Approaches to multidrug-resistant organism prevention and control in long-term care facilities for older people: a systematic review and meta-analysis

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Review

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Abstract

Background: Current guidelines recommend infection prevention and control (IPC) interventions to limit the spread of multidrug-resistant organisms (MDROs) in long-term care facilities (LTCFs). Despite clear evidence of benefits in acute-care hospital settings, the effectiveness of IPC programmes in LTCFs has not been quantified.

Objective: To investigate the effects of IPC interventions on MDRO colonization and infections in LTCFs.

Data sources: Ovid MEDLINE, EMBASE, and CINAHL from inception to September 2020.

Eligibility criteria: Original and peer-reviewed articles examining the post-intervention effects of IPC interventions on MDRO colonization and infections in LTCFs for older adults.

Interventions: i) Horizontal interventions: administrative engagement, barrier precautions, education, environmental cleaning, hand hygiene, performance improvement, and source control; and ii) vertical intervention: decolonization.

Study appraisal and synthesis: We employed random-effects meta-analysis to estimate the pooled risk ratios (pRRs) for Methicillin-resistant Staphylococcus aureus (MRSA) colonization by intervention durations; and conducted subgroup analyses on different intervention components. Study quality was assessed using Cochrane risk of bias tools.

Results: Of 3877 studies initially identified, 19 were eligible for inclusion (eight randomized controlled trials (RCTs) and 11 non-RCTs). Studies reported outcomes associated with MRSA (15 studies), Vancomycin-resistant Enterococci (VRE) (four studies), Clostridium difficile (two studies), and Gram-negative bacteria (GNB) (two studies). Eleven studies included in the meta-analysis. The pRRs were closed to unity regardless of intervention durations (long: RR 0.81 [95%CI 0.60-1.10]; medium: RR 0.81 [95%CI 0.25-2.68]; short: RR 0.95 [95%CI 0.53-1.69]). All studies involving active administrative engagement reported reductions. The risk of bias was high in all but two studies.

Conclusions: Our meta-analysis did not show beneficial effects from IPC interventions on MRSA reductions in LTCFs. Administrative engagement was crucial in all programmes with reductions. Before more evidence is available, LTCFs should elucidate their goals and weigh cautiously for the benefits and risks before implementing IPC interventions, which may have potential negative impacts on residents. An alternative approach would be to reinforce strict compliance to standard precautions through administrative engagement. We call for high-quality trials with detailed execution and exit plans to refine the existing IPC strategies in LTCFs.

Introduction

The emergence of multidrug-resistant organisms (MDRO) is a major public health concern in the 21st century **[1]**. It limits the effective antimicrobial treatment options for infections and increases the morbidity, mortality, and health care costs in health care settings worldwide **[2–4]**.

Long-term care facilities for older people (short for “LTCFs”) play an important and unique role in MDRO transmission. They have long been regarded as reservoirs for antimicrobial resistance (AMR). Prevalence studies reported up to 32% of residents in LTCFs were colonized with Methicillin-resistant Staphylococcus aureus (MRSA) **[5–7]**. The homelike environment, where residents assemble in close proximity, such as frequently share recreation and dining areas, increases the risk of MRSA acquisition **[8,9]**. The high prevalence can also be attributable to the clustering of vulnerable individuals, who are often older, have chronic illnesses, and require external devices for sustained nursing care. These high-risk individuals commute between LTCFs and hospitals for medical appointments **[10,11]**, facilitating the intra- and inter-facility transmission of MDROs **[12]**.

Although research and development of new antibiotics are considered the most direct approach to combat MDROs, financial and technical challenges, such as low profitability yield and lengthy clinical testing, hinder the process **[13]**. Evidence suggests significant associations between levels of antibiotic consumption and the incidence of antibiotic resistance at both the individual and community levels **[14,15]**. As a result, the use of antibiotics alone is not a sustainable solution to avert the AMR crisis.

Infection prevention and control (IPC) provides an alternative and practical solution to reduce MDRO colonization and prevent harms caused by MDRO infections. This approach comprises two types of interventions: horizontal and vertical. Horizontal interventions aim to control the transmission of multiple pathogens simultaneously by implementing standardized practices, while vertical strategies target to reduce the transmission of specific pathogens with active screening programmes **[16]**. National and local guidelines recommend IPC interventions to control MDRO transmission in LTCFs **[17–19]**. Both strategies in LTCFs are predominately adopted from acute-care settings or based on consensus opinions from experts. Recent narrative reviews have described the types of interventions without summarizing the data **[20–22]**. Studies quantifying intervention effects on MDROs are mostly conducted in acute-care hospitals, which have different contact patterns from LTCFs **[23,24]**. A 2013 Cochrane review attempted to assess the effects of IPC interventions on MDRO transmission in LTCFs **[25]**, but identified only one

clustered randomized controlled trial (RCT), and hence could not provide any pooled effect estimates **[26]**. That RCT reported interventions improved staff practice but had no effects on the prevalence of MRSA among residents. Two other systematic reviews showed contrasting findings in reducing general infection rates in LTCFs **[27,28]**. Lee et al. supported the effectiveness of behavioral change strategies using education, monitoring, and feedback with 17 studies **[27]**, while Uchida's team reported no effect of interventions from 24 articles **[28]**. But both of them have not addressed MDRO infections. Although the number of studies has increased over the years, the evidence has not been updated and remains inconclusive.

