**Appendix 1: PRISMA Checklist.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic**  | **#** | **Checklist item**  | **Reported on page #**  |
| **TITLE**  |  |
| Title  | 1 | Identify the report as a systematic review, meta-analysis, or both.  | Title page |
| **ABSTRACT**  |  |
| Structured summary  | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.  | 1 |
| **INTRODUCTION**  |  |
| Rationale  | 3 | Describe the rationale for the review in the context of what is already known.  | 2-3 |
| Objectives  | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | 3 |
| **METHODS**  |  |
| Protocol and registration  | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.  | 3 |
| Eligibility criteria  | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | 4 |
| Information sources  | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | 3 |
| Search  | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.  | 3-4 |
| Study selection  | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).  | 4 |
| Data collection process  | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | 4-5 |
| Data items  | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.  | 4-5 |
| Risk of bias in individual studies  | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.  | 5 |
| Summary measures  | 13 | State the principal summary measures (e.g., risk ratio, difference in means).  | 5 |
| Synthesis of results  | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.  | 5 |
| Risk of bias across studies  | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).  | N/Ap |
| Additional analyses  | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.  | 5 |
| **RESULTS**  |  |
| Study selection  | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.  | 5, Figure 1 (p. 15) |
| Study characteristics  | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.  | 5-6 |
| Risk of bias within studies  | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).  | 6, Figure 2 (p. 16) |
| Results of individual studies  | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.  | 6-8, Table 1 (p. 18-19), Figure 3 (p. 17) |
| Synthesis of results  | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.  | 6-8, Figure 3 (p. 17) |
| Risk of bias across studies  | 22 | Present results of any assessment of risk of bias across studies (see Item 15).  | N/Ap |
| Additional analysis  | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).  | 6-8 |
| **DISCUSSION**  |  |
| Summary of evidence  | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).  | 9-10 |
| Limitations  | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).  | 10 |
| Conclusions  | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research.  | 11 |
| **FUNDING**  |  |
| Funding  | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.  | 1 |

