOPIC: (apron*) OR TOPIC: (mask*) OR TOPIC: (barrier*)
Indexes=SCI-EXPANDED, SSCI, CPCI-S Timespan=All years

#3
TS=(contact precaution*) OR TS=(universal precaution*) OR TS=(droplet precaution*) OR TS=(airborne precaution*) OR TS=(isolation precaution*) OR TS=(contact isolation) OR TS=(patient isolation) OR TS=(ward isolation OR ward isolated OR ward closure) OR TS=(unit isolation) OR TS=(cohort nursing) OR TS=(control measure)
Indexes=SCI-EXPANDED, SSCI, CPCI-S Timespan=All years

#4
#3 OR #2
Indexes=SCI-EXPANDED, SSCI, CPCI-S Timespan=All years

#5
#4 AND #1
Indexes=SCI-EXPANDED, SSCI, CPCI-S Timespan=All years

**EBSCO CINAHL (1982 to 5 June 2015), searched 5 June 2015**

S71 S56 OR S70

S70 S43 AND S69

S69 S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68

S68 (MH "Quasi-Experimental Studies+")

S67 (MH "Pretest-Posttest Design+")

S66 TI effect* or AB effect*

S65 TI evaluat* or AB evaluat*

S64 TI intervention* or AB intervention*

S63 TI impact or AB impact

S62 TI time series or AB time series

S61 TI experiment* or AB experiment*

S60 (MH "Comparative Studies")

S59 TI random* or AB random*

S58 TI control* or AB control*

S57 (MH "Clinical Trials+")

S56 S43 AND S55

S55 S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54

S54 MH "Quantitative Studies"

S53 TI placebo* or AB placebo*

S52 MH "Placebos"

S51 TI random* allocat* or AB random* allocat*

S50 MH "Random Assignment"

S49 TI randomi?ed control* trial* or AB randomi?ed control* trial*

S48 AB ( singl* or doubl* or trebl* or tripl* ) and AB ( blind* or mask* )

S47 TI ( singl* or doubl* or trebl* or tripl* ) and TI ( blind* or mask* )

S46 TI clinic* N1 trial* or AB clinic* N1 trial*

S45 PT Clinical trial

S44 MH "Clinical Trials+"

S43 S42 and S18

S42 S41 or S40 or S39 or S38 or S37 or S36 or S35 or S34 or S33 or S32 or S31 or S30 or S29 or S28 or S27 or S26 or S25 or S24 or S23 or S22 or S21 or S20 or S19

S41 TI control measure* or AB control measure*

S40 TI ( handwashing or hand washing ) or AB ( handwashing or hand washing )

S39 TI cohort patient* or AB cohort patient*

S38 TI cohort nursing or AB cohort nursing

S37 TI ward closure or AB ward closure

S36 TI isolation unit* or AB isolation unit*

S35 TI ward* isolat* or AB ward* isolat*

S34 TI patient isolat* or AB patient isolat*

S33 (MH "Patient Isolation")

S32 TI contact isolation or AB contact isolation

S31 TI isolation precaution* or AB isolation precaution*

S30 TI airborne precaution* or AB airborne precaution*

S29 TI droplet precaution* or AB droplet precaution*

S28 TI universal precaution* or AB universal precaution*

S27 TI contact precaution* or AB contact precaution*

S26 TI barrier* or AB barrier*

S25 TI mask* or AB mask*

S24 (MH "Masks")

S23 TI apron* and AB apron*

S22 TI gown* and AB gown*

S21 TI glove* or AB glove*

S20 (MH "Gloves")

S19 (MH "Protective Clothing")

S18 S17 or S16

S17 TX mrsa or emrsa or mdro

S16 S15 and S7

S15 S14 or S13 or S12 or S11 or S10 or S9 or S8

S14 TI antibiotic resistan* or AB antibiotic resistan*

S13 TI multi drug resistan* or AB multi drug resistan*

S12 TI oxacillin* resistan* or AB oxacillin* resistan*

S11 TI penicillin* resistan* or AB penicillin* resistan*

S10 TI meticillin resistan* or AB meticillin resistan*

S9 TI methicillin resistan* or AB methicillin resistan*

S8 (MH "Methicillin Resistance")

S7 S6 or S5 or S4 or S3 or S2 or S1

S6 TI staphylococcal bacteraemia or AB staphylococcal bacteraemia

S5 TI staphylococcal bacteremia or AB staphylococcal bacteremia

S4 TI staphylococcal infect* or AB staphylococcal infect*

S3 (MH "Staphylococcal Infections+")

S2 TI staphylococcus aureus or AB staphylococcus aureus

S1 (MH "Staphylococcus Aureus")

**Ovid British Nursing Index (1985 to 6 July 2010), searched 6 July 2010**

1 staphylococcus aureus.ti,ab.

