S1 file. PRISMA Checklist (1)

Section/topic	#	Checklist item	Included?
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	✓
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.	✓
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	✓
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	✓
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.	✓
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.	✓
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.	✓
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**S2 file**
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).	✓
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.	✓
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	✓

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.	✓
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	✓
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	✓
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).	✓
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	✓
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.	**Fig 1**
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.	✓
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).	✓
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.	**Fig 2, 3**
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	**Fig 2, 3**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	✓
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	**S4/5 files**
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).	✓
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).	✓
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	✓
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.	✓

S2 file. Literature search strategy (list of search terms)

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(((('carbapenem'/exp/mj OR 'carbapenem derivative'/exp/mj OR 'imipenem'/mj OR 'meropenem'/mj OR 'ertapenem'/mj OR 'doripenem'/mj OR 'panipenem'/mj OR 'betamipron'/mj OR 'biapenem'/mj OR 'beta lactam antibiotic'/mj OR 'carbapenemase'/mj OR 'beta lactamase'/mj OR 'metallo beta lactamase'/mj) AND ('antibiotic resistance'/de OR 'antibiotic sensitivity'/de)) OR 'carbapenem resistant Enterobacteriaceae'/de OR 'carbapenemase producing Enterobacteriaceae'/exp OR (((carbapenem* OR imipenem* OR meropenem* OR ertapenem* OR doripenem* OR betamipron* OR biapenem*) NEAR/6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa)) OR ((carbapenemase OR kpc OR ndm OR vim OR imp OR oxa) NEAR/3 produc*) OR ((((β-lactamase OR βlactamase OR beta-lactamase OR betalactamase) NEAR/3 produc*) OR ((β-lactam OR βlactam OR beta-lactam OR betalactam) NEAR/6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa))) NOT ('extended spectrum' OR esbl))):ab,ti) AND ('Enterobacteriales'/exp OR 'Enterobacteriaceae infection'/exp OR (Enterobacter* OR escherichia* OR 'e coli' OR shigella* OR edwardsiella* OR salmonella* OR citrobacter* OR klebsiella* OR enterobacter* OR serratia* OR proteus OR yersinia* OR hafnia* OR morganella*):ab,ti) AND ('risk factor'/exp OR 'protection'/de OR 'epidemiology'/de OR 'prevalence'/de OR 'causality'/de OR 'epidemic'/de OR 'reservoir'/de OR 'prevention'/de OR 'prevention'/lnk OR (((risk* OR protecti* OR reinforc* OR enabl* OR predispos*) NEAR/3 factor*) OR epidemiolog* OR outbreak OR prevalence OR epidemic* OR endemic* OR causalit* OR reservoir* OR (environment* NEAR/3 (role OR source)) OR prevent*):ab,ti) AND ('hospital'/exp OR 'hospitalization'/exp OR 'hospital management'/exp OR 'multicenter study'/exp OR 'tertiary health care'/exp OR 'secondary health care'/exp OR 'patient'/exp OR (hospital* OR ward OR wards OR icu OR ((intensive OR critical) NEAR/3 care) OR department* OR nosocomial* OR ((healthcare OR health-care) NEAR/3 (related* OR tertiar* OR secondar*)) OR (medical* NEAR/3 (centre* OR center*)) OR (nation* NEAR/3 stud*) OR multicent* OR multi-cent* OR single-cent* OR clinic OR clinics OR patient*):ab,ti) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim)

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(((exp "Carbapenems"/ OR *"beta-Lactams"/ OR *"beta-Lactamases"/) AND ("Drug Resistance, Microbial"/ OR "Drug Resistance, Bacterial"/)) OR *"beta-Lactam Resistance"/ OR (((carbapenem* OR imipenem* OR meropenem* OR ertapenem* OR doripenem* OR betamipron* OR biapenem*) ADJ6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa)) OR ((carbapenemase OR kpc OR ndm OR vim OR imp OR oxa) ADJ3 produc*) OR ((((beta-lactamase OR betalactamase) ADJ3 produc*) OR ((beta-lactam OR betalactam) ADJ6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa))) NOT ("extended spectrum" OR esbl))).ab,ti,kf.) AND (exp "Enterobacteriaceae"/ OR exp "Enterobacteriaceae Infections"/ OR (Enterobacter* OR escherichia* OR "e coli" OR shigella* OR