**Appendix 2. Medline search strategy**

Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®

|  |  |  |
| --- | --- | --- |
| **#** | **Searches** | **Results** |
| 1 | ((("Carbapenemase-Producing" or "Carbapenemase Producing") adj5 Enterobacteriaceae) or "CP-Enterobacteriaceae" or CPE).tw,kf. | 5346 |
| 2 | Enterobacteriaceae/ or exp Enterobacteriaceae Infections/ or ((Enterobacter$ adj3 (infection? or outbreak?)) or Enterobacter$ or "Coliform Bacill$").tw,kf. | 126231 |
| 3 | beta-Lactamases/ or ("beta-Lactamase" or "beta Lactamaseor carbapenemase" or (((multidrug or "multiple drug" or multi-drug) adj3 resistan$) and (carbapenem? or thienamycin? or imipenem))).tw,kf. | 29348 |
| 4 | 2 and 3 | 10335 |
| 5 | 1 or 4 | 15169 |
| 6 | Critical Illness/ or Recovery of function/ or Prognosis/ or Disease-Free Survival/ or Medical Futility/ or Treatment Outcome/ or exp Therapeutic Index/ or exp Treatment Failure/ or Bacteremia/ or Endotoxemia/ or Disease Transmission, Infectious/ or Basic Reproduction Number/ or Infectious Disease Incubation Period/ or Infectious Disease Transmission, Patient-to-Professional/ or Infectious Disease Transmission, Professional-to-Patient/ or Infectious Disease Transmission, Vertical/ or ((critical$ adj3 (illness$ or ill)) or (function adj3 recover$) or ((prognos?s or prognostic) adj3 factor?) or (("disease free" or "event free" or "progression free" or disease-free or event-free or progression-free) adj4 survival?) or ((medical or treatment?) adj3 futil$) or ((outcome? or clinical or patient-relevant or "patient relevant") adj5 (treatment or effective$ or efficacy or rehabilitation)) or (treatment adj3 (effective$ or efficacy)) or (therapeutic adj3 (index or indices)) or ((treatment or rescue?) adj3 failure?) or bacteremia? or endotoxemia? or ((disease? or pathogen? or infection? or autochthonous or environmental or "close contact") adj5 transmission?) or (incubation adj5 (disease? or pathogen? or infection?)) or ((number or ratio or rate) adj4 "basic reproduct$")).tw,kf. | 1872732 |
| 7 | exp Hospitalization/ or exp "Outcome Assessment (Health Care)"/ or Patient Outcome Assessment/ or Patient Reported Outcome Measures/ or Critical Care Outcomes/ or Minimal Clinically Important Difference/ or Watchful Waiting/ or (((hospitalization? or ((length? or hospital) adj3 stay?) or ((discharge adj3 planning) or readmission?) or (voluntary adj3 admission) or ((nursing or clinical) adj3 (handoff? or "hand off?" or "hand over?" or handover)) or (care adj3 transition?) or (outcome? adj3 (assessment? or research or stud$ or measure? or "critical care")) or (patient adj3 (admission? or discharge? or handoff? or "hand off?" or "hand over?" or handover or "sign out?" or signout? or signover? or transfer? or transition? or turfing? or dumping)) or (patient or patient-centered or "patient centered")) adj5 outcome adj5 (assessment? or research or reported)) or "Minimal Clinically Important Difference" or (Watchful adj2 Waiting?)).tw,kf. | 1120997 |
| 8 | Mortality/ or Hospital mortality/ or Fatal outcome/ or Cause of Death/ or Survival rate/ or Life expectancy/ or Life tables/ or (mortalit$ or fatalit$ or death or (fatal adj3 outcome?) or (survival adj3 (rate? or time?)) or (life adj3 (expectanc$ or extension)) or "years of potential life lost" or ((extension or table? or expectanc$) adj4 life)).tw,kf. | 1495115 |
| 9 | exp comorbidity/ or exp morbidity/ or (comorbidit$ or multimorbidit$ or morbidit$ or prevalence? or incidence?).tw,kf. | 1681742 |
| 10 | (HR-PRO or HRPRO or HRQL or HRQoL or QL or QoL).ti,ab. or quality of life.mp. or (health index\* or health indices or health profile\*).ti,ab. or health status.mp. or ((patient or self or child or parent or carer or proxy) adj (appraisal\* or appraised or report or reported or reporting or rated or rating\* or based or assessed or assessment\*)).ti,ab. or ((disability or function or functional or functions or subjective or utility or utilities or wellbeing or well being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire\* or profile or profiles or scale or scales or score or scores or status or survey or surveys)).ti,ab. | 625006 |
| 11 | "Value of Life"/ or Quality of Life/ or Quality-Adjusted Life Years/ or exp health status indicators/ or quality of life.ti,kf. or ((instrument or instruments) adj3 quality of life).ab. or ("quality adjusted life" or (qaly\* or qald\* or qale\* or qtime\* or life year or life years) or "disability adjusted life" or daly\* or (sf36 or "sf 36" or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six) or (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6) or (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight) or (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve) or (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen) or (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty) or (hql or hqol or h qol or hrqol or hr qol) or (hye or hyes) or (health\* adj2 year\* adj2 equivalent\*) or (pqol or qls) or (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb) or "nottingham health profile\*" or "sickness impact profile" or (health adj3 (utilit\* or status)) or (utilit\* adj3 (valu\* or measur\* or health or life or estimat\* or elicit\* or disease or score\* or weight)) or (preference\* adj3 (valu\* or measur\* or health or life or estimat\* or elicit\* or disease or score\* or instrument or instruments)) or disutilit\* or rosser or "willingness to pay" or "standard gamble\*" or (time trade off or time tradeoff or tto) or (hui or hui1 or hui2 or hui3) or (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual) or "duke health profile" or "functional status questionnaire" or "dartmouth coop functional health assessment\*").ti,ab,kf. | 518121 |
| 12 | (cost$ or cost benefit analys$ or health care costs).mp. | 603155 |
| 13 | (co or de or mo or ec or ep or et or mo or py or pd).fs. | 8317524 |
| 14 | 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 | 10944805 |
| 15 | 5 and 14 | 11015 |
| 16 | Animals/ not (Animals/ and Humans/) | 4426113 |
| 17 | 15 not 16 | 9829 |
| 18 | ("clinical conference" or comment or congresses or "conference abstract" or dissertation or editorial or festschrift or "historical article" or letter or news or "newspaper article" or summary or addresses or biography or "case reports" or directory or interview or lectures or "legal cases" or legislation or "patient education handout" or "popular works" or "consensus development conference" or " consensus development conference, nih" or " practice guideline").pt. | 3973545 |
| 19 | 17 not 18 | 8722 |
| 20 | limit 19 to yr="2008 -Current" | 5701 |
| 21 | limit 20 to english language | 5238 |