2 (staphylococc* and Infectio*).ti,ab.

3 (staphylococc* and (bacteremia or bacteraemia)).ti,ab.

4 1 or 2 or 3

5 (methicillin* and resistan*).ti,ab.

6 (penicillin* and resistan*).ti,ab.

7 (oxacillin* and resistan*).ti,ab.

8 multi drug resistan*.mp.

9 antibiotic resistan*.mp.

10 5 or 6 or 7 or 8 or 9

11 4 and 10

12 mrsa.mp.

13 emrsa.mp.

14 mdro.mp.

15 11 or 12 or 13 or 14

16 glove*.ti,ab.

17 gown*.ti,ab.

18 apron*.ti,ab.

19 mask*.ti,ab.

20 barrier*.ti,ab.

21 contact precaution*.ti,ab.

22 universal precaution*.ti,ab.

23 droplet precaution*.ti,ab.

24 airborne precaution*.ti,ab.

25 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

26 isolation precaution*.ti,ab.

27 contact isolation.ti,ab.

28 patient* isolation.ti,ab.

29 (ward* and isolation).ti,ab.

30 patient* isolated.ti,ab.

31 (ward* and isolated).ti,ab.

32 ward* closure.ti,ab.

33 unit isolation.ti,ab.

34 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33

35 cohort nursing.ti,ab.

36 cohort patient*.ti,ab.

37 handwashing.ti,ab.

38 hand washing.ti,ab.

39 hand hygiene.ti,ab.

40 control measure*.ti,ab.

41 35 or 36 or 37 or 38 or 39 or 40

42 25 or 34 or 41

43 15 and 42

**ProQuest Dissertations & Theses A&I (1639 to 11 June 2015), searched 11 June 2015**

all ("methicillin-resistant Staphylococcus aureus" OR "mrsa" OR "emrsa" OR "mdro" OR ("staphylococcus aureus" AND "resistant")) AND ti(barrier* OR glove* OR gown* OR mask* OR handwashing OR "hand washing" OR precaution* OR isolation OR "ward closure" OR "cohort nursing" OR "care bundling")

**Trials registers**

***Clinicaltrials.gov. Searched 6 June 2015***

**Advanced search**

**Conditions**

(nosocomial OR bacterial infections OR gram positive OR cross infection OR health care associated infections OR Staphylococcus aureus OR Staphylococcal infections OR Methicillin resistance OR Methicillin resistant Staphylococcus aureus OR MRSA)

**Intervention**

(gloves OR gowns OR aprons OR masks OR barrier precautions OR contact precautions OR universal precautions OR droplet precautions OR airborne precautions OR isolation precautions OR isolation OR “cohort nursing” OR hand hygiene OR infection control)

**Total results: 308 records**

***Clinical Trials Search Portal (WHO), searched 6 June 2015***

**Title**

nosocomial OR bacterial infections OR gram positive OR cross infection OR health care associated infections OR Staphylococcus aureus OR Staphylococcal infections OR Methicillin resistance OR Methicillin resistant Staphylococcus aureus OR MRSA

AND

**Condition**

nosocomial OR bacterial infections OR gram positive OR cross infection OR health care associated infections OR Staphylococcus aureus OR Staphylococcal infections OR Methicillin resistance OR Methicillin resistant Staphylococcus aureus OR MRSA

Register is ALL; Recruitment status is ALL;

**Total results: 624 records**

***International Standard Randomised Controlled Trial Number Register, searched 31 July 2014***

metaRegister of Controlled Trials (mRCT): ISRCTN Register; The Wellcome Trust (UK) - subset from ISRCTN Register; Action Medical Research (UK) - subset from ISRCTN Register; UK trials (UK) - subset from ISRCTN Register, UK trials only

Stragey: aureus OR MRSA OR gloves OR gown OR apron OR mask OR barrier OR droplet OR infection control

**Total results: 129 records**

## Appendix 3. List of potential confounders

1. Case mix
2. Length of stay
3. Seasonal effects
4. Strain type and properties of the organism
5. Numbers colonised on admission
6. Patient crowding/bed occupancy
7. Proportion of patients in isolation
8. Staffing levels
9. Staffing workloads
10. Hand-hygiene compliance

11. Handwashing agents used
12. MRSA clearance therapy (for studies considering MRSA)
13. Antibiotic consumption
14. Ward closures
15. Staff-patient contact patterns
16. Compliance with contact precautions
17. Processing of isolates
18. Screening practice or frequency
19. Colonisation pressure (the ratio of MRSA carrier–days to total patient-days)

Adapted from Cooper 2003 and Stone 2007 (no systematic review process was done to identify or select these factors).

