Cost-effectiveness of antimicrobial treatment for inpatients with carbapenem-resistant *Klebsiella pneumoniae* infection: a systematic review of economic evidence

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ABSTRACT

Objectives: The objective of this review was to evaluate the cost-effectiveness of antimicrobial therapy for patients with carbapenem-resistant *Klebsiella pneumoniae* infection.

Introduction: Among the main multi-resistant microorganisms, carbapenem-resistant *K. pneumoniae* is responsible for the mortality of 40% of patients following 30 days of infection. Treatment for carbapenem-resistant *K. pneumoniae* infection entails the use of high-cost antimicrobials. Inappropriate use of antimicrobials can increase the cost of treatment fourfold. This review aimed to evaluate the cost-effectiveness of antimicrobial therapy treatment for patients with carbapenem-resistant *K. pneumoniae* infection to better inform decision making in hospital services.

Inclusion criteria: The review included studies on participants 18 years or over with carbapenem-resistant *K. pneumoniae* infection who had undergone antimicrobial therapy in hospital and acute care services. Studies that compared the cost-effectiveness of different antimicrobial therapy for carbapenem-resistant *K. pneumoniae* infection were included. Outcome measures were cost per unit of effect expressed in clinical outcome units; this included cost per avoided death, cost per prevention of sepsis and cost per duration of stay. Economic studies with a cost-effectiveness design were considered, as well as modeling studies.

Methods: A three-step search strategy was utilized to locate studies published in English, Spanish or Portuguese, with no date restrictions. Two independent reviewers screened titles and abstracts and the full texts of potentially relevant studies for eligibility. Methodological quality was assessed by two independent reviewers using the JBI critical appraisal checklist for economic evaluations. Data were extracted from included studies using the standardized JBI data extraction tool. Data were synthesized using narrative, tables and the JBI Dominance Ranking Matrix.

Results: This review identified eight studies that evaluated the cost-effectiveness of different treatments for carbapenem-resistant *K. pneumoniae* infection. The results of this study demonstrated that there was no gold standard treatment for carbapenem-resistant *K. pneumoniae* infection, hence treatment was generally directed by colonization pressure and resistance profiles. Furthermore, due to the moderate quality and limited number of studies, there was high uncertainty of the values of the cost-effectiveness ratio.

Conclusions: Ofloxacin appears to be the most cost-effective treatment; however, conclusions are limited due to the small number and low quality of studies.

Keywords Cost-effectiveness; costs and cost analysis; health care economics and organizations; *Klebsiella pneumoniae*

JBI Database System Rev Implement Rep 2019; 17(12):2417–2451.

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EA is the Editor-in-Chief of the JBI Database of Systematic Reviews and Implementation Reports *and was not involved in the editorial processing of this manuscript.*

DOI: 10.11124/JBISRIR-D-18-00019

Introduction

Treatment of bacterial infections accounts for a significant proportion of healthcare spending. The cost of medicines, in general, can represent more than 20% of health expenses, and incorrect prescriptions, doses, treatment time and wrong antimicrobial therapy can increase treatment costs by up to 36%.[1-4] The major clinical consequences of inappropriate antimicrobial treatment are changes in the expected therapeutic effect, adverse reactions, drug dependence and appearance of multidrug-resistant bacteria.[5-7]

Multidrug-resistant bacteria require the use of increasingly potent antimicrobials.[5-9] The risk of transmission of multidrug-resistant bacteria is recognized as a global public health concern, more so because *Enterobacteriaceae* are common, natural inhabitants of our microbiota. Infection with these bacteria causes prolonged hospitalization and high mortality rates.[10,11] In the United States (US), multidrug-resistant bacteria cause 2 million infections and 23,000 deaths each year.[12] The impact of infections on direct and indirect healthcare costs amounts to approximately US$20 billion and US$25 billion per annum, respectively.[11] The financial burden of infection may be even greater in low-income and middle-income countries.[11] For example, pharmaceutical purchases (including antimicrobial agents) constitute an estimated 70% of out-of-pocket health expenditure in India, 43% in Pakistan and 20% in Brazil.[11,13,14]

Among multidrug-resistant *Enterobacteriaceae*, carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is a notable pathogen.[15-18] CRKP is an opportunistic, hospital-associated pathogen, accounting for about 33% of all gram-negative infections.[19,20] CRKP is the most common multidrug-resistant *Enterobacteriaceae* in the US. Following the first description of CRKP from clinical isolates in the late 1990s in North Carolina, cases were identified in all US states by 2017.[21,22] Globally, CRKP was responsible for 1% of hospital infections in 2001, which rose to 30% in 2008, with an incidence rate of 2.93 cases per 100,000 person-years.[23] Between 2001 and 2011, the proportion of carbapenem-resistant *Enterobacteriaceae* increased from 1% to 4%, and the percentage of CRKP rose from 2% to 10%.[24-26] Cases of CRKP infection have been reported in almost all regions of the world beyond North America, including Europe,[27,28] Asia,[29-31] Australia[32] and South America.[33,34] CRKP infection is very high in endemic countries (Argentina, Brazil, China, Colombia, Greece, Israel, Italy, Poland, Taiwan and the US); this worldwide growth in the incidence of multidrug-resistant *K. pneumoniae* reflects multifactorial dissemination processes that include the spread of high-risk global genetic lineages.[35,36]

CRKP infection causes pneumonia; endocarditis; septicemia and extra-intestinal, urinary tract, bloodstream and surgical wound infections. Untreated, the mortality rate of CRKP infection is higher than 40% within 30 days of infection.[15,27,29-31,37-39] Risk factors for infection with CRKP include long periods of hospitalization, mechanical ventilation, organ or stem cell transplantation, and previous treatment with antimicrobial agents.[39-44]

Therapy for multidrug-resistant *K. pneumoniae* infection involves limited drug options. Limited drug options lead to inadequate management, which prolongs hospitalization time, increases morbidity and mortality, and contributes to higher healthcare costs.[45-49] Therapy for *K. pneumoniae* infection commonly includes a combination of antimicrobials, such as tigecycline and polymyxin, in addition to carbapenem and aminoglycoside, and this combination therapy is directed towards decreasing resistance and reducing mortality.[15,20,43] Resistance of *K. pneumoniae* against the top four antibiotic classes has increased over recent years, including third-generation cephalosporins, aminoglycosides, fluoroquinolones and carbapenem.[50]

CRKP represents a significant health problem in the hospital setting, and treatment with the range of antimicrobials has clinical and economic impact; for example, use of high-cost drugs can result in expenses higher than US$52 per day.[6,7] Inadequate use of antimicrobials can increase the cost of treatment fourfold as well as increase mortality rates.[39-44]

In light of this, budget constraints in various government sectors, including health, have led to the need for treatment protocols aimed at a balance between cost and effectiveness.[51,52] Because of increasing costs with marginal effectiveness, the debate over incorporation of CRKP therapy into the healthcare system has become even more pressing. Therefore, the aim of this review was to evaluate the cost-effectiveness of antimicrobial therapy for

patients with CRKP infection to better inform decision making in hospital services.

Review question

What is the cost-effectiveness of antimicrobial therapy for patients with CRKP infection worldwide?

Inclusion criteria

Participants

This review considered studies including participants 18 years or over with CRKP infection. Studies using preventive antimicrobial treatment for inpatients exclusively colonized with CRKP were excluded. Colonization refers to the presence of bacteria in the body without causing infection or disease in the person.

Interventions and comparators

This review considered studies that compared different antimicrobial therapy, such as amoxicillin, cefepime, ceftriaxone, ciprofloxacin, ertapenem, imipenem, levofloxacin, metronidazole, nitrofurantoin, ofloxacin, piperacillin-tazobactam and tigecycline. We considered any dose of administration and treatment time.

Context

This review considered studies conducted in the hospital setting and acute care services. Studies investigating cost-effectiveness of in-hospital treatment were included, independent of the study perspective and country of study.

Outcomes

To be included, studies must have estimated the cost relative to the effectiveness of an antimicrobial therapeutic option. Eligible outcomes were estimates of cost per unit of effect expressed in clinical outcome units. We considered studies that included cost per avoided death, cost per prevention of sepsis, and cost per duration of stay.

Types of studies

This review included economic studies with a cost-effectiveness design but excluded cost-benefit and cost-utility analyses. Studies modeling cost-effectiveness were also included with those providing empirical data. Studies published in English, Spanish or Portuguese were considered for inclusion.

Methods

The objectives, inclusion criteria and methods of analysis for this review were specified in advance and documented in an *a priori* protocol.[53] The conduct and reporting of this systematic review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Joanna Briggs Institute Reviewer's Manual.[54-56]

Search strategy

A comprehensive search aimed to find both published and unpublished studies. A three-step search strategy was utilized in this review. An initial limited search of PubMed was undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article.

A second search using all identified keywords and index terms was undertaken across all included databases. Thirdly, the reference lists of all reports and articles were searched for additional studies. No date limitations or other restrictions were applied to the search. Search strategies for all the databases and sources searched are provided in Appendix I. Databases searched included:

- CEA (Cost-Effectiveness Analysis Registry)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- Embase (Excerpta Medica Database)
- HEED (Health Economic Evaluation Database)
- HTA (Health Technology Assessment Database)
- LILACS (Literature of the Latin American and Caribbean Health Sciences)
- NHS EED (National Health Service Economic Evaluation Database)
- PubMed (US National Library of Medicine-National Institutes of Health)
- Science Direct
- Web of Science

The search for gray literature included Bank of CAPES for theses and dissertations, MedNar, Google Scholar, NYAM (New York Academy of Medicine), Open Access Theses and Dissertations and WorldWideScience.org.

Study selection

All citation records from the search were uploaded into Covidence (Veritas Health Innovation, Melbourne, Australia) and duplicates removed. Two independent reviewers (WMS, JYM) screened titles and abstracts for the evaluation against the inclusion criteria for the review. Potentially eligible studies were retrieved in full, and their details imported into Covidence. The full texts of retrieved studies were assessed against the inclusion criteria (WMS, JYM). Reasons for exclusion of full-text studies were recorded. There was no disagreement among the reviewers during the study selection process.

Assessment of methodological quality

Eligible studies were critically appraised by two independent reviewers (WMS, JYM) at the study level for methodological quality using the standardized critical appraisal instrument for economic evaluations in the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; Joanna Briggs Institute, Adelaide, Australia).[55] All studies, regardless of their methodological quality, underwent data extraction and synthesis. There was no disagreement among the reviewers during the methodological quality assessment.

We determined the level of methodological quality as follows: fair quality = less than 40% of the items presented; moderate quality = between 41 and 80% of the items presented; good quality = more than 80% of the items presented.

Data extraction

Descriptive and outcome economic data were extracted using the standardized data extraction tool from JBI SUMARI.[55] Extracted data included year, country and currency, setting/perspective, participant characteristics, time of therapy, source of effectiveness data, effectiveness reference, source of cost, treatment, effectiveness of therapy, cost measure, cost total, cost-effectiveness analysis, incremental cost-effectiveness ratio and sensitivity analysis.

Data synthesis

Data extracted from included studies were analyzed and summarized using narrative, tables and the JBI Dominance Ranking Matrix (DRM).[55] The decision matrix has three possible outcomes for the cost of an intervention of interest balanced against health outcomes[55]:

- Reject intervention: the intervention has higher cost and similar effectiveness, similar costs and lower effectiveness, or higher cost and lower effectiveness.
- Unclear: the intervention has lower cost and lower effectiveness, similar cost and similar effectiveness, or higher cost and higher effectiveness.
- Favor intervention: the intervention has lower cost and similar effectiveness, similar costs and higher effectiveness, or lower cost and higher effectiveness.

Results

Study selection

The search returned 4327 records; from this total, 615 duplicates were removed. From the remaining 3712 records, 3666 were excluded following title and abstract screening. Forty-six potentially relevant studies were retrieved for assessment of full text against the review eligibility criteria, following which, 38 were excluded, resulting in eight included studies (Figure 1; Appendix II).[57-64] Figure 1 demonstrates the results of the search and selection process.[54]

Three studies[62-64] did not include a cost-effectiveness evaluation; however, these studies provided data on treatment costs and effectiveness between the groups.

Characteristics of included studies

The studies included in this review were published between 1999 and 2016. Key characteristics of the eight included studies are presented in Table 1.[57-64]

One study was an economic modeling study.[61] The included studies investigated multiple infection sites including urinary,[61] upper respiratory,[62] intra-abdominal[59,60,63] and general.[57,58,64]

Four studies were from South Asia,[57,58,63,64] three from the United States,[60-62] and one from Europe.[59] The official currency present in the studies was the American dollar,[57,59-62,64] and the Indian rupee.[58,63]

Four studies did not provide demographic information about participants[57,59,61,62]; however, one of these was a model economic evaluation based on other studies.[61] Of the included studies where participant information was available, among the total number of participants (918), the majority were males (64.0%–73.1%) between 40 and 80 years of age.[58,60,63,64]

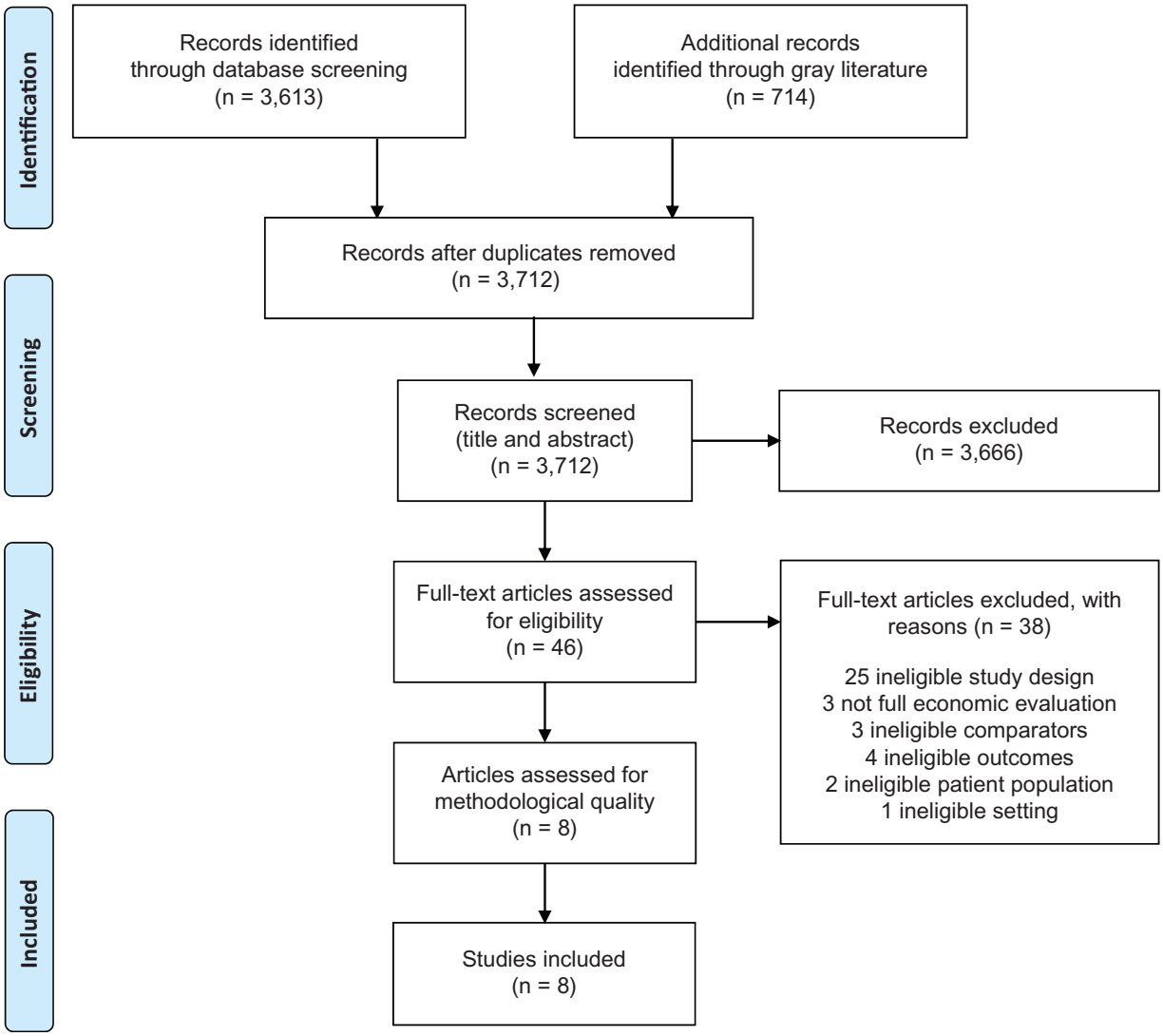

Figure 1: Search results and study selection and inclusion process[54]