In light of this, our systematic review aims to renew the existing evidence and quantify the effects of IPC interventions on MDRO transmission, in terms of reductions in colonization and associated infections in LTCFs, and to evaluate the quality of current evidence.

Methods

Search strategies and selection criteria

We searched for studies published from inception to September 2020 with the following electronic databases: "Ovid MEDLINE", "Ovid MEDLINE Epub ahead of print", In-Process & Other Non-Indexed Citations", "EMBASE", and "CINAHL". A combination of search terms encompassing four domains was developed: MDROs, LTCFs, IPC interventions, and colonization or infections **(see Additional file 1)**. The study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework **[29]**. We include original, peer-reviewed articles that examined changes of MDRO colonization in the human body and infections following IPC interventions, but neither the outbreak reports nor studies without facility-specific estimates.

This review focuses on prevalent and clinically concerned MDROs in LTCFs: MRSA, Vancomycin-resistant Enterococci (VRE), multidrug-resistant gram-negative bacteria (MDR-GNB), those producing extended-spectrum beta-lactamases, and others that are resistant to multiple classes of antimicrobial agents (i.e., Carbapenem-resistant Enterobacteriaceae (CRE), Carbapenemase-producing Enterobacteriaceae, and Clostridium difficile (C.diff.)) **[30]**.

We defined an LTCF as a public or private residential institution that primarily provides a high level of long-term personal and nursing care assistance to individuals who cannot live independently. Our review included studies specific to LTCFs for older people but excluded those facilities that provided specialized nursing care to other populations or adopted different care models from LTCFs **[31]**.

We categorized eight IPC interventions into either horizontal or vertical groups. Horizontal strategies included: (i) administrative engagement, (ii) barrier precautions, (iii) education, (iv) environmental cleaning, (v) hand hygiene, (vi) performance improvement, and (vii) source control; vertical intervention included decolonization only. We describe each IPC intervention in detail in an additional table **(see Additional file 2)**.

The primary outcome is MRSA colonization among residents in our study settings, where colonization referred to bacteria multiplication in the body without causing any infections. The microbiological assessment indicated the culture positivity in specimens from colonized individuals. We counted multiple positive cultures from the same resident as one colonization episode. "Acquisition" is interpreted as synonymous with "colonization". The secondary outcomes are other MDRO colonization and all MDRO infections.

Data extraction and quality assessment

Two authors (VW, YH) independently extracted data and assessed study quality. They identified the articles and subsequently screened through the full-text papers. Three categories of data were extracted: study characteristics, methodologies, and measured outcomes. The reference lists of relevant review articles from the search were screened for additional studies. We excluded any extended studies in the meta-analysis to avoid duplicate data.

The study quality was assessed using the revised Cochrane risk-of-bias tool (ROB2) for RCTs **[32]**, and the Cochrane Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool for non-randomized studies **[33]**. The risk of bias of each study was graded as high, with some concerns, and low in ROBs; similarly, it was graded as serious, moderate, and low in ROBINS-I. The risk-of-bias visualization tool synthesized the assessment and presented in plot **[34]**.

Any disagreements in data extraction and quality assessment were resolved by consensus between VW and YH or through consultation with a third reviewer (KOK).

Statistical analysis

Meta-analyses were performed using a random-effects model to estimate the pooled risk ratios (pRRs) with 95% confidence intervals (CIs). With the number of studies less than three or diverse measured outcomes for pooled analysis due to differences in definitions and assessment methods, only narrative synthesis of results were performed. We conducted meta-analyses on MRSA colonization and narrative syntheses on other outcomes. In addition to visual inspection of forest plots, we quantified the heterogeneity across studies using the I^2-statistics. Contour-enhanced funnel plot and Egger's test were used to evaluate the publication bias, particularly small-study effects **[35,36]**. However, the tests were

not conducted for subgroup meta-analyses with fewer than ten studies, as the power of the tests would be too low to differentiate chance from real asymmetry **[37]**.

Previous studies suggested that the effects of interventions varied by intervention durations **[38,39]**. Subgroup analyses by short (less than five months), medium (six to 11 months), and long (12 months or longer) durations were conducted. We further summarized pRRs by different combinations of interventions for studies reporting a long duration. Finally, post hoc sensitivity analyses were performed only to studies with concurrent control to assess the robustness of the results.

The package "metaphor" of R Studio version 4.0.2 was used to perform the meta-analyses and subgroup statistical analyses **[40,41]**. A p-value of less than 0.05 was considered statistically significant.

Results

Record retrieval

The search strategy identified 3877 articles. Following removal of duplicates, 2776 articles remained. After screening titles and abstracts, 129 articles were included for full-text review **(Fig. 1)**. Nineteen articles met the inclusion criteria and were included in the systematic review **[26,42–59]**.