## Appendix 4. Risk of bias judgement criteria for non ITS studies

### 1. Random sequence generation (*selection bias*)

***Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence***

**Low risk of bias**

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots or minimisation (minimisation may be implemented without a random element, and this is considered to be equivalent to being random).

**High risk of bias**

Either of the following.

- The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach (often called 'quasi-randomisation'), for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; or sequence generated by some rule based on hospital or clinic record number.
- Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorisation of participants, for example: allocation by judgement of the clinician; allocation by preference of the participant; allocation based on the results of a laboratory test or a series of tests; or allocation by availability of the intervention.

Non-randomised studies (including quasi-randomised) will be scored as being at 'high risk' for this domain.

**Unclear risk of bias**

Insufficient information about the sequence generation process is available to permit a judgement of 'low risk' or 'high risk'.

### 2. Allocation concealment (*selection bias*)

***Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.***

**Low risk of bias**

Any of the following.

- Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.
- In cluster designs:
  * the unit of allocation was by institution, team or professional, and allocation was performed on all units at the start of the study (EPOC 2013c); and
  * the risk of recruitment bias is low:
    - ☐ recruitment of participants occurs **prior** to the point at which clusters are randomised; or
    - ☐ recruitment of participants occurs **after** clusters are randomised, but strategies to avoid recruitment bias have been put in place. For example, blinding participants or recruiters, or both to the cluster allocation.

**High risk of bias**

Either of the following.

- Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; or any other explicitly unconcealed procedure. Non-randomised studies (including quasi-randomised) will be scored as being at 'high risk' for this domain.
- In cluster designs, the risk of recruitment bias is high: recruitment of participants occurs **after** clusters are randomised with no strategies to avoid recruitment bias in place. In these instances, the allocation of the cluster is often known to the recruiter and may influence selection of participants for the trial and the application of any inclusion and exclusion criteria, thus negating the randomisation procedure (Brierley 2012).

**Unclear risk of bias**

Either of the following.

- Insufficient information available to permit a judgement of 'low risk' or 'high risk'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.
- In cluster designs, the risk of recruitment bias is unclear (insufficient information available to permit a judgement of 'low risk' or 'high risk').

Recruitment bias is a type of selection bias. It occurs when the recruiter knows the allocation scheme, therefore this knowledge can influence selection of participants for the trial and the application of any inclusion and exclusion criteria, thus negating the randomisation procedure (Brierley 2012).

**3. Imbalance in baseline characteristics *in terms of clusters or individuals (selection bias)***

This domain will be assessed for NRS or cluster randomised designs (not for RCTs with allocation at the individual level with an adequate sample size as we will assume that baseline imbalances in these designs are caused by chance). See Appendix 3 for the list of potential confounders to be considered.

***Low risk of bias***

| Characteristics | NRS with allocation at the individual level | RCT or NRS with allocation at the group level |
|---|---|---|
| **Individuals** | • More than 80% of prognostic indicators (see Appendix 3) are reported and they are similar at baseline; or<br>• More than 80% of prognostic indicators (see Appendix 3) are reported and there are imbalances, but they are controlled for at the design or analysis stage of the study | • More than 80% of prognostic indicators (see Appendix 3) are reported and they are similar at baseline; or<br>• More than 80% of prognostic indicators (see Appendix 3) are reported and there are imbalances, but they are controlled for at the design or analysis stage of the study. |
| **Clusters** | • Not applicable | • There are no relevant imbalances in the numbers of clusters allocated; or<br>• There are relevant imbalances in the numbers of clusters allocated, but they are controlled for at the analysis stage of the study |

***High risk of bias***

| Characteristics | NRS with allocation at the individual level | RCT or NRS with allocation at the group level |
|---|---|---|
| **Individuals** | • More than 20% of prognostic indicators (see Appendix 3) are imbalanced and were not controlled at the design or analysis stage of the study | • More than 20% of prognostic indicators (see Appendix 3) are imbalanced and were not controlled at the design or analysis stage of the study; or |

(Continued)

| | | |
|---|---|---|
| **Clusters** | • Not applicable | • There are relevant imbalances in the numbers of clusters allocated that were not controlled for at the analysis stage of the study |

***Unclear risk of bias***

Insufficient information available to permit a judgement of 'low risk' or 'high risk', for example, in NRS, less than 80% of the prognostic factors (Appendix 3) were reported.