The reported outcomes across the included studies were treatment efficacy[57-64] and survival rate.[64] All studies utilized direct costs from various sources that included prescription of antimicrobial drug therapy; cost of dosage preparation, dispensing and administration; therapeutic drug monitoring; treatment of adverse events; and treatment failure.[57-64]

Sixteen antimicrobials were utilized in these studies, including amoxicillin,[61] cefepime combined with amoxicillin/clavulanic acid,[64] ceftriaxone plus metronidazole,[59] ceftriaxone,[57,58] ceftriaxone-sulbactam plus metronidazole,[63] ciprofloxacin,[62] ciprofloxacin plus metronidazole,[59,60] ertapenem,[59] imipenem,[62] levofloxacin,[57,58] nitrofurantoin,[61] ofloxacin,[61] piperacillin plus tazobactam,[60] piperacillin-tazobactam plus metronidazole,[63] tigecycline[64] and trimethoprim plus sulfamethoxazole.[61]

Methodological quality

The overall methodological quality of the included studies was moderate (Table 2). No studies had a well-defined question/objective (Q1). They did not inform in a clear way the objective/question of the

Table 1: Characteristics of included studies

Study	Year, country	Setting/ perspective	Population characteristic	Prevalence CRKP (%)	Site of infection	Source of effectiveness data	Treatment	Daily dose (mg)	Treatment days	Time horizon (days)	Eff. Tx (%)	Cost measure	Cost value*
Paladino *et al.*[60]	1995–1997, U.S./ Canada	Hospital	Male: 64% Age: 48 (±19.0)	NA	Intra-abdominal	Treatment efficacy	Ciprofloxacin Metronidazole	800 2000	5–14	49	75	Hospital day* Drug cipro Drug metro	1130.00 21.29 1.49
							Piperacillin-tazobactam	13,000	5–14	49	65	Hospital day* Drug pipe-tazo	1130.00 12.52
Thomas *et al.*[58]	2014, India	Hospital	Male: 68.5% Age 41–60: 43.6% 61–80: 35.3%	18.9	General	Treatment efficacy	Ceftriaxone	NA	3–10	NA	73	Mean per patient	49.45 Indian rupees
							Levofloxacin	NA	3–10	NA	100	Mean per patient	95.13 Indian rupees
Sriram *et al.*[57]	NA, India	Hospital	NA	18.9	General	Treatment efficacy	Ceftriaxone	NA	3–10	NA	73	Mean per patient	1.06
							Levofloxacin	NA	3–10	NA	100	Mean per patient	1.77
Rosenberg[61]	NA, U.S.	Hospital	NA	NA	Urinary	Treatment efficacy	Amoxicillin	NA	7	NA	52	NA	NA
							Nitrofurantoin	NA	7	NA	76	NA	NA
							Ofloxacin	NA	7	NA	96	NA	NA
							Trimethoprim/ sulfamethoxazole	NA	7	NA	87	NA	NA
Kolbin *et al.*[59]	NA, Russia	Hospital	NA	NA	Intra-abdominal	Treatment efficacy	Ceftriaxone metronidazole	NA	NA	NA	NA	Mean per patient	2579.00
							Ciprofloxacin plus metronidazole	NA	NA	NA	NA	Mean per patient	3153.00
							Ertapenem	NA	NA	NA	NA	Mean per patient	2860.00
Caldwell *et al.*[62]	NA, U.S.	Hospital	NA	NA	General	Treatment efficacy	Ciprofloxacin	1200	3–7	44	77	Drug + hospital day	31,054.00
							Imipenem	3000	3–7	44	50	Drug + hospital day	51,504.56
Jadhav *et al.*[63]	2013–2015, India	Hospital	Male: 73.1% Age: 58.9 (±13.7)	19.1	Intra-abdominal	Treatment efficacy	Ceftriaxone sulbactan Metronidazol	3000 4000	7.93±0.90	NA	62.5	Mean per patient	12,820.26 Indian rupees
							Piperacillin-tazobactam Metronidazol	13,500 4000	11.16±1.42	NA	39.13	Mean per patient	35,923.16 Indian rupees
Ji *et al.*[64]	2011–2012, China	Hospital	Male: 60.6% Age: 65.4 (±17.0)	100.0	General	Treatment efficacy Survival rate	Cefepime Amoxicillin/clavulanic acid	1000 1200	9 (4.8–15.5)	NA	57.7	Drug cost per day	108.00
							Tigecycline	100	9 (6.5–14.5)	NA	68.0	Drug cost per day	321.00

CRKP: carbapenem-resistant *Klebsiella pneunomiae*; Eff. Tx: effectiveness of treatment; NA: not available; U.S.: United States.
*Cost in U.S. dollars unless otherwise specified.

Table 2: Assessment of methodological quality of included studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Quality of study
Caldwell *et al.*[62]	N	Y	Y	Y	Y	Y	U	N	N	N	Y	Moderate
Jadhav S *et al.*[63]	N	Y	Y	Y	Y	Y	U	N	N	N	Y	Moderate
Ji S *et al.*[64]	N	Y	Y	Y	Y	Y	U	N	N	N	Y	Moderate
Kolbin AS *et al.*[59]	N	Y	U	U	U	U	U	N	N	U	U	Fair
Paladino JA *et al.*[60]	N	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Good
Rosenberg M[61]	N	Y	U	Y	U	U	U	N	U	Y	U	Fair
Sriram S *et al.*[57]	N	Y	N	Y	U	N	U	N	N	Y	Y	Fair
Thomas B *et al.*[58]	N	Y	N	Y	U	N	U	N	N	N	Y	Fair
Total (%)	–	100	50	88	50	50	-	13	13	38	75	

Y: yes; U: unclear; N: no.
Critical appraisal checklist for economic evaluations:
(Q1) Is there a well-defined question? (Q2) Is there comprehensive description of alternatives? (Q3) Are all important and relevant costs and outcomes for each alternative identified? (Q4) Has clinical effectiveness been established? (Q5) Are costs and outcomes measured accurately? (Q6) Are costs and outcomes valued credibly? (Q7) Are costs and outcomes adjusted for differential timing? (Q8) Is there an incremental analysis of costs and consequences? (Q9) Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences? (Q10) Do study results include all issues of concern to users? (Q11) Are the results generalizable to the setting of interest in the review?

studies, the statement and perspective of the studies, and if the studies were used for decision making. All studies provided a comprehensive description of alternatives for treatment (Q2). Most of the studies demonstrated that clinical effectiveness had been established (Q4) and results were generalizable to the setting of interest in the review (Q11).

It was unclear in the included studies if costs and outcomes had been adjusted for differential timing (Q7). Studies did not present information about the discount rate used and only presented information about the time frame over which the study was conducted. Four studies demonstrated all important and relevant costs and outcomes for each alternative (Q3).

Fifty percent of the studies did not measure costs and outcomes accurately (Q5); methods used to take measures were not provided, nor were any limitations of the methods used provided. Half of the studies evaluated the costs, and the results were evaluated with credibility and reliability (Q6).

Seven studies did not present an incremental analysis of costs and consequences (Q8). They did not present any analysis that reports a measure that demonstrated the alteration in costs and benefits for the intervention and comparator for a marginal shift in resources from the comparator to the intervention. Furthermore, the authors of only one study[60] conducted a sensitivity analysis to investigate uncertainty in estimates of costs or outcomes (Q9). The results of the study included all issues of interest to the perspective that was elaborated (Q10).

Review findings

Classification of studies using the dominance ranking framework

The findings from the included studies are summarized using the dominance ranking framework, which demonstrated the analysis of a comparator and an intervention for the treatment of CRKP infection (see Tables 3-16).

Using amoxicillin as a comparator, interventions based on nitrofurantoin (Table 3) or ofloxacin (Table 4) demonstrated less cost and more clinical effectiveness.[61] Levofloxacin demonstrated more cost and more clinical effectiveness when compared to ceftriaxone (Table 5).[57,58]

Using ciprofloxacin–metronidazole as a comparator, interventions based on piperacillin-tazobactam (Table 6), ceftriaxone–metronidazole (Table 7) and ertapenem (Table 8) demonstrated less cost and less clinical effectiveness, less cost and equal clinical effectiveness, and less cost and more clinical effectiveness, respectively.[59,60]

Table 3: Economic evaluation of amoxicillin versus nitrofurantoin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use nitrofurantoin (use amoxicillin)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use nitrofurantoin (do not use amoxicillin)
	0	+	
Rosenberg[61]	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Interventions based on ceftriaxone/metronidazole demonstrated less cost and less clinical efficiency in comparison to ertapenem (Table 9).[59] Intervention based on ofloxacin demonstrated less cost and more clinical effectiveness in comparison to nitrofurantoin (Table 10).[61]

Using trimethoprim/sulfamethoxazole as a comparator, interventions based on amoxicillin (Table 11) or nitrofurantoin (Table 12), and ofloxacin (Table 13) demonstrated more cost and less clinical effectiveness, and equal cost and more clinical effectiveness, respectively.[61]

Table 4: Economic evaluation of amoxicillin versus ofloxacin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ofloxacin (use amoxicillin)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ofloxacin (do not use amoxicillin)
	0	+	
Rosenberg[61]	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 5: Economic evaluation of ceftriaxone versus levofloxacin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use levofloxacin (use ceftriaxone)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
Thomas et al.,[58] Sriram et al.[57]	+	+	Further analysis required
	-	0	Use levofloxacin (do not use ceftriaxone)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Presentation of findings on incremental cost-effectiveness measures

Over half of the studies did not present incremental analyses.[57-59,61,62] The intervention based on ceftriaxone-sulbactam plus metronidazole demonstrated less cost and more clinical effectiveness as compared to piperacillin-tazobactam plus metronidazole (Table 14).[63] The intervention based on

Table 6: Economic evaluation of ciprofloxacin-metronidazole versus piperacillin-tazobactam: three-by-three matrix dominanceclassification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use piperacillintazobactam (use ciprofloxacin-metronidazole)
	0	-	
	+	0	
Paladino et al.[60]	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use piperacillintazobactam (do not use ciprofloxacin-metronidazole)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 7: Economic evaluation of ciprofloxacin-metronidazole versus ceftriaxone/metronidazole: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ceftriaxone/metronidazole (use ciprofloxacin-metronidazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
Kolbin et al.[59]	-	0	Use ceftriaxone/metronidazole (do not use ciprofloxacin-metronidazole)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

tigecycline demonstrated more cost and less clinical effectiveness compared to cefepime combined with amoxicillin/clavulanic acid (Table 15).[64]

Using ciprofloxacin as a comparator, interventions based on imipenem demonstrated more cost and more clinical effectiveness (Table 16).[62]

Discussion

Of the 16 different treatments examined, nine were monotherapy[57-59,61,62,64] and seven were multidrug therapy.[59-61,63,64] The literature recommends a combination of therapies to decrease the resistance to monotherapy, because this factor can significantly

Table 8: Economic evaluation of ciprofloxacin-metronidazole versus ertapenem: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ertapenem (use ciprofloxacin-metronidazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ertapenem (do not use ciprofloxacin-metronidazole)
	0	+	
Kolbin et al.[59]	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 9: Economic evaluation of ertapenem versus ceftriaxone/metronidazole: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ceftriaxone/metronidazole (use ertapenem)
	0	-	
	+	0	
Kolbin et al.[59]	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ceftriaxone/metronidazole (do not use ertapenem)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

impact the cost of antimicrobial treatment in the long term.[20,65-67] Even so, it is important to highlight that some of these studies were performed before these recommendations were made, and hence, conclusions about cost-effectiveness can vary depending on when a given primary study was published.