**Appendix 3. Study and patient characteristics**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First-Author and Publication Year** | **Country of Publication** | **Study Design** | **Study Setting** | **No. Cases** | **No. Controls** | **Mean Age (SD) Cases** | **Mean Age (SD) Controls** | **Sex (%) Female Cases** | **Sex (%) Female Controls** | **Most Common Infection Cases (Enzyme-Bacteria)** | **Control Group Definition** | **Main Comorbidities (%)** |
| Ben-David et al. 201228 | Israel | Retrospective Cohort | Sheba University-Affiliated Medical Tertiary Center | 42 | 150 | 73 (IQR 27)‡ | C1 - 71 (IQR 28); C2 - 73 (IQR 22)‡ | 33% | C1 - 43%; C2 - 46% | BSI (KPC-KP) | C1 – CS-KP (n=85); C2 - ESBL-KP (n=65) | Cases - Chronic Renal Failure (39%); SKP, Malignancy (42%); ESBLKP, Malignancy, Diabetes Mellitus and Stroke (33%) |
| Daikos et al. 200921 | Greece | Prospective Cohort | Three Tertiary-CareHospitals | 14 | 148 | NR†  | NR† | NR† | NR† | BSI (VIM-KP) | C1 – VIM (-) (n=95); C2 – VIM (+) CS (n=53) | NR† |
| Falcone et al. 200922 | Italy | Prospective Cohort | University Hospital Umberto I | 7 | 22 |  68 (49–79) ‡ | 61.5 (20–81) ‡ | 28.57% | 31.82% | UTI (VIM-EC) | VIM (-) | Cases - Cirrhosis (42.8%) and Neoplasm (42.8%); Controls - Neoplasm (36.3%) |
| Fraenkel-Wandel et al. 201630 | Israel | Matched Case-Control\* | Shaare Zedek Medical Centre, University-Affiliated Hospital | 68 | 136 | 73 (17) | 72 (17) | 46% | 44% | BSI – Bacteremia (KPC-KP) | CS ESBL-KP | NA |
| López-González et al. 201731 | Spain | Retrospective Cohort | Hospital Clínico San Carlos, Tertiary, Urban, Teaching Hospital | 38 | 34 | 81.5 (69-84) ‡ | 80 (68-85) ‡ | 65.8% | 44.1% | UTI (KPC, n=17 ; OXA, n=13 – 81% KP and 10% EC) | Colonized with CPE | Cases - Congestive heart failure (28.9%); Controls - Peripheral Vascular disease (23.5%) and Tumor without metastasis (23.5%) |
| Lubbert et al. 201432 | Germany | Retrospective Matched Cohort | Leipzig University Hospital, Germany, Large Single-Center | 8 | 18 | 52.3 (12.5) † | 54.8 (7) † | 37.5% | 27.8% | Pneumonia (KPC-KP) | CS KPC (-) liver transplant patients | Cases - Liver Cirrhosis (62.5%); Controls - Liver Cirrhosis (61.1%) |
| McLaughlin et al. 201429 | United States | Retrospective Cohort | Northwestern MemorialHospital, Teaching Hospital | 15 | 60 | 59.5 (11.3) | 59.6 (17) | 53% | 53.3% | BSI (KPC-KP) | KPC (-) pan-susceptible except for ampicillin | Cases - Diabetes and renal dysfunction (20%); Controls - Diabetes and renal dysfunction (16.7%) |
| **First-Author and Publication Year** | **Country of Publication** | **Study Design** | **Study Setting** | **No. Cases** | **No. Controls** | **Mean Age (SD) Cases** | **Mean Age (SD) Controls** | **Sex (%) Female Cases** | **Sex (%) Female Controls** | **Most Common Infection Cases (Enzyme-Bacteria)** | **Control Group Definition** | **Main Comorbidities (%)** |
| Mouloudi et al. 201434 | Greece | Matched Case-Control\* | ICU of Hippokration General Hospital, Tertiary-Care Teaching Hospital - Liver Transplantation Center | 17 | 34 | 54 (44-66) ‡ | 55 (26-66) ‡ | 41.2% | 44.1% | BSI after orthotropic liver transplant (KPC-KP) | No CR-KP Infection | Cases - Hepatocellular Carcinoma (47%); Controls - Alcohol Hepatitis (35.2%) |
