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Review

Umbrella review of economic evaluations of interventions for the prevention and management of healthcare-associated infections in adult hospital patients

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Background: Healthcare-associated infections (HCAIs) result in worse outcomes for patients and greater financial burden. An estimated 4.8 million HCAIs occurred in hospitals across Europe in 2022–23. Sixty-four percent of antibiotic-resistant infections in Europe are associated with healthcare. It is therefore vital to identify cost-effective interventions.

Aim: To summarize the cost-effectiveness evidence of interventions addressing HCAIs in hospitals.

Methods: An umbrella review was conducted to identify evidence on the cost-effectiveness of antimicrobial stewardship, infection prevention and control, and microbiology and diagnostic stewardship interventions for the prevention and clinical management of HCAIs in adult hospital patients. Medline, Embase, and EconLit databases were searched. A qualitative synthesis was undertaken.

Findings: Twenty-four systematic reviews met the inclusion criteria, with 101 separate analyses extracted and grouped into 10 intervention and 14 infection/organism categories, across various countries and settings. Most evidence focused on screening followed by contact precautions, isolation and/or decolonization, with selective screening most cost-effective. Most infection prevention and control bundles were cost-effective, although interventions were heterogeneous. The evidence base was sparse for the remaining intervention categories, with more research required. The limited evidence suggests that standalone environmental cleaning, hand hygiene, diagnostics, surveillance, antimicrobial stewardship, and decolonization interventions were mostly cost-effective. The cost-effectiveness of standalone personal protective equipment, and education and training interventions was mixed. Most interventions focused on meticillin-resistant *Staphylococcus aureus* and other Gram-positive infections, with more research needed on Gram-negative infections. The comparator was unclear in many extracted analyses.

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Conclusions: Cost-effective interventions to address HCAIs in hospitals exist, although more evidence is needed for most interventions.

Introduction

Healthcare-associated infections (HCAIs) are defined as 'an infection occurring in a patient during the process of care in a hospital or other health care facility, which was not present or incubating at the time of admission. This includes infections acquired in the hospital, but appearing after discharge, and occupational infections among staff of the facility' [1]. Data collected by the European Centre for Disease Prevention and Control estimated that 4.8 million HCAIs occurred annually in acute care hospitals across Europe in 2022—23, which was up from 4.5 million in 2016—17 and 3.2 million in 2011—12 [2—4]. HCAIs lead to worse outcomes for patients, including poorer health, longer hospital stays and even death, resulting in greater financial burden for healthcare payers. Furthermore, HCAIs are often resistant to antibiotics, with 64% of all infections with antibiotic-resistant bacteria across Europe associated with healthcare [5]. Antibiotic-resistant infections resulted in almost 36,000 attributable deaths across Europe in 2020 [6].

There is therefore a clear need for cost-effectiveness evidence to support decision-making on the most appropriate interventions for the prevention and clinical management of HCAIs, and infections resistant to antibiotics, in the context of limited healthcare budgets. Capturing intervention outcomes with a generic measure, such as quality-adjusted life-years (QALYs) or disability-adjusted life-years (DALYs), as well as condition-specific measures, such as infections avoided, is vital for decision-makers to rationally allocate resources. It is also important to consider the context of the intervention, as an intervention that is cost-effective in one setting is not necessarily cost-effective in another and may depend on factors such as the incidence of infections, prevalence of antibiotic resistance, and organization of healthcare systems.

Multiple systematic reviews have recently been published examining the cost-effectiveness of different interventions tackling HCAIs and antimicrobial resistance (AMR) [7—12]. An umbrella review (i.e. a systematic review of systematic reviews) was therefore appropriate to meet the aims of this review [13]. Specifically, the objective was to summarize the cost-effectiveness evidence of interventions addressing HCAIs and AMR in hospitals. To achieve this objective, we sought to answer the following research question: What is the cost-effectiveness of antimicrobial stewardship (ABS), infection prevention and control (IPC), and microbiology and diagnostic stewardship (MDS) for the prevention and clinical management of HCAIs in adult hospital patients, with a particular focus on infections resistant to antibiotics?

Methods

The umbrella review was registered on PROSPERO (CRD42024544387) [14]. A rapid methodological approach was applied according to best practice [15]. The review was reported in line with the latest Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Appendix S2) [16].

Eligibility criteria

The PICO (Participants, Interventions, Comparisons, Outcomes) framework was used to establish the eligibility criteria. Retrieved records were included if they met the following criteria: peer-reviewed systematic review; adult hospital patients; ABS, IPC and MDS interventions for the prevention and clinical management of HCAIs, including infections resistant to antibiotics, compared to an alternative intervention option (e.g. standard practice, no intervention); reporting cost-effectiveness evidence. Reviews that only considered low- and/or middle-income countries were excluded.

ABS is a coherent set of integrated actions with the aim to promote the responsible and appropriate use of antimicrobials, such as education, auditing, broad-spectrum antibiotic restrictions, and shortening of treatment duration. IPC consists of interventions such as guidance and standards, education and training, hand hygiene, personal protective equipment (PPE), environmental cleaning and governance. MDS consists of interventions such as microbiological testing and rapid diagnostic workflows to enable targeted therapy of appropriate antimicrobials.

The PROSPERO protocol reports the inclusion/exclusion criteria in detail [14].

Identification of reviews

Four key concepts were used to create the search strategy: (1) HCAI, (2) AMR, (3) economic evaluation and (4) systematic review. Search strategies were created by an information scientist, N. Pearce-Smith, and peer-reviewed by a second information scientist. Known papers were used to test the effectiveness of the search strategy. Databases were searched using the following strategy: (1 OR 2) AND 3 AND 4. The full search strategy is presented in Supplementary Appendix S3. OVID Medline ALL (1946 to April 9th, 2024), OVID Embase (1974 to April 9th, 2024) and EBSCO EconLit (1996 to April 3rd, 2024) were searched on April 10th, 2024 with no date or language limits to identify studies. Deduklick was used to deduplicate studies [17]. Included reviews were used for backward and forward citation searching using citationchaser [18]. Records were exported to EndNote for deduplication and to identify systematic reviews to be screened.

All records were screened by at least one reviewer. A randomly selected 20% sample of records was independently screened on title/abstract and full text in Rayyan by E.A. and J.P. to ensure that the inclusion/exclusion criteria were applied appropriately, with disagreements resolved by consensus [19]. The remaining records were screened by J.P.

Reasons for exclusion were documented at full text review (Figure 1).

The corrected covered area (CCA) was calculated to measure the level of publication overlap in the included reviews, i.e. the same underlying studies being included in multiple reviews. The CCA divides the frequency of repeated occurrences of the index publication (i.e. the first occurrence of an underlying study) in other reviews by the product of index publications and reviews, reduced by the number of index publications [20]. The CCA can vary from 0%, no overlap of underlying studies, to 100%, complete overlap. Overlap of 0–5% is considered 'slight', 6–10% 'moderate', 11–15% 'high', and >15% 'very high', and the selection of reviews should be critically assessed when the degree of overlap is substantial [21]. Only underlying studies that contributed to the data extracted for this umbrella review were included in the CCA calculation.

Data extraction

A bespoke data extraction form was created in Excel and finalized after piloting. Specific data extraction items are reported in Supplementary Appendix S4. Data from a randomly selected 20% of included reviews was independently extracted by E.A. and J.P. to ensure that the appropriate data were extracted, with disagreements resolved by consensus. J.P. extracted data from the remaining reviews.

Data were extracted separately for each intervention–infection/organism combination reported by a review. For example, if a review reported the cost-effectiveness of hand hygiene interventions for HCAIs, environmental cleaning for HCAIs, and decolonization for meticillin-resistant *Staphylococcus aureus* (MRSA), data were extracted for each of the analyses in three separate rows in the data extraction form.

Quality assessment

The quality of included reviews was assessed using the JBI Checklist for Systematic Reviews and Research Synthesis [22]. The critical appraisal tool is made up of 11 items, each with one of four options: yes, no, unclear, not applicable. To assess the overall quality of a review, a score of 1 was awarded for a yes, 0 for a no or unclear, and non-applicable items were excluded. A review scoring >70% was classified as high quality, 50–70% medium quality, and <50% low quality [23,24].