**4. Imbalance of baseline outcome measurement (assessments to be made per outcome or group of outcomes)**

***Low risk of bias***

Either of the following.

- The outcome was measured prior to the intervention, and no important differences were present across study groups.
- The outcome was measured prior to the intervention, and it was imbalanced but appropriate adjusted analysis was performed (e.g. analysis of covariance).

***High risk of bias***

The outcome was measured prior to the intervention, and important differences were present and not adjusted for in analysis.

***Unclear risk of bias***

The baseline measure of the outcome was not reported (if RCTs have no baseline measure of outcome, score 'unclear').

Note: If scoring 'high risk' or 'unclear risk' but there are sufficient data in the paper to do an adjusted analysis (e.g. baseline adjustment analysis), the criteria should be scored as 'low risk'.

**5. Blinding of participants and personnel (performance bias)**

***Performance bias due to knowledge of the allocated interventions by participants and personnel during the study***

**Low risk of bias**

Either of the following.

- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.

**High risk of bias**

Either of the following.

- No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.

**Unclear risk of bias**

Either of the following.

- Insufficient information available to permit a judgement of 'low risk' or 'high risk'.
- The study did not address this outcome.

We decided that we would assess this domain for each study as whole, as we assumed that the lack of blinding of participants or healthcare providers would affect the actual results of all the review outcomes, with all of them being affected in a similar manner.

**6. Blinding of outcome assessment (detection bias; assessments to be made for each outcome (or class of outcomes))**

***Detection bias due to knowledge of the allocated interventions by outcome assessors***

**Low risk of bias**

Either of the following.

- Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
- No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding.

**High risk of bias**

Either of the following.

- No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding.
- Blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.

**Unclear risk of bias**

Either of the following.

- Insufficient information available to permit a judgement of ‘low risk’ or ‘high risk’.
- The study did not address this outcome.

**7. Incomplete outcome data (attrition bias; assessments to be made for each outcome (or class of outcomes))**

***Attrition bias due to amount, nature or handling of incomplete outcome data***

**Low risk of bias**

Any of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to the true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

**High risk of bias**

Any of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size.
- ‘As-treated’ analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

**Unclear risk of bias**

Either of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of ‘low risk’ or ‘high risk’ (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

Note: If scoring 'unclear' or 'high', but there are sufficient data in the paper to do an adjusted analysis (e.g. from 'per protocol analysis to intention-to-treat analysis) the criteria should be scored as 'low risk of bias'.

Note: in this domain loss of clusters in cluster-designs will be also assessed.

**8. Selective reporting (reporting bias)**

***Reporting bias due to selective outcome reporting***

**Low risk of bias**

Either of the following.

- The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon). For example, all relevant outcomes in the methods section are reported in the results section.

**High risk of bias**

Any of the following.

- Not all of the study's pre-specified primary outcomes have been reported.
- One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub-scales) that were not pre-specified.
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

**Unclear risk of bias**

Insufficient information available to permit a judgement of 'low risk' or 'high risk'. It is likely that the majority of studies will fall into this category.

**9. Protection against contamination**

In a controlled trial, contamination refers to the inadvertent application of the intervention being evaluated to people in the control group; or the inadvertent failure to apply the intervention to people assigned to the intervention group (Higgins 2005). Cluster allocation usually reduces the likelihood of contamination.

***Low risk of bias***

Allocation was by group level (such as ward or hospital) and it is unlikely that the control group received the intervention, or that there was an inadvertent failure to apply the intervention to people assigned to the intervention group.

***High risk of bias***

It is likely that contamination occurred.

***Unclear risk of bias***

- Professionals were allocated within a clinic or practice but it is possible that communication between intervention and control professionals could have occurred (e.g. physicians within practices were allocated to intervention or control).
- Insufficient information available to permit a judgement of low or high risk of bias.

**10. Timing of the assessment of the outcomes (Assessments to be made for each outcome (or class of outcomes))**

***Low risk of bias***

The timing of the outcome assessment was similar in all groups.

***High risk of bias***

The timing of the outcome assessment was not similar in all groups: for example, studies with non-concurrent controls where seasonality is an issue (i.e. if January to June comprises the intervention group and July to December the control group, the 'seasons' could have caused a spurious effect).

***Unclear risk of bias***

Insufficient information available to permit a judgement.

**11. Statistical methods taking the clustering into account (only for cluster designs)**

***Low risk of bias***

The cluster-design was analysed by correct statistical methods, taking the clustering into account. Ways to avoid unit-of-analysis errors in cluster-designs include any of the following (see *Cochrane Handbook for Systematic Reviews of Interventions* 16.3.3, Higgins 2011b).