| Mouloudi et al. 201033 | Greece | Nested Case-Control Studies | ICU of Hippokration General Hospital, Tertiary-Care Teaching Hospital - Liver Transplantation Center | 37 | 22 | MBL – 56 (17-81); KPC – 47 (25–79) ‡ | 50.5 (15–78) ‡ | MBL – 27.8%; KPC - 21.1% | 22.7 | BSI (KPC-KP, n=19 ; VIM-KP, n=18) | CS | MBL - Surgery (55.6%); KPC - Surgery (52.6%); Controls - Surgery (54.5%) |
| Papadimitriou-Olivgeris et al. 201335 | Greece | Prospective Cohort | ICU of University Hospital of Patras, Teaching Hospital | 37 | 127 | NR† | NR† | NR† | NR† | NR (KPC-KP) | KPC-KP Colonized | Cases - Obesity (17.7%); Controls - Obesity (27.4%) |
| Qureshi et al. 201236 | United States | Nested Case-Control Studies\* | Three tertiary medical centres in the Northeastern USA (New York, Massachusetts, and Pennsylvania) | 19 | 51 | NR† | NR† | NR† | NR† | BSI – Bacteremia (KPC-KP) | ESBL-producing, but KPC (-) | KPC - Malignancy (40%); ESBL - Diabetes (38.1%) |
| Sánchez-Romero et al. 201137 | Spain | Case-Control\* | Tertiary Care University Hospital Puerta de Hierro Majadahonda | 28 | 55 | 55.4 (12.6) | NR† | 32.1% | NR† | Pneumonia (VIM-KP) | CS | Cases - Cardiovascular (38.2%); Controls - Cardiovascular (43.6%) |
| **First-Author and Publication Year** | **Country of Publication** | **Study Design** | **Study Setting** | **No. Cases** | **No. Controls** | **Mean Age (SD) Cases** | **Mean Age (SD) Controls** | **Sex (%) Female Cases** | **Sex (%) Female Controls** | **Most Common Infection Cases (Enzyme-Bacteria)** | **Control Group Definition** | **Main Comorbidities (%)** |
| Sbrana et al. 201623 | Italy | Matched Case-Control\* | Medical-surgical-trauma ICU | 30 | 60 | 57 (18) | 56 (18) | 17% | 22% | Ventilator associated pneumonia (KPC-KP) | KPC-KP Colonized | 40% comorbidity in case and control (heart failure, renal replacement therapy, COPD, and/or insulin-dependent diabetes mellitus) |
| Shilo et al. 201324 | Israel | Matched Case-Control\* | Shaare Zedek Medical Centre, University-Affiliated Hospital | 135 | 127 |  77 (14) | 80 (13) |  54% | 58% | Bacteriuria, possibility of UTI (KPC-KP) | ESBL-producing CS KP  | Cases - Physical Disability (64%); Controls - Physical Disability (54%) |
| Tascini et al. 201525 | Italy | Matched Case-Control\* | Tertiary-Care UniversityHospital | 6 | 21 | NR† | 70 (9) | NR† | 24% | Diabetic Foot Infection (KPC-KP) | No KPC-KP colonization or Diabetic Foot Infection | NR; Charlson index was comparable for cases and controls |
| Torres-González et al. 201626 | Mexico | Matched Case-Control\* | Tertiary care hospital for patients with complex medical and surgical problems | 27 | 108 | 48.2 (15.5) | C1 - 59.3 (18); C2 - 51.4 (20) | 66.6% | C1 - 70.4%; C2 - 55.6% | UTI (OXA –*E.* *Coli*, n=17*;* KP, n=6) | C1 - third-generation cephalosporin and CS (n=54); C2 - ESBL-producing CS (n=54) | Cases - Kidney Transplant (11%) and Billary Duct injury (11%); Controls - NR |
| Tumbarello et al. 201427 | Italy | Matched Case-Control\* | Databases maintained by microbiology laboratories of five full-service teaching hospitals | 426 | 231 | 68.5 (56–78)‡ | NR† | 44.1% | NR† | BSI (KPC-KP) | KPC-KP Colonized, but no true infection | Cases - Cardiovascular disease (39.2%); Controls - Cardiovascular disease (45.5%)  |