Quality was assessed independently by E.A. and J.P. for a randomly selected 20% of included reviews to ensure the checklist was applied appropriately, with disagreements resolved by consensus. J.P. assessed the quality of the remaining reviews.

Data synthesis

A qualitative synthesis was undertaken given the heterogeneity in the geographies, settings, conditions, and interventions of interest, and the natural variation in country-specific unit costs and different cost-effectiveness guidelines.

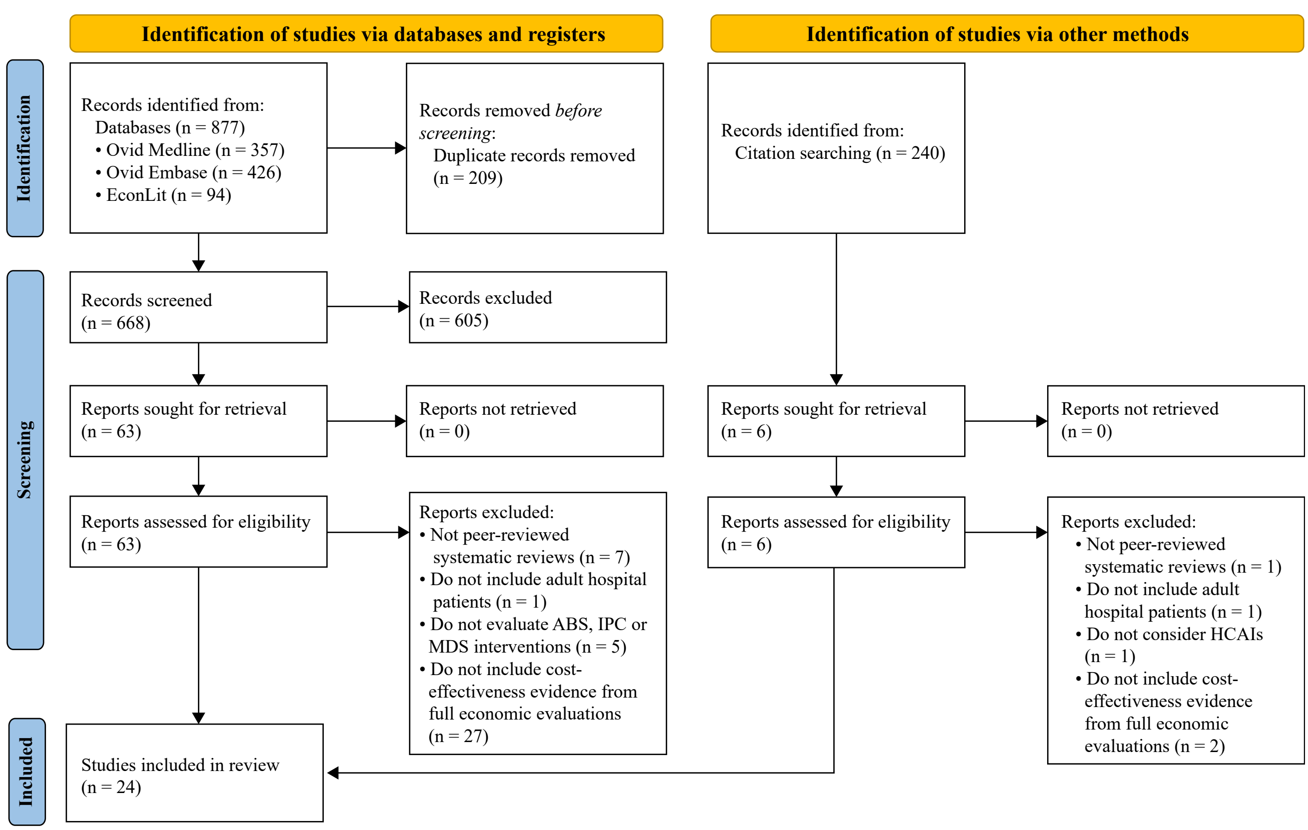


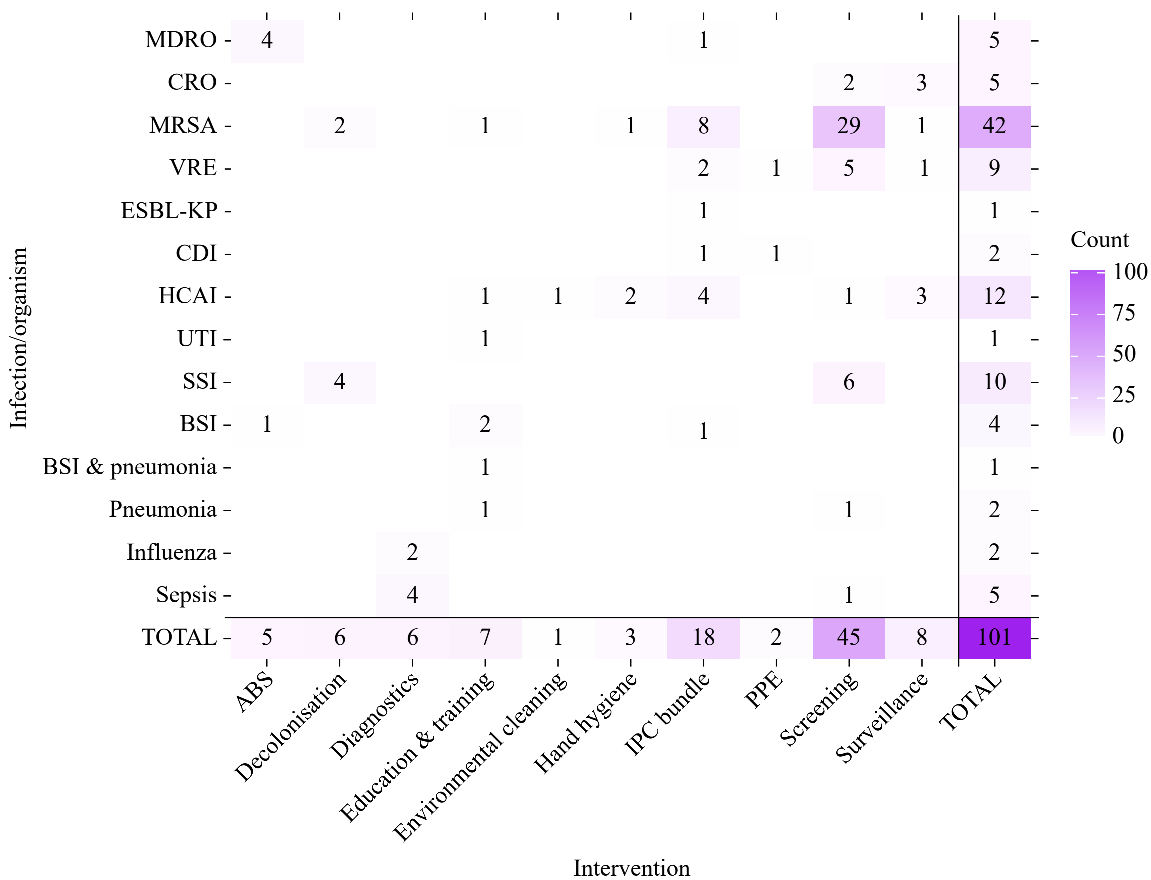
Figure 1. PRISMA flow diagram for identification of studies. ABS, antimicrobial stewardship; IPC, infection prevention and control; MDS, microbiology and diagnostic stewardship; HCAI, healthcare-associated infection.

Therefore, quantitative data analysis was not undertaken. Instead, descriptive conclusions on the cost-effectiveness of different interventions were drawn, based on the evidence presented in the included systematic reviews. Interested readers can find the quantitative data extracted from the included reviews in the full data extraction provided in Supplementary Appendix S6.

Interventions that were conceptually similar were grouped into one of 10 categories: (1) ABS; (2) screening followed by contact precautions, isolation, decolonization, or a combination of these; (3) IPC bundle (i.e. multimodal interventions incorporating more than one infection control activity); or standalone (4) decolonization (i.e. interventions to eliminate or reduce patient colonization); (5) diagnostics (i.e. method of diagnosis); (6) environmental cleaning (i.e. cleaning and disinfection of surfaces and equipment); (7) hand hygiene (i.e. cleaning hands); (8) PPE (i.e. specialist clothing or equipment); (9) surveillance (i.e. ongoing monitoring of HCAIs); and (10) education and training (i.e. material to promote appropriate behaviours and procedures).