edwardsiella* OR salmonella* OR citrobacter* OR klebsiella* OR enterobacter* OR serratia* OR proteus OR yersinia* OR hafnia* OR morganella*).ab,ti,kf.) AND ("Risk Factors"/ OR "epidemiology"/ OR "prevalence"/ OR "causality"/ OR "epidemics"/ OR "Disease Reservoirs"/ OR "prevention and control ".xs. OR (((risk* OR protecti* OR reinforc* OR enabl* OR predispos*) ADJ3 factor*) OR epidemiolog* OR outbreak OR prevalence OR epidemic* OR endemic* OR causalit* OR reservoir* OR (environment* ADJ3 (role OR source)) OR prevent*).ab,ti,kf.) AND (exp "Hospitals"/ OR exp "Hospitalization"/ OR exp "Hospital Administration"/ OR "multicenter study"/ OR "Patients"/ OR (hospital* OR ward OR wards OR icu OR ((intensive OR critical) ADJ3 care) OR department* OR nosocomial* OR ((healthcare OR health-care) ADJ3 (related* OR tertiar* OR secondar*)) OR (medical* ADJ3 (centre* OR center*)) OR (nation* ADJ3 stud*) OR multicent* OR multi-cent* OR single-cent* OR clinic OR clinics OR patient*).ab,ti,kf.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt.

Cochrane CENTRAL

((((carbapenem* OR imipenem* OR meropenem* OR ertapenem* OR doripenem* OR betamipron* OR biapenem*) NEAR/6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa)) OR ((carbapenemase OR kpc OR ndm OR vim OR imp OR oxa) NEAR/3 produc*) OR ((((β-lactamase OR βlactamase OR beta-lactamase OR betalactamase) NEAR/3 produc*) OR ((β-lactam OR βlactam OR beta-lactam OR betalactam) NEAR/6 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa))) NOT ('extended spectrum' OR esbl))):ab,ti) AND ((Enterobacter* OR escherichia* OR 'e coli' OR shigella* OR edwardsiella* OR salmonella* OR citrobacter* OR klebsiella* OR enterobacter* OR serratia* OR proteus OR yersinia* OR hafnia* OR morganella*):ab,ti) AND ((((risk* OR protecti* OR reinforc* OR enabl* OR predispos*) NEAR/3 factor*) OR epidemiolog* OR outbreak OR prevalence OR epidemic* OR endemic* OR causalit* OR reservoir* OR (environment* NEAR/3 (role OR source)) OR prevent*):ab,ti) AND ((hospital* OR ward OR wards OR icu OR ((intensive OR critical) NEAR/3 care) OR department* OR nosocomial* OR ((healthcare OR health-care) NEAR/3 (related* OR tertiar* OR secondar*)) OR (medical* NEAR/3 (centre* OR center*)) OR (nation* NEAR/3 stud*) OR multicent* OR multi-cent* OR single-cent* OR clinic OR clinics OR patient*):ab,ti)

Web of Science

TS=(((((carbapenem* OR imipenem* OR meropenem* OR ertapenem* OR doripenem* OR betamipron* OR biapenem*) NEAR/5 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa)) OR ((carbapenemase OR kpc OR ndm OR vim OR imp OR oxa) NEAR/2 produc*) OR ((((β-lactamase OR βlactamase OR beta-lactamase OR betalactamase) NEAR/2 produc*) OR ((β-lactam OR βlactam OR beta-lactam OR betalactam) NEAR/5 (resist* OR multiresist* OR susceptib* OR sensitivit* OR nonsusceptib* OR kpc OR ndm OR vim OR imp OR oxa))) NOT ("extended spectrum" OR esbl)))) AND ((Enterobacter* OR escherichia* OR "e coli" OR shigella* OR edwardsiella* OR salmonella* OR citrobacter* OR klebsiella* OR enterobacter* OR serratia* OR proteus OR yersinia* OR hafnia* OR morganella*)) AND ((((risk* OR protecti* OR reinforc* OR enabl* OR predispos*) NEAR/2 factor*) OR epidemiolog* OR outbreak OR prevalence OR epidemic* OR endemic* OR causalit* OR reservoir* OR (environment* NEAR/2 (role OR source)) OR prevent*)) AND ((hospital* OR ward OR

wards OR icu OR ((intensive OR critical) NEAR/2 care) OR department* OR nosocomial* OR ((healthcare OR health-care) NEAR/2 (related* OR tertiar* OR secondar*)) OR (medical* NEAR/2 (centre* OR center*)) OR (nation* NEAR/2 stud*) OR multicent* OR multi-cent* OR single-cent* OR clinic OR clinics OR patient*))) AND Dt=(article)

Google scholar

"carbapenem resistant Enterobacteriaceae" "risk|protective factors"|epidemiology|prevalence|epidemic|endemic|causality|reservoir hospitals|ward|wards|icu|nosocomial|multicenter

S3 file. Study Quality assessment using the STROBE guideline (2).