\*Main outcomes of interest in our study were measured using a cohort study design and therefore the study was appraised as a prospective cohort study

‡ Median (Range), specified if IQR

† Calculated Manually or NR, which means we were unable to calculate manually

C1 – Control Group 1 ; C2 – Control Group 2

CS – Carbapenem-Susceptible ; CR – Carbapenem-Resistant ; ESBL – Extended Spectrum Beta-Lactamase; CPE – Carbapenemase-producing Enterobacteriaceae

BSI – Bloodstream Infection

KP - *Klebsiella Pneumoniae* ; EC - *Enterobacter cloacae*

**Appendix 4. Quality appraisal results by study**



**Appendix 5. Quality appraisal results for cohort and case control studies**

|  |  |
| --- | --- |
| **Paper Citation (Author; Year)** | **Critical Appraisal Questions** |
| **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** |
| Daikos 2009 | Y | Y | Y | Y | Y | Y | N | Y | Y | NA | Y |
| Falcone 2009 | Y | Y | Y | Y | N | U | U | Y | Y | NA | Y |
| Fraenkel-Wandel 2016 | Y | Y | Y | Y | Y | U | U | Y | Y | NA | Y |
| López-González 2017 | Y | Y | Y | Y | U | U | U | Y | Y | NA | Y |
| C. Lubbert | Y | Y | Y | Y | Y | Y | Y | Y | Y | NA | Y |
| E. Mouloudi 2014 | Y | Y | Y | Y | Y | Y | Y | Y | Y | NA | Y |
| M. Papadimitriou-Olivgeris 2013 | Y | Y | Y | Y | N | Y | Y | Y | Y | NA | Y |
| Qureshi 2012 | N | Y | Y | Y | Y | Y | Y | Y | N | Y | Y |
| Sanchez-Romero 2011 | Y | Y | Y | Y | Y | Y | Y | Y | Y | NA | Y |
| Sbrana 2016 | Y | Y | Y | Y | Y | Y | Y | U | U | NA | Y |
| Shilo 2013 | Y | Y | Y | U | Y | Y | Y | Y | Y | NA | Y |
| Tascini 2015 | Y | Y | Y | Y | Y | Y | Y | Y | Y | NA | Y |
| Torres-Gonzalez 2016 | Y | Y | Y | Y | Y | U | U | U | Y | NA | Y |
| Tumbarello 2014 | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Y |
| Ben-David 2012 | Y | Y | Y | U | N | Y | Y | Y | Y | NA | Y |
| McLaughlin 2014 | Y | Y | Y | Y | Y | Y | Y | Y | Y | NA | Y |