HCAIs were grouped into one of 14 infection/organism categories, depending on the level of detail reported by the review: (1) multidrug-resistant organisms (MDROs); (2) carbapenem-resistant organisms (CROs); (3) MRSA; (4) vancomycin-resistant enterococci (VRE); (5) extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* (ESBL-KP); (6) *Clostridioides difficile* infection (CDI); (7) HCAI; (8) urinary tract infection (UTI); (9) surgical site infection (SSI); (10) bloodstream infection (BSI); (11) BSI and pneumonia; (12) pneumonia; (13) influenza; (14) sepsis. HCAIs were categorized based on how the HCAI of interest was reported in the given systematic review. The infection/organism categories include various levels of detail because of the differences in reporting results across the included systematic reviews. For example, MDROs and CROs were both included as separate categories, even though CROs are a subset of MDROs, because some reviews reported results across all MDROs of interest, whereas others focused on specific subsets. Similarly, HCAI was included as a category since — although all other included categories are a subset of HCAIs — some reviews reported results across all HCAIs of interest, so it was not feasible to disaggregate the infection/organism any further.

The quantity of evidence was summarized in a heat map, with infection/organism on the vertical axis, intervention on the horizontal axis, and a count for the number of analyses extracted for each intervention—infection/organism combination (Figure 2). Darker shades signify a higher count. Although some of the intervention—infection/organism



Infection/organism	ABS	Decolonisation	Diagnostics	Education & training	Environmental cleaning	Hand hygiene	IPC bundle	PPE	Screening	Surveillance	TOTAL
MDRO	4						1				5
CRO									2	3	5
MRSA		2		1		1	8		29	1	42
VRE							2	1	5	1	9
ESBL-KP							1				1
CDI							1	1			2
HCAI				1	1	2	4		1	3	12
UTI				1							1
SSI		4							6		10
BSI	1			2			1				4
BSI & pneumonia				1							1
Pneumonia				1					1		2
Influenza			2								2
Sepsis			4						1		5
TOTAL	5	6	6	7	1	3	18	2	45	8	101

Figure 2. Quantity of evidence heatmap by intervention and infection/organism category. ABS, antimicrobial stewardship; IPC, infection prevention and control; PPE, personal protective equipment; MDRO, multidrug-resistant organism; CRO, carbapenem-resistant organism; MRSA, meticillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; ESBL-KP, extended-spectrum β-lactamase-producing *Klebsiella pneumoniae*; CDI, *Clostridioides difficile* infection; HCAI, healthcare-associated infection; UTI, urinary tract infection; SSI, surgical site infection; BSI, bloodstream infection.

combinations in Figure 2 are not applicable or feasible in practice (e.g. decolonization for ESBL-KP), the figure succinctly provides a comprehensive and detailed summary of the quantity of evidence identified.

The cost-effectiveness result of each extracted analysis was grouped into one of three mutually exclusive categories: yes — intervention was cost-effective; mixed — cost-effectiveness was context dependent; no — intervention was not cost-effective. The cost-effectiveness results were also summarized in a heat map, with a count of each cost-effectiveness category for the intervention—infection/organism combination (Figure 3). Darker shades signify a higher count. Analyses were excluded from the cost-effectiveness heat map if the cost-effectiveness comparator was unclear, or if the intervention and comparator were grouped in the same intervention category (e.g. polymerase chain reaction (PCR) compared to culture test for screening MRSA). If a review reported that it found no cost-effectiveness evidence for a particular intervention it was also excluded from the heat map.

The narrative write-up was presented by intervention category and organized by infection/organism within this. Information is provided on intervention, cost-effectiveness, comparator and setting, if it was more specific than hospital-wide. An overview of the synthesized findings for each intervention category is presented in Table I, which includes information on the quantity (i.e. number of reviews included) and quality (i.e. overall score on the JBI checklist) of evidence.

Results

Figure 1 shows that a total of 668 unique records were retrieved through the database searches, with 605 excluded after title/abstract screening. Of the 63 records screened on full text, 23 reviews were included. Backward and forward citation searching of these 23 reviews identified 240 unique records. Two hundred and thirty-four records were excluded after title/abstract screening and five were excluded after full text screening. Therefore, a total of 24 reviews were included for synthesis in this umbrella review.

Study characteristics

Characteristics of the included systematic reviews are presented in Supplementary Appendix S1, with full data extraction provided in Supplementary Appendix S6.

Publication year ranged from 2003 to 2024, with most ($N = 13$) of the reviews published from 2020 onwards. Search term periods ran up to 2023 for two reviews. Half of the reviews did

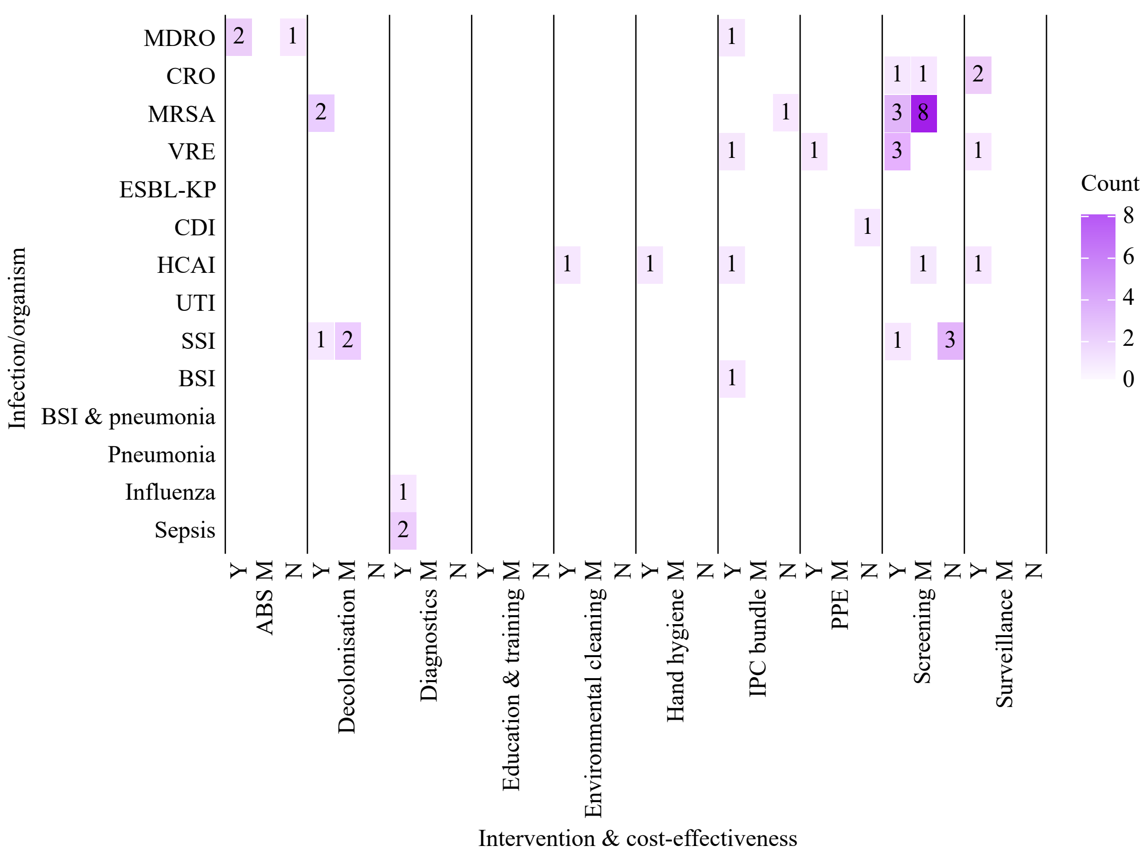


Figure 3. Cost-effectiveness heatmap by intervention and infection/organism category. Y, yes, intervention was cost-effective; M, mixed, cost-effectiveness was context dependent; N, no, intervention was not cost-effective; ABS, antimicrobial stewardship; IPC, infection prevention and control; PPE, personal protective equipment; MDRO, multidrug-resistant organism; CRO, carbapenem-resistant organism; MRSA, meticillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; ESBL-KP, extended-spectrum β-lactamase-producing *Klebsiella pneumoniae*; CDI, *Clostridioides difficile* infection; HCAI, healthcare-associated infection; UTI, urinary tract infection; SSI, surgical site infection; BSI, bloodstream infection.