Characteristics of included studies

Among the 19 articles included, there were eight RCTs **[26,42,45–47,51,54,55]**, eight uncontrolled before-after studies **[43,44,48–50,53,57,58]**, one controlled before-after studies **[52]**, and two interrupted time-series studies **[56,59]**. One article was an extended study of another **[42,46]**. Two articles were from the same study but presented different outcomes **[54,55]**. Fifteen identified studies associated with MRSA **[26,42,44–52,54,55,58,59]**, four with VRE **[51,53,56,59]**, two with C.diff. **[56,57]**, and two with GNB **[43,51]**. Twelve studies were conducted in the United States **[44,49–59]**, four in Europe **[26,42,46,48]**, two in Asia **[45,47]**, and one in the Middle East **[43] (**Table 1**)**.

Table 1
Characteristics of included studies

Author (year)	Country	Study design	Control type	MDRO type	Measured outcomes	Staff compliance measured	Interventions (duration, months)	No. of residents analyzed (baseline)	Summary findings
Baldwin et al. (2010) [26]	Northern Ireland	Clustered RCT	Concurrent	MRSA	Colonization	Y	ED + PI (3, 6, 12)	793	No effect.
Bellini et al. (2015) [42]	Switzerland	Clustered RCT	Concurrent	MRSA	Colonization; infections	N	DC + EC + ED (12)	4750	No effect.
Ben-David et al. (2019)[43]	Israel	Uncontrolled before-after	Historical	CRE	Acquisition	N	AE + BP + ED + PI (84)	~ 20000	Reduction.
Bowler et al. (2010) [44]	United States	Uncontrolled before-after	Historical	MRSA	Colonization	N	DC + EC + ED (13)	687	Reduction.
Chuang et al. (2015) [45]	Hong Kong SAR, China	Clustered RCT	Concurrent	MRSA	Colonization	Y	BP + EC + ED + HH + PI (6, 9, 12, 15)	2776	No effect.
Hequet et al. (2017) [46]	Switzerland	Clustered RCT	Concurrent	MRSA	Colonization	N	DC + EC + ED (12, 60)	NS	No effect.
Ho et al. (2012)[47]	Hong Kong SAR, China	Clustered RCT	Concurrent	MRSA	Infections	Y	AE + ED + HH + PI (4)	2407	Reduction.
Horner et al. (2012) [48]	United Kingdom	Uncontrolled before-after	Historical	MRSA	Colonization	Y	ED + PI (6, 9, 12, 18, 24)	2237	No effect.
Jaqua-Stewart et al. (1999) [49]	United States	Uncontrolled before-after	Historical	MRSA	Colonization; infections	N	BP + DC + ED + SC (12, 39)	42	Reduction.
Kauffman et al. (1993)[50]	United States	Uncontrolled before-after	Historical	MRSA	Colonization	N	DC (7, 5)	321	Reduction.
Mody et al. (2015) [51]	United States	Clustered RCT	Concurrent	MRSA; VRE; GNB	Colonization; infections	Y	BP + ED + HH + PI (24)	418	Reduction.
Morgan et al. (2019) [52]	United States	Controlled before-after	Concurrent	MRSA	Acquisition; infections	N	BP (48)	75414	No effect.
Ostrowsky et al. (2001)[53]	United States	Uncontrolled before-after	Historical	VRE	Colonization	Y	BP + EC + ED + HH (12, 24)	5221	Reduction.
Peterson et al. (2016)[54]	United States	Clustered RCT	Concurrent	MRSA	MRSA infections	N	DC + EC + ED + SC (12, 24)	7069	Reduction.
Schora et al. (2014) [55]	United States	Clustered RCT	Concurrent	MRSA	Colonization	N	DC + EC + ED + SC (12, 24)	4424	Reduction.
Schweon et al. (2013)[59]	United States	Uncontrolled interrupted time series	Historical	MRSA; VRE; C.diff.	Infections	Y	AE + ED + HH + PI (22)	NS	No effect.
Silverblatt et al. (2000)[56]	United States	Uncontrolled interrupted time series	Historical	VRE	Colonization	N	BP + DC + ED + HH (28)	NS	Absence of outcome.

Abbreviations:

AE, administrative engagement; BP, barrier precautions; BSI, bloodstream infection; C.diff., Clostridium difficile; DC, decolonization; ED, education; EC, environmental cleaning; GNB, Gram-negative bacteria; HH, hand hygiene; MRSA, methicillin-resistant Staphylococcus aureus; PI, performance improvement; NS, not specified; SC, source control; UC, usual care; VRE, vancomycin-resistant enterococci

Author (year)	Country	Study design	Control type	MDRO type	Measured outcomes	Staff compliance measured	Interventions (duration, months)	No. of residents analyzed (baseline)	Summary findings
Singh et al. (2018) [57]	United States	Uncontrolled before-after	Historical	C.diff	C.diff infections	N	AE + BP + EC + ED + HH (33)	~ 9381	Reduction.
Thomas et al. (1989)[58]	United States	Uncontrolled before-after	Historical	MRSA	Colonization; MRSA infections	N	BP + ED (3)	164	Reduction.
Abbreviations:									
AE, administrative engagement; BP, barrier precautions; BSI, bloodstream infection; C.diff., Clostridium difficile; DC, decolonization; ED, education; EC, environmental cleaning; GNB, Gram-negative bacteria; HH, hand hygiene; MRSA, methicillin-resistant Staphylococcus aureus; PI, performance improvement; NS, not specified; SC, source control; UC, usual care; VRE, vancomycin-resistant enterococci									