Considering the therapeutic group of each antimicrobial, a beta-lactam was prescribed in over half of the therapies, followed by imidazole derivatives

Table 10: Economic evaluation of nitrofurantoin versus ofloxacin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ofloxacin (use nitrofurantoin)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ofloxacin (do not nitrofurantoin)
	0	+	
Rosenberg[61]	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 11: Economic evaluation of trimethoprim/sulfamethoxazole versus amoxicillin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
Rosenberg[61]	+	-	Do not use amoxicillin (use trimethoprim/sulfamethoxazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use amoxicillin (do not use trimethoprim/sulfamethoxazole)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

and quinolone antimicrobials. The beta-lactam based therapy, especially carbapenem antibiotics, are used with increasing frequency for the treatment of multidrug-resistant gram-negative nosocomial pathogens.[2,20,68] The imidazole group is highly active against gram-negative anaerobic bacteria, and is usually prescribed with another antimicrobial to potentiate the clinical efficacy.[69,70] The increasing incidence of fluoroquinolone resistance is observed in hospitals that use carbapenem

Table 12: Economic evaluation of trimethoprim/sulfamethoxazole versus nitrofurantoin: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
Rosenberg[61]	+	-	Do not use nitrofurantoin (use trimethoprim/sulfamethoxazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use nitrofurantoin (do not use trimethoprim/sulfamethoxazole)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 13: Economic evaluation of trimethoprim/sulfamethoxazole versus ofloxacin: three-by-three matrix dominance is classifying for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ofloxacin (use trimethoprim/sulfamethoxazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ofloxacin (do not use trimethoprim/sulfamethoxazole)
Rosenberg[61]	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

antibiotics as the first choice of treatment, which leads to an even greater dependence on carbapenem therapy.[20,71]

Other older antimicrobials including fosfomycin or nitrofurantoin have been discussed for use in noninvasive infections such as urinary tract infections, but data relating to clinical efficacy are absent. However, there are new multidrug-resistant bacteria within existing classes of pathogens, and presently there are no new antimicrobials in the later

Table 14: Economic evaluation of piperacillin-tazobactam + metronidazole versus ceftriaxone-sulbactam + metronidazole: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use ceftriaxone-sulbactam + metronidazole (use piperacillin-tazobactam + metronidazole)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use ceftriaxone-sulbactam + metronidazole (do not use piperacillin-tazobactam + metronidazole)
	0	+	
Jadhav et al.[63]	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

Table 15: Economic evaluation of cefepime combined with amoxicillin/clavulanic acid versus tigecycline: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
Ji et al.[64]	+	-	Do not use tigecycline (use cefepime combined with amoxicillin/clavulanic acid)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
	+	+	Further analysis required
	-	0	Use tigecycline (do not use cefepime combined with amoxicillin/ clavulanic acid)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

phases of development with activity against these bacteria.[20]

The variablity in prescriptions of antimicrobials can impact the cost and effectiveness of the therapy.[72,73] Some of the studies were conducted for a specific site of infection, while three of them were done for widespread infection.[57,58,62] The efficacy of the antimicrobials can change according to the site of infection because some of them have less dispersibility for a specific site of infections.[74,75] Nevertheless, the general recommendation for the treatment of CRKP infection is to start treatment with clinical

Table 16: Economic evaluation of ciprofloxacin versus imipenem: three-by-three matrix dominance classification for cost-effectiveness outcomes/findings

Studies	Cost	Clinical effectiveness	Decision
	+	-	Do not use imipenem (use ciprofloxacin)
	0	-	
	+	0	
	-	-	Further analysis required
	0	0	Neutral
Caldwell et al.[62]	+	+	Further analysis required
	-	0	Use imipenem (do not use ciprofloxacin)
	0	+	
	-	+	

(+) indicates greater cost/effectiveness; (-) indicates lesser cost/effectiveness; 0 indicates comparable cost/effectiveness

evaluation, regardless of the results of laboratory testing.[76-79]

Cost-effective treatments identified in this review were ciprofloxacin-metronidazole, ertapenem, levofloxacin or ofloxacin. However, there was not a single primary study comparing these antimicrobials. The different types of therapy identified by this review are supported in the literature, but there is no gold standard for the treatment of CRKP.[80] The findings of this review cannot be generalizable to other populations or healthcare settings because of the complex processes in the hospital-based context.

Limitations of the review

Results of this review should be considered with caution because of some limitations. The first limitation was the difference in the prevalence of CRKP infections in the studies, which can influence the efficacy of the therapies. None of the included studies were designed exclusively to investigate the treatment of CRKP infection. In three of the studies, approximately 20% of the bacteria examined were Klebsiella species, whereas four studies did not specify the distribution of the bacteria. One study did not specify the distribution of the bacteria but did indicate that the predominant bacterium was *Escherichia coli*.[61] Additionally, the study considered any dose of administration and time of treatment factor, increasing the study's homogeneity; however, these factors vary depending on the patient's weight and site of infection of the bacteria, as well as the severity of the infection. Therefore, it was not possible to perform a standardized study of these factors, as well as to evaluate the dose-effect relationship of the treatment.

Furthermore, the economic model presented in the studies did not consider the patient's final outcome (death or survival) after infection. Hence, the studies only allowed the evaluation of an intermediate outcome (success or therapeutic failure).

Conclusions

This review identified eight studies that evaluated the cost-effectiveness of different treatments for CRKP infections. The results of this study demonstrate that there is no gold standard treatment for CRKP infection; the treatment is generally directed by colonization pressure and resistance profiles. Furthermore, due to the moderate quality and the limited number of studies, it is possible to have different values of the cost-effectiveness ratio for each treatment.

Recommendations for practice

This review showed that there is no gold standard treatment for CRKP infection; the treatment for multidrug-resistant *K. pneumoniae* should be directed by colonization pressure and resistance profiles. This evaluation is culturally acceptable, but cannot be transferable/applicable to most of the population infected by this bacterium. Also, it is easily adaptable in a variety of circumstances such as varying purchase prices of the medications or co-infections with other bacteria, and different indications for hospitalization. This is a safe practice to providing the best treatment available, according to the willingness of each institution to pay. Based on the JBI levels of evidence for economic reviews,[81] the overall recommendations for practice of this review are level 5 moderate and/or poor quality (insufficient coverage of costs and health effects, no discounting, no sensitivity testing, time period covered insufficient). Therefore, we recommend that the treatment be performed based on the minimum inhibitory concentration test and be adjusted according to the site of infection.

Recommendations for research

The current review has shown a clear need for additional research on the cost-effectiveness of the treatment of CRKP infection. The studies included in this review did not include analyses exclusive for CRKP infection, and this uncertainty and variability between studies can impact the results demonstrated.

Prospective research is essential to support the evidence on the best cost-effective treatment of CRKP infection, and should incorporate different analyses of this bacteria and consider the different sites of infection.

In future, a quantitative meta-analysis of new published data of different therapies could be conducted, which may lead to robust and generalizable conclusions so the data can be used to construct a solid economic model.

Funding

This study was funded in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - PDSE - 88881.133309/2016-01.

References

1. Vieira FS. Impact of recent decisions and discussions on the Brazilian Public Health System financing. Saúde Debate 2016;40(109):187–99.
2. Wirtz VJ, Hogerzeil HV, Gray AL, Bigdeli M, de Joncheere CP, Ewen MA, *et al*. Essential medicines for universal health coverage. Lancet 2017;389(10067):403–76.
3. Boing AC, Bertoldi AD, Peres KG. Socioeconomic inequalities in expenditures and income committed to the purchase of medicines in Southern Brazil. Rev Saúde Pública 2011;45(5): 897–905.
4. Costa NR, Engstrom EM, Siqueira SAV. Public Policy and the Institutional Role of the Ministry of Health in Brazil. Ciênc Saúde Coletiva 2017;22(5):1394–11394.
5. Santana RS, Viana Ade C, Santiago Jda S, Menezes MS, Lobo IM, Marcellini PS. The cost of excessive postoperative use of antimicrobials: the context of a public hospital. Rev Col Bras Cir 2014;41(3):149–54.
6. Oliveira AC, Paula AO. Discontinuation of antimicrobials and costs of treating patients with infection. Acta Paul Enferm 2012;25(spe2):68–74.
7. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T 2015;40(4):277–83.
8. Lee GC, Burgess DS. Treatment of Klebsiella pneumoniae carbapenemase (KPC) infections: a review of published case series and case reports. Ann Clin Microbiol Antimicrob 2012;11(1):32.
9. Rafailidis PI, Falagas ME. Options for treating carbapenem-resistant Enterobacteriaceae. Curr Opin Infect Dis 2014;27(6):479–83.
10. Iredell J, Brown J, Tagg K. Antibiotic resistance in Enterobacteriaceae: mechanisms and clinical implications. BMJ 2016;352:h6420.
11. Colomb-Cotinat M, Lacoste J, Brun-Buisson C, Jarlier V, Coignard B, Vaux S. Estimating the morbidity and mortality associated with infections due to multidrug-resistant bacteria (MDRB), France, 2012. Antimicrob Resist Infect Control 2016;5:56.
12. Guh AY, Bulens SN, Mu Y, Jacob JT, Reno J, Scott J, *et al*. Epidemiology of carbapenem-resistant Enterobacteriaceae in 7 US communities, 2012–2013. JAMA 2015;314(14): 1479–87.
13. Miranda GMD, Mendes ACG, Silva ALA. The challenge of organizing a universal and efficient National Health System in the Brazilian federal pact. Saude Soc 2017;26(2):329–35.
14. Mengue SS, Bertoldi AD, Boing AC, Tavares NUL, Pizzol TSD, Oliveira MA, *et al*. National Survey on Access, Use and Promotion of Rational Use of Medicines (PNAUM): household survey component methods. Rev Saúde Pública 2016;50(Suppl 2):4s.
15. Lee GC, Burgess DS. Treatment of Klebsiella pneumoniae carbapenemase (KPC) infections: a review of published case series and case reports. Ann Clin Microbiol Antimicrob 2012;11:32–41.
16. Iovleva A, Doi Y. Carbapenem-resistant Enterobacteriaceae. Clin Lab Med 2017;37(2):303–15.
17. Paterson DL. Resistance in gram-negative bacteria: enterobacteriaceae. Am J Med 2006;119(6 Suppl 1):S20–8.
18. Bush K. Carbapenemases: Partners in crime. J Glob Antimicrob Resist 2013;1(1):7–16.
19. Meletis G. Carbapenem resistance: overview of the problem and future perspectives. Ther Adv Infect Dis 2016;3(1):15–21.
20. Arnold RS, Thom KA, Sharma S, Phillips M, Johnson JK, Morgan DJ. Emergence of Klebsiella pneumoniae carbapenemase (KPC)-producing bacteria. South Med J 2011;104(1):40–5.
21. Swathi CH, Chikala R, Ratnakar KS, Sritharan V. A structural, epidemiological & genetic overview of Klebsiella pneumoniae carbapenemases (KPCs). Indian J Med Res 2016;144(1): 21–31.
22. Nordmann P, Cuzon G, Naas T. The real threat of Klebsiella pneumoniae carbapenemase-producing bacteria. Lancet Infect Dis 2009;9(4):228–36.
23. Snitkin ES, Zelazny AM, Thomas PJ, Stock F, Henderson DK, Palmore TN, *et al*. Tracking a hospital outbreak of carbapenem-resistant Klebsiella pneumoniae with whole-genome sequencing. Sci Transl Med 2012;4(148):148ra16.
24. Marquez P, Terashita D, Dassey D, Mascola L. Population-based incidence of carbapenem-resistant Klebsiella pneumoniae along the continuum of care, Los Angeles County. Infect Control Hosp Epidemiol 2013;34(2):144–50.
25. David S, Reuter S, Harris SR, Glasner C, Feltwell T, Argimon S, *et al*. Epidemic of carbapenem-resistant Klebsiella pneumoniae in Europe is driven by nosocomial spread. Nat Microbiol 2019;4(11):1919–29.
26. Xu L, Sun X, Ma X. Systematic review and meta-analysis of mortality of patients infected with carbapenem-resistant Klebsiella pneumoniae. Ann Clin Microbiol Antimicrob 2017;16(1):18–30.
27. Kuai S, Shao H, Huang L, Pei H, Lu Z, Wang W, *et al*. KPC-2 carbapenemase and DHA-1 AmpC determinants carried on the same plasmid in Enterobacter aerogenes. J Med Microbiol 2014;63(Pt 3):367–70.
28. Hoenigl M, Valentin T, Zarfel G, Wuerstl B, Leitner E, Salzer HJF, *et al*. Nosocomial outbreak of Klebsiella pneumoniae carbapenemase-producing Klebsiella oxytoca in Austria. Antimicrob Agents Chemother 2012;56(4):2158–61.
29. Lamoureaux TL, Frase H, Antunes NT, Vakulenko SB. Antibiotic resistance and substrate profiles of the class A carbapenemase KPC-6. Antimicrob Agents Chemother 2012;56(11):6006–8.
30. Leavitt A, Navon-Venezia S, Chmelnitsky I, Schwaber MJ, Carmeli Y. Emergence of KPC-2 and KPC-3 in carbapenem-resistant Klebsiella pneumoniae strains in an Israeli hospital. Antimicrob Agents Chemother 2007;51(8):3026–9.
31. Wei ZQ, Du XX, Yu YS, Shen P, Chen YG, Li LJ. Plasmid-Mediated KPC-2 in a Klebsiella pneumoniae isolate from China. Antimicrob Agents Chemother 2007;51(2):763–5.