Table I
Results of the qualitative data synthesis

Intervention	No. reviews included	Reference(s)	Synthesized findings	Quality of evidence
ABS	4	[7,8,11,26]	Generally, ABS interventions were cost-effective, including dedicated ABS team consultations. Cost-effectiveness of point-of-care test guided antibiotic prescribing compared to standard practice was context dependent.	All four reviews were rated as high quality.
Decolonization	4	[7,8,27,28]	Generally, decolonization was cost-effective, including universal decolonization for MRSA in ICU compared to no decolonization, and decolonization for MRSA compared to patient isolation. Cost-effectiveness of preoperative and perioperative decolonization for SSI compared to standard practice was context dependent.	All four reviews were rated as high quality.
Diagnostics	2	[29,30]	Diagnostic interventions were cost-effective, including molecular and procalcitonin testing compared to standard practice, and point-of-care testing compared to clinical judgement and laboratory testing.	Both reviews were rated as medium quality.
Education and training	3	[9,27,31]	Evidence on the cost-effectiveness of standalone education and training interventions was mixed, with one review not finding any studies that met their minimum quality criteria. Simulation-based education interventions were cost-effective, whereas the cost-effectiveness of local protocols, guidelines and patient safety programmes was context dependent. The cost-effectiveness of a national guideline for MRSA was not cost-effective. The comparator was unclear for all interventions.	All three reviews were rated as high quality.
Environmental cleaning	1	[9]	Environmental cleaning interventions were cost-effective compared to standard practice.	The review was rated as high quality.
Hand hygiene	3	[9,27,32]	Hand hygiene improvement interventions were cost-effective for healthcare workers and patients, compared to standard practice.	All three reviews were rated as high quality.
IPC bundle	9	[7,9,27,31–36]	IPC bundle interventions were mostly cost-effective, although there was considerable heterogeneity between the interventions that were included in the nine reviews. The comparator was also unclear in many of the analyses.	All nine reviews were rated as high quality.
PPE	2	[7,9]	Evidence on the cost-effectiveness of PPE is mixed. Gown and glove usage for VRE was cost-effective in ICU compared to glove usage alone, whereas glove and gown usage for CDI was not cost-effective for healthcare workers or visitors compared to standard practice.	Both reviews were rated as medium quality.
Screening followed by contact precaution, isolation,	18	[7–9,28,30–43]	Selective screening of high-risk patients or settings was cost-effective compared to do nothing and, in many cases, universal screening. Universal screening was cost-	Fifteen of the reviews were rated as high quality, with the other three of

decolonization, or a combination			effective in some contexts, particularly where prevalence and transmission of the infection/organism is high. Evidence on the cost-effectiveness of screening and decolonization was mixed, with results highly context dependent. Rapid diagnostic screening was cost-effective compared to standard screening techniques.	medium quality.
Surveillance	5	[7–10,12]	Surveillance interventions were cost-effective compared to standard practice and do nothing. Surveillance of CROs in ICU was cost-effective compared to do nothing, as was surveillance of VRE compared to standard practice and do nothing. Cost-effectiveness of WGS compared to standard techniques was context dependent.	All five reviews were rated as high quality.

ABS, antimicrobial stewardship; IPC, infection prevention and control; PPE, personal protective equipment; ICU, intensive care unit; MRSA, meticillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci; CRO, carbapenem-resistant organism; CDI, *Clostridioides difficile* infection; SSI, surgical site infection; WGS, whole-genome sequencing.

not explicitly state the geographical area of interest ($N = 12$), although among those that did, most considered global evidence ($N = 8$). Most reviews considered hospital interventions across all specialties ($N = 18$), while others focused on certain specialties, such as orthopaedics and medical or surgical units. Half of the reviews only reported results for one intervention type ($N = 12$), while several considered five or more ($N = 3$).

Eighteen reviews presented results for a single infection/organism, whereas the others considered multiple ($N = 6$). Some reviews reported results for HCAIs in general, whereas others focused on specific infections or organisms. The number of underlying studies included in each review varied from five to 383. However, not all underlying studies provided cost-effectiveness evidence, as some reviews also considered other outcomes, such as clinical effectiveness. The CCA, which measures the level of overlap in the underlying studies, was 1.5%, which equates to slight overlap (i.e. 0–5%) and is therefore within acceptable limits [20,21].

Quality assessment

Results of the quality assessment of the included reviews are provided in Appendix S5, broken down by each of the 11 items of the JBI Checklist for Systematic Reviews and Research Synthesis. Twenty of the 24 reviews were classified as high quality, with six scoring 100%, five scoring 90% and nine scoring 80%. The four other reviews were of medium quality, with scores ranging from 50% to 70%.

Information on the quality assessment tool used in each review, and the overarching results of the assessment, are provided in the full data extraction (Supplementary Appendix S6). Well-established quality assessment tools were used by most reviews ($N = 18$) to assess the risk of bias in their included studies, such as the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [25]. However, several created a bespoke tool ($N = 4$) and two reviews did not conduct any formal quality assessment. In summary, among the reviews that provided an overall summary of their quality assessment, the quality of the underlying studies varied. Only three reviews, all published from 2017 onwards, reported an overall high quality of evidence. Four reviews reported that the quality of evidence was generally low, and over half of the included studies in one review were excluded from the synthesis as they did not meet the minimum quality criteria. Most reviews reported that the quality of evidence was moderate, or moderate to low. Other reviews reported overall quality assessment scores but did not comment on whether it equated to low-, medium- or high-quality evidence.

Data synthesis

In total, 101 analyses were extracted from the 24 reviews, with data extracted separately for each intervention–infection/organism combination reported in each review.

Figure 2 shows the quantity of evidence identified for each intervention and infection/organism in a heat map. Screening followed by contact precautions, isolation, decolonization, or a combination of these, was the most common intervention, making up 45% of the analyses, followed by IPC bundle (18%), surveillance (8%), and education and training (7%). Evidence was most limited for environmental cleaning (1%) and PPE (2%).

The most common infection/organism was MRSA, accounting for 42% of the analyses. This was followed by analyses that reported on HCAI (12%) and SSI (10%). ESBL-KP, UTI, and BSI and pneumonia were each considered in only one analysis (1%).

A tabular summary of the qualitative data synthesis of the 101 analyses is provided in Table I. The heat map in Figure 3 presents the cost-effectiveness results graphically for the 45 analyses where the cost-effectiveness comparator was known and was not grouped in the same intervention category as the intervention.

A detailed summary of findings is presented below, organized by intervention category, and by infection/organism within this. An overarching summary of the results is then given.

Antimicrobial stewardship

Four of the 24 reviews considered the cost-effectiveness of ABS interventions, presenting five intervention–infection/organism combinations. All four reviews were rated high quality. Point-of-care (POC) test guided antibiotic prescribing was found to be cost-effective for MDROs compared to standard practice in one review [7], although cost-effectiveness varied by the country of interest in another review, with the comparator unclear [8]. The intervention was not cost-effective in a third review due to costs and antibiotic prescribing increasing in a maternity unit, when compared to standard practice [11]. Another review found that dedicated ABS team consultations were cost-effective for BSIs, although the comparator was unclear [8]. Finally, a fourth review also found that ABS interventions were cost-effective for MDROs compared to standard practice [26].

Decolonization

Four high-quality reviews presented evidence on the cost-effectiveness of standalone decolonization interventions, including six intervention–infection/organism combinations. In the context of MRSA, universal decolonization in intensive care unit (ICU) patients was cost-effective compared to interventions without decolonization, with decolonization also cost-effective compared to patient isolation [7,8]. Perioperative decolonization for SSI was cost-effective versus placebo in gastrointestinal surgery [27], although for cardiothoracic surgery the cost-effectiveness depended on willingness-to-pay (WTP) per SSI prevented, when compared to doing nothing [28]. One review also reported that preoperative decolonization for SSI was cost-effective for surgery, although the comparator was unclear, and in orthopaedic surgery it was only found to be cost-effective under certain efficacy and compliance scenarios, when compared to standard practice [28].