NA, Not applicable; N, No; U, Unclear; Y, Yes

**Questions:** 1. Were the two groups similar and recruited from the same population?; 2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?; 3. Was the exposure measured in a valid and reliable way?; 4. Were confounding factors identified?; 5. Were strategies to deal with confounding factors stated?; 6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?; 7. Were the outcomes measured in a valid and reliable way?; 8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?; 9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?; 10. Were strategies to address incomplete follow up utilized?; 11. Was appropriate statistical analysis used?

|  |  |
| --- | --- |
| **Paper Citation (Author Year)** | **Critical Appraisal Questions** |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Mouloudi 2010 | N | N | Y | Y | Y | Y | Y | Y | Y | Y |

N, No; Y, Yes

**Questions:** 1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?; 2. Were cases and controls matched appropriately?; 3. Were the same criteria used for identification of cases and controls?; 4. Was exposure measured in a standard, valid and reliable way?; 5. Was exposure measured in the same way for cases and controls?; 6. Were confounding factors identified?; 7. Were strategies to deal with confounding factors stated?; 8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?; 9. Was the exposure period of interest long enough to be meaningful?; 10. Was appropriate statistical analysis?

**Appendix 6. Summary of data extraction categorized by health outcomes and sequelae**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Sample Size Cases** | **Sample Size Controls** | **Cases Results (%)** | **Control Results (%)** | **Risk Difference (%)** |
| **Category: Mortality** |
| In-Hospital |
| Ben-David et al. 201228 | 42 | 150 | 69.0% | 30.0% | 39.0% |
| Fraenkel-Wandel et al. 201630 | 68 | 136 | 64.7% | 39.7% | 25.0% |
| Lubbert et al. 201432 | 8 | 18 | 75.0% | 11.1% | 63.9% |
| McLaughlin et al. 201429 | 15 | 60 | 33.3% | 11.7% | 21.7% |
| Mouloudi et al. 201033 | 37 | 22 | 67.6% | 40.9% | 26.7% |
| Shilo et al. 201324 | 135 | 127 | 28.9% | 25.2% | 3.7% |
| Tumbarello et al. 201427 | 426 | 231 | 38.3% | 18.6% | 19.6% |
| Falcone et al. 200922 | 7 | 22 | 42.9% | 27.3% | 15.6% |
| Intensive Care Unit |
| Papadimitriou-Olivgeris et al. 201335 | 37 | 127 | 59.5% | 32.3% | 27.2% |
| Mouloudi et al. 201033 | 37 | 22 | 56.8% | 40.9% | 15.8% |
| Mouloudi et al. 201434 | 17 | 34 | 82.4% | 32.4% | 50.0% |
| Sbrana et al. 201623 | 30 | 60 | 20.0% | 23.3% | -3.3% |
| Attributable to Infection |
| Ben-David et al. 201228 | 42 | 150 | 47.6% | 18.7% | 29.0% |
| Mouloudi et al. 201033 | 37 | 22 | 27.0% | 13.6% | 13.4% |
