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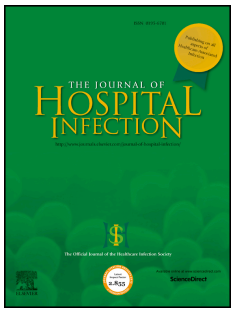

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B.G. Mitchell, S.J. Dancer, M. Anderson, E. Dehn

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Review

Risk of organism acquisition from prior room occupants: a systematic review and meta-analysis

B.G. Mitchell[a,b,*], S.J. Dancer[c], M. Anderson[a], E. Dehn[a]

[a]*Avondale College of Higher Education, Faculty of Arts, Nursing and Theology, Wahroonga, NSW, Australia*

[b]*Faculty of Health Sciences, Australian Catholic University, Watson, Australian Capital Territory, Australia*

[c]*Department of Microbiology, Hairmyres Hospital, East Kilbride, UK*

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[*]Corresponding author. Address: Avondale College of Higher Education, 185 Fox Valley Rd, Wahroonga, NSW 2076, Australia. Tel.: +61 2 9487 9630.

E-mail address: +61 2 9487 9630.

SUMMARY

A systematic review and meta-analysis was conducted to determine the risk of pathogen acquisition for patients associated with prior room occupancy. The analysis was also broadened to examine any differences in acquisition risk between Gram-positive and Gram-negative organisms. A search using Medline/PubMed, Cochrane and CINHAL yielded 2577 citations between 1984 and 2014. Reviews were assessed in accordance with the international prospective register of systematic reviews (PROSPERO). Just seven articles met the inclusion criteria, namely: (a) papers were peer reviewed, (b) pathogen acquisition prevalence rates were reported, (c) articles were written in English; and (d) had minimal or no risk of bias based on the Newcastle–Ottawa Scale (NOS). One study was an extension of a previous study and was discarded. Employing NOS provided little difference between the studies, with five studies receiving eight-star and two studies receiving seven-star ratings, respectively. Overall, pooled acquisition odds ratio for study pathogens (meticillin-resistant *Staphylococcus aureus*; vancomycin-resistant enterococcus; *Clostridium difficile*; acinetobacter; extended-spectrum β-lactamase-producing coliforms; pseudomonas) was 2.14 [95% confidence interval (CI): 1.65–2.77]. When comparing data between Gram-positive and Gram-negative organisms, the pooled acquisition odds ratio for Gram-negatives was 2.65 (95% CI: 2.02–3.47) and 1.89 (95% CI: 1.62–2.21) for Gram positives. The findings have important implications for infection control professionals, environmental cleaning services and patients, since current practices fail to adequately reduce acquisition risk. Although there may be non-preventable

sources of acquisition, revised practices require collaborative work between all responsible staff in order to reduce this risk to a minimum.

Keywords:

Acquisition

Cleaning

Infection control

Prior room occupancy

Introduction

The discovery and provision of antibiotics is one of the most important advances in modern medicine and underpins much of medical practice today. However, resistance to antimicrobial agents is now a major health issue and threatens the management of infection.[1] The evolution of resistant strains may occur naturally or follow exchange of resistance genes from other organisms in a pressured environment.[1] In high-income countries, antibiotic consumption in hospitals, communities, and agriculture has encouraged and sustains resistant strains.[2] Infections caused by multi-resistant organisms are becoming difficult or even impossible to treat, resulting in higher morbidity and mortality.[3] This has led to a greater focus on infection prevention and control, particularly in healthcare institutions.