Diagnostics

Two reviews considered the cost-effectiveness of standalone diagnostic interventions, presenting evidence on six intervention–infection/organism combinations. Both reviews were rated medium quality. Molecular testing, including PCR, was cost-effective for sepsis when compared to standard practice, as was procalcitonin testing [29]. Similarly, POC testing for influenza and respiratory syncytial virus was cost-effective compared to clinical judgement and laboratory testing [30].

Education and training

Three high-quality reviews synthesized evidence on the cost-effectiveness of standalone education and training interventions, providing evidence on seven intervention–infection/organism combinations. One review did not find any studies that met the minimum quality criteria necessary for inclusion in their synthesis [9]. Another found that national guidelines for the prevention and control of MRSA in Germany were not cost-effective [31].

Simulation-based education interventions were cost-effective for central-line-associated BSIs in ICUs and hospitals more widely, as was an ICU patient safety programme, whereas guidelines to reduce the use of catheters were not cost-effective for urinary tract infections (UTIs) [27]. Finally, an oral care protocol in surgical ICUs was cost-effective in the context of ventilator-associated pneumonia [27]. However, the comparator was unclear for all education and training interventions.

Environmental cleaning

One high-quality review provided evidence of the cost-effectiveness of standalone environmental cleaning for HCAIs, finding that such interventions were cost-effective when compared to standard practice [9].

Hand hygiene

Three high-quality reviews summarized evidence on standalone hand hygiene interventions, each considering one intervention–infection/organism combination. One review found that hand hygiene interventions were cost-effective for HCAIs in hospitals, although the comparator was unclear [27]. Another review reported that they were cost-effective for healthcare workers (HCWs) and patients, but not for visitors, when compared to standard practice [9]. Finally, a third review found that hand hygiene interventions were cost-effective when considering MRSA in medical and surgical units, although the comparator was unclear [32].

IPC bundle

Nine high-quality reviews synthesized evidence on IPC bundles, including a total of 18 intervention–infection/organism combinations. One review reported that a proactive IPC programme – incorporating enhanced hand hygiene, environmental cleaning, increased nurse-to-patient ratio, and replacement of disposable supplies – was cost-effective compared to doing nothing for MDROs [7].

Another review found that four different IPC bundles were cost-effective for MRSA, including an ICU search-and-destroy policy, targeted surveillance alongside contact isolation, dedicated IPC personnel, pre-emptive isolation and screening without decolonization, and two other interventions combining various components of IPC [31]. A third review found that two IPC bundles for MRSA, including a search-and-destroy policy, were cost-effective, although another intervention that implemented Centers for Disease Control and Prevention contact precaution recommendations was not cost-effective, compared to glove use alone [32]. An IPC bundle made up of hand hygiene, PPE, and single room isolation to tackle MRSA was cost-effective, as was another IPC bundle addressing MRSA in a university hospital [33,34]. However, the comparator was unclear for all but one of the analyses considering MRSA.

An IPC bundle of 15 interventions for VRE was cost-effective in an oncology ward compared to screening and contact precautions only, as was a similar IPC bundle for VRE in medical and surgical units, although the comparator was unclear [32,35]. An IPC bundle to address an outbreak of ESBL-KP was cost-effective, although the comparator was unclear [27]. Similarly, a multimodal IPC bundle for CDI was cost-saving from the hospital perspective and produced better health outcomes [36]. Again, the comparator was unclear.

With respect to HCAIs, one review found that two different IPC bundles, one including hand hygiene, oral care, and central-line catheter care, were cost-effective, although the comparator was unclear [27]. Similarly, multimodal IPC bundles tackling HCAIs were cost-effective compared to standard practice [9]. However, another review found that the cost-effectiveness of an HCAI IPC bundle including hand hygiene, cultural change, surveillance, education, and training depended on the geographical region [36]. The same review also reported that an IPC bundle incorporating a care bundle, culture change, and performance feedback was cost-effective for BSIs when compared to standard practice [36].

Personal protective equipment

Two high-quality reviews presented evidence on standalone PPE interventions, each considering one intervention—infection/organism combination. One found that gown and glove usage for VRE in ICU was cost-effective compared to glove usage alone [7]. However, another reported that glove and gown usage to tackle CDI was not cost-effective compared to standard practice, for both HCWs and visitors [9].

Screening

Eighteen reviews synthesized evidence on screening followed by contact precautions, isolation, decolonization, or a combination of these. Fifteen of the reviews were high quality and three were medium quality. These studies included 45 intervention—infection/organism combinations.

Twenty-nine of these combinations considered MRSA. Selective screening of high-risk patients or settings was the most cost-effective approach [7,8,36—38], although universal screening was cost-effective in some instances where the prevalence of MRSA was high [37,38].

One review reported that universal rapid PCR screening for MRSA at admission was not cost-effective, and neither was presurgical PCR screening, although the comparator for both was unclear [31]. On the other hand, another review reported that universal single-culture MRSA screening was cost-effective compared to doing nothing, as was rapid PCR screening compared to standard practice [7]. Preadmission screening was found to be cost-effective if it prevented transmission of MRSA to as few as six patients, although the comparator was unclear [34]. Another review also found that PCR screening for MRSA was cost-effective, but the comparator was unclear, while the cost-effectiveness of screening using rapid diagnostics was dependent on the willingness-to-pay for averted isolation days [32]. Furthermore, rapid diagnostic screening was reported to be cost-effective compared to laboratory testing [30].

Screening, isolation, and decolonization of MRSA was cost-effective compared to do nothing, particularly when targeted towards high-risk patients and in scenarios with high MRSA transmission rates [7]. Another review reported the same, including for selective screening and screening of ICU patients, although the comparator was unclear [31]. The same authors also found evidence that universal MRSA screening and isolation was cost-effective compared to targeted screening, as was screening and isolation for ICU patients [31]. However, a further review reported that screening and isolation of high-risk patients on admission was cost-effective, although the comparator was unclear [33].

Moreover, screening and isolation was only found to be cost-effective if the prevalence of MRSA was high enough, isolation beds were utilized, and enough MRSA infections were averted and not substituted by meticillin-susceptible infections [39]. Screening and pre-emptive isolation, before receiving the results, was not cost-effective compared to no pre-emptive isolation [31]. Results for screening and decolonization were mixed, with one review reporting that it was likely to be cost-effective [8], while another found that it was not cost-effective compared to screening without decolonization [31].

With respect to CROs, one review found that screening and decolonization for carbapenem-resistant Enterobacteriaceae (CRE) in ICU patients was cost-effective compared to do nothing, whereas universal screening for carbapenemase-producing Enterobacterales was only cost-effective compared to doing nothing if prevalence levels were high enough [7].

Another review reported that VRE screening of high-risk hospital patients was cost-effective compared to doing nothing and standard practice, as was admission screening and active surveillance of ICU patients [35]. The review also found that VRE screening, contact precaution, and gown usage for HCWs and visitors was cost-effective compared to the same intervention without gown usage.

One review synthesized results across all HCAIs, finding that selective screening of high-risk patients was likely to be cost-effective across general wards and ICU, while there was no strong evidence that universal screening was cost-effective [9]. However, there was evidence that universal screening and decolonization was cost-effective in surgical departments. On the other hand, two reviews found that universal decolonization was more cost-effective for *Staphylococcus aureus* SSI than preoperative screening and decolonization in orthopaedic wards [40,41]. Another review found that the cost-effectiveness of screening and decolonization for SSI was context dependent [28]. Specifically, universal decolonization was cost-effective compared to screening and decolonization, and compared to doing nothing, in orthopaedic wards. However, preoperative screening and decolonization in orthopaedic wards was cost-effective in other settings if the intervention reduced the relative revision rate by at least 10%. Screening and decolonization in a general ward was also cost-effective compared to doing nothing, although it was unlikely to be cost-effective on a maternity ward.

Finally, rapid PCR screening for sepsis or suspected BSI in ICU patients was likely to be cost-effective compared to blood culture screening [42], as was screening for early disease detection in hospital patients with pneumococcal disease compared to standard practice [43].