Effectiveness of IPC interventions on MRSA colonization

Of the 12 studies on MRSA colonization, the directions of intervention effects were divided: half of the studies found insignificant or no effects **[26,42,45,46,48,52]**, while the other half reported significant reductions **[44,49–51,55,58]**. Seven studies involved at least three intervention components **[42,44–46,49,51,55]**. The most common interventions were education (83%) **[26,42,44–46,48,49,51,55,58]**, decolonization (50%) **[42,44,46,49,50,55]**, and environmental cleaning (42%) **[42,44–46,55] (Fig. 2)**. The interventions included in each studies are summarized in a table **(see Additional file 3)**. Two studies evaluated the individual effects of barrier precautions and decolonization. One showed that barrier precautions alone did not affect MRSA acquisition controlling for patient demographics, comorbidity, and year of admission (odds ratio, 0.97 [95%CI 0.85–1.12]; p = 0.71) **[52]**, while the other reported decolonizing both the nares and wounds yielded a reduction in mean monthly colonization rate from 22.7–11.5% (p = 0.0001) **[50]**. Only four studies reported changes in compliance followed by the interventions: three on hand hygiene **[26,45,48]**, and one on barrier precautions **[51]**. However, the evaluation methods were not standardized **(see Additional file 4)**.

We excluded Hequet et al. (2017) since it is a follow-up study from Bellini et al. (2015) **[42,46]**. Our meta-analysis of 11 articles showed that IPC interventions were not associated with the reductions in MRSA colonization regardless of the intervention durations (long: pRR 0.81 [95%CI 0.60–1.10]; medium: pRR 0.81 [95%CI 0.25–2.68]; short: pRR 0.95 [95%CI 0.53–1.69]) **[26,42,44,45,48–52,55,58]**. We present the forest plot for studies evaluating MRSA colonization in an additional figure **(see Additional file 5)**. Nevertheless, IPC interventions including decolonization reported reductions, albeit statistically insignificant, in colonization (range: pRR 0.34 [95%CI 0.22–0.53] to 0.88 [95%CI 0.71–1.10]) while interventions involving barrier precautions (range: pRR 1.00 [95%CI 0.75–1.33] to 1.02 [95%CI 0.74–1.41]) and education (pRR 1.06 [95%CI 0.91–1.23]) had no effects on MRSA colonization **(Fig. 3)**. Our findings did not change when restricted only to studies with concurrent control (long: pRR 0.94 [95%CI 0.83–1.07]; medium: pRR 1.01 [95%CI 0.10-10.21]; short: RR 0.96 [95%CI 0.73–1.26]). The sensitivity analysis demonstrated a significant drop in the I^2 with long-term interventions to 1% (p = 0.41); the I^2 with medium-term interventions reduced only slightly to 77% (p = 0.04); and, the I^2 short-term intervention remained unchanged at 0%. The forest plot for sensitivity analysis is included as an additional figure **(see Additional file 6)**.

Effectiveness of IPC interventions on other outcomes

Three studies employing altogether barrier precautions, hand hygiene and education reported either reduced VRE colonization or free from new acquisition **[51,53,56]**. Of the two studies reporting reductions, one reported a cluster- and covariate-adjusted hazard ratio (HR) of 0.85 [95%CI 0.45–1.60] (p = 0.61) **[51]**, while another found a relative risk of 0.30 [95%CI 0.20–0.70] (p = 0.001) **[53]**. Two studies, which included barrier precautions, education, and performance improvement in their IPC programme, found decreases in GNB acquisition. One of them reporting administrative engagement decreased CRE acquisition from 0.5 per 10 000 patient-days at baseline to 0.3 per 10 000 patient-days two years after implementation **[43]**. The other study, which also included hand hygiene, reported an insignificant cluster- and covariate-adjusted HR of 0.90 [95%CI 0.60–1.33] (p = 0.59) **[51]**. There were nine studies evaluating the effects of IPC interventions on infections, of which six reported reductions **[47,49,51,54,57,58]**, one had no infection episodes **[42]**, and two found no effects **[52,59]**. The six studies reporting reductions in infections summarized their results in various metrics with two reporting significant rate ratios ranged from 0.54 [95%CI 0.30–0.97] to 0.61

[95%CI 0.38–0.97] (p = 0.04) **[47,51]** and four showing relative reductions in infection rates ranging from 25.9–99.7% **[49,54,57,58]**. The opportunity for meta-analyses in other outcomes was limited due to heterogeneity in study designs and lack of studies.

Effectiveness of IPC interventions on MDRO outcomes involving administrative engagement

All studies actively involving the administrations reported reductions in either colonization or infections **[43,47,57,59]**, although one did not reach 5% significant level **[59]**. Among the studies that did not result in outcome reductions, both alluded their failures to lack of organizational commitment **[26,45]**.