- The analysis is conducted at the same level as the allocation.
- The analysis is conducted at the level of the individual while accounting for the clustering in the data. Such an analysis might be based on a 'multilevel model', a 'variance components analysis' or a 'generalised estimating equations (GEEs)', among other techniques.

***High risk of bias***

The cluster-design was analysed by incorrect statistical methods, not taking the clustering into account. Such analyses tend to create a 'unit of analysis error' and produce over-precise results (the standard error of the estimated intervention effect is too small) and P values that are too small. Although they do not lead to biased estimates of effect, if they remain uncorrected, they will receive too much weight in a meta-analysis.

***Unclear risk of bias***

Insufficient information available to permit a judgement.

## Appendix 5. Risk of bias judgement criteria for ITS studies

**1. Was the intervention independent of other changes?**

***Low risk of bias***

Either of the following.

- There are compelling arguments that the intervention occurred independently of other changes over time and the outcome was not influenced by other confounding variables/historic events during study period. If events/variables identified, note what they are.
- There is no evidence of seasonality being an issue; the study considers at least 12 monthly data points before and 12 monthly data points after the intervention.

***High risk of bias***

Either of the following.

- Reported that intervention was not independent of other changes in time.
- There is evidence of seasonality being an issue: the study does not consider at least 12 monthly data points before and 12 monthly data points after the intervention (for example, if January to June comprises the pre-intervention period and July to December the post, could the 'seasons' have caused a spurious effect).

***Unclear risk of bias***

Insufficient information available to permit a judgement of 'low risk' or 'high risk.

**2. Was the shape of the intervention effect pre-specified?**

***Low risk of bias***

Point of analysis is the point of intervention or a rational explanation for the shape of intervention effect was given by the authors. Where appropriate, this should include an explanation if the point of analysis is not the point of intervention.

***High risk of bias***

It is clear that the condition above for low risk of bias is not met.

***Unclear risk of bias***

Insufficient information available to permit a judgement of 'low risk' or 'high risk'.

**3. Was the intervention unlikely to affect data collection? (Assessments to be made for each outcome (or class of outcomes))**

***Low risk of bias***

Reported that intervention itself was unlikely to affect data collection (for example, sources and methods of data collection were the same before and after the intervention).

***High risk of bias***

The intervention itself was likely to affect data collection (for example, any change in source or method of data collection reported).

***Unclear risk of bias***

Insufficient information available to permit a judgement of ‘low risk’ or ‘high risk’.

**4. Blinding of outcome assessment (detection bias; assessments to be made for each outcome (or class of outcomes))**

***Low risk of bias***

Either of the following.

- Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
- No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding.

***High risk of bias***

Either of the following.

- No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding.
- Blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.

***Unclear risk of bias***

Either of the following.

- Insufficient information available to permit a judgement of ‘low risk’ or ‘high risk’.
- The study did not address this outcome.

**5. Incomplete outcome data (attrition bias; assessments to be made for each outcome (or class of outcomes))**

***Low risk of bias***

Missing outcome measures were unlikely to bias the results (e.g. the proportion of missing data was similar in the pre- and post-intervention periods or the proportion of missing data was less than the effect size i.e. unlikely to overturn the study result).

***High risk of bias***

Missing outcome data was likely to bias the results. Score 'unclear' if not specified in the paper (do not assume 100% follow-up unless stated explicitly).

***Unclear risk of bias***

Insufficient information available to permit a judgement of 'low risk’ or ‘high risk’ (do not assume 100% follow-up unless stated explicitly).

**6. Was the study free from selective outcome reporting? (reporting bias)**

***Low risk of bias***

Either of the following.

- The study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon). For example, all relevant outcomes in the methods section are reported in the results section.

***High risk of bias***

Any of the following.

- Not all of the study’s pre-specified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods or subsets of the data (e.g. sub-scales) that were not pre-specified.
- One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).

- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

***Unclear risk of bias***

Insufficient information available to permit a judgement of 'low risk' or 'high risk'. It is likely that the majority of studies will fall into this category.