Surveillance

Five high-quality reviews synthesized evidence on the cost-effectiveness of surveillance interventions, covering eight intervention–infection/organism combinations. One found that surveillance for HCAIs was cost-effective compared to standard practice [9]. A second found that whole-genome sequencing (WGS) was cost-effective for HCAI surveillance [12], while a third reported that such interventions were only cost-effective if they were clinically effective enough [10], and the comparator in both was unclear. In the context of MRSA, WGS for surveillance was cost-effective compared to standard practice where the infrastructure already exists and prevalence of MRSA is high enough [7].

A state-wide electronic registry for CRE was found to be cost-effective compared to do nothing, while active PCR surveillance in a surgical ICU was also cost-effective for CRE compared to no surveillance [7]. Similarly, surveillance and decontamination strategies for CRE in ICUs was cost-effective, although the comparator was unclear [8]. Finally, active surveillance of VRE was cost-effective compared to standard practice and doing nothing [7].

Summary of the results

In summary, hand hygiene and environmental cleaning was cost-effective compared to standard practice, although the evidence base was limited. Diagnostic interventions were cost-effective compared to standard practice, although the evidence base was limited, as was surveillance compared to standard practice and doing nothing. ABS and decolonization interventions were generally cost-effective, although results were context dependent for some analyses. IPC bundles were mostly cost-effective, although there was considerable intervention heterogeneity, and the comparator was often unclear. Selective screening of high-risk patients or settings was cost-effective compared to doing nothing and, in many cases, universal screening. Universal screening was cost-effective in some contexts, particularly where prevalence and transmission of the infection/organism was high. Evidence on the cost-effectiveness of standalone education and training interventions was mixed, and the comparator was unclear for each of the analyses. The cost-effectiveness of PPE was also mixed. There was considerable geographical variation in the underlying studies, with many reviews considering global evidence, which is important to note given that the cost-effectiveness of an intervention is often dependent on the context of its implementation (e.g. prevalence, healthcare setting, willingness to pay).

Discussion

Twenty-four systematic reviews were synthesized to provide a comprehensive overview of the cost-effectiveness of ABS, IPC, and MDS interventions for the prevention and clinical management of HCAIs in adult hospital patients, with a particular focus on infections resistant to antibiotics.

There was a considerable lack of cost-effectiveness evidence for most of the intervention categories. Other than IPC bundle interventions, and screening, followed by contact precautions, isolation, decolonization, or a combination of these, no intervention had more than ten analyses extracted. Moreover, except for these two categories, no intervention type was considered in more than five of the 24 reviews. Quantity of evidence does not necessarily equate to quality or strength of evidence, as one high-quality study is often more insightful than many low-quality studies. However, lack of evidence can indicate that an area is under-researched. It is worth noting that not all intervention–infection/organism combinations are applicable or feasible in practice (e.g. decolonization for ESBL-KP), but many that are feasible had no evidence.

Screening, followed by contact precautions, isolation, decolonization, or a combination of these, had the largest quantity of evidence. Selective screening of high-risk patients or settings was generally more cost-effective, although universal screening was cost-effective in some cases where prevalence and transmission were high. This is likely to be a result of the high costs associated with universal screening. If prevalence and transmission is low, the cost of universal screening is unlikely to be offset by the clinical benefit, as only a relatively small proportion of patients will test positive and receive an alternative treatment pathway and the clinical benefits associated with it.

Among screening interventions, the majority addressed MRSA. In fact, considerably more evidence was identified for MRSA than any other infection/organism across all intervention categories. This is probably because of the longevity of MRSA, which emerged in the early 1960s and remains a political priority into the 21st century [44]. CRE, for example, did not emerge until decades later [45]. Furthermore, a high proportion of economic evaluations are conducted in high-income countries, where MRSA rates are relatively high compared to other organism–drug combinations [46], which may also explain the large evidence base.

Although most of the evidence focuses on Gram-positive infections – such as MRSA and VRE – Gram-negative infections such as CRE have developed into considerable public health issues [47]. This is because of their high resistance to antibiotics and their tendency to infect already high-risk patients, such as those in ICUs [48]. Despite this, there was very little evidence on the cost-effectiveness of interventions tackling Gram-negative infections, and those that did were focused on screening and surveillance. More cost-effectiveness evidence is therefore required to identify appropriate interventions to tackle this growing concern, particularly with respect to non-screening and non-surveillance interventions.

IPC bundle interventions had the second largest quantity of evidence, with 18 analyses. Overall, they were mostly cost-effective. However, only four IPC bundle analyses were included in the cost-effectiveness heat map (Figure 3), as the comparator was unclear in most. This was also a problem with the wider evidence base, with the comparator unclear in 41 of the 101 analyses that were extracted. It is unclear whether this was an issue with primary studies not reporting their comparator, or systematic reviews not capturing the information appropriately. Regardless, it is important for the intervention and comparator to be clearly reported when presenting cost-effectiveness evidence to enable policymakers to make informed resource allocation decisions based on the results.

Due to the nature of the IPC bundle category, defined as multimodal interventions targeting more than one infection control activity, there was considerable heterogeneity between the interventions. For example, the category included interventions ranging from comprehensive 'search-and-destroy' policies that incorporated contact precautions, dedicated IPC personnel, patient and staff cohorting, surveillance, pre-emptive isolation and screening with decolonization; to enhanced hand hygiene alongside contact precaution and PPE use. It is therefore not appropriate to assume that a potential IPC bundle will be cost-effective because of the evidence presented in this review, where most were reported to be cost-effective, given the considerable differences between the interventions.

This is part of a wider issue with the evidence base. Even when considering more homogeneous categories, interventions are typically evaluated as a single entity, despite being made up of several interventions in practice. For example, screening interventions also include contact precautions, isolation and/or decolonization, as do many surveillance interventions. Despite this, cost-effectiveness results are commonly presented for the overarching intervention, making it hard to identify specifically which components were and were not cost-effective.

Even when considering perfectly homogeneous interventions, cost-effectiveness can vary considerably depending on the context of implementation. As demonstrated by the evidence for ABS, decolonization, education and training, screening, and surveillance interventions, cost-effectiveness can vary depending on infection type, prevalence, transmission, healthcare provider, WTP for health benefits, reimbursement systems and geography. Given the heterogeneity of interventions that are often evaluated as a single entity, and the potential impact of the context of implementation, it can be difficult to draw conclusions about the cost-effectiveness of an intervention beyond the specific setting it was evaluated in. The very nature of an umbrella review (i.e. a systematic review of systematic reviews) means that we could not analyse the context of the underlying studies nor therefore the impact that this context (e.g. WTP) may have had on the cost-effectiveness results. Our review necessarily synthesized the evidence as it was reported by the included reviews, rather than examining the underlying studies. It is therefore important that future research attempts to disentangle the impact of the individual components that often make up an overarching intervention, and considers how the wider context directly influences the cost-effectiveness of an intervention, so that policymakers can better understand the circumstances under which a particular intervention may be cost-effective in their context.

Moreover, in evaluating cost-effectiveness it is important to understand the components of cost, both in terms of the cost savings generated through infections prevented, as well as the costs incurred through implementation of the intervention itself. Costs of HCAI are largely driven by additional length of hospital stay due to infection, but, due to common use of inappropriate methodologies to estimate this key cost component, infection costs have historically been overestimated [49—51]. Similarly, costs of implementing the intervention itself are often ignored. Specifically, none of the included reviews or underlying analyses explicitly considered the implementation strategy used for the intervention of interest, the costs associated with its implementation (rather than those associated directly with the intervention), or the cost-effectiveness of the implementation. Future research should therefore look to distinguish between the cost of an intervention and the cost of its implementation, to allow insights into the cost, outcome, and cost-effectiveness of different implementation strategies for a given intervention. Ideally, economic evaluations should not only report costs, but also the resource utilization that underlies them (e.g. number of diagnostic procedures, treatment duration), as these can be converted into setting-specific costs, facilitating comparisons between countries [52].

ABS interventions were generally cost-effective, although in some instances results were mixed. One potential explanation for interventions that address AMR infections not being found cost-effective is that analyses may not account for the secondary cost of antibiotic consumption, as highlighted by Painter *et al.* in their review of economic evaluations of interventions addressing AMR [8]. This cost incorporates how changes in consumption affect the risk of resistance developing and therefore the cost associated with it [53]. Therefore, it is recommended that future economic evaluations explicitly incorporate these costs into their analyses, given that most patients diagnosed with HCAI are treated with antibiotics. Even where the impact of antibiotic use on resistance has been incorporated into economic evaluations, results have been subject to considerable uncertainty regarding the evolution of resistance and its associated health outcomes and costs [54]. This is largely due to the challenges associated with estimating how antimicrobial use will affect the long-term incidence of AMR. This is therefore an important area for future research, if the full costs and outcomes associated with AMR-related interventions are to be incorporated into economic evaluations.