Study quality

The risk of bias among 19 studies was generally high **(Fig. 4a and 4b)**. Of the eight RCTs **[26,42,45–47,51,54,55]**, all but one were at high risk of bias **[47]**. The only one with "some concerns" of bias reported significant reductions in MRSA infections requiring hospitalization following the implementation of a multimodal strategy **[47]**. The main reason for downgrading was that most studies did not appropriately adjust for the imbalance of missing outcome data in the analytical stage. The risk of bias assessment using ROB2 tool is presented in an additional table **(see Additional file 7)**. Similarly, we rated the risk of bias of one non-RCTs as "moderate" **[48]**, while others were as "serious" **[43,44,49,50,52,53,56–59]**. Unadjusted confounders without randomization was the main cause of degradation. The risk of bias assessment using ROBINS-I is available **(see Additional file 8)**. The controlled before-after study with a moderate-level risk of bias reported a small but insignificant increase in MRSA colonization after the implementation of an IPC programme [48].

Publication bias and small study effects

Funnel plot suggests differences in intervention tendency effects among smaller and larger studies **(see Additional file 9)**. Results from the majority of moderate-sized studies were statistically insignificant but that among studies with small sample size was generally significant. Small-sized studies with low methodological quality produced exaggerated positive intervention effect estimates. Egger's test also supports the presence of small study effects (intercept=-4.05; p = 0.03).

Discussion

Principal findings

This systematic review provides an up-to-date, critically appraised, and comprehensive literature syntheses of IPC interventions' effect on MDRO risk in LTCFs. Evidence was overall low in quality. Our meta-analysis did not demonstrate a significant decrease in MRSA colonization following IPC interventions. While the pooled estimates varied by intervention types, none produced significant results of which vertical intervention reduced MRSA colonization but horizontal interventions had no effects. Some smaller studies with low methodological quality produced exaggerated positive intervention effect estimates. IPC interventions may reduce VRE and GNB colonization while they had inconsistent effects on MDRO infections. Notably, administrative engagement is a core component in all successful IPC programmes to curtail MDRO colonization in LTCFs.

Comparison with previous literature

The decision to implement a "search and destroy" approach in LTCFs is controversial. While the MDRO control and prevention policies vary by settings, IPC interventions that rely upon identification, isolation, and decolonization of carriers, are commonly employed in acute-care hospitals. However, given the existing inconsistent supportive evidence on its effectiveness to MDRO control, implementation challenges in long-term care settings, and potential adverse impacts on the residents, a similar approach would have to be refined when adopting in resource-deficient LTCFs.

This review adds to the existing knowledge in several ways.

First, in line with the rising number of studies have questioned the benefits of barrier precautions in LTCFs **[60]**, this review did not find any supporting evidence on its effectiveness on MRSA reductions. An intervention study in the United States found barrier precautions had no impact on MRSA acquisition and infections **[52]**. Discontinuing barrier precautions was also not associated with the infection rates surge in a recent meta-analysis **[61]**. While evidence has not yet confirmed the effectiveness of barrier precautions, the detrimental impacts on residents have to be considered. Adopting barrier precautions constrains residents mobility and thus results in social stigma and isolation **[8]**. A systematic review summarized four main adverse outcomes related to barrier precautions: (i) less patient-health care worker contact time, (ii) delays in care and more non-infectious adverse events, (ii) increased patient depression and anxiety symptoms, and (iv) decreased patient satisfaction with care **[62]**. A survey revealed that isolation increased anxiety of both patients and family members **[63]**. Barrier precautions also imposes burden to health care workers, which compromises the compliance of hand hygiene and use of personal protective equipment as the number of isolated patients increases **[64]**. Overall, the risks of barrier precautions to residents seemed to offset its benefits on MDRO control in LTCFs.

Second, in terms of vertical intervention, the insignificant result also raises the questions on the long-run decolonization effects. Decolonization did not result in significant reductions in MRSA colonization. Although the use of decolonization among patients at risk of infections for a short period was supported **[65]**, its long-term use remains inconclusive. The effect of decolonization is temporary. A pilot study found a mean recolonization time of 3.8 weeks in an outpatient chronic haemodialysis unit **[66]**. Multiple colonization further complicates the effectiveness of

decolonization therapy in LTCFs, that decolonizing a single organism may not be adequate in reducing the risk of transmission. A nested case-control study reported that residents colonized with multidrug-resistant Acinetobacter baumannii were more likely to be colonized with another type of GNB **[67]**. Besides, decolonization therapy can lead to adverse reactions and increased secondary drug resistance. Of the patients decolonized with mupirocin in an RCT, 25% developed gastrointestinal adverse reactions, and 5% progressed into a high-level of drug resistance **[68]**. Therefore, the risk of MDRO colonization should be weighed against that of decolonization therapy.

Third, the role of administration has proven to be crucial in various contexts. A few studies suggested the direct and indirect benefits of engaging administrative commitment. A semi-structured interview of 20 clinicians revealed how hospital administrative engagement facilitated interventions in reducing surgical-site infections **[69]**. Similarly, a Thai national survey described an association between good-to-excellent administrative support and high adherence to environmental disinfection **[70]**. A cross-sectional survey reported that hospitals with more effective leadership showed better compliance in hand hygiene and less likely to report implementation barriers **[71]**. The health belief model can explain the association **[72,73]**: as perceived barriers to action is one of the six key factors that influence health behaviours, a supportive administrative engagement not only eliminates perceived barriers to implementation but also promotes learning, allocates adequate resources, and creates a facilitative and collaborative environment **[74]**.