## Appendix 6. Grouping of outcomes for RoB assessment

| RoB domain | Assessment level | Factor for grouping the outcomes | Groups of outcomes | Entries in the RoB tool |
|---|---|---|---|---|
| **Imbalance in baseline outcome measurements** | Outcome | None | RoB assessed for each outcome | One for each outcome |
| **Blinding of outcome assessment** | Outcome | Susceptibility of the measurement to lack or incomplete blinding of outcome assessment | **a. Low susceptibility**<br>Judged by the review authors as not likely to be influenced by lack or incomplete of blinding | Blinding of outcome assessment (detection bias)<br>(Low susceptibility: MRSA to MSSA ratios; length of stay; antibiotic use; all cause mortality) |
| | | | **b. High susceptibility**<br>Judged by the review authors as likely to be influenced by lack or incomplete of blinding | Blinding of outcome assessment (detection bias)<br>(High susceptibility: remaining outcomes not listed above) |
| **Was the intervention unlikely to affect data collection?** | Outcome | Susceptibility of the data collection to be affected by the introduction of the intervention | **a. Low susceptibility**<br>Judged by the review authors as not likely to be influenced by lack or incomplete of blinding | Susceptibility data collection to the intervention<br>(Low susceptibility: MRSA to MSSA ratios; length of stay; antibiotic use; all cause mortality) |
| | | | **b. High susceptibility**<br>Judged by the review authors as likely to be influenced by lack or incomplete of blinding | Susceptibility data collection to the intervention<br>(High susceptibility: remaining outcomes not listed above) |
| **Timing of the assessments of the outcomes** | Outcome | None | RoB assessed for each outcome | One for each outcome |
| **Incomplete outcome data** | Outcome | None | RoB assessed for each outcome | One for each outcome |

## HISTORY

Protocol first published: Issue 2, 2008
Review first published: Issue 7, 2015

| Date | Event | Description |
|---|---|---|
| 7 September 2010 | Amended | Contact details updated. |
| 3 August 2010 | Amended | Contact details updated. |
| 7 August 2009 | Amended | Contact details updated. |
| 11 November 2008 | Amended | Contact details updated |
| 9 May 2008 | Amended | External source of support added |
| 18 April 2008 | Amended | Converted to new review format. |
| 10 January 2008 | New citation required and major changes | Substantive amendment |

## CONTRIBUTIONS OF AUTHORS

Jesus López-Alcalde (JLA): conceived, designed and coordinated the review. Extracted data, checked the quality of the data extraction, and analysed and interpreted data. Wrote and edited the review. Advised on the review and approved the final review prior to submission. Secured funding. Wrote to study authors/experts/companies. Is the guarantor of the review.
Marta Mateos (MM): analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Wrote to study authors/experts/companies.
Marcela Guevara (MG): analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Wrote to study authors/experts/companies.
Lucieni Oliveira Conterno (LOC): analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Wrote to study authors/experts/companies.
Iván Solà (IS): conceived and designed the review. Analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Performed previous work that was the foundation of the current review.
Sheila Cabir (SC): extracted data, checked the quality of the data extraction, and analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Performed translations.
Xavier Bonfill (XB): conceived, designed and coordinated the review. Analysed and interpreted data. Performed part of writing and editing the review. Advised on the review and approved the final review prior to submission. Secured funding and performed previous work that was the foundation of the current review.

**Contributions of editorial base:**Â
Nicky Cullum: edited the review, advised on methodology, interpretation and review content. Approved the final reviewÂ prior to submission.
Sally Bell-Syer: coordinated the editorial process. Advised on methodology, interpretation and content. Edited the review.
Ruth Foxlee: designed the search strategy, Amanda Briant ran the searches.

## DECLARATIONS OF INTEREST

JLA: in 2011 JLA was paid by Angelini for participating as a speaker in one session (1 hour) about evidence-based medicine (not related to the topic of this review)
MM: none known
MG: none known
LOC: none known
IS: none known
SC: none known
XB: none known

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### Internal sources

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## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

On occasion we followed different methods from those detailed in the protocol because we could not apply the methods we had laid out due to the absence of included studies, or because we found a preferable alternative. It is noteworthy that the review protocol was published in 2008; since then the *Cochrane Handbook for Systematic Reviews of Interventions* has been updated several times, and the Cochrane Editorial Unit also developed its 'Methodological Expectations of Cochrane Intervention Reviews (MECIR)' (MECIR Conduct 2013). Therefore, we incorporated changes that need to be implemented for future updates of the review. Below we detail the particular modifications made in each section.

### Review information

- Francisco Job Neto retired from the review team, while Xavier Bonfill and Sheila Cabir joined.

### Objectives

- The objectives reported in the protocol were "To determine whether the wearing of gloves, gowns and/or masks by any person in the hospital setting in contact with an inpatient colonised or infected with MRSA, reduces the transmission of MRSA in the hospital setting". We decided to rephrase these objectives to make it explicit that we also aimed to assess the effects of the use of these barrier precautions in the immediate environment of the MRSA patient (this refers to entering the room of the MRSA patient without planning to establish any contact with him or her).