In their review of economic evaluations of interventions to tackle HCAIs, Rice *et al.* found that no analyses of education and training interventions met the minimum quality criteria required to be included in their synthesis [9]. Interestingly, it appeared to be the only review that explicitly drew attention to an intervention where no robust evidence was identified. Naturally, reviews focused on interventions for which they identified cost-effectiveness evidence. However, generally, they did not identify interventions where no evidence was found. Given that reporting where no evidence was identified is just as important as reporting where evidence was found, this is something future systematic reviews should incorporate in the presentation of their results.

For specific analyses to be included in their comparison of the cost-effectiveness of different interventions, Painter *et al.* required the outcome to be measured in QALYs or DALYs [8]. Economic evaluations that utilize generic outcome measures, such as QALYs and DALYs, are referred to as cost—utility analyses. Generic outcome measures allow for incremental cost-effectiveness ratios (ICERs) to be estimated, such as cost per QALY or cost per DALY, which is the ratio of the difference in costs to the difference in outcomes between two interventions. ICERs with generic outcome measures, rather than condition-specific measures, allow for the comparison of interventions across different disease areas, which is vital for decision-makers to appropriately allocate resources across healthcare systems. Condition-specific outcomes, on the other hand, are particularly useful when decision-makers are faced with fixed infection specialist budgets. Economic evaluations with condition-specific outcomes, such as infection-specific mortality, are referred to as cost-effectiveness analyses (CEAs). Many analyses extracted for this review reported a generic outcome measure, mostly QALYs. Many also utilized condition-specific measures, including infections avoided, patients admitted, length of stay, and more. Future research should prioritize using generic measures, alongside condition-specific measures, to capture outcomes associated with the intervention and enable both CEA and CUA to be undertaken.

The major strength and originality of our review is its breadth and comprehensiveness. Evidence has been synthesized from all identified systematic reviews examining the cost-effectiveness of ABS, IPC, and MDS interventions tackling HCAIs, with a particular focus on those resistant to antibiotics. This has been achieved without compromising on quality or rigour, with best practice guidelines followed for methodology [15] and reporting [16]. As a result, a comprehensive overview of the quantity (Figure 2) and quality (Supplementary Appendix S5) of the evidence base is provided, as well as a summary of the cost-effectiveness of different interventions, by infection/organism (Figure 3 and Table I). Furthermore, 20 (83%) of the 24 reviews were high quality, with the other four (17%) medium quality. No reviews were low quality. This suggests that the results of our review have a reasonable degree of reliability.

The findings of this umbrella review should be considered in light of several limitations. First, there is no established approach to estimate an overall quality assessment score based on the JBI Checklist for Systematic Reviews and Research Synthesis. A transparent, objective approach was adopted, based on the scoring system applied in another review that used the same quality assessment tool [24]. However, the scoring system assumes that all 11 items in the checklist are of equal importance, which may not be the case. Second, given the nature of an umbrella review, we did not formally assess the quality of the underlying studies that were synthesized in the included systematic reviews. Thus, it was challenging to draw conclusions about the quality of the underlying evidence base. However, where reported, we did extract and synthesize information on the overarching quality of the underlying studies. Moreover, twenty of the included reviews were high quality, with the others medium quality. The high quality of the included reviews suggests they appropriately accounted for the quality of the underlying studies when synthesizing the evidence. Third, our search strategy used the validated built-in review filter in Medline and Embase to limit hits to systematic reviews (Supplementary Appendix S3). The filters have good specificity, meaning that most hits will be genuine systematic reviews, but lower sensitivity, meaning that studies that are not indexed as systematic reviews or do not have clear systematic review terms may be missed. This approach was taken due to time and resource constraints. However, all known papers were retrieved by this search strategy, and the included reviews were used for backward and forward citation searching to identify any systematic reviews that may have been missed by the search. Despite these limitations, this umbrella review utilizes well-established methodologies to provide a comprehensive summary of the cost-effectiveness of ABS, IPC, and MDS interventions tackling HCAIs.

Conclusion

The objective of this research was to summarize the cost-effectiveness of interventions addressing HCAIs and AMR in hospitals. Most of the cost-effectiveness evidence was focused on screening, followed by contact precautions, isolation, and/or decolonization, with selective screening generally more cost-effective. IPC bundles had the second largest evidence base and were mostly found to be cost-effective, although there was considerable heterogeneity between the interventions. The evidence also suggested that standalone environmental cleaning, hand hygiene, diagnostics, surveillance, ABS, and decolonization were mostly cost-effective. However, the evidence base was sparse, as it was for education and training, and PPE interventions, and more research is required. Importantly, cost-effectiveness can vary depending on the context of implementation (e.g. prevalence, transmission, healthcare provider, WTP); therefore policymakers should consider their setting and that of the evidence base before deciding on implementing a specific intervention. Future research should also account for this in economic evaluations, explicitly exploring how the context changes the cost-effectiveness. Even where there is a relatively large evidence base, such as with screening interventions, the majority is focused on MRSA and other Gram-positive infections. Due to the public health threat posed by Gram-negative infections, considerably more research is required in this area. Further recommendations for future research are also made based on the findings, including for economic evaluations to try to untangle the cost-effectiveness of the specific components of an overarching intervention, consider the secondary cost of antibiotic consumption, and use generic, as well as clinical, outcome measures. The intervention and comparators of interest should clearly be defined when cost-effectiveness evidence is presented, and systematic reviews of such evidence should report where no evidence is found for relevant interventions.

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Conflict of interest statement
None declared.

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Ethics statement
Not required.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2025.01.006.

References

[1] Ducel G, Fabry J, Nicolle L. Prevention of hospital acquired infections: a practical guide. Geneva: WHO; 2002.

[2] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2022—2023. Stockholm: ECDC; 2024.

[3] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2016—2017. Stockholm: ECDC; 2023.

[4] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2011—2012. Stockholm: ECDC; 2013.

[5] Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. Lancet Infect Dis 2019;19:56—66.

[6] European Centre for Disease Prevention and Control. Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016—2020. Stockholm: ECDC; 2022.

[7] Allel K, Hernandez-Leal MJ, Naylor NR, Undurraga EA, Abou Jaoude GJ, Bhandari P, et al. Costs-effectiveness and cost components of pharmaceutical and non-pharmaceutical interventions affecting antibiotic resistance outcomes in hospital patients: a systematic literature review. BMJ Global Health 2024;9(2).

[8] Painter C, Faradiba D, Chavarina KK, Sari EN, Teerawattananon Y, Aluzaite K, et al. A systematic literature review of economic evaluation studies of interventions impacting antimicrobial resistance. Antimicrob Resist Infect Control 2023;12:69.

[9] Rice S, Carr K, Sobiesuo P, Shabaninejad H, Orozco-Leal G, Kontogiannis V, et al. Economic evaluations of interventions to prevent and control health-care-associated infections: a systematic review. Lancet Infect Dis 2023;23:e228—39.

[10] Price V, Ngwira LG, Lewis JM, Baker KS, Peacock SJ, Jauneikaite E, et al. A systematic review of economic evaluations of whole-genome sequencing for the surveillance of bacterial pathogens. Microb Genom 2023;9(2).

[11] Tolley A, Bansal A, Murerwa R, Howard Dicks J. Cost-effectiveness of point-of-care diagnostics for AMR: a systematic review. J Antimicrob Chemother 2024;79:1248—69.

[12] Tran M, Smurthwaite KS, Nghiem S, Cribb DM, Zahedi A, Ferdinand AD, et al. Economic evaluations of whole-genome sequencing for pathogen identification in public health surveillance and health-care-associated infections: a systematic review. Lancet Microbe 2023;4:e953—62.

[13] Belbasis L, Bellou V, Ioannidis JP. Conducting umbrella reviews. BMJ Med 2022;1(1).