It is now acknowledged that the healthcare environment may play a key role in facilitating the transmission of important pathogens associated with healthcare infections.[4,5] These pathogens include vancomycin-resistant enterococci (VRE), *Clostridium difficile* and meticillin-resistant *Staphylococcus aureus* (MRSA).[4–8] Such organisms are able to survive in the environment for days or even weeks, posing an ongoing risk of transmission and acquisition to hospital patients.[4,9] In recent years, there has been more interest from infection control staff, clinicians, health planners and government on maintaining a clean environment.[10–13] Nevertheless, what constitutes a clean environment and how to achieve this is beyond the scope and purpose of this study. A review paper by Dancer explored this issue in detail and summarizes the current evidence base.[4]

Despite advances in technology, increased attention towards cleanliness and new cleaning practices, studies have shown that if a patient is admitted to a room where the prior occupant was colonized or infected with a hospital pathogen, there is an increased risk of the next patient acquiring the same organism.[6,14,15] Such studies are pivotal for supporting the notion that the environment plays an important role in infection transmission. They provide evidence that, despite our best efforts to date, the risk of acquiring a multidrug-resistant organism or *C. difficile* increases as a direct result of patient placement, regardless of any other infection prevention strategies including hand hygiene. Further, these studies justify a

move to impose scientific standards for measuring microbial soil and environmental cleanliness in order to gauge the cleaning effect and infection risk to patients.[12]

This systematic review and meta-analysis of published literature investigates the acquisition risk associated with prior room occupancy. Specifically applicable to hospitalized patients, the review determines whether being admitted to a room where the prior occupant was colonized or infected with an organism increases the risk of acquiring that organism. Differences in the risk of acquisition between Gram-positive and Gram-negative organisms are also explored.

Methods

Protocol and registration

The protocol for conducting this review can be accessed on the international prospective register of systematic reviews (PROSPERO), which is available at www.york.ac.uk/inst/crd with the registration number CRD42015016273. Prior to registration, the protocol was assessed by a reviewer who was independent of the study team.

Eligibility criteria

We conducted a systematic review of observational (cross-sectional, cohort, and case control) studies published in the last 30 years regarding hospitalized patients who had acquired organisms from prior room occupants. Publications were included if they reported acquisition prevalence rates, and only peer-reviewed material was considered. All grey material, non-peer-reviewed literature (e.g. conference abstracts, letters to editors, etc.) and reviews were excluded. Papers written in languages other than English were also excluded.

Studies must have examined exposure or acquisition in a hospitalized population where the prior room occupant was colonized or infected with a specific organism. For the purpose of this review, eligible organisms were acinetobacter, *Escherichia coli*, klebsiella, pseudomonas, enterobacter, citrobacter, proteus, serratia, enterococcus, *C. difficile*, *S. aureus*, MRSA, and VRE.

Information sources

The electronic bibliographic databases Medline/PubMed, Cochrane and CINHAL were searched for material published between January 1st, 1984 and December 1st, 2014. Searches were conducted for words in the title or abstract. The search filters used were the 30-year publication time-period, articles published in English and studies conducted on humans. The reference lists of the studies identified from the electronic databases and included in this study were subsequently hand-searched for additional studies.

The names of the specific organisms and the terms ‘prior room occupancy’, ‘occupancy’ and ‘acquisition’ were used to search the bibliographic databases. The names of

the specific organisms searched with the other stated keywords were 'Acinetobacter', '*Escherichia coli*', 'Klebsiella', 'Pseudomonas', 'Enterobacter', 'Citrobacter', 'Proteus', 'Serratia', 'Enterococcus', '*Clostridium difficile*', '*Staphylococcus aureus*', 'methicillin-resistant *Staphylococcus aureus*' and 'vancomycin-resistant Enterococcus'. Where relevant both extended-spectrum β-lactamase (ESBL) and non-ESBL strains were included for Gram-negative organisms.

Study selection

The titles and abstracts of all the publications identified in the electronic databases were examined and assessed for relevance and appropriateness to the review question. Those not relevant were excluded. Of the remaining articles, the full text was reviewed to further assess eligibility. The remaining articles were deemed to have data relevant to the systematic review and meta-analysis.

The study selection process and other stages of the review were performed by two trained research assistants. Ten percent of the original articles retrieved in the initial search were selected at random and reviewed by an experienced research member as a cross-check against study eligibility. Any discrepancies in either the application of the inclusion or exclusion criteria were resolved by two members of the research team.