Strengths and limitations

This study and its evidence base are affected by some inherent limitations. **First**, in the majority of the studies, very few data on adherence to IPC interventions was reported. However, the compliance of health care workers to IPC interventions greatly influences the assessment of their effectiveness. This bias would potentially shrink the estimates of the intervention effects toward the null. **Second**, the multiplicity of outcome measures could limit the potential to synthesize results. Most studies assessing multicomponent interventions increased the challenges of elucidating the effects of single-component interventions. Third, there was a presence of misclassification bias as studies did not report the routine interventions as a part of the IPC bundles. **Fourth**, we limited our meta-analysis to studies that reported MRSA colonization. However, this approach is prone to a high level of heterogeneity across studies due to different outcome definitions, study designs, and intervention components. Although we have grouped interventions into eight categories and performed subgroup analyses to identify the source of heterogeneity, it is still difficult to draw a definitive conclusion. **Fifth**, we found only two moderate-quality studies, and they provided inconsistent evidence of benefits. The low quality of study affects the internal validity of our review.

Despite the limitations, our review provides the first comprehensive synthesis of the association between IPC interventions and MDRO colonization and infections in LTCFs. In the absence of a clear benefit in LTCFs, strict compliance to standard precautions, which generally includes hand hygiene, environmental cleaning, and staff education, remains the optimal approach in curtailing the spread of MDROs. The effectiveness of an IPC programme relies on organizational commitment. Specifically, an engaged administration with clearly defined goals promotes compliance through adequate resource allocation and consultations to the frontline staff to identify and remove implementation barriers. For interventions that have potential negative impacts on residents, the trade-off between benefits and risks has to be evaluated carefully. Facility managers should construct a detailed execution plan specifying the timing, target groups, and exit strategy before implementation.

Conclusions

The proliferation of AMR limits treatment options of patients, from acute-care hospitals to LTCFs, and is no longer adequately addressed solely by research and development of antibiotics. Apart from curtailing inappropriate use of antibiotics, IPC interventions are rational steps in reducing the colonization and infection risks. However, existing evidence suggested IPC interventions without administrative engagement offers little effects on MDRO control. Securing the administrative commitment, LTCFs can reinforce the standard precautions in routine care of residents and weigh cautiously before applying barrier precautions and decolonization. Prospective studies can explore how strategies promoting prudent use of antibiotics, for instance, antimicrobial stewardship programmes and point-of-care testing, can work hand in hand with the refined IPC strategies to formulate a comprehensive programme in LTCFs.

List Of Abbreviations

AMR: Antimicrobial resistance

C.diff.: Clostridium difficile

CI: Confidence intervals

CRE: Carbapenem-resistant Enterobacteriaceae

GNB: Gram-negative bacteria

HR: Hazard ratio

IPC: Infection prevention and control

KOK: Kin On Kwok

LTCF: Long-term care facility

MDR: Multidrug-resistant

MDRO: Multidrug-resistant organism

MRSA: Methicillin-resistant Staphylococcus aureus

PRISMA: Preferred reporting items for systematic reviews and meta-analyses

P: P-value

pRR: Pooled risk ratios

RCT: Randomized controlled trial

ROB2: Revised Cochrane risk-of-bias

ROBINS-I: Cochrane risk of bias in non-randomized studies of interventions

RR: Risk ratios

VRE: Vancomycin-resistant Enterococci

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

This review was based on data extracted from published papers available in the public domain.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KOK and VW wrote the manuscript. KOK, VW, SYSW and WIW conceptualized the study, VW and HY collected and analyzed data, and approved the final version. KOK contributed to the funding of the research. All authors reviewed and approved the manuscript.