32. Chang LW, Buising KL, Jeremiah CJ, Cronin K, Poy Lorenzo YS, Howden BP, *et al*. Managing a nosocomial outbreak of carbapenem-resistant Klebsiella pneumoniae: an early Australian hospital experience. Intern Med J 2015;45(10):1037–43.
33. Villegas MV, Lolans K, Correa A, Suarez CJ, Lopez JA, Vallejo M, *et al*. First detection of the plasmid-mediated class A carbapenemase KPC-2 in clinical isolates of Klebsiella pneumoniae from South America. Antimicrob Agents Chemother 2006;50(8):2880–2.
34. Correa A, Montealegre MC, Mojica MF, Maya JJ, Rojas LJ, De La Cadena EP, *et al*. First report of a Pseudomonas aeruginosa isolate coharboring KPC and VIM carbapenemases. Antimicrob Agents Chemother 2012;56(10):5422–3.
35. Toth A, Damjanova I, Puskas E, Janvari L, Farkas M, Dobak A, *et al*. Emergence of a colistin-resistant KPC-2-producing Klebsiella pneumoniae ST258 clone in Hungary. Eur J Clin Microbiol Infect Dis 2010;29(7):765–9.
36. Zarkotou O, Pournaras S, Voulgari E, Chrysos G, Prekates A, Voutsinas D, *et al*. Risk factors and outcomes associated with acquisition of colistin-resistant KPC-producing Klebsiella pneumoniae: A matched case–control study. J Clin Microbiol 2010;48(6):2271–4.
37. Peleg AY, Franklin C, Bell JM, Spelman DW. Dissemination of the metallo-beta-lactamase gene blaIMP-4 among gram-negative pathogens in a clinical setting in Australia. Clin Infect Dis 2005;41(11):1549–56.
38. Hirakata Y, Izumikawa K, Yamaguchi T, Takemura H, Tanaka H, Yoshida R, *et al*. Rapid detection and evaluation of clinical characteristics of emerging multiple-drug-resistant gram-negative rods carrying the metallo-beta-lactamase gene blaIMP. Antimicrob Agents Chemother 1998;42(8):2006–11.
39. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis 2011;53(1):60–7.
40. Orsi GB, Falcone M, Venditti M. Surveillance and management of multidrug-resistant microorganisms. Expert Rev Anti Infect Ther 2011;9(8):653–79.
41. Souli M, Galani I, Antoniadou A, Papadomichelakis E, Poulakou G, Panagea T, *et al*. An outbreak of infection due to beta-Lactamase Klebsiella pneumoniae Carbapenemase 2-producing K. pneumoniae in a Greek University Hospital: molecular characterization, epidemiology, and outcomes. Clin Infect Dis 2010;50(3):364–73.
42. Thabit AK, Crandon JL, Nicolau DP. Antimicrobial resistance: impact on clinical and economic outcomes and the need for new antimicrobials. Expert Opin Pharmacother 2015;16(2):159–77.
43. Tumbarello M, Viale P, Viscoli C, Trecarichi EM, Tumietto F, Marchese A, *et al*. Predictors of mortality in bloodstream infections caused by Klebsiella pneumoniae carbapenemase-producing K. pneumoniae: importance of combination therapy. Clin Infect Dis 2012;55(7):943–50.
44. Owens RC Jr, Rice L. Hospital-based strategies for combating resistance. Clin Infect Dis 2006;42(Suppl 4):S173–81.
45. Millan LS, Benedette CEM, Maximo LZ, Almeida PCCd, Gomes DS, Gemperli R, *et al*. Bloodstream infections by multidrug-resistant bacteria in patients in an intensive care unit for the treatment of burns: a 4-year-experience. Rev Bras Cir Plast 2012;27(3):374–8.
46. Kaki R, Elligsen M, Walker S, Simor A, Palmay L, Daneman N. Impact of antimicrobial stewardship in critical care: a systematic review. J Antimicrob Chemother 2011;66(6):1223–30.
47. Cantey JB, Milstone AM. Bloodstream infections: epidemiology and resistance. Clin Perinatol 2015;42(1):1–16.
48. McGowan JE. Economic impact of antimicrobial resistance. Emerg Infect Dis 2001;7(2):286–92.
49. Bratu S, Tolaney P, Karumudi U, Quale J, Mooty M, Nichani S, *et al*. Carbapenemase-producing Klebsiella pneumoniae in Brooklyn, NY: molecular epidemiology and in vitro activity of polymyxin B and other agents. J Antimicrob Chemother 2005;56(1):128–32.
50. Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21st century. Perspect Medicin Chem 2014;6:25–64.
51. Greenberg D, Earle C, Fang CH, Eldar-Lissai A, Neumann PJ. When is cancer care cost-effective? A systematic overview of cost-utility analyses in oncology. J Natl Cancer Inst 2010;102(2):82–8.
52. Soárez PC, Soares MO, Novaes HMD. Decision modeling for economic evaluation of health technologies. Ciênc Saúde Coletiva 2014;19(10):4209–22.
53. dos Santos WM, Matuoka JY, Secoli SR. Cost-effectiveness of the antimicrobial treatment for inpatients infected with Klebsiella pneumoniae carbapenemase: a systematic review protocol. JBI Database System Rev Implement Rep 2018;16(2):336–44.
54. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009;6(7):e1000097.
55. Gomersall JS, Jadotte YT, Xue YF, Lockwood S, Riddle D, Preda A. Chapter 6: systematic reviews of economic evaluation evidence. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual [Internet]. Adelaide: Joanna Briggs Institute. 2014 [cited Mar 17, 2019]. Available from: https://reviewersmanual.joannabriggs.org/.
56. dos Santos WM, Secoli SR, Püschel VAA. The Joanna Briggs Institute approach for systematic reviews. Rev Lat Am Enfermagem 2018;26:e3074.
57. Sriram S, Aiswaria V, Cijo AE, Mohankumar T. Antibiotic sensitivity pattern and cost-effectiveness analysis of antibiotic therapy in an Indian tertiary care teaching hospital. J Res Pharm Pract 2013;2(2):70–4.
58. Thomas B, Matthew L, Jose J, Rathinavelu M, Shanmugam S, Kumar K. Assessment of antibiotic sensitivity pattern of microorganisms and their cost-effectiveness at a private corporate hospital in south India. Asian J Pharm Clin Res 2014;7(5):155–9.

59. Kolbin AS, Sidorenko S, Zagorodnikova K, Klimko N, Koroleva O. Pharmacoeconomic analysis of the effects of secondary bacterial resistance in the multi-departmental hospital on treatment efficacy in complicated abdominal infections. Value Health 2010;13(3):A73.
60. Paladino JA, Gilliland-Johnson KK, Adelman MH, Cohn SM. Pharmacoeconomics of ciprofloxacin plus metronidazole vs. piperacillin-tazobactam for complicated intra-abdominal infections. Surg Infect (Larchmt) 2008;9(3):325–33.
61. Rosenberg M. Pharmacoeconomics of treating uncomplicated urinary tract infections. Int J Antimicrob Agents 1999;11(3–4):247–51.
62. Caldwell JW, Singh S, Johnson RH. Clinical and economic evaluation of subsequent infection following intravenous ciprofloxacin or imipenem therapy in hospitalized patients with severe pneumonia. J Antimicrob Chemother 1999;43(Suppl A):129–34.
63. Jadhav S, Sawant N. Comparative pharmacoeconomics and efficacy analysis of a new antibiotic adjuvant entity and piperacillin-tazobactam for the management of intra-abdominal infections: A retrospective study. Asian Pac J Trop Dis 2016;6(1):32–9.
64. Ji S, Lv F, Du X, Wei Z, Fu Y, Mu X, *et al*. Cefepime combined with amoxicillin/clavulanic acid: a new choice for the KPC-producing K. pneumoniae infection. Int J Infect Dis 2015;38:108–14.
65. dos Santos WM, Secoli SR. Economic burden of inpatients infected with Klebsiella pneumoniae carbapenemase. Einstein (São Paulo) 2019;17(4):1–8.
66. Damas P, Garweg C, Monchi M, Nys M, Canivet J-L, Ledoux D, *et al*. Combination therapy versus monotherapy: a randomised pilot study on the evolution of inflammatory parameters after ventilator associated pneumonia [ISRCTN31976779]. Crit Care 2006;10(2):R52.
67. Paul M, Carmeli Y, Durante-Mangoni E, Mouton JW, Tacconelli E, Theuretzbacher U, *et al*. Combination therapy for carbapenem-resistant Gram-negative bacteria. J Antimicrob Chemother 2014;69(9):2305–9.
68. Yigit H, Queenan AM, Anderson GJ, Domenech-Sanchez A, Biddle JW, Steward CD, *et al*. Novel carbapenem-hydrolyzing β-lactamase, KPC-1, from a carbapenem-resistant strain of Klebsiella pneumoniae. Antimicrob Agents Chemother 2001;45(4):1151–61.
69. Samuelson J. Why Metronidazole Is Active against both Bacteria and Parasites. Antimicrob Agents Chemother 1999;43(7):1533–41.
70. Löfmark S, Edlund C, Nord CE. Metronidazole is still the drug of choice for treatment of anaerobic infections. Clin Infect Dis 2010;50(suppl 1):S16–23.
71. Endimiani A, Carias LL, Hujer AM, Bethel CR, Hujer KM, Perez F, *et al*. Presence of plasmid-mediated quinolone resistance in Klebsiella pneumoniae isolates possessing blaKPC in the United States. Antimicrob Agents Chemother 2008;52(7):2680–2.
72. Wong D, Spellberg B. Leveraging antimicrobial stewardship into improving rates of carbapenem-resistant Enterobacteriaceae. Virulence 2017;8(4):383–90.
73. Kim NH, Han WD, Song KH, Seo HK, Shin MJ, Kim TS, *et al*. Successful containment of carbapenem-resistant Enterobacteriaceae by strict contact precautions without active surveillance. Am J Infect Control 2014;42(12):1270–3.
74. Levison ME, Levison JH. Pharmacokinetics and pharmacodynamics of antibacterial agents. Infect Dis Clin North Am 2009;23(4). 791-vii.
75. Leekha S, Terrell CL, Edson RS. General principles of antimicrobial therapy. Mayo Clin Proc 2011;86(2):156–67.
76. Morrill HJ, Pogue JM, Kaye KS, LaPlante KL. Treatment options for carbapenem-resistant Enterobacteriaceae infections. Open Forum Infect Dis 2015;2(2):ofv050.
77. Falagas ME, Lourida P, Poulikakos P, Rafailidis PI, Tansarli GS. Antibiotic treatment of infections due to carbapenem-resistant Enterobacteriaceae: systematic evaluation of the available evidence. Antimicrob Agents Chemother 2014;58(2):654–63.
78. Yamamoto M, Pop-Vicas AE. Treatment for infections with carbapenem-resistant Enterobacteriaceae: what options do we still have? Crit Care 2014;18(3):229.
79. Lee C-S, Doi Y. Therapy of infections due to carbapenem-resistant gram-negative pathogens. Infect Chemother 2014;46(3):149–64.
80. van Duin D. Carbapenem-resistant Enterobacteriaceae: What we know and what we need to know. Virulence. 2017; 8(4):379-82.81.
81. Joanna Briggs Institute. JBI Levels of Evidence [internet]. 2013 [cited Apr 17, 2019]. Available from: https://joannabriggs.org/sites/default/files/2019-05/JBI-Levels-of-evidence_2014_0.pdf.

Appendix I: Search strategy

Searches conducted on April 30, 2019

CEA (Cost Effectiveness Analysis Registry)

Search ID no.	Search formula	Records retrieved
#1.	(Klebsiella pneumoniae) OR (Klebsiella rhinoscleromatis) OR (Klebsiella) OR (Enterobacteriaceae) OR (Enterobacteria) OR (Enteric Bacteria) OR (Coliform Bacilli) OR (Sodalis) OR (Paracolobactrum) OR (Ewingella) OR (Leclercia) OR (Gram-Negative Facultatively Anaerobic Rods) OR (Gram Negative Facultatively Anaerobic Rods) OR (Gram-Negative Bacteria) OR (Gram Negative Bacteria) OR (Gamma Proteobacteria) OR (Proteobacteria gamma) OR (Proteobacteria) OR (Bacteria, Purple) OR (Purple Bacteria) OR (Klebsiella Infections) OR (Infections, Klebsiella) OR (Klebsiella Infection) OR (Enterobacteriaceae Infections) OR (Enterobacterial Infections) OR (Infections, Enterobacterial) OR (Enterobacterial Infection) OR (Infection, Enterobacterial) OR (Infections, Enterobacteriaceae) OR (Enterobacteriaceae Infection) OR (Infection, Enterobacteriaceae) OR (Gram-Negative Bacterial Infections) OR (Gram Negative Bacterial Infections) OR (Infections, Gram-Negative Bacterial) OR (Bacterial Infection, Gram-Negative) OR (Gram-Negative Bacterial Infection) OR (Infection, Gram-Negative Bacterial) OR (Infections, Gram Negative Bacterial) OR (Bacterial Infections, Gram-Negative) OR (Bacterial Infections, Gram Negative)	8
#2.	(Cost Effectiveness) OR (Effectiveness, Cost) OR (Cost-Utility Analysis) OR (Analyses, Cost-Utility) OR (Analysis, Cost-Utility) OR (Cost Utility Analysis) OR (Cost-Utility Analyses) OR (Economic Evaluation) OR (Economic Evaluations) OR (Evaluation, Economic) OR (Evaluations, Economic) OR (Marginal Analysis) OR (Analyses, Marginal) OR (Analysis, Marginal) OR (Marginal Analyses) OR (Cost-Effectiveness Analysis) OR (Analysis, Cost-Effectiveness) OR (Cost Effectiveness Analysis) OR (economics, pharmaceutical) OR (pharmacoeconomics)	2,625
#3.	#1 AND #2	3

CENTRAL (Cochrane Central Register of Controlled Trials)

Search ID no.	Search formula	Records retrieved
#1.	((Klebsiella pneumoniae) OR (Klebsiella rhinoscleromatis) OR (Klebsiella) OR (Enterobacteriaceae) OR (Enterobacteria) OR (Enteric Bacteria) OR (Coliform Bacilli) OR (Sodalis) OR (Paracolobactrum) OR (Ewingella) OR (Leclercia) OR (Gram-Negative Facultatively Anaerobic Rods) OR (Gram Negative Facultatively Anaerobic Rods) OR (Gram-Negative Bacteria) OR (Gram Negative Bacteria) OR (Gamma Proteobacteria) OR (Proteobacteria gamma) OR (Proteobacteria) OR (Bacteria, Purple) OR (Purple Bacteria) OR (Klebsiella Infections) OR (Infections, Klebsiella) OR (Klebsiella Infection) OR (Enterobacteriaceae Infections) OR (Enterobacterial Infections) OR (Infections, Enterobacterial) OR (Enterobacterial Infection) OR (Infection, Enterobacterial) OR (Infections, Enterobacteriaceae) OR (Enterobacteriaceae Infection) OR (Infection, Enterobacteriaceae) OR (Gram-Negative Bacterial Infections) OR (Gram Negative Bacterial Infections) OR (Infections, Gram-Negative Bacterial) OR (Bacterial Infection, Gram-Negative) OR (Gram-Negative Bacterial Infection) OR (Infection, Gram-Negative Bacterial) OR (Infections, Gram Negative Bacterial) OR (Bacterial Infections, Gram-Negative) OR (Bacterial Infections, Gram Negative)) in Title, Abstract, Keywords	3,881
#2.	((Cost Effectiveness) OR (Effectiveness, Cost) OR (Cost-Utility Analysis) OR (Analyses, Cost-Utility) OR (Analysis, Cost-Utility) OR (Cost Utility Analysis) OR (Cost-Utility Analyses) OR (Economic Evaluation) OR (Economic Evaluations) OR (Evaluation, Economic) OR (Evaluations, Economic) OR (Marginal Analysis) OR (Analyses, Marginal) OR (Analysis, Marginal) OR (Marginal Analyses) OR (Cost-Effectiveness Analysis) OR (Analysis, Cost-Effectiveness) OR (Cost Effectiveness Analysis) OR (economics, pharmaceutical) OR (pharmacoeconomics)) in Title, Abstract, Keywords	50,067
#3.	#1 AND #2	195

CINAHL (Cumulative Index to Nursing and Allied Health Literature)

Search ID no.	Search formula	Records retrieved
#1.	(Klebsiella pneumoniae) OR (Klebsiella rhinoscleromatis) OR (Klebsiella) OR (Enterobacteriaceae) OR (Enterobacteria) OR (Enteric Bacteria) OR (Coliform Bacilli) OR (Sodalis) OR (Paracolobactrum) OR (Ewingella) OR (Leclercia) OR (Gram-Negative Facultatively Anaerobic Rods) OR (Gram Negative Facultatively Anaerobic Rods) OR (Gram-Negative Bacteria) OR (Gram Negative Bacteria) OR (Gamma Proteobacteria) OR (Proteobacteria gamma) OR (Proteobacteria) OR (Bacteria, Purple) OR (Purple Bacteria) OR (Klebsiella Infections) OR (Infections, Klebsiella) OR (Klebsiella Infection) OR (Enterobacteriaceae Infections) OR (Enterobacterial Infections) OR (Infections, Enterobacterial) OR (Enterobacterial Infection) OR (Infection, Enterobacterial) OR (Infections, Enterobacteriaceae) OR (Enterobacteriaceae Infection) OR (Infection, Enterobacteriaceae) OR (Gram-Negative Bacterial Infections) OR (Gram Negative Bacterial Infections) OR (Infections, Gram-Negative Bacterial) OR (Bacterial Infection, Gram-Negative) OR (Gram-Negative Bacterial Infection) OR (Infection, Gram-Negative Bacterial) OR (Infections, Gram Negative Bacterial) OR (Bacterial Infections, Gram-Negative) OR (Bacterial Infections, Gram Negative)	15,219
#2.	(Cost Effectiveness) OR (Effectiveness, Cost) OR (Cost-Utility Analysis) OR (Analyses, Cost-Utility) OR (Analysis, Cost-Utility) OR (Cost Utility Analysis) OR (Cost-Utility Analyses) OR (Economic Evaluation) OR (Economic Evaluations) OR (Evaluation, Economic) OR (Evaluations, Economic) OR (Marginal Analysis) OR (Analyses, Marginal) OR (Analysis, Marginal) OR (Marginal Analyses) OR (Cost-Effectiveness Analysis) OR (Analysis, Cost-Effectiveness) OR (Cost Effectiveness Analysis) OR (economics, pharmaceutical) OR (pharmacoeconomics)	28,182
#3.	#1 AND #2	39