Data collection process

A paper-based data extraction form was designed for the purpose of extracting data for the systematic review and meta-analysis. Data were extracted by research assistants and were cross-checked by one researcher. No attempt was made to contact the authors of papers that contained missing data or unclear information.

Risk of bias in individual studies

An assessment of quality and risk of bias in the final papers included in the review was conducted using the Newcastle–Ottawa Scale (NOS). Recommended by the Cochrane Collaboration, NOS is a risk-of-bias assessment tool for observational studies.[14,16] The content validity and inter-rater reliability of this tool has been established.[16] The tool enables a maximum of nine stars to be awarded to an individual study.

Summary measures and synthesis of results

Statistical analyses were undertaken using Review Manager software (Revman 5.3; Cochrane Collaboration, Oxford, UK). The pooled prevalence estimates [and 95% confidence interval (CI)] of acquisition were calculated and compared, with a sub-analysis by the type of organism genus and by Gram-negative and Gram-positive organisms, using a random-effects meta-analysis model based on the DerSimonian and Laird method. This method incorporates an estimate of the between-study variation into both the study weights and the standard error

of the estimate of the common effect. The precision of an estimate from each included study was represented by the inverse of the variance of the outcome pooled across all the studies.

The heterogeneity among the studies was assessed using the Cochran Q statistic where $P < 0.05$ was considered statistically significant. The I^2 statistic was used to determine the degree of heterogeneity.

Results

Study selection

The electronic database searches identified 2577 potential studies. After 801 duplicates had been removed, 1879 articles remained for title and abstract screening. After applying the inclusion and exclusion criteria, seven papers (3.7%) were retained for data analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart describing the studies identified from the search strategy and reasons for exclusion is shown in Figure 1.

Overview of study characteristics

Study characteristics are listed in Table I. Three studies examined more than one organism, and all but two studies were conducted outside the USA.[6,15,17,18] All studies were single site and published in the last 10 years. There was only one study that examined acquisition in a setting other than intensive care.[18]

The study undertaken by Datta *et al*. was an extension of the study undertaken by Huang *et al*., but also included an intervention.[6,17] The data from the Datta *et al*. study were not included in the meta-analysis as the baseline data provided had already been reported in the Huang *et al*. study.[6,17] Therefore, six studies were included in the meta-analysis, and these studies were all observational.[6,15,18–21] The NOSbias tool demonstrated few overall differences between the studies. Five of the seven studies obtained an eight-star rating with the two other studies receiving seven-stars. There was therefore no reason to exclude any of the studies from the meta-analysis, apart from the Datta study for the reasons already described.[17] NOS prompted a review of potential confounders and how these were managed in each study (Table II).

Synthesis of results

Of 4643 patients who were admitted into a room where the prior room occupant had either any of the studied organisms (i.e. VRE; MRSA; Gram-negative bacilli, including EBSL producers; *C. difficile*; *Acinetobacter baumannii* or *Pseudomonas aeruginosa*), 287 (6.2%) were shown to acquire the same species of organism. In comparison, of 34,886 patients who were not admitted into a room where the prior room occupant had one of these organisms, 1112 (3.2%) acquired the studied organism(s).

The pooled acquisition odds ratio (OR) for all the organisms included in the six studies was 2.14 (95% CI: 1.65–2.77). There was heterogeneity between the studies (I^2 = 67%, $P < 0.001$). Figure 2 shows a forest plot of the included studies with analyses undertaken for the various study organisms. When comparing the data between Gram-positive and Gram-negative organisms, the pooled acquisition OR for Gram-negative organisms was 2.65 (95% CI: 2.02–3.47) and 1.89 (95% CI: 1.62–2.21) for Gram-positive organisms (heterogeneity: $tau^2 = 0.04$; $I^2 = 78\%$; overall effect size: $Z = 4.70$, $P < 0.001$). For Gram-negative organisms, *A. baumannii* had the highest OR (4.53; 95% CI: 2.32–8.86).