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Figures

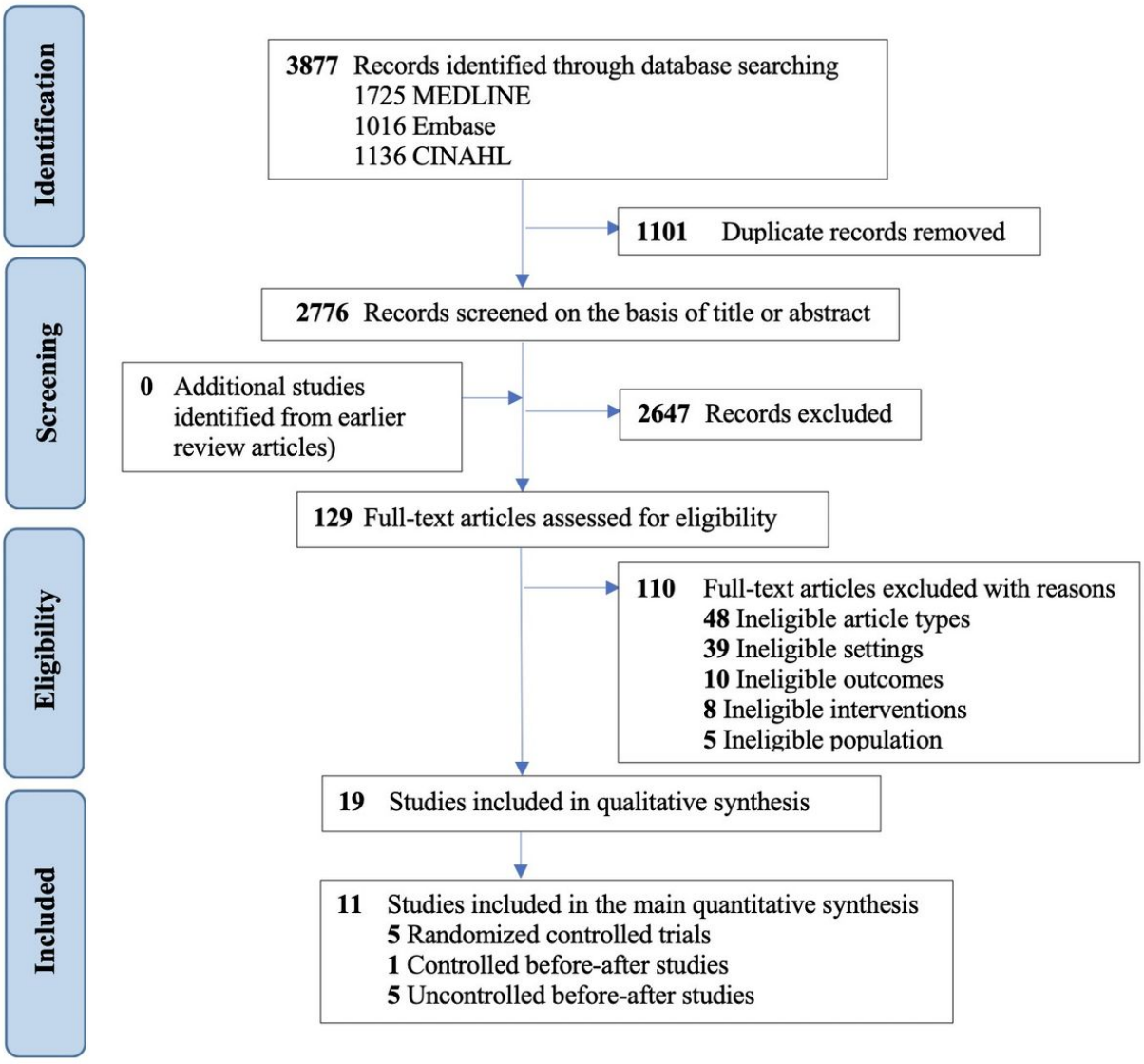

Figure 1

PRISMA flow diagram.

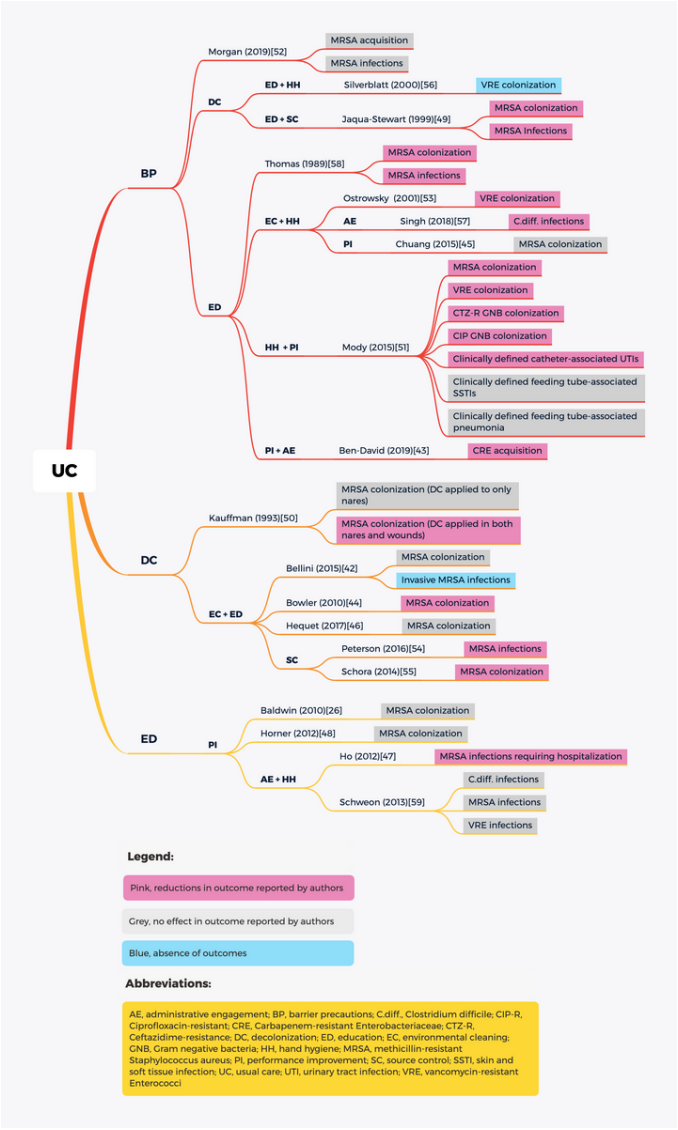

Figure 2

Components and outcomes of included studies.