| Torres-Gonzalez et al. 201626 | 27 | 108 | 11.1% | 7.4% | 3.7% |
| Mortality Inappropriate Antibiotics |
| Fraenkel-Wandel et al. 201630 | 68 | 136 | 64.0% | 35.4% | 28.6% |
| 14-Day |
| Daikos et al. 200921 | 14 | 148 | 42.9% | 16.9% | 26.0% |
| Sànchez-Romero et al. 201137 | 28 | 55 | 46.4% | 30.9% | 15.5% |
| 28-Day |
| Qureshi et al. 201236 | 19 | 51 | 47.4% | 27.5% | 19.9% |
| 30-Day |
| López-González et al. 201731 | 38 | 34 | 34.2% | 11.8% | 22.4% |
| 90-Day |
| López-González et al. 201731 | 38 | 34 | 18.4% | 8.8% | 9.6% |
| Tascini et al. 201525 | 6 | 21 | 66.7% | 4.8% | 61.9% |
| **Category: Sequelae** |
| Relapse |
| Falcone et al. 200922 | 7 | 22 | 71.4% | 0.0% | 71.4% |
| Secondary Bloodstream Infection |
| Falcone et al. 200922 | 7 | 22 | 71.4% | 40.9% | 30.5% |
| Lubbert et al. 201432 | 8 | 18 | 62.5% | 11.1% | 51.4% |
| Sbrana et al. 201623 | 30 | 60 | 66.7% | N/A | N/A |
| Torres-Gonzalez et al. 201626 | 27 | 108 | 22.2% | 19.4% | 2.8% |
| Functional Status - Dependent |
| Fraenkel-Wandel et al. 201630 | 68 | 136 | 19.1% | 28.7% | -9.6% |
| Length of Infection in Days |
| McLaughlin et al. 201429 | 15 | 60 | 3 (3-4) | 3 (3-5) | N/A |
|  | **Sample Size Cases** | **Sample Size Controls** | **Cases Results (%)** | **Control Results (%)** | **Risk Difference (%)** |
| **Category: Antibiotic Therapy** |
| Duration of Antibiotic Therapy in Days |
| Falcone et al. 200922 (Mean, CI) | 7 | 22 | 29.7 [CI, 21.5 to 37.8] | 23.6 [CI, 10.3 to 36.8] | N/A |
| McLaughlin et al. 201429 (Post-Infection)\* | 15 | 60 | 13 (8-18) | 6.5 (4-10) | N/A |
| Sbrana et al. 201623 (Post-Colonization)\* | 30 | 60 | 4 (2-5) | 1 (0-3) | N/A |
| Full-Course Completed |
| López-González et al. 201731 | 38 | 34 | 81.6% | 64.7% | 16.9% |
| Appropriate Antibiotics Administered |
| Fraenkel-Wandel et al. 201630 | 68 | 136 | 44.2% | 39.7% | 4.5% |
| **Category: Length of Stay** |
| Post-Infection Stay in Days |
| Ben-David et al. 201228\* | 42 | 150 | 18 (22) | CS-KP - 9 (16); ESBL-KP - 16 (34) | N/A |
| Hospital Stay in Days |
| Falcone et al. 200922 (Mean, CI) | 7 | 22 | 41.6 [CI, 22.4 to 60.7] | 29.7 [CI, 21.5 to 37.8] | N/A |
| Fraenkel-Wandel et al. 201630\*  | 68 | 136 | 36 (21–55) | 32 (15–63) | N/A |
| López-González et al. 201731\* | 38 | 34 | 34.5 (21-53) | 25.5 (13-41) | N/A |
| Lubbert et al. 201432 (Mean (SD)) | 8 | 18 | 87 (47.3) | 42.7 (23.7) | N/A |
| Shilo et al. 201324 (Mean (SD)) | 135 | 127 | 28 (33) | 22 (28) | N/A |
| Torres-Gonzalez et al. 201626\* | 27 | 108 | 21 (8–15) | CS - 15 (7-32) ; CS ESBL-producing - 15 (11-35) | N/A |

\*Median (interquartile range)

CI, confidence interval; NA, not available; SD, standard deviation; ESBL, extended-spectrum beta-lactamase; KP, *Klebsiella pneumoniae* ; CS, carbapenem susceptible