Further sub-analyses were undertaken comparing the data from *C. difficile* against the MRSA studies; MRSA against the VRE studies; *Klebsiella* species and *E. coli* ESBL-producing Gram-negative bacilli (where identified within studies) with *P. aeruginosa* against *A. baumannii*. No statistically significant differences were identified. There were also no significant differences in acquisition between ESBL-producing organisms and MRSA or VRE.

The study undertaken by Datta *et al*. evaluated the effect of targeted feedback, increased education and the use of cleaning cloths saturated with a disinfectant.[17] The acquisition of both MRSA and VRE decreased from 3.0% to 1.5% and from 3.0% to 2.2%, respectively. Patients in rooms previously occupied by MRSA-colonized or -infected patients had an increased risk of MRSA acquisition before the intervention and a decreased risk of acquisition after the intervention. An increased risk of acquisition remained for patients in rooms occupied by VRE before and after the intervention.[17] The lack of data on antibiotic use was a stated limitation of this study.

Discussion

The findings of our systematic review support the notion that admission to a room previously occupied by a patient infected and/or colonized with a specific pathogen is a risk factor for acquisition. Our study identified seven articles which explored the relationship between acquisition and prior room occupancy. We undertook a meta-analysis of six of these articles. The analysis of the combined data from these studies overwhelmingly indicated an increased risk of acquisition. The sub-analysis suggested that regardless of the organism – VRE, MRSA, ESBL-producing Gram negative bacilli, *A. baumannii* or *P. aeruginosa* – the risk of acquisition increases. A comparison of risk between Gram-negative and Gram-positive organisms indicated a greater pooled acquisition rate for Gram-negative organisms. This difference remained even after excluding *C. difficile* from the Gram-positive group and *A. baumannii* from the Gram-negative group. A meta-regression of the studies was not possible

as the key data on age, sex and colonization pressure were either incomplete or absent for the majority of patients.

Micro-organisms survive in the environment for different lengths of time. For organisms relevant to this review, on dry inanimate surfaces, *S. aureus* including MRSA can survive up to seven months; *C. difficile* spores up to five months; *Enterococcus* spp., including VRE, five days to four months; *Acinetobacter* spp. three days to five months; and *P. aeruginosa* 6 h to 16 months.[9] Overall, Gram-negative bacteria have been reported to persist longer than Gram-positive bacteria.[9,22] This may in part explain the higher risk identified for acquisition from prior room occupants with a Gram-negative organism, compared with Gram-positive organism, although the difference was not significant. Hydric reservoirs may increase the risk of survival of Gram-negative bacteria. *E. coli, Klebsiella* spp. and *Pseudomonas* spp. can survive for more than a year under certain conditions.[9] Organisms from water outlets have the potential to colonize and infect patients, with sinks forming a potential reservoir for Gram-negative bacteria.[23–26] Biofilms, which may establish in sink traps, can display greater capacity for antimicrobial resistance and tolerance to chlorine and other disinfectants.[23]

This systematic review and meta-analysis have important implications for infection control professionals, environmental cleaning services, administrators, and the wider public. The findings will assist infection control staff and hospital managers in understanding and managing the risks associated with the determination of room placement. Knowing the status of the prior room occupant may serve as important information in decision-making. For environmental cleaning services and administrators, this review suggests that current cleaning practices fail to reduce the risk of acquisition. There is a need for renewed interest and emphasis on hospital cleaning, and particularly discharge or terminal cleaning. As such, this requires all responsible parties to work together to find methods that reduce this risk to an acceptable level.