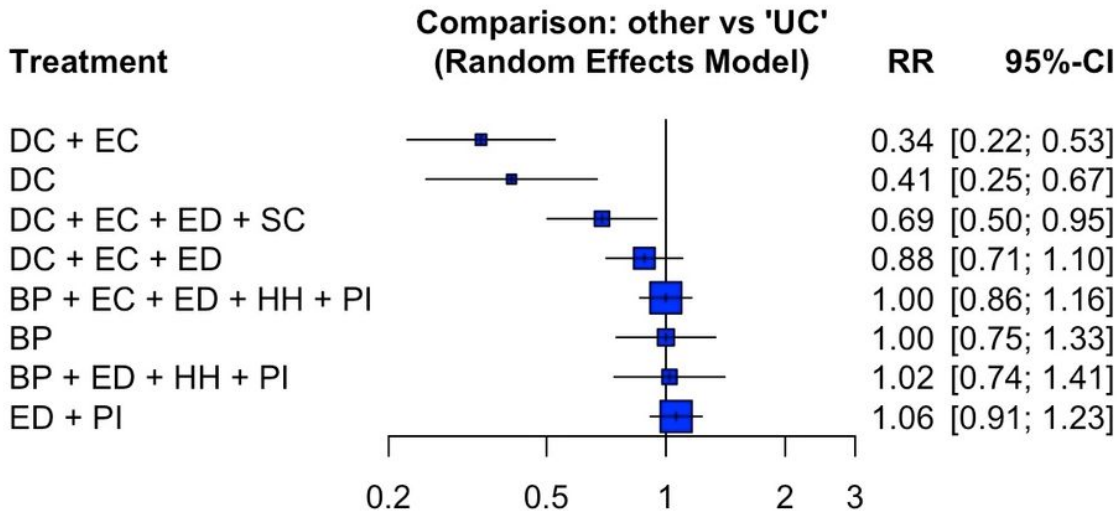

Figure 3

Forest plot for studies evaluating the long-term intervention effects on MRSA colonization by components.

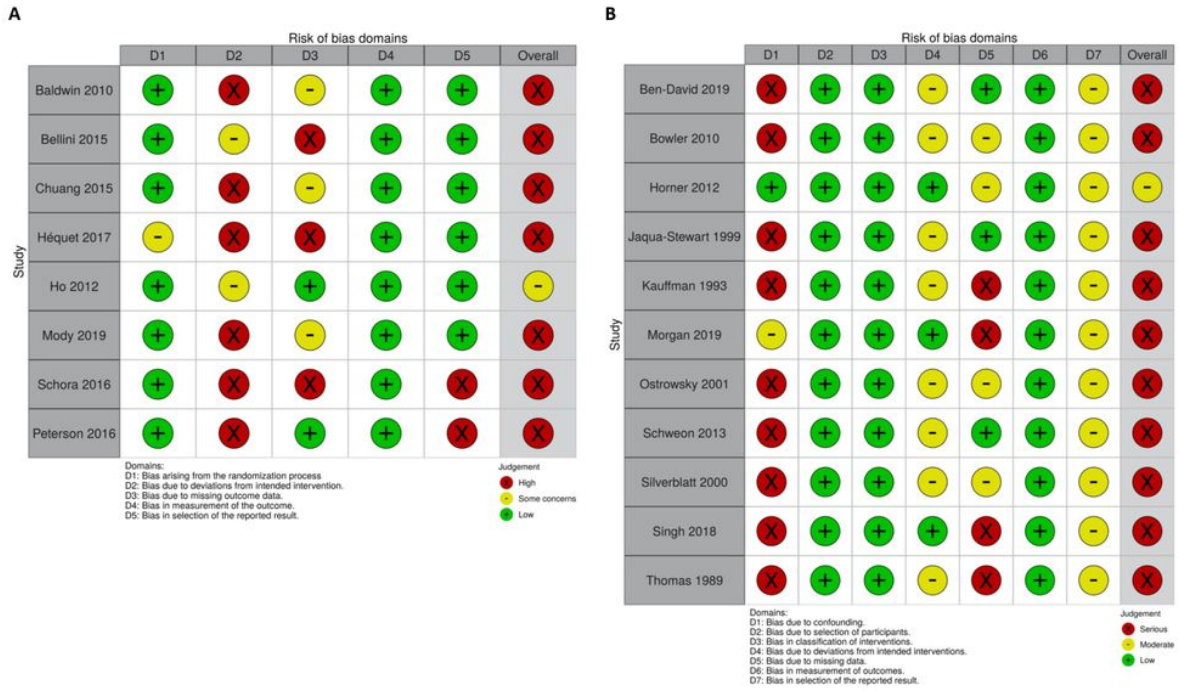

Figure 4

a. Risk of bias plot for randomized controlled trials. b. Risk of bias plot for non-randomized studies.

Supplementary Files

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