Table A. Quality assessment scores of the 52 articles describing risk factors related to antibiotic exposure for the acquisition of CRE, included in the random-effects meta-analysis study.

Study	1		2	3	4	5	6		7	8	9	10	11	12						13			14			15	16			17	18	19	20	21	22	Total
	a	b					a	b						a	b	c	d	e	a	b	c	a	b	c		a	b	c							
Low quality (≤15)																																				
Karaaslan (2016)	1	1	1	1	1	1	1	1	−	−	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	−	1	N/A	1	1	−	−	1	1	**15**
Tuon (2012)	1	1	1	1	1	1	−	N/A	−	1	−	−	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**15**
Borer (2012)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	−	−	1	N/A	1	1	−	1	1	−	**15**
de Jager (2015)	1	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	−	1	N/A	1	1	1	−	1	−	**15**
Moderate quality (16-18)																																				
Maldonado (2015)	1	1	1	1	1	−	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	−	1	N/A	1	1	1	−	1	1	**16**
Sánchez-Romero (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	−	−	−	1	**16**
Daikos (2010)	−	1	1	1	−	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**17**
Dizbay (2014)	−	1	1	1	1	−	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	−	**17**
Gagliotti (2014)	1	1	1	1	1	1	1	1	−	1	−	−	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**17**
Orsi (2013)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	1	−	**17**
Patel (2008)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**17**
Petrikkos (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	−	−	−	1	**17**
Gasink (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**17**
Maseda (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	−	1	**17**
Falagas (2007)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**17**
Ahn (2014)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	−	**18**
Cheng (2016)	−	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	1	**18**
Garbati (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Hussein (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	1	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	−	**18**
Kwak (2005)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Mills (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Schwartz-Niederman (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Papadimitriou-Olivgeris (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	−	−	1	1	**18**
Papadimitriou-Olivgeris (2015)	−	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	1	1	**18**
Wang (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Ma (2014)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Wu (2011)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	−	**18**
Candevir (2015)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	−	1	1	1	1	−	**18**
Hayakawa (2014)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	1	1	**18**
Jiao (2015)	1	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**18**
Liu (2012)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Schwaber (2008)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Teo (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Kritsotakis (2011)	1	1	1	1	1	1	1	1	−	1	1	1	1	1	1	N/A	1	1	1	−	N/A	−	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**18**
Ling (2015)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Zhao (2014)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**

High quality (≥19)																																						
Chang (2011)	1	1	1	1	1	1	1	1	1	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**19**
Hu (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**19**
Jeon (2008)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	1	**19**
Satlin (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**19**
Torres-Gonzalez (2015)	1	1	1	1	1	1	1	N/A	−	1	1	1	1	1	1	N/A	1	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	1	−	**19**
Dautzenberg (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	−	**19**
Chitnis (2012)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	−	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	1	**19**

Abbreviations: N/A, not available.

Table B. Quality assessment scores of the 59 articles describing other risk factors for the acquisition of CRE, included in the random-effects meta-analysis study.