Whereas consideration of the surface environment is obviously a key feature in the current review, the role of ventilation should not be discounted. There is a growing body of evidence supporting the notion that aerial dispersal of some pathogens may contaminate the environment and contribute to further acquisition regardless of manual cleaning strategies.[27–32] Spores of *C. difficile* may remain airborne for up to 48 h after a colonized patient is discharged from a room, despite terminal cleaning taking place. This area requires further research and exploration. Cross-transmission of pathogens may also occur via the hands of healthcare workers, clothing, and shared equipment.[33–36]

In addition to those already employed, we need to consider the use of advanced cleaning technologies and concurrent interventions involving the patient.[37] Whereas regular

and conscientious cleaning is a necessity for eliminating pathogens, it is not the only mechanism for keeping surfaces free from microbes. There are some high-tech solutions currently receiving attention, including the so-called 'self-sanitizing' surfaces. It is possible that treating or coating hospital surfaces liable to contamination by pathogens could kill or inhibit microbes in order to disrupt transmission to patients. Hard metals such as copper and silver have long been investigated for their antimicrobial properties, and now novel technologies such as light-activated titanium dioxide-containing surfaces are attracting attention.[38] Other novel innovations include automated robot delivery of disinfectants or microbiocidal light for terminal cleaning, UVC light fixtures, microfibre cloths and mops and novel disinfectants such as electrolysed water.[4] Our study supports the need to improve hospital design, as often the limited availability of single rooms makes the placement of patients challenging. For the wider public, our study opens up a discussion about what is deemed acceptable risk. For a layperson, it would be difficult to explain why, just because the last person in the room had an infection/colonization, the new admission has an increased risk of acquiring that same organism – particularly since additional cleaning measures are often in place when the infection status of patients is known.

To our knowledge, this is the first systematic review exploring the acquisition of organisms in hospital from prior room occupants. The findings were constrained by the limitations of the individual studies reviewed, for example, the inability to conduct meta-regression due to the lack of data, different approaches to testing the efforts of the participants, potential variations in microbiological testing methods, the presumption of acquisition based on epidemiological evidence, and the inability to account for colonization pressure. Colonization pressure – the proportion of patients colonized by a particular organism – has been shown to be an important factor in acquisition.[39] A standardized and simple method to quantify colonization pressure will assist in accurately assessing the effect that this pressure may have on the cross-transmission of bacteria.[40] If studies employ and document such a method, it will aid future systematic reviews and meta-analyses on this topic.

A systematic review of the literature identified evidence to suggest that admission to a room previously occupied by a carrier of observed bacteria is a risk factor for subsequent acquisition. A meta-analysis of the combined data from included studies overwhelmingly indicated an increased risk of acquisition. The findings support the need for infection control professionals and hospital bed managers to manage the risks associated with the determination of room placement. Our study suggests that current environmental cleaning practices fail to reduce the risk of acquisition. To reduce the risk of acquisition, we should

consider the use of novel approaches to improve cleaning, the use of new cleaning technologies and interventions involving the patient.[4] Further research on the role of aerial persistence and dispersal of organisms and subsequent acquisition in addition to studies accounting for colonization pressure are required.

Conflict of interest statement

One of the authors of this paper was an author of one of the studies included in the meta-analysis. This author played no role in evaluating the bias related to this study, and the eligibility of this study for inclusion was verified independently by two other authors.

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Table I

Overview of studies

Study	Publication year	Study duration	Study setting (country)	Study design	Organisms evaluated
Huang *et al.*[6]	2005	20 months	USA	Cohort	VRE, MRSA
Mitchell *et al.*[18]	2014	24 months	Australia	Cohort	MRSA
Datta *et al.*[17]	2011	20 months	USA	Cohort	VRE, MRSA
Ajao *et al.*[19]	2013	93 months	USA	Cohort	ESBL-producing Gram negative
Drees *et al.*[20]	2008	14 months	USA	Cohort	VRE
Nseir *et al.*[15]	2011	12 months	France	Cohort	*Acinetobacter baumannii*, ESBL-producing Gram negative, *Pseudomonas aeruginosa*
Shaughnessy *et al.*[21]	2011	16 months	USA	Cohort	*Clostridium difficile*

VRE, vancomycin-resistant enterococci; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended spectrum β-lactamase.