Embase (Excerpta Medica Database)

Search ID no.	Search formula	Records retrieved
#1.	'klebsiella pneumoniae':ti,ab,kw OR 'klebsiella rhinoscleromatis':ti,ab,kw OR 'klebsiella':ti,ab,kw OR 'enterobacteriaceae':ti,ab,kw OR 'enterobacteria':ti,ab,kw OR 'enteric bacteria':ti,ab,kw OR 'coliform bacilli':ti,ab,kw OR 'sodalis':ti,ab,kw OR 'paracolobactrum':ti,ab,kw OR 'ewingella':ti,ab,kw OR 'leclercia':ti,ab,kw OR 'gram-negative facultatively anaerobic rods':ti,ab,kw OR 'gram negative facultatively anaerobic rods':ti,ab,kw OR 'gram-negative bacteria':ti,ab,kw OR 'gram negative bacteria':ti,ab,kw OR 'gammaproteobacteria':ti,ab,kw OR 'gamma proteobacteria':ti,ab,kw OR 'proteobacteria gamma':ti,ab,kw OR 'proteobacteria':ti,ab,kw OR 'bacteria, purple':ti,ab,kw OR 'purple bacteria':ti,ab,kw OR 'klebsiella infections':ti,ab,kw OR 'infections, klebsiella':ti,ab,kw OR 'klebsiella infection':ti,ab,kw OR 'enterobacteriaceae infections':ti,ab,kw OR 'enterobacterial infections':ti,ab,kw OR 'infections, enterobacterial':ti,ab,kw OR 'enterobacterial infection':ti,ab,kw OR 'infection, enterobacterial':ti,ab,kw OR 'infections, enterobacteriaceae':ti,ab,kw OR 'enterobacteriaceae infection':ti,ab,kw OR 'infection, enterobacteriaceae':ti,ab,kw OR 'gram-negative bacterial infections':ti,ab,kw OR 'gram negative bacterial infections':ti,ab,kw OR 'infections, gram-negative bacterial':ti,ab,kw OR 'bacterial infection, gram-negative':ti,ab,kw OR 'gram-negative bacterial infection':ti,ab,kw OR 'infection, gram-negative bacterial':ti,ab,kw OR 'infections, gram negative bacterial':ti,ab,kw OR 'bacterial infections, gram-negative':ti,ab,kw OR 'bacterial infections, gram negative':ti,ab,kw	106,806

(*Continued*)		
Search ID no.	**Search formula**	**Records retrieved**
#2.	'cost effectiveness':ti,ab,kw OR 'effectiveness, cost':ti,ab,kw OR 'effectiveness, cost':ti,ab,kw OR 'effectiveness, cost':ti,ab,kw OR 'effectiveness, cost':ti,ab,kw OR 'effectiveness, cost':ti,ab,kw OR 'cost-utility analyses':ti,ab,kw OR 'economic evaluation':ti,ab,kw OR 'economic evaluations':ti,ab,kw OR 'evaluation, economic':ti,ab,kw OR 'evaluations, economic':ti,ab,kw OR 'marginal analysis':ti,ab,kw OR 'analyses, marginal':ti,ab,kw OR 'analysis, marginal':ti,ab,kw OR 'marginal analyses':ti,ab,kw OR 'cost-effectiveness analysis':ti,ab,kw OR 'analysis, cost-effectiveness':ti,ab,kw OR 'cost effectiveness analysis':ti,ab,kw OR 'economics, pharmaceutical':ti,ab,kw OR 'pharmacoeconomics':ti,ab,kw	91,489
#3.	#1 AND #2	97

HEED (Health Economic Evaluation Database) – powered by Wiley

Search ID no.	Search formula	Records retrieved
#1.	(''Klebsiella pneumoniae'' OR ''Klebsiella rhinoscleromatis'' OR ''Klebsiella'' OR ''Enterobacteriaceae'' OR ''Enterobacteria'' OR ''Enteric Bacteria'' OR ''Coliform Bacilli'' OR ''Sodalis'' OR ''Paracolobactrum'' OR ''Ewingella'' OR ''Leclercia'' OR ''Gram-Negative Facultatively Anaerobic Rods'' OR ''Gram Negative Facultatively Anaerobic Rods'' OR ''Gram-Negative Bacteria'' OR ''Gram Negative Bacteria'' OR ''Gamma Proteobacteria'' OR ''Proteobacteria gamma'' OR ''Proteobacteria'' OR ''Bacteria, Purple'' OR ''Purple Bacteria'' OR ''Klebsiella Infections'' OR ''Infections, Klebsiella'' OR ''Klebsiella Infection'' OR ''Enterobacteriaceae Infections'' OR ''Enterobacterial Infections'' OR ''Infections, Enterobacterial'' OR ''Enterobacterial Infection'' OR ''Infection, Enterobacterial'' OR ''Infections, Enterobacteriaceae'' OR ''Enterobacteriaceae Infection'' OR ''Infection, Enterobacteriaceae'' OR ''Gram-Negative Bacterial Infections'' OR ''Gram Negative Bacterial Infections'' OR ''Infections, Gram-Negative Bacterial'' OR ''Bacterial Infection, Gram-Negative'' OR ''Gram-Negative Bacterial Infection'' OR ''Infection, Gram-Negative Bacterial'' OR ''Infections, Gram Negative Bacterial'' OR ''Bacterial Infections, Gram-Negative'' OR ''Bacterial Infections, Gram Negative'') in Abstract	15,247
#2.	(''Cost Effectiveness'' OR ''Effectiveness, Cost'' OR ''Cost-Utility Analysis'' OR ''Analyses, Cost-Utility'' OR ''Analysis, Cost-Utility'' OR ''Cost Utility Analysis'' OR ''Cost-Utility Analyses'' OR ''Economic Evaluation'' OR ''Economic Evaluations'' OR ''Evaluation, Economic'' OR ''Evaluations, Economic'' OR ''Marginal Analysis'' OR ''Analyses, Marginal'' OR ''Analysis, Marginal'' OR ''Marginal Analyses'' OR ''Cost-Effectiveness Analysis'' OR ''Analysis, Cost-Effectiveness'' OR ''Cost Effectiveness Analysis'' OR ''economics, pharmaceutical'' OR ''pharmacoeconomics'') in Abstract	23,460
#3.	#1 AND #2	29

HTA (Health Technology Assessment Database)

Search ID no.	Search formula	Records retrieved
#1.	(Klebsiella pneumoniae) OR (Klebsiella rhinoscleromatis) OR (Klebsiella) OR (Enterobacteriaceae) OR (Enterobacteria) OR (Enteric Bacteria) OR (Coliform Bacilli) OR (Sodalis) OR (Paracolobactrum) OR (Ewingella) OR (Leclercia) OR (Gram-Negative Facultatively Anaerobic Rods) OR (Gram Negative Facultatively Anaerobic Rods) OR (Gram-Negative Bacteria) OR (Gram Negative Bacteria) OR (Gamma Proteobacteria) OR (Proteobacteria gamma) OR (Proteobacteria) OR (Bacteria, Purple) OR (Purple Bacteria) OR (Klebsiella Infections) OR (Infections, Klebsiella) OR (Klebsiella Infection) OR (Enterobacteriaceae Infections) OR (Enterobacterial Infections) OR (Infections, Enterobacterial) OR (Enterobacterial Infection) OR (Infection, Enterobacterial) OR (Infections, Enterobacteriaceae) OR (Enterobacteriaceae Infection) OR (Infection, Enterobacteriaceae) OR (Gram-Negative Bacterial Infections) OR (Gram Negative Bacterial Infections) OR (Infections, Gram-Negative Bacterial) OR (Bacterial Infection, Gram-Negative) OR (Gram-Negative Bacterial Infection) OR (Infection, Gram-Negative Bacterial) OR (Infections, Gram Negative Bacterial) OR (Bacterial Infections, Gram-Negative) OR (Bacterial Infections, Gram Negative)	7
#2.	(Cost Effectiveness) OR (Effectiveness, Cost) OR (Cost-Utility Analysis) OR (Analyses, Cost-Utility) OR (Analysis, Cost-Utility) OR (Cost Utility Analysis) OR (Cost-Utility Analyses) OR (Economic Evaluation) OR (Economic Evaluations) OR (Evaluation, Economic) OR (Evaluations, Economic) OR (Marginal Analysis) OR (Analyses, Marginal) OR (Analysis, Marginal) OR (Marginal Analyses) OR (Cost-Effectiveness Analysis) OR (Analysis, Cost-Effectiveness) OR (Cost Effectiveness Analysis) OR (economics, pharmaceutical) OR (pharmacoeconomics)	2,974
#3.	#1 AND #2	2

LILACS (Literature of the Latin American and Caribbean Health Sciences)

Search ID no.	Search formula	Records retrieved
#1.	(tw:(Klebsiella pneumoniae)) OR (tw:(Klebsiella rhinoscleromatis)) OR (tw:(Klebsiella)) OR (tw:(Enterobacteriaceae)) OR (tw:(Enterobacteria)) OR (tw:(Enteric Bacteria)) OR (tw:(Coliform Bacilli)) OR (tw:(Sodalis)) OR (tw:(Paracolobactrum)) OR (tw:(Ewingella)) OR (tw: Leclercia)) OR (tw:(Gram-Negative Facultatively Anaerobic Rods)) OR (tw:(Gram Negative Facultatively Anaerobic Rods)) OR (tw:(Gram-Negative Bacteria)) OR (tw:(Gram Negative Bacteria)) OR (tw:(Gammaproteobacteria)) OR (tw:(gamma Proteobacteria)) OR (tw:(Proteobacteria gamma)) OR (tw:(Proteobacteria)) OR (tw:(Bacteria, Purple)) OR (tw:(Purple Bacteria)) OR (tw:(Klebsiella Infections)) OR (tw:(Infections, Klebsiella)) OR (tw:(Klebsiella Infection)) OR (tw:(Enterobacteriaceae Infections)) OR (tw:(Enterobacterial Infections)) OR (tw:(Infections, Enterobacterial)) OR (tw:(Enterobacterial Infection)) OR (tw:(Infection, Enterobacterial)) OR (tw:(Infections, Enterobacteriaceae)) OR (tw:(Enterobacteriaceae Infection)) OR (tw:(Infection, Enterobacteriaceae)) OR (tw:(Gram-Negative Bacterial Infections)) OR (tw:(Gram Negative Bacterial Infections)) OR (tw:(Infections, Gram-Negative Bacterial)) OR (tw:(Bacterial Infection, Gram-Negative)) OR (tw:(Gram-Negative Bacterial Infection)) OR (tw:(Infection, Gram-Negative Bacterial)) OR (tw:(Infections, Gram Negative Bacterial)) OR (tw:(Bacterial Infections, Gram-Negative)) OR (tw:(Bacterial Infections, Gram Negative))	7,473

(*Continued*)

Search ID no.	Search formula	Records retrieved
#2.	(tw:(Cost Effectiveness)) OR (tw:(Effectiveness, Cost)) OR (tw:(Cost-Utility Analysis)) OR (tw:(Analyses, Cost-Utility)) OR (tw:(Analysis, Cost-Utility)) OR (tw:(Cost Utility Analysis)) OR (tw:(Cost-Utility Analyses)) OR (tw:(Economic Evaluation)) OR (tw:(Economic Evaluations)) OR (tw:(Evaluation, Economic)) OR (tw:(Evaluations, Economic)) OR (tw:(Marginal Analysis)) OR (tw:(Analyses, Marginal)) OR (tw:(Analysis, Marginal)) OR (tw:(Marginal Analyses)) OR (tw:(Cost-Effectiveness Analysis)) OR (tw:(Analysis, Cost-Effectiveness)) OR (tw:(Cost Effectiveness Analysis)) OR (tw:(economics, pharmaceutical)) OR (tw:(pharmacoeconomics))	6,124
#3.	#1 AND #2	4

PubMed

Search ID no.	Search formula	Records retrieved
#1.	(Klebsiella pneumoniae[Title/Abstract] OR Klebsiella pneumoniae[MeSH Terms]) OR (Klebsiella rhinoscleromatis[Title/Abstract] OR Klebsiella rhinoscleromatis[MeSH Terms]) OR (Klebsiella[Title/Abstract] OR Klebsiella[MeSH Terms]) OR (Enterobacteriaceae[Title/Abstract] OR Enterobacteriaceae[MeSH Terms]) OR (Enterobacteria[Title/Abstract] OR Enterobacteria[MeSH Terms]) OR (Enteric Bacteria[Title/Abstract] OR Enteric Bacteria[MeSH Terms]) OR (Coliform Bacilli[Title/Abstract] OR Coliform Bacilli[MeSH Terms]) OR (Sodalis[Title/Abstract] OR Sodalis[MeSH Terms]) OR (Paracolobactrum[Title/Abstract] OR Paracolobactrum[MeSH Terms]) OR (Ewingella[Title/Abstract] OR Ewingella[MeSH Terms]) OR (Leclercia[Title/Abstract] OR Leclercia[MeSH Terms]) OR (Gram-Negative Facultatively Anaerobic Rods[Title/Abstract] OR Gram-Negative Facultatively Anaerobic Rods[MeSH Terms]) OR (Gram Negative Facultatively Anaerobic Rods[Title/Abstract] OR Gram Negative Facultatively Anaerobic Rods[MeSH Terms]) OR (Gram-Negative Bacteria[Title/Abstract] OR Gram-Negative Bacteria[MeSH Terms]) OR (Gram Negative Bacteria[Title/Abstract] OR Gram Negative Bacteria[MeSH Terms]) OR (Gammaproteobacteria[Title/Abstract] OR Gammaproteobacteria[MeSH Terms]) OR (gamma Proteobacteria[Title/Abstract] OR gamma Proteobacteria[MeSH Terms]) OR (Proteobacteria gamma[Title/Abstract] OR Proteobacteria gamma[MeSH Terms]) OR (Proteobacteria[Title/Abstract] OR Proteobacteria[MeSH Terms]) OR (Bacteria, Purple[Title/Abstract] OR Bacteria, Purple[MeSH Terms]) OR (Purple Bacteria[Title/Abstract] OR Purple Bacteria[MeSH Terms]) OR (Klebsiella Infections[Title/Abstract] OR Klebsiella Infections[MeSH Terms]) OR (infections, Klebsiella[Title/Abstract] OR Infections, Klebsiella[MeSH Terms]) OR (Klebsiella Infection[Title/Abstract] OR Klebsiella Infection[MeSH Terms]) OR (Enterobacteriaceae Infections[Title/Abstract] OR Enterobacteriaceae Infections[MeSH Terms]) OR (Enterobacterial Infections[Title/Abstract] OR Enterobacterial Infections[MeSH Terms]) OR (Infections, Enterobacterial[Title/Abstract] OR Infections, Enterobacterial[MeSH Terms]) OR (Enterobacterial Infection[Title/Abstract] OR Enterobacterial Infection[MeSH Terms]) OR (Infection, Enterobacterial[Title/Abstract] OR Infection, Enterobacterial[MeSH Terms]) OR (Infections, Enterobacteriaceae[Title/Abstract] OR Infections, Enterobacteriaceae[MeSH Terms]) OR (Enterobacteriaceae Infection[Title/Abstract] OR Enterobacteriaceae Infection[MeSH Terms]) OR (Infection, Enterobacteriaceae[Title/Abstract] OR Infection, Enterobacteriaceae[MeSH Terms]) OR (Gram-Negative Bacterial Infections[Title/Abstract] OR Gram-Negative Bacterial Infections[MeSH Terms]) OR (Gram Negative Bacterial Infections[Title/Abstract] OR Gram Negative Bacterial Infections[MeSH Terms]) OR (Infections, Gram-Negative Bacterial[Title/Abstract] OR Infections, Gram-Negative Bacterial[MeSH Terms]) OR (Bacterial Infection, Gram-Negative[Title/Abstract] OR Bacterial Infection, Gram-Negative[MeSH Terms]) OR (Gram-Negative Bacterial Infection[Title/Abstract] OR Gram-Negative Bacterial Infection[MeSH Terms]) OR (Infection, Gram-Negative Bacterial[Title/Abstract] OR Infection, Gram-Negative Bacterial[MeSH Terms]) OR (Infections, Gram Negative Bacterial[Title/Abstract] OR Infections, Gram Negative Bacterial[MeSH Terms]) OR (Bacterial Infections, Gram-Negative[Title/Abstract] OR Bacterial Infections, Gram-Negative[MeSH Terms]) OR (Bacterial Infections, Gram Negative[Title/Abstract] Bacterial Infections, Gram Negative[MeSH Terms])	964,685