### Criteria for considering studies for this review

#### Type of studies

- The protocol did not detail that we would include experimental designs only; it reported that RCT, Q-RCT, CBA, and ITS would be eligible, defined according to the EPOC Group criteria (EPOC 2007). However, the application of these criteria did not allow us to separate 'outbreak reports' and 'observational studies' from 'experimental studies'. This distinction is key according to the *Outbreak Reports and Intervention Studies Of Nosocomial infection* (ORION) statement, as 'experimental studies' are less prone to bias when assessing the effects of infection control interventions (Stone 2007). For this reason, we decided to assess explicit study design features to decide on the experimental character of the studies. In particular, we considered that the minimum requirements for a study to be defined as experimental would be a prospective assessment of baseline, a prospective allocation of the intervention and a prospective assessment of outcomes.
- The 'study design labels' used in this review (detailed in tables 13.2.2 and 13.2.b of the *Cochrane Handbook for Systematic Reviews of Interventions* (Reeves 2011)), were not the same than those used in the protocol. This is justified by the fact that this chapter of the *Cochrane Handbook* was not published at the time of writing the protocol.
- For deciding on study design eligibility, we considered the 'study design features' detailed in tables 13.2.2 and 13.2.b of the *Cochrane Handbook* (Reeves 2011). This was not planned in the protocol due to this chapter was not published at the time of writing the protocol. We judged that the approach proposed in chapter 13 is useful to decide on the inclusion of non-randomised studies, as the terminology and classification systems used for these study designs are inconsistent, which may lead to a low reliability when deciding on which studies to include (Hartling 2010).
- The protocol did not detail explicitly that the stepped wedge design in RCTs or CI-RCTs would be eligible trial types.
- The protocol did not report that in vitro laboratory-based studies would be excluded.

#### Type of participants

- The protocol defined a 'participant' as the person on whom the outcome was measured. However, the review defined 'participant' according to the CONSORT statement definition, that is, the study subject who is selected to take part in a trial (CONSORT glossary 2014).

### Type of interventions

The protocol did not specify that we would consider:

- the use of gloves, gowns, aprons or masks for interactions with the patient's environment as an eligible intervention.
- any comparator provided that it allowed the effect of gloving, gowning or masking on MRSA transmission to be separated out. This criterion was found to be key during the selection process of the studies in order to increase the consistency of the decisions.

### Types of outcomes measures

- We used the term 'healthcare-associated' instead of 'nosocomial' (used in the protocol) as it is more widely used (CDC 2014).
- The protocol did not state that we would not exclude any study solely because no outcomes of interest were reported.
- The protocol did not state that issues of equity and relevance of evidence to specific populations would be assessed.

## Search methods for identification of studies

- Initially we searched the Cochrane Infectious Diseases Group Specialised Register (5 January 2009), but we decided not to continue searching this source as it did not contain relevant records.
- We searched the BNI only up to 6 July 2010 as we did not have access to this database after this date.
- The protocol stated that we planned to access MEDLINE via PubMed, but we accessed it via OVID.
- The protocol stated that we planned to combine the MEDLINE, EMBASE and CINAHL search strategies with validated methodological filters, however, we did not combine MEDLINE with any methodological filter, in order to gain sensitivity.
- For EMBASE and CINAHL we used the most recent filters available.
- We checked the abstracts from relevant conferences in the field, which we did not plan to do in the protocol.

## Selection of studies

- The protocol did not report that we would not exclude studies solely on the basis of reporting of the outcome data, that we would complete a PRISMA flow chart, or our approach to multiple reports of the same included study.
- For the review JLA assessed the eligibility of all the references and full texts, while in the protocol he had been assigned to the first half of the titles and abstracts and full texts.

## Data extraction and management

In the review we state that:

- we would have adapted the data extraction form to several relevant existing guidelines (Stone 2007; Boutron 2008; Schulz 2010; NRSMG 2011; Reeves 2011; Campbell 2012; EPOC 2013b; MECIR Conduct 2013; Hoffmann 2014), some of these were not available when the protocol was published.
- had any study been included, we would have created a graphical depiction of the experimental and control interventions using the Pat Plot tool (Perera 2007); this was not reported in the protocol.
- had we included a study with more than two intervention arms, the review would include only the intervention and control groups that met the eligibility criteria; this was not detailed in the protocol.
- we would have examined any relevant retraction statements and errata for relevant information regarding each included study; this was not reported in the protocol.
- although the protocol stated that there would always be dual data extraction, we decided that this would be the case at least for outcome data (and if possible for the remainder study characteristics).