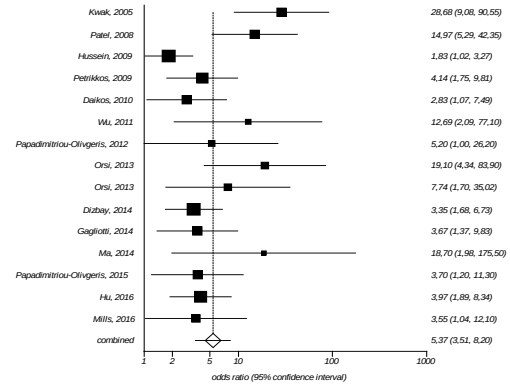
Study	1		2	3	4	5	6		7	8	9	10	11	12						13			14			15	16			17	18	19	20	21	22	Total
	a	b					a	b						a	b	c	d	e	a	b	c	a	b	c		a	b	c							
Low quality (≤15)																																				
Mittal (2016)	−	1	1	1	−	1	1	−	−	1	−	1	1	1	1	1	−	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**13**
de Jager (2015)	1	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	−	1	N/A	1	1	1	−	1	−	**15**
Karaaslan (2016)	1	1	1	1	1	1	1	1	−	−	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	−	1	N/A	1	1	−	−	1	1	**15**
Freire (2015)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	−	−	1	1	1	1	N/A	1	1	−	−	−	−	**15**
Marchaim (2008)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	−	1	N/A	1	1	−	−	−	−	**15**
Tuon (2012)	1	1	1	1	1	1	−	N/A	−	1	−	−	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**15**
Moderate quality (16-18)																																				
Nouvenne (2014)	1	1	1	1	1	1	1	N/A	−	−	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**16**
Pereira (2015)	1	1	1	1	−	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**16**
Freire (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	−	−	**16**
Sánchez-Romero (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	−	−	−	1	**16**
Giuffrè (2013)	−	1	1	1	1	1	1	N/A	−	1	−	−	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	−	−	1	1	1	**16**
Madueno (2017)	1	1	1	1	−	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	−	1	−	1	−	**16**
Gasink (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**17**
Marchaim (2012)	−	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	1	1	**17**
Miller (2016)	1	1	1	1	1	1	1	1	−	−	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**17**
Orsi (2013)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	1	−	**17**
Ben-David, 2012	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	−	1	−	1	N/A	1	1	1	1	1	−	**17**
Kim (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	−	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**17**
Maseda (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	−	1	**17**
Patel (2008)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	−	**17**
Daikos (2010)	−	1	1	1	−	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**17**
Dizbay (2014)	−	1	1	1	1	−	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	−	**17**
Petrikkos (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	−	−	−	1	**17**
Tian (2016)	−	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	−	1	**17**
Vergara-López (2015)	1	1	1	1	1	1	1	1	−	1	−	−	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**17**
Gallagher (2014)	1	1	1	1	1	1	1	1	−	1	1	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	−	−	1	N/A	1	1	1	1	−	−	**17**
Bhargava (2014)	1	1	1	1	1	1	1	1	−	−	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	−	**18**
Liu (2012)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Papadimitriou-Olivgeris (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	−	−	1	1	**18**
Papadimitriou-Olivgeris (2015)	−	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	1	1	**18**
Schwaber (2008)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Garbati (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Gregory (2010)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Hayakawa (2014)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	1	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	−	−	1	1	**18**
Mills (2016)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Zhao (2014)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Candevir (2015)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	−	1	1	1	1	−	**18**
Cheng (2016)	−	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	1	**18**
Freire (2016)	1	1	1	1	1	1	1	N/A	−	1	−	−	1	1	1	N/A	N/A	1	1	−	N/A	1	1	1	1	1	1	N/A	1	1	1	1	1	1	**18**
Jiao (2015)	1	1	1	1	−	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**18**
Ling (2015)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Papadimitriou-Olivgeris (2013)	1	1	1	1	1	−	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	1	1	**18**

Teo (2012)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Hussein (2009)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	1	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	−	**18**
Lee (2013)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	−	1	−	1	1	**18**
Wu (2011)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	−	**18**
Mouloudi (2010)	1	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	N/A	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**18**
Poole (2016)	−	1	1	1	1	1	1	N/A	−	1	−	1	1	1	1	1	N/A	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**18**
High quality (≥19)																																			
Schwartz-Niederman (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	−	**18**
Chang (2011)	1	1	1	1	1	1	1	1	1	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**19**
Chitnis (2012)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	−	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	1	**19**
Kofteridis (2014)	1	1	1	1	1	1	1	1	−	1	1	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	−	1	1	−	1	1	**19**
Satlin (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	1	1	**19**
Torres-Gonzalez (2015)	1	1	1	1	1	1	1	N/A	−	1	1	1	1	1	1	N/A	1	1	1	1	N/A	1	1	1	1	1	1	N/A	1	1	1	−	1	−	**19**
da Silva (2016)	1	1	1	1	1	1	1	1	1	1	−	1	1	1	1	N/A	1	1	1	1	N/A	−	1	N/A	1	1	1	N/A	1	1	−	1	1	1	**19**
Jeon (2008)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	−	1	**19**
Bleumin (2012)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	N/A	1	1	1	−	N/A	1	1	N/A	1	1	1	N/A	1	1	1	−	−	1	**19**
Dautzenberg (2016)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	−	**19**
Swaminathan (2013)	1	1	1	1	1	1	1	1	−	1	−	1	1	1	1	N/A	1	1	1	1	N/A	1	1	N/A	1	1	1	N/A	1	1	1	1	1	1	**20**

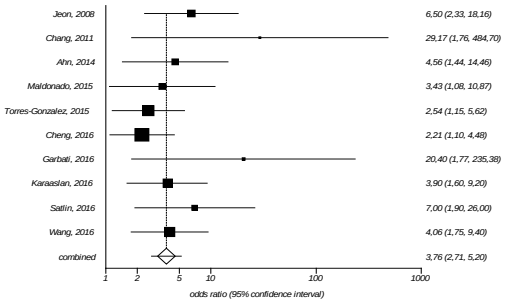
Abbreviations: N/A, not available.