(*Continued*)		
Search ID no.	**Search formula**	**Records retrieved**
#2.	(Cost Effectiveness[Title/Abstract] OR Cost Effectiveness[MeSH Terms]) OR (Effectiveness, Cost[Title/Abstract] OR Effectiveness, Cost[MeSH Terms]) OR (Cost-Utility Analysis[Title/Abstract] OR Cost-Utility Analysis[MeSH Terms]) OR (Analyses, Cost-Utility[Title/Abstract] OR Analyses, Cost-Utility[MeSH Terms]) OR (Analysis, Cost-Utility[Title/Abstract] OR Analysis, Cost-Utility[MeSH Terms]) OR (Cost Utility Analysis[Title/Abstract] OR Cost Utility Analysis[MeSH Terms]) OR (Cost-Utility Analyses[Title/Abstract] OR Cost-Utility Analyses[MeSH Terms]) OR (Economic Evaluation[Title/Abstract] OR Economic Evaluation[MeSH Terms]) OR (Economic Evaluations[Title/Abstract] OR Economic Evaluations[MeSH Terms]) OR (Evaluation, Economic[Title/Abstract] OR Evaluation, Economic[MeSH Terms]) OR (Evaluations, Economic[Title/Abstract] OR Evaluations, Economic[MeSH Terms]) OR (Marginal Analysis[Title/Abstract] OR Marginal Analysis[MeSH Terms]) OR (Analyses, Marginal[Title/Abstract] OR Analyses, Marginal[MeSH Terms]) OR (Analysis, Marginal[Title/Abstract] OR Analysis, Marginal[MeSH Terms]) OR (Marginal Analyses[Title/Abstract] OR Marginal Analyses[MeSH Terms]) OR (Cost-Effectiveness Analysis[Title/Abstract] OR Cost-Effectiveness Analysis[MeSH Terms]) OR (Analysis, Cost-Effectiveness[Title/Abstract] OR Analysis, Cost-Effectiveness[MeSH Terms]) OR (Cost Effectiveness Analysis[Title/Abstract] OR Cost Effectiveness Analysis[MeSH Terms]) OR (economics, pharmaceutical[Title/Abstract] OR economics, pharmaceutical[MeSH Terms]) OR (pharmacoeconomics[Title/Abstract] OR pharmacoeconomics[MeSH Terms])	149,413
#3.	#1 AND #2	2,801

NHS EED (National Health Service Economic Evaluation Database)

Search ID no.	**Search formula**	**Records retrieved**
#1.	(Klebsiella pneumoniae) OR (Klebsiella rhinoscleromatis) OR (Klebsiella) OR (Enterobacteriaceae) OR (Enterobacteria) OR (Enteric Bacteria) OR (Coliform Bacilli) OR (Sodalis) OR (Paracolobactrum) OR (Ewingella) OR (Leclercia) OR (Gram-Negative Facultatively Anaerobic Rods) OR (Gram Negative Facultatively Anaerobic Rods) OR (Gram-Negative Bacteria) OR (Gram Negative Bacteria) OR (Gamma Proteobacteria) OR (Proteobacteria gamma) OR (Proteobacteria) OR (Bacteria, Purple) OR (Purple Bacteria) OR (Klebsiella Infections) OR (Infections, Klebsiella) OR (Klebsiella Infection) OR (Enterobacteriaceae Infections) OR (Enterobacterial Infections) OR (Infections, Enterobacterial) OR (Enterobacterial Infection) OR (Infection, Enterobacterial) OR (Infections, Enterobacteriaceae) OR (Enterobacteriaceae Infection) OR (Infection, Enterobacteriaceae) OR (Gram-Negative Bacterial Infections) OR (Gram Negative Bacterial Infections) OR (Infections, Gram-Negative Bacterial) OR (Bacterial Infection, Gram-Negative) OR (Gram-Negative Bacterial Infection) OR (Infection, Gram-Negative Bacterial) OR (Infections, Gram Negative Bacterial) OR (Bacterial Infections, Gram-Negative) OR (Bacterial Infections, Gram Negative)	57
#2.	(Cost Effectiveness) OR (Effectiveness, Cost) OR (Cost-Utility Analysis) OR (Analyses, Cost-Utility) OR (Analysis, Cost-Utility) OR (Cost Utility Analysis) OR (Cost-Utility Analyses) OR (Economic Evaluation) OR (Economic Evaluations) OR (Evaluation, Economic) OR (Evaluations, Economic) OR (Marginal Analysis) OR (Analyses, Marginal) OR (Analysis, Marginal) OR (Marginal Analyses) OR (Cost-Effectiveness Analysis) OR (Analysis, Cost-Effectiveness) OR (Cost Effectiveness Analysis) OR (economics, pharmaceutical) OR (pharmacoeconomics)	18,215
#3.	#1 AND #2	32

Science Direct

Search ID no.	Search formula	Records retrieved
#1.	(Tak(“Klebsiella pneumoniae”)) OR (Tak(“Klebsiella rhinoscleromatis”)) OR (Tak(“Klebsiella”)) OR (Tak(“Enterobacteriaceae”)) OR (Tak(“Enterobacteria”)) OR (Tak(“Enteric Bacteria”)) OR (Tak(“Coliform Bacilli”)) OR (Tak(“Sodalis”)) OR (Tak(“Paracolobactrum”)) OR (Tak(“Ewingella”)) OR (Tak(“Leclercia”)) OR (Tak(“Gram-Negative Facultatively Anaerobic Rods”)) OR (Tak(“Gram Negative Facultatively Anaerobic Rods”)) OR (Tak(“Gram-Negative Bacteria”)) OR (Tak(“Gram Negative Bacteria”)) OR (Tak(“Gammaproteobacteria”)) OR (Tak(“gamma Proteobacteria”)) OR (Tak(“Proteobacteria gamma”)) OR (Tak(“Proteobacteria”)) OR (Tak(“Bacteria, Purple”)) OR (Tak(“Purple Bacteria”)) OR (Tak(“Klebsiella Infections”)) OR (Tak(“Infections, Klebsiella”)) OR (Tak(“Klebsiella Infection”)) OR (Tak(“Enterobacteriaceae Infections”)) OR (Tak(“Enterobacterial Infections”)) OR (Tak(“Infections, Enterobacterial”)) OR (Tak(“Enterobacterial Infection”)) OR (Tak(“Infection, Enterobacterial”)) OR (Tak(“Infections, Enterobacteriaceae”)) OR (Tak(“Enterobacteriaceae Infection”)) OR (Tak(“Infection, Enterobacteriaceae”)) OR (Tak(“Gram-Negative Bacterial Infections”)) OR (Tak(“Gram Negative Bacterial Infections”)) OR (Tak(“Infections, Gram-Negative Bacterial”)) OR (Tak(“Bacterial Infection, Gram-Negative”)) OR (Tak(“Gram-Negative Bacterial Infection”)) OR (Tak(“Infection, Gram-Negative Bacterial”)) OR (Tak(“Infections, Gram Negative Bacterial”)) OR (Tak(“Bacterial Infections, Gram-Negative”)) OR (Tak(“Bacterial Infections, Gram Negative”))	39,448
#2.	(Tak(“Cost Effectiveness”)) OR (Tak(“Effectiveness, Cost”)) OR (Tak(“Cost-Utility Analysis”)) OR (Tak(“Analyses, Cost-Utility”)) OR (Tak(“Analysis, Cost-Utility”)) OR (Tak(“Cost Utility Analysis”)) OR (Tak(“Cost-Utility Analyses”)) OR (Tak(“Economic Evaluation”)) OR (Tak(“Economic Evaluations”)) OR (Tak(“Evaluation, Economic”)) OR (Tak(“Evaluations, Economic”)) OR (Tak(“Marginal Analysis”)) OR (Tak(“Analyses, Marginal”)) OR (Tak(“Analysis, Marginal”)) OR (Tak(“Marginal Analyses”)) OR (Tak(“Cost-Effectiveness Analysis”)) OR (Tak(“Analysis, Cost-Effectiveness”)) OR (Tak(“Cost Effectiveness Analysis”)) OR (Tak(“economics, pharmaceutical”)) OR (Tak(“pharmacoeconomics”))	19,156
#3.	#1 AND #2	27

Web of Science

Search ID no.	Search formula	Records retrieved
#1.	(TS = (Klebsiella pneumoniae)) OR (TS = (Klebsiella rhinoscleromatis)) OR (TS = (Klebsiella)) OR (TS = (Enterobacteriaceae)) OR (TS = (Enterobacteria)) OR (TS = (Enteric Bacteria)) OR (TS = (Coliform Bacilli)) OR (TS = (Sodalis)) OR (TS = (paracolobacterum)) OR (TS = (eungella)) OR (TS = (Leclercia)) OR (TS = (Gram-Negative Facultatively Anaerobic Rods)) OR (TS = (Gram Negative Facultatively Anaerobic Rods)) OR (TS = (Gram Negative Bacteria)) OR (TS = (Gram-Negative Bacteria)) OR (TS = (Gammaproteobacteria)) OR (TS = (gamma Proteobacteria)) OR (TS = (Proteobacteria gamma)) OR (TS = (Proteobacteria)) OR (TS = (Bacteria, Purple)) OR (TS = (Purple Bacteria)) OR (TS = (Klebsiella Infections)) OR (TS = (Infections, Klebsiella)) OR (TS = (Klebsiella Infection)) OR (TS = (Enterobacteriaceae Infections)) OR (TS = (Enterobacterial Infections)) OR (TS = (Infections, Enterobacterial)) OR (TS = (Enterobacterial Infection)) OR (TS = (Infection, Enterobacterial)) OR (TS = (Infections, Enterobacteriaceae)) OR (TS = (Enterobacteriaceae Infection)) OR (TS = (Infection, Enterobacteriaceae)) OR (TS = (Gram-Negative Bacterial Infections)) OR (TS = (Gram Negative Bacterial Infections)) OR (TS = (Infections, Gram-Negative Bacterial)) OR (TS = (Bacterial Infection, Gram-Negative)) OR (TS = (Gram-Negative Bacterial Infection)) OR (TS = (Infection, Gram-Negative Bacterial)) OR (TS = (Infections, Gram Negative Bacterial)) OR (TS = (Bacterial Infections, Gram-Negative)) OR (TS = (Bacterial Infections, Gram Negative))	143,290

(*Continued*)		
Search ID no.	**Search formula**	**Records retrieved**
#2.	(TS = (Cost Effectiveness)) OR (TS = (Effectiveness, Cost)) OR (TS = (Cost-Utility Analysis)) OR (TS = (Analyses, Cost-Utility)) OR (TS = (Analysis, Cost-Utility)) OR (TS = (Cost Utility Analysis)) OR (TS = (Cost-Utility Analyses)) OR (TS = (Economic Evaluation)) OR (TS = (Economic Evaluations)) OR (TS = (Evaluation, Economic)) OR (TS = (Evaluations, Economic)) OR (TS = (Marginal Analysis)) OR (TS = (Analyses, Marginal)) OR (TS = (Analysis, Marginal)) OR (TS = (Marginal Analyses)) OR (TS = (Cost-Effectiveness Analysis)) OR (TS = (Analysis, Cost-Effectiveness)) OR (TS = (Cost Effectiveness Analysis)) OR (TS = (economics, pharmaceutical)) OR (TS = (pharmacoeconomics))	253,386
#3.	#1 AND #2	384

Bank of CAPES for theses and dissertations

Search ID no.	**Search formula**	**Records retrieved**
#1.	(''Klebsiella pneumoniae'' OR ''Klebsiella rhinoscleromatis'' OR ''Klebsiella'' OR ''Enterobacteriaceae'' OR ''Enterobacteria'' OR ''Enteric Bacteria'' OR ''Coliform Bacilli'' OR ''Sodalis'' OR ''Paracolobactrum'' OR ''Ewingella'' OR ''Leclercia'' OR ''Gram-Negative Facultatively Anaerobic Rods'' OR ''Gram Negative Facultatively Anaerobic Rods'' OR ''Gram-Negative Bacteria'' OR ''Gram Negative Bacteria'' OR ''Gamma Proteobacteria'' OR ''Proteobacteria gamma'' OR ''Proteobacteria'' OR ''Bacteria, Purple'' OR ''Purple Bacteria'' OR ''Klebsiella Infections'' OR ''Infections, Klebsiella'' OR ''Klebsiella Infection'' OR ''Enterobacteriaceae Infections'' OR ''Enterobacterial Infections'' OR ''Infections, Enterobacterial'' OR ''Enterobacterial Infection'' OR ''Infection, Enterobacterial'' OR ''Infections, Enterobacteriaceae'' OR ''Enterobacteriaceae Infection'' OR ''Infection, Enterobacteriaceae'' OR ''Gram-Negative Bacterial Infections'' OR ''Gram Negative Bacterial Infections'' OR ''Infections, Gram-Negative Bacterial'' OR ''Bacterial Infection, Gram-Negative'' OR ''Gram-Negative Bacterial Infection'' OR ''Infection, Gram-Negative Bacterial'' OR ''Infections, Gram Negative Bacterial'' OR ''Bacterial Infections, Gram-Negative'' OR ''Bacterial Infections, Gram Negative'')	2,488
#2.	(''Cost Effectiveness'' OR ''Effectiveness, Cost'' OR ''Cost-Utility Analysis'' OR ''Analyses, Cost-Utility'' OR ''Analysis, Cost-Utility'' OR ''Cost Utility Analysis'' OR ''Cost-Utility Analyses'' OR ''Economic Evaluation'' OR ''Economic Evaluations'' OR ''Evaluation, Economic'' OR ''Evaluations, Economic'' OR ''Marginal Analysis'' OR ''Analyses, Marginal'' OR ''Analysis, Marginal'' OR ''Marginal Analyses'' OR ''Cost-Effectiveness Analysis'' OR ''Analysis, Cost-Effectiveness'' OR ''Cost Effectiveness Analysis'' OR ''economics, pharmaceutical'' OR ''pharmacoeconomics'')	598
#3.	#1 AND #2	0