Table II

Potential confounders and management

Potential confounder	Study					
	Drees *et al.*[20]	Huang *et al.*[6]	Nseir *et al.*[15]	Shaughnessy *et al.*[21]	Ajao *et al.*[19]	Mitchell *et al.*[18]
Antibiotic use	Collected and included in analysis	No adjustment[a]	Collected and included in analysis	Not discussed	Collected and included in analysis	Not discussed
Hand hygiene compliance	Considered[b]	Not discussed	Not discussed	Not discussed	Not collected[a]	Considered[b]
Comorbidities	Collected and included in analysis	Collected and included in analysis	Collected and included in analysis	Collected and included in analysis	Collected and included in analysis	Collected and included in analysis
Indwelling devices: drains, PICC lines, central lines, mechanical ventilation	Limited[c]	Not discussed	Collected and included in analysis[e]	Not discussed[d]	Not discussed	Not discussed
Selection bias: screened upon admission/entered into study	Limited bias. Admission, twice weekly and discharge	Limited bias. Admission and weekly	Limited bias. Admission and weekly	Unclear bias[f]	Limited bias. Admission, weekly and discharge	Limited bias. Admission and weekly

Colonization pressure	Collected and included in analysis	Not discussed	Collected and included in analysis	Not discussed	Collected and included in analysis	Not discussed
Length of stay	Considered	Considered	Considered	Considered	Considered	Considered
Type of patient rooms/areas studied	Private	Private	Private	Private	Private	Shared and private

PICC, peripherally inserted central catheter.

Not discussed: no discussion in the context of the study results. This includes no adjustment for this confounder or not stated as a limitation.

'Private' refers to a single room, not a shared room.

[a]Discussed as a limitation.

[b]No difference during the identified study period.

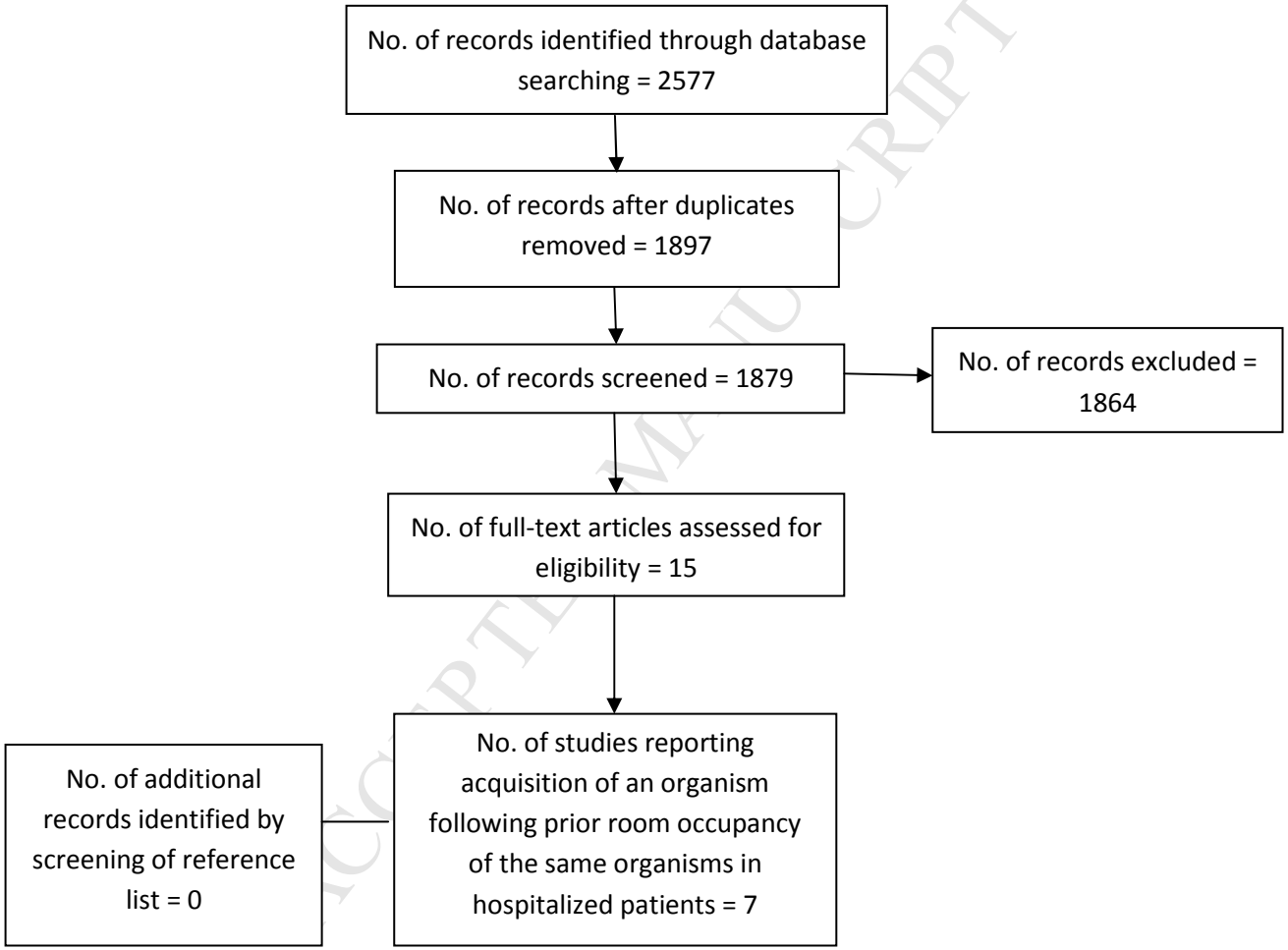
[c]Mechanical ventilation collected and included in the analysis.