S4 file. Forest plots of additional meta-analyses of antibiotic exposure as risk factor and/or protective factor for the acquisition of carbapenem-resistant Enterobacteriaceae.

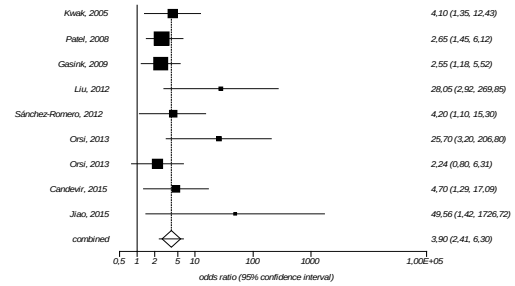
1A. Carbapenem use



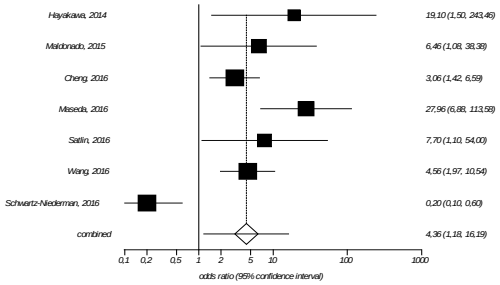
1B. Carbapenem use



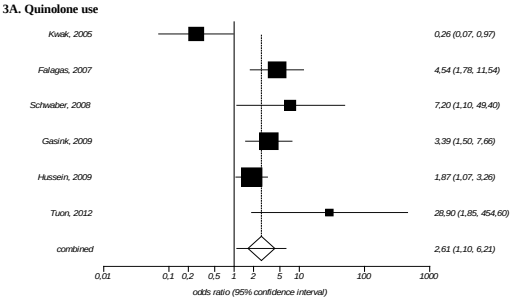
2A. Cephalosporin use



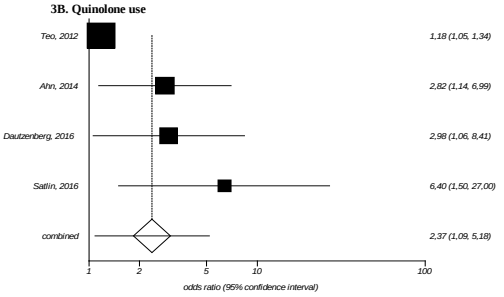
2B. Cephalosporin use



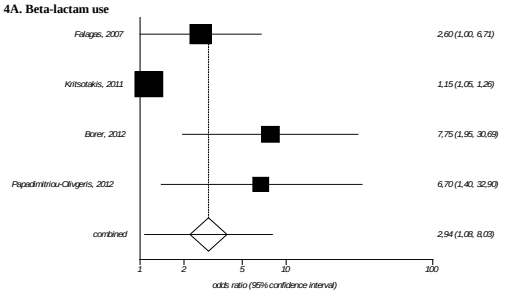
3A. Quinolone use



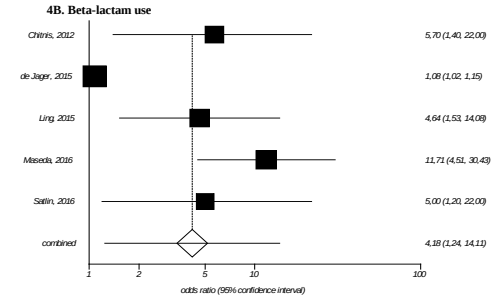
3B. Quinolone use



4A. Beta-lactam use



4B. Beta-lactam use



5A. Glycopeptide use

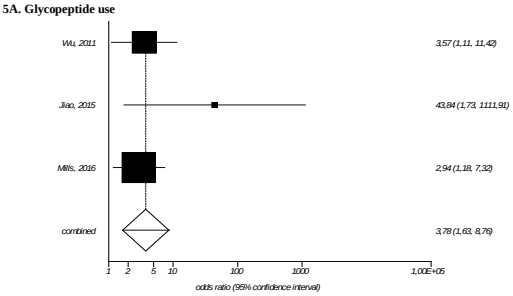


Figure A.The effect of studied Enterobacteriaceae species on the overall risk estimate. A)Studies only including *K. pneumoniae* isolates, B) other studies (e.g. all CRE, *Enterobacter* spp.)