MedNar

Search ID no.	Search formula	Records retrieved
#1.	(''Klebsiella pneumoniae'' OR ''Klebsiella rhinoscleromatis'' OR ''Klebsiella'' OR ''Enterobacteriaceae'' OR ''Enterobacteria'' OR ''Enteric Bacteria'' OR ''Coliform Bacilli'' OR ''Sodalis'' OR ''Paracolobactrum'' OR ''Ewingella'' OR ''Leclercia'' OR ''Gram-Negative Facultatively Anaerobic Rods'' OR ''Gram Negative Facultatively Anaerobic Rods'' OR ''Gram-Negative Bacteria'' OR ''Gram Negative Bacteria'' OR ''Gamma Proteobacteria'' OR ''Proteobacteria gamma'' OR ''Proteobacteria'' OR ''Bacteria, Purple'' OR ''Purple Bacteria'' OR ''Klebsiella Infections'' OR ''Infections, Klebsiella'' OR ''Klebsiella Infection'' OR ''Enterobacteriaceae Infections'' OR ''Enterobacterial Infections'' OR ''Infections, Enterobacterial'' OR ''Enterobacterial Infection'' OR ''Infection, Enterobacterial'' OR ''Infections, Enterobacteriaceae'' OR ''Enterobacteriaceae Infection'' OR ''Infection, Enterobacteriaceae'' OR ''Gram-Negative Bacterial Infections'' OR ''Gram Negative Bacterial Infections'' OR ''Infections, Gram-Negative Bacterial'' OR ''Bacterial Infection, Gram-Negative'' OR ''Gram-Negative Bacterial Infection'' OR ''Infection, Gram-Negative Bacterial'' OR ''Infections, Gram Negative Bacterial'' OR ''Bacterial Infections, Gram-Negative'' OR ''Bacterial Infections, Gram Negative'') in title	633
#2.	(''Cost Effectiveness'' OR ''Effectiveness, Cost'' OR ''Cost-Utility Analysis'' OR ''Analyses, Cost-Utility'' OR ''Analysis, Cost-Utility'' OR ''Cost Utility Analysis'' OR ''Cost-Utility Analyses'' OR ''Economic Evaluation'' OR ''Economic Evaluations'' OR ''Evaluation, Economic'' OR ''Evaluations, Economic'' OR ''Marginal Analysis'' OR ''Analyses, Marginal'' OR ''Analysis, Marginal'' OR ''Marginal Analyses'' OR ''Cost-Effectiveness Analysis'' OR ''Analysis, Cost-Effectiveness'' OR ''Cost Effectiveness Analysis'' OR ''economics, pharmaceutical'' OR ''pharmacoeconomics'') in title	1,076
#3.	#1 AND #2	224

Google Scholar

Search ID no.	Search formula	Records retrieved
#1.	allintitle: ''Klebsiella pneumoniae''	16,800
#2.	allintitle: ''Klebsiella rhinoscleromatis''	75
#3.	allintitle: ''Klebsiella''	33,200
#4.	allintitle: ''Enterobacteriaceae''	12,400
#5.	allintitle: ''Enterobacteria''	2,110
#6.	allintitle: ''Enteric Bacteria''	1,820
#7.	allintitle: ''Coliform Bacilli''	77
#8.	allintitle: ''Sodalis''	642
#9.	allintitle: ''Paracolobactrum''	75
#10.	allintitle: ''Ewingella''	55
#11.	allintitle: ''Leclercia''	157
#12.	allintitle: ''Gram-Negative Facultatively Anaerobic Rods''	7
#13.	allintitle: ''Gram Negative Facultatively Anaerobic Rods''	7
#14.	allintitle: ''Gram-Negative Bacteria''	9,210
#15.	allintitle: ''Gram Negative Bacteria''	9,210
#16.	allintitle: ''Gammaproteobacteria''	240

(*Continued*)

Search ID no.	Search formula	Records retrieved
#17.	allintitle: "gamma Proteobacteria"	74
#18.	allintitle: "Proteobacteria gamma"	22
#19.	allintitle: "Proteobacteria"	1,480
#20.	allintitle: "Bacteria, Purple"	50
#21.	allintitle: "Purple Bacteria"	1,220
#22.	allintitle: "Klebsiella Infections"	194
#23.	allintitle: "Infections, Klebsiella"	34
#24.	allintitle: "Klebsiella Infection"	223
#25.	allintitle: "Enterobacteriaceae Infections"	241
#26.	allintitle: "Enterobacterial Infections"	33
#27.	allintitle: "Infections, Enterobacterial"	0
#28.	allintitle: "Enterobacterial Infection"	24
#29.	allintitle: "Infection, Enterobacterial"	0
#30.	allintitle: "Infections, Enterobacteriaceae"	7
#31.	allintitle: "Enterobacteriaceae Infection"	60
#32.	allintitle: "Infection, Enterobacteriaceae"	5
#33.	allintitle: "Gram-Negative Bacterial Infections"	237
#34.	allintitle: "Gram Negative Bacterial Infections"	237
#35.	allintitle: "Infections, Gram-Negative Bacterial"	2
#36.	allintitle: "Bacterial Infection, Gram-Negative"	0
#37.	allintitle: "Gram-Negative Bacterial Infection"	110
#38.	allintitle: "Infection, Gram-Negative Bacterial"	0
#39.	allintitle: "Infections, Gram Negative Bacterial"	2
#40.	allintitle: "Bacterial Infections, Gram-Negative"	3
#41.	allintitle: "Bacterial Infections, Gram Negative"	3
#42.	allintitle: "Cost Effectiveness"	99,500
#43.	allintitle: "Effectiveness, Cost"	2,740
#44.	allintitle: "Cost-Utility Analysis"	2,220
#45.	allintitle: "Analyses, Cost-Utility"	4
#46.	allintitle: "Analysis, Cost-Utility"	83
#47.	allintitle: "Cost Utility Analysis"	2,220
#48.	allintitle: "Cost-Utility Analyses"	194
#49.	allintitle: "Economic Evaluation"	37,400
#50.	allintitle: "Economic Evaluations"	2,370
#51.	allintitle: "Evaluation, Economic"	687
#52.	allintitle: "Evaluations, Economic"	56
#53.	allintitle: "Marginal Analysis"	493
#54.	allintitle: "Analyses, Marginal"	2

(*Continued*)

Search ID no.	Search formula	Records retrieved
#55.	allintitle: "Analysis, Marginal"	76
#56.	allintitle: "Marginal Analyses"	10
#57.	allintitle: "Cost-Effectiveness Analysis"	13,500
#58.	allintitle: "Analysis, Cost-Effectiveness"	640
#59.	allintitle: "Cost Effectiveness Analysis"	13,500
#60.	allintitle: "economics, pharmaceutical"	10
#61.	allintitle: "pharmacoeconomics"	2,270
#62.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #42 OR #43	5
#63.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #44 OR #45	5
#64.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #46 OR #47	4
#65.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #48 OR #49	4
#66.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #50 OR #51	0
#67.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #52 OR #53	0
#68.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #54 OR #55	0
#69.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #56 OR #57	0
#70.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #58 OR #59	0
#71.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) AND #60 OR #61	0
#72.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #42 OR #43	0
#73.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #44 OR #45	0
#74.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #46 OR #47	0
#75.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #48 OR #49	0
#76.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #50 OR #51	0
#77.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #52 OR #53	0
#78.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #54 OR #55	0
#79.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #56 OR #57	0
#80.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #58 OR #59	0
#81.	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16) AND #60 OR #61	0
#82.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #42 OR #43	0
#83.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #44 OR #45	0
#84.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #46 OR #47	0
#85.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #48 OR #49	0
#86.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #50 OR #51	0
#87.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #52 OR #53	0
#88.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #54 OR #55	0
#89.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #56 OR #57	0
#90.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #58 OR #59	0
#91.	(#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24) AND #60 OR #61	0
#92.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #42 OR #43	0

(*Continued*)		
Search ID no.	**Search formula**	**Records retrieved**
#93.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #44 OR #45	0
#94.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #46 OR #47	0
#95.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #48 OR #49	0
#96.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #50 OR #51	0
#97.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #52 OR #53	0
#98.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #54 OR #55	0
#99.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #56 OR #57	0
#100.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #58 OR #59	0
#101.	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32) AND #60 OR #61	0
#102.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #42 OR #43	0
#103.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #44 OR #45	0
#104.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #46 OR #47	0
#105.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #48 OR #49	0
#106.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #50 OR #51	0
#107.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #52 OR #53	0
#108.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #54 OR #55	0
#109.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #56 OR #57	0
#110.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #58 OR #59	0
#111.	(#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41) AND #60 OR #61	0

*This database has a limit in the number of characters in the search field.

NYAM (New York Academy of Medicine)

Search ID no.	Search formula	Records retrieved
#1.	(kw,wrdl: Klebsiella pneumoniae) OR (kw,wrdl: Klebsiella rhinoscleromatis) OR (kw,wrdl: Klebsiella) OR (kw,wrdl: Enterobacteriaceae) OR (kw,wrdl: Enterobacteria) OR (kw,wrdl: Enteric Bacteria) OR (kw,wrdl: Coliform Bacilli) OR (kw,wrdl: Sodalis) OR (kw,wrdl: Paracolobactrum) OR (kw,wrdl: Ewingella) OR (kw,wrdl: Leclercia) OR (kw,wrdl: Gram-Negative Facultatively Anaerobic Rods) OR (kw,wrdl: Gram Negative Facultatively Anaerobic Rods) OR (kw,wrdl: Gram-Negative Bacteria) OR (kw,wrdl: Gram Negative Bacteria) OR (kw,wrdl: Gammaproteobacteria) OR (kw,wrdl: gamma Proteobacteria) OR (kw,wrdl: Proteobacteria gamma) OR (kw,wrdl: Proteobacteria) OR (kw,wrdl: Bacteria, Purple) OR (kw,wrdl: Purple Bacteria) OR (kw,wrdl: Klebsiella Infections) OR (kw,wrdl: Infections, Klebsiella) OR (kw,wrdl: Klebsiella Infection) OR (kw,wrdl: Enterobacteriaceae Infections) OR (kw,wrdl: Enterobacterial Infections) OR (kw,wrdl: Infections, Enterobacterial) OR (kw,wrdl: Enterobacterial Infection) OR (kw,wrdl: Infection, Enterobacterial) OR (kw,wrdl: Infections, Enterobacteriaceae) OR (kw,wrdl: Enterobacteriaceae Infection) OR (kw,wrdl: Infection, Enterobacteriaceae) OR (kw,wrdl: Gram-Negative Bacterial Infections) OR (kw,wrdl: Gram Negative Bacterial Infections) OR (kw,wrdl: Infections, Gram-Negative Bacterial) OR (kw,wrdl: Bacterial Infection, Gram-Negative) OR (kw,wrdl: Gram-Negative Bacterial Infection) OR (kw,wrdl: Infection, Gram-Negative Bacterial) OR (kw,wrdl: Infections, Gram Negative Bacterial) OR (kw,wrdl: Bacterial Infections, Gram-Negative) OR (kw,wrdl: Bacterial Infections, Gram Negative)	78

(*Continued*)		
Search ID no.	**Search formula**	**Records retrieved**
#2.	(kw,wrdl: Cost Effectiveness) OR (kw,wrdl: Effectiveness, Cost) OR (kw,wrdl: Cost-Utility Analysis) OR (kw,wrdl: Analyses, Cost-Utility) OR (kw,wrdl: Analysis, Cost-Utility) OR (kw,wrdl: Cost Utility Analysis) OR (kw,wrdl: Cost-Utility Analyses) OR (kw,wrdl: Economic Evaluation) OR (kw,wrdl: Economic Evaluations) OR (kw,wrdl: Evaluation, Economic) OR (kw,wrdl: Evaluations, Economic) OR (kw,wrdl: Marginal Analysis) OR (kw,wrdl: Analyses, Marginal) OR (kw,wrdl: Analysis, Marginal) OR (kw,wrdl: Marginal Analyses) OR (kw,wrdl: Cost-Effectiveness Analysis) OR (kw,wrdl: Analysis, Cost-Effectiveness) OR (kw,wrdl: Cost Effectiveness Analysis) OR (kw,wrdl: economics, pharmaceutical) OR (kw,wrdl: pharmacoeconomics) OR	758
#3.	#1 AND #2	0

ProQuest Dissertations and Theses

Search ID no.	Search formula	Records retrieved
#1.	(''Klebsiella pneumoniae'' OR ''Klebsiella rhinoscleromatis'' OR ''Klebsiella'' OR ''Enterobacteriaceae'' OR ''Enterobacteria'' OR ''Enteric Bacteria'' OR ''Coliform Bacilli'' OR ''Sodalis'' OR ''Paracolobactrum'' OR ''Ewingella'' OR ''Leclercia'' OR ''Gram-Negative Facultatively Anaerobic Rods'' OR ''Gram Negative Facultatively Anaerobic Rods'' OR ''Gram-Negative Bacteria'' OR ''Gram Negative Bacteria'' OR ''Gamma Proteobacteria'' OR ''Proteobacteria gamma'' OR ''Proteobacteria'' OR ''Bacteria, Purple'' OR ''Purple Bacteria'' OR ''Klebsiella Infections'' OR ''Infections, Klebsiella'' OR ''Klebsiella Infection'' OR ''Enterobacteriaceae Infections'' OR ''Enterobacterial Infections'' OR ''Infections, Enterobacterial'' OR ''Enterobacterial Infection'' OR ''Infection, Enterobacterial'' OR ''Infections, Enterobacteriaceae'' OR ''Enterobacteriaceae Infection'' OR ''Infection, Enterobacteriaceae'' OR ''Gram-Negative Bacterial Infections'' OR ''Gram Negative Bacterial Infections'' OR ''Infections, Gram-Negative Bacterial'' OR ''Bacterial Infection, Gram-Negative'' OR ''Gram-Negative Bacterial Infection'' OR ''Infection, Gram-Negative Bacterial'' OR ''Infections, Gram Negative Bacterial'' OR ''Bacterial Infections, Gram-Negative'' OR ''Bacterial Infections, Gram Negative'')	5,702
#2.	(''Cost Effectiveness'' OR ''Effectiveness, Cost'' OR ''Cost-Utility Analysis'' OR ''Analyses, Cost-Utility'' OR ''Analysis, Cost-Utility'' OR ''Cost Utility Analysis'' OR ''Cost-Utility Analyses'' OR ''Economic Evaluation'' OR ''Economic Evaluations'' OR ''Evaluation, Economic'' OR ''Evaluations, Economic'' OR ''Marginal Analysis'' OR ''Analyses, Marginal'' OR ''Analysis, Marginal'' OR ''Marginal Analyses'' OR ''Cost-Effectiveness Analysis'' OR ''Analysis, Cost-Effectiveness'' OR ''Cost Effectiveness Analysis'' OR ''economics, pharmaceutical'' OR ''pharmacoeconomics'')	6,273
#3.	#1 AND #2	0