[d]Confounder potentially of limited relevance to the infection studied.

[e]Data on central venous catheter, arterial catheter, urinary catheter, tracheostomy, and mechanical ventilation included.

[f]*Clostridium difficile* infection cases were reviewed to ensure that the patients had not been diagnosed with *Clostridium difficile* infection within the previous three months. Unclear whether the non-exposed patients were colonized.

Figure 1. PRISMA flowchart summarizing the search strategy.



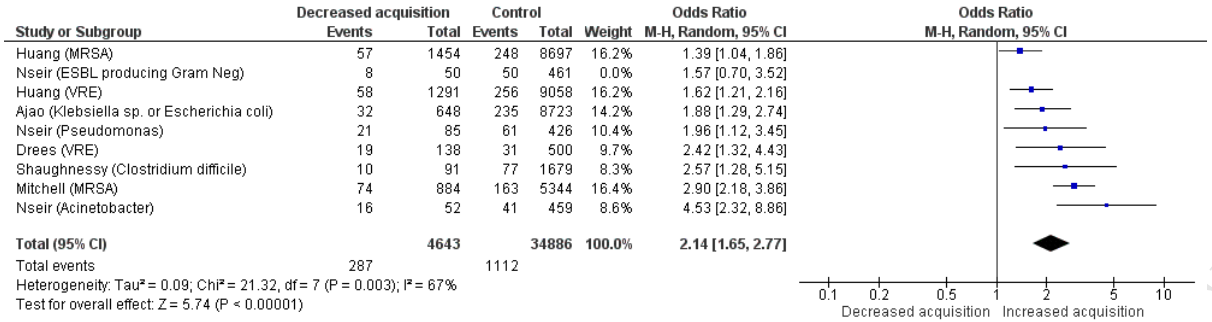


Figure 2. Risk of acquisition from prior room occupants by organism. M-H, Mantel–Haenszel; VRE, vancomycin-resistant enterococci; MRSA, meticillin-resistant *Staphylococcus aureus*; Ajao *et al*.'s study involved extended spectrum β-lactamase producing *Klebsiella* or *Escherichia coli* organisms. Acinetobacter: *Acinetobacter baumannii*; Pseudomonas: *Pseudomonas aeruginosa.* It was not possible to separate *Klebsiella* sp. and *Escherichia coli* data in the Ajao *et al*. study.

Author queries

1. Please confirm full postal address and telephone number for corresponding author.
2. Conflict of interest statement: please name authors referred to.
3. Fig. 2 caption: M-H defined correctly?