## Assessment of risk of bias in included studies

In the protocol we did not plan to:

- assess the RoB according to the domains proposed by the Cochrane Collaboration's new RoB tool (Higgins 2011a), and the new Cochrane EPOC group guidance (EPOC 2013c), as they were not available at the time of its submission.
- to assess the RoB for each outcome (or class of similar outcomes).
- summarize the RoB for each outcome (or class of similar outcomes) in two different manners, that is, 'within each study' and 'across studies'.
- assess the 'blinding of participants and personnel' and 'blinding of outcome assessment' separately.
- assess the domain 'timing of the outcomes assessments'; we considered it vital to discard the presence of seasonal effects that could have influence on MRSA outcome data, for example, there may be a higher bed occupancy in winter months, which can generate changes in MRSA rates.
- assess inter-rater reliability for the key domains only.

- report the results of assessments of confounders in an additional table.
- justify judgements of RoB and provide this information in the RoB tables.
- incorporate the summary assessments of the RoB for each outcome across studies into explicit measures of the quality of evidence for each important outcome using the GRADE system.
- assess RoB of cluster designs, or provide details of how we would do it.

We stated in the protocol, "All the quality assessment criteria will be considered equally important in terms of their contribution to study validity", however, we defined 'key domains' for the analysis.

### Measures of treatment effect

- The protocol did not report this section, as it was not present in RevMan 4, but was introduced with RevMan 5.

### Unit of analysis issues

- In the protocol we did not plan to re-analyse the results of the included studies with unit of analysis errors, however, due to the paucity of studies expected, we plan to do it for future updates of this review.
- In the protocol we did not plan to assess whether count data had been treated erroneously as dichotomous data in the included studies.
- In this section of the protocol we stated that we planned to examine whether the method of analysis of CBA studies accounted for eventual baseline differences of the outcomes, however, we planned to do this as part of the RoB assessment ('imbalance in baseline characteristics (selection bias)').
- In the protocol we did not cover issues relating to 'Sample size calculation', 'Outcome of interest is an event that may re-occur' and 'Additional analysis issues' in this section. We decided to add them, as they are relevant to the review topic.

### Dealing with missing data

- In the protocol we did not state explicitly how we would deal with missing data. This section was added to the protocol.

### Assessment of heterogeneity

- RevMan 4.2, the software used to construct the protocol, did not allow us to detail this information in an independent section. However, the information presented in this review was detailed according to the protocol plan, although in a more detailed manner.

### Assessment of reporting biases

- In the protocol we did not state explicitly how we would deal with reporting biases (this section was not available in RevMan 4.2).

### Data synthesis

The protocol stated that:

- we would use RevMan 4.2 but we used RevMan 5.3;
- we would meta-analyse RCTs and Q-RCTs only. However, due the low number of included studies expected for future review updates, if the meta-analysis is appropriate and the study design eligible, we will not exclude of the meta-analysis any included study based on its design;
- we would meta-analyse only those studies with a low RoB. However, due the low number of studies expected to be included in future updates of the review, we now plan to meta-analyse all the included studies regardless of their RoB. The impact of this decision will be assessed through sensitivity analysis.

The protocol did not state that the narrative analysis of the included studies would provide a descriptive presentation of the results, grouped by outcome.

### Subgroup analysis and investigation of heterogeneity

- As we intend to meta-analyse NRS too, we plan to determine whether the adjustment of the estimates may be a potential factor for explaining heterogeneity.
- In the protocol we did not specify that "If sufficient studies had been available, we would have used a formal statistical test to compare the results of the subgroups. If subgroup analyses had been conducted, we would have followed the subgroup analysis plan specified in the protocol without undue emphasis on particular findings (MECIR Conduct 2013)".

### Sensitivity analysis

- In the protocol we did not specify that sensitivity analysis would be restricted to the review's primary outcomes, or that the statistical model chosen for meta-analysis would be tested.

- We decided to modify the sensitivity analyses to be performed in future updates of the review in order to focus on key methodological aspects that would allow us to assess the robustness of results. We did not plan to perform the following sensitivity analyses in the protocol:
  * repeat the meta-analysis to assess the effect of including only studies that report nosocomial MRSA colonisation, infection, bacteraemia or pneumonia.
  * repeat the meta-analysis to assess the effect of including only RCT designs.
  * repeat the meta-analysis to assess the effect of including only CBA designs.
  * repeat the meta-analysis to assess the effect of including only ITS designs.

### Appendix 1: Glossary

We added some terms in the review.

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Masks; *Methicillin-Resistant Staphylococcus aureus; *Protective Clothing; Cross Infection [prevention & control] [*transmission]; Gloves, Protective; Staphylococcal Infections [prevention & control] [*transmission]

### MeSH check words

Female; Humans