WorldWideScience.org

Search ID no.	Search formula	Records retrieved
#1.	(''Klebsiella pneumoniae'' OR ''Klebsiella rhinoscleromatis'' OR ''Klebsiella'' OR ''Enterobacteriaceae'' OR ''Enterobacteria'' OR ''Enteric Bacteria'' OR ''Coliform Bacilli'' OR ''Sodalis'' OR ''Paracolobactrum'' OR ''Ewingella'' OR ''Leclercia'' OR ''Gram-Negative Facultatively Anaerobic Rods'' OR ''Gram Negative Facultatively Anaerobic Rods'' OR ''Gram-Negative Bacteria'' OR ''Gram Negative Bacteria'' OR ''Gamma Proteobacteria'' OR ''Proteobacteria gamma'' OR ''Proteobacteria'' OR ''Bacteria, Purple'' OR ''Purple Bacteria'' OR ''Klebsiella Infections'' OR ''Infections, Klebsiella'' OR ''Klebsiella Infection'' OR ''Enterobacteriaceae Infections'' OR ''Enterobacterial Infections'' OR ''Infections, Enterobacterial'' OR ''Enterobacterial Infection'' OR ''Infection, Enterobacterial'' OR ''Infections, Enterobacteriaceae'' OR ''Enterobacteriaceae Infection'' OR ''Infection, Enterobacteriaceae'' OR ''Gram-Negative Bacterial Infections'' OR ''Gram Negative Bacterial Infections'' OR ''Infections, Gram-Negative Bacterial'' OR ''Bacterial Infection, Gram-Negative'' OR ''Gram-Negative Bacterial Infection'' OR ''Infection, Gram-Negative Bacterial'' OR ''Infections, Gram Negative Bacterial'' OR ''Bacterial Infections, Gram-Negative'' OR ''Bacterial Infections, Gram Negative'') in title	1,613
#2.	(''Cost Effectiveness'' OR ''Effectiveness, Cost'' OR ''Cost-Utility Analysis'' OR ''Analyses, Cost-Utility'' OR ''Analysis, Cost-Utility'' OR ''Cost Utility Analysis'' OR ''Cost-Utility Analyses'' OR ''Economic Evaluation'' OR ''Economic Evaluations'' OR ''Evaluation, Economic'' OR ''Evaluations, Economic'' OR ''Marginal Analysis'' OR ''Analyses, Marginal'' OR ''Analysis, Marginal'' OR ''Marginal Analyses'' OR ''Cost-Effectiveness Analysis'' OR ''Analysis, Cost-Effectiveness'' OR ''Cost Effectiveness Analysis'' OR ''economics, pharmaceutical'' OR ''pharmacoeconomics'') in title	2,077
#3.	#1 AND #2	472

Appendix II: Studies ineligible following full text review

No.	Article	Reason
1.	Amodio-Groton M, Madu A, Madu CN, Briceland LL, Seligman M, McMaster P, *et al.* Sequential parenteral and oral ciprofloxacin regimen versus parenteral therapy for bacteremia: a pharmacoeconomic analysis. Ann Pharmacother Jun 1996;30(6):596-602.	Ineligible study design
2.	Benfield P, Chrisp P. Imipenem/cilastatin: a pharmacoeconomic appraisal of its use in intra-abdominal infections. Pharmacoeconomics Jun 1992;1(6):443-59.	Ineligible study design
3.	Bijie H, Kulpradist S, Manalaysay M, Soebandrio A. In vitro activity, pharmacokinetics, clinical efficacy, safety and pharmacoeconomics of ceftriaxone compared with third and fourth generation cephalosporins: review. J Chemother Feb 2005;17(1):3-24.	Ineligible study design
4.	Blanchette LM, Kut JL, Nicolau DP, Nailor MD. Clinical comparison of ertapenem and cefepime for treatment of infections caused by AmpC beta-lactamase-producing Enterobacteriaceae. Scand J Infect Dis 2014;46(11):803-8.	Ineligible study design
5.	Boucher BA. Role of aztreonam in the treatment of nosocomial pneumonia in the critically ill surgical patient. Am J Surg Feb 2000;179(2A Suppl):45S-50S.	Ineligible study design
6.	Burke JP, Pestotnik, SL. Antibiotic use and microbial resistance in intensive care units: impact of computer-assisted decision support. J Chemother. Dec 1999;11(6):530-5.	Ineligible study design
7.	Burrichter PJ, Murabito A, Sohn CA, Lentnek, AL. Comparative efficacy, safety and cost of cefazolin given two vs four times daily for urinary tract infections caused by common pathogens in hospitalized adults. Adv Ther 1984;1(4):247-255.	Ineligible study design
8.	Cong ZH, Xu LJ, Guan YH, Li XD. Pharmaceutical-economic analysis and efficacy evolution of piperacillin/sulbactam in treatment of hospital acquired pneumonia. Chinese J Antibiot 2011;36(3):228-232.	Ineligible study design
9.	Cox CE. Cost-effective management of complicated urinary tract infections. Adv Ther. Jul-Aug 1995;12(4):222-35.	Ineligible study design
10.	Cutro SR, Holzman R, Dubrovskaya Y, Chen XJ, Ahuja T, Scipione MR, *et al.* Extended-Infusion versus standard-infusion piperacillin-tazobactam for sepsis syndromes at a tertiary medical center. Antimicrob Agents Chemother. Aug 2014;58(8):4470-5.	Ineligible study design
11.	Davis R, Bryson HM. Ceftriaxone. A pharmacoeconomic evaluation of its use in the treatment of serious infections. Pharmacoeconomics. 1994;6(3):249-69.	Ineligible comparator
12.	Goodpasture HC, Gerlach EH, Jones RN, Peterie JD. Optimal cefotaxime dosing for gram-negative bacteremia: Effective trough serum bactericidal titers and drug concentrations 8 and 12 hr after 1- or 2-gm infusions. Diagn Microbiol Infect Dis 1988;9(2):97-103.	Ineligible comparator
13.	Harwan WA, Abbassi MM, El-Attar MM, Farid SF. Pharmacoeconomic study of antibiotics used in the treatment of lower respiratory tract infections in ICU patients: A case study in an Egyptian hospital. Bulletin of Faculty of Pharmacy, Cairo University 2014/06/01/ 2014;52(1):135-144.	Ineligible patient population
14.	Kauf TL, Prabhu VS, Medic G, Borse RH, Miller B, Gaultney J, *et al.* Cost-effectiveness of ceftolozane/tazobactam compared with piperacillin/tazobactam as empiric therapy based on the in-vitro surveillance of bacterial isolates in the United States for the treatment of complicated urinary tract infections. BMC Infect Dis Apr 28 2017;17(1):314.	Ineligible outcomes

(*Continued*)

No.	Article	Reason
15.	Kaur K, Gupta A, Sharma A, Walia G, Singh B, Kaur K. Evaluation of efficacy and tolerability of cefotaxime and sulbactam versus cefepime and tazobactam in patients of urinary tract infection-a prospective comparative study. J Clin Diagn Res Nov 2014;8(11):HC05-8.	Ineligible study design
16.	Kolar M, Htoutou Sedlakova M, Urbanek K, Uvizl R, Adamus M, Imwensi OP. Antibiotic therapy of hospital-acquired pneumonia and its pharmacoeconomics. Am J Health Syst Pharm. Sep 15 Mar 2000;57(18):1711-2.	Ineligible study design
17.	Kolar M, Htoutou Sedlakova M, Urbanek K, Uvizl, R, Adamus M, Imwensi OP. Antibiotic therapy of hospital-acquired pneumonia and its pharmacoeconomics. Klin Mikrobiol Infekc Lek Mar 2016;22(1):4-12.	Ineligible study design
18.	Kolbin AS, Sidorenko SV, Zagorodnikova KA, Musatov VB, Iakovlev AA. Clinical and economic expedience of ertapenem therapy of complicated urinary tract infection. Antibiot Khimioter 2011;56(1-2):35-42.	Ineligible study design
19.	Kollef KE, Schramm GE, Wills AR, Reichley RM, Micek ST, Kollef MH. Predictors of 30-day mortality and hospital costs in patients with ventilator-associated pneumonia attributed to potentially antibiotic-resistant gram-negative bacteria. Chest. 2008 Aug;134(2):281-287.	Ineligible study design
20.	Lin HA, Yang YS, Wang JX, Lin HC, Lin DY, Chiu CH, *et al.* Comparison of the effectiveness and antibiotic cost among ceftriaxone, ertapenem, and levofloxacin in treatment of community-acquired complicated urinary tract infections. J Microbiol Immunol Apr 2016;49(2):237-242.	Ineligible setting/ context
21.	Lipsky BA, Napolitano LM, Moran GJ, Vo L, Nicholson S, Chen S, *et al.* Economic outcomes of inappropriate initial antibiotic treatment for complicated skin and soft tissue infections: a multicenter prospective observational study. Diagn Microbiol Infect Dis Jun 2014;79(2):266-272.	Ineligible study design
22.	Madan AK. Use of ciprofloxacin in the treatment of hospitalized patients with intra-abdominal infections. Clin Ther Oct 2004;26(10):1564-77.	Ineligible study design
23.	Molton J, Phillips R, Gandhi M, Yoong J, Lye D, Tan TT, *et al.* Oral versus intravenous antibiotics for patients with Klebsiella pneumoniae liver abscess: study protocol for a randomized controlled trial. Trials. Oct 31 2013;14:364.	Ineligible study design
24.	Otter JA, Burgess P, Davies F, Mookerjee S, Singleton J, Gilchrist M, *et al.* Counting the cost of an outbreak of carbapenemase-producing Enterobacteriaceae: an economic evaluation from a hospital perspective. Clin Microbiol Infec 2017;23:188-96.	Ineligible study design
25.	Periti P. Pharmacoeconomic evaluation of once-daily aminoglycoside treatment. J Chemother Aug 1995;7(4):380-94.	Ineligible study design
26.	Prabhu V, Foo J, Ahir H, Sarpong E, Merchant S. Cost-effectiveness of ceftolozane/tazobactam plus metronidazole compared with piperacillin/tazobactam as empiric therapy for the treatment of complicated intra-abdominal infections based on the in-vitro surveillance of bacterial isolates in the UK. J Med Econ Aug 2017;20(8):840-849.	Ineligible outcomes
27.	Quintanilha JCF, Duarte NDC, Lloret GR, Visacri MB, Mattos KPH, Dragosavac D *et al.* Colistin and polymyxin B for treatment of nosocomial infections in intensive care unit patients: pharmacoeconomic analysis. Int J Clin Pharm. 2019 ;41(1):74-80.	Ineligible study design
28.	Reyes-Lopez A, Jimenez L, Perezbolde C, Pastor, V. Economic evaluation of ertapenem in the treatment of sepsis from enterobacteria producing beta-lactamases of extended spectrum (blees) at the Mexico children's hospital "federico gomez". Value Health May 2016;19(3):A218-A218.	Ineligible patient population

(*Continued*)

No.	Article	Reason
29.	Reynolds R, Gupchup G, Borrego M, Raisch D, Netravali S. Comparing differences in clinical effectiveness, nephrotoxicity, and cost-effectiveness of aminoglycoside therapy between alternative dosing protocols. Value Health. 2001;4(2)136-7.	Ineligible patient population
30.	Siegel R, Alicea M, Lee A, Blaiklock R. Comparison of 7 versus 10 days of antibiotic therapy for hospitalized patients with uncomplicated community-acquired pneumonia: a prospective, randomized, double-blind study. Am J Ther 1999;6(4):217-222.	Ineligible study design
31.	Simon MS, Sfeir MM, Calfee DP, Satlin MJ. Cost-effectiveness of ceftazidime-avibactam for treatment of carbapenem-resistant Enterobacteriaceae bacteremia and pneumonia. Antimicrob Agents Chemother. 2019;pii:AAC.00897-19.	Ineligible outcomes
32.	Stewardson AJ, Marimuthu K, Sengupta S, Allignol A, El-Bouseary M5 Carvalho MJ, *et al.* Effect of carbapenem resistance on outcomes of bloodstream infection caused by Enterobacteriaceae in low-income and middle-income countries (PANORAMA): a multinational prospective cohort study. Lancet Infect Dis. 2019;19(6):601-610.	Ineligible study design
33.	Tramarin A, Bragagnolo L, Tolley K, Sartorelli S, Tositti G, Lazzarini L, *et al.* The application of cost effectiveness analysis to derive a formulary for urinary tract infections. J Chemother. Apr 2002;14(2):166-74.	Ineligible study design
34.	Xu F, Zhao P, Luo Y, Kuang F, Liu L, Liu C. Evaluation of antibacterial activity of amoxycillin sodium and clavulanate potassium and the pharmacoeconomics in the therapy of acute respiratory infection. Chinese J Pediatr 2003;41(5):352-356.	Ineligible study design
35.	Yaqub A, Khan Z. Comparison of early intravenous to oral switch amoxicillin/clavulanate with parenteral ceftriaxone in treatment of hospitalized patients with community acquired pneumonia. Pak J Med Sci 2005;21(3):259-266.	Ineligible study design
36.	Young M, Plosker G. Piperacillin/tazobactam in moderate to severe bacterial infections. Dis Manag Health Out 2002;10(3):195-199.	Ineligible study design
37.	Young M, Plosker GL. Piperacillin/tazobactam - A pharmacoeconomic review of its use in moderate to severe bacterial infections. Pharmacoeconomics 2001;19(11):1135-1175.	Ineligible study design
38.	Zilberberg MD, Mody SH, Chen J, Shorr AF. Cost-effectiveness model of empiric doripenem compared with imipenem-cilastatin in ventilator-associated pneumonia. Surg Infect (Larchmt). 2010;11(5):409-17.	Ineligible outcomes