[14] Pollard J, Agnew E, Pearce-Smith N, Pouwels KB, Salant N, Robotham J. Umbrella review of economic evaluations of interventions for the prevention and management of healthcare-associated infections: PROSPERO protocol. PROSPERO; 2024. CRD42024544387.

[15] Garritty C, Hamel C, Trivella M, Gartlehner G, Nussbaumer-Streit B, Devane D, et al. Updated recommendations for the Cochrane rapid review methods guidance for rapid reviews of effectiveness. BMJ 2024;384:e076335.

[16] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372.

[17] Borissov N, Haas Q, Minder B, Kopp-Heim D, von Gernler M, Janka H, et al. Reducing systematic review burden using Deduklick: a novel, automated, reliable, and explainable deduplication algorithm to foster medical research. Systemat Rev 2022;11(1):172.

[18] Haddaway NR, Grainger MJ, Gray CT. Citationchaser: a tool for transparent and efficient forward and backward citation chasing in systematic searching. Res Synth Methods 2022;13:533—45.

[19] Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systemat Rev 2016;5:1—10.

[20] Pieper D, Antoine S-L, Mathes T, Neugebauer EA, Eikermann M. Systematic review finds overlapping reviews were not mentioned in every other overview. J Clin Epidemiol 2014;67:368—75.

[21] Kirvalidze M, Abbadi A, Dahlberg L, Sacco LB, Calderón-Larrañaga A, Morin L. Estimating pairwise overlap in umbrella reviews: considerations for using the corrected covered area (CCA) index methodology. Res Synth Methods 2023;14:764—7.

[22] Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. JBI Evid Implement 2015;13:132—40.

[23] Kachabian S, Seyedmajidi S, Tahani B, Naghibi Sistani MM. Effectiveness of educational strategies to teach evidence-based dentistry to undergraduate dental students: a systematic review. Evidence-Based Dentistry 2024;25:53—4.

[24] George PP, Molina JAD, Heng BH. The methodological quality of systematic reviews comparing intravitreal bevacizumab and alternates for neovascular age related macular degeneration: a systematic review of reviews. Ind J Ophthalmol 2014;62:761—7.

[25] Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. MDM Policy Pract 2022;7(1):23814683211061097.

[26] Ibrahim NH, Maruan K, Mohd Khairy HA, Hong YH, Dali AF, Neoh CF. Economic evaluations on antimicrobial stewardship programme: a systematic review. J Pharm Pharmaceut Sci 2017;20:397—406.

[27] Arefian H, Vogel M, Kwetkat A, Hartmann M. Economic evaluation of interventions for prevention of hospital acquired infections: a systematic review. PloS One 2016;11(1):e0146381.

[28] McFarland A, Reilly J, Manoukian S, Mason H. The economic benefits of surgical site infection prevention in adults: a systematic review. J Hosp Infect 2020;106:76—101.

[29] Rojas-Garcia P, van der Pol S, van Asselt ADI, Postma MJ, Rodriguez-Ibeas R, Juarez-Castello CA, et al. Diagnostic testing for sepsis: a systematic review of economic evaluations. Antibiotics (Basel) 2021;11(1).

[30] Lingervelder D, Koffijberg H, Kusters R, Ijzerman MJ. Health economic evidence of point-of-care testing: a systematic review. PharmacoEconomics-Open 2021;5:157—73.

[31] Farbman L, Avni T, Rubinovitch B, Leibovici L, Paul M. Cost-benefit of infection control interventions targeting methicillin-resistant *Staphylococcus aureus* in hospitals: systematic review. Clin Microbiol Infect 2013;19:E582—93.

[32] Tchouaket Nguemeleu E, Beogo I, Sia D, Kilpatrick K, Seguin C, Baillot A, et al. Economic analysis of healthcare-associated infection prevention and control interventions in medical and surgical units: systematic review using a discounting approach. J Hosp Infect 2020;106:134—54.

[33] 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 Technol Assessm (Winchester, England) 2003;7:1—194.

[34] 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. Am J Infect Control 2006;34:484–94.
[35] MacDougall C, Johnstone J, Prematunge C, Adomako K, Nadolny E, Truong E, et al. Economic evaluation of vancomycin-resistant enterococci (VRE) control practices: a systematic review. J Hosp Infect 2020;105:53–63.
[36] Price L, MacDonald J, Melone L, Howe T, Flowers P, Currie K, et al. Effectiveness of national and subnational infection prevention and control interventions in high-income and upper-middle-income countries: a systematic review. Lancet Infect Dis 2018;18:e159–71.
[37] Halim NIBA, Rahman NABA, Zin NBM, Baba MSB, Rahman NIA, Haque M. A systematic review on prevention of methicillin-resistant *Staphylococcus aureus* infection by pre-admission screening: the cost effectiveness and practicality. Systemat Rev Pharm 2016;7:1–19.
[38] McGinigle KL, Gourlay ML, Buchanan IB. The use of active surveillance cultures in adult intensive care units to reduce methicillin-resistant *Staphylococcus aureus*-related morbidity, mortality, and costs: a systematic review. Clin Infect Dis 2008;46:1717–25.
[39] Loveday HP, Pellowe CM, Jones SRLJ, 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). J Hosp Infect 2006;63:S45–70.
[40] Chen AF, Wessel CB, Rao N. *Staphylococcus aureus* screening and decolonization in orthopaedic surgery and reduction of surgical site infections. Clin Orthopaed Relat Res 2013;471:2383–99.
[41] Ribau AI, Collins JE, Chen AF, Sousa RJ. Is preoperative *Staphylococcus aureus* screening and decolonization effective at reducing surgical site infection in patients undergoing orthopedic surgery? A systematic review and meta-analysis with a special focus on elective total joint arthroplasty. J Arthroplasty 2021;36:752–766.e6.
[42] D'Onofrio V, Salimans L, Bedenic B, Cartuyvels R, Barisic I, Gyssens IC. The clinical impact of rapid molecular microbiological diagnostics for pathogen and resistance gene identification in patients with sepsis: a systematic review. Open Forum Infect Dis 2020;7(10).
[43] Shiri T, Khan K, Keaney K, Mukherjee G, McCarthy ND, Petrou S. Pneumococcal disease: a systematic review of health utilities, resource use, costs, and economic evaluations of interventions. Value Health 2019;22:1329–44.
[44] Cookson B. Five decades of MRSA: controversy and uncertainty continues. Lancet 2011;378(9799):1291–2.
[45] Meletis G. Carbapenem resistance: overview of the problem and future perspectives. Ther Adv Infect Dis 2016;3:15–21.
[46] Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022;399(10325):629–55.
[47] UK Government. Confronting antimicrobial resistance 2024 to 2029. London. 2024.
[48] Oliveira J, Reygaert WC. Gram-Negative Bacteria. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. PMID: 30855801.
[49] Nelson RE, Nelson SD, Khader K, Perencevich EL, Schweizer ML, Rubin MA, et al. The magnitude of time-dependent bias in the estimation of excess length of stay attributable to healthcare-associated infections. Infect Control Hosp Epidemiol 2015;36:1089–94.
[50] Graves N, Harbarth S, Beyersmann J, Barnett A, Halton K, Cooper B. Estimating the cost of health care-associated infections: mind your p's and q's. Clin Infect Dis 2010;50:1017–21.
[51] De Angelis G, Murthy A, Beyersmann J, Harbarth S. Estimating the impact of healthcare-associated infections on length of stay and costs. Clin Microbiol Infect 2010;16:1729–35.
[52] Robotham JV, Tacconelli E, Vella V, de Kraker ME. Synthesizing pathogen- and infection-specific estimates of the burden of antimicrobial resistance in Europe for health-technology assessment: gaps, heterogeneity, and bias. Clin Microbiol Infect 2024;30:S1–3.
[53] Shrestha P, Cooper BS, Coast J, Oppong R, Do Thi Thuy N, Phodha T, et al. Enumerating the economic cost of antimicrobial resistance per antibiotic consumed to inform the evaluation of interventions affecting their use. Antimicrob Resist Infect Control 2018;7:1–9.
[54] Roope LS, Morrell L, Buchanan J, Ledda A, Adler AI, Jit M, et al. Overcoming challenges in the economic evaluation of interventions to optimise antibiotic use. Commun Med 2024;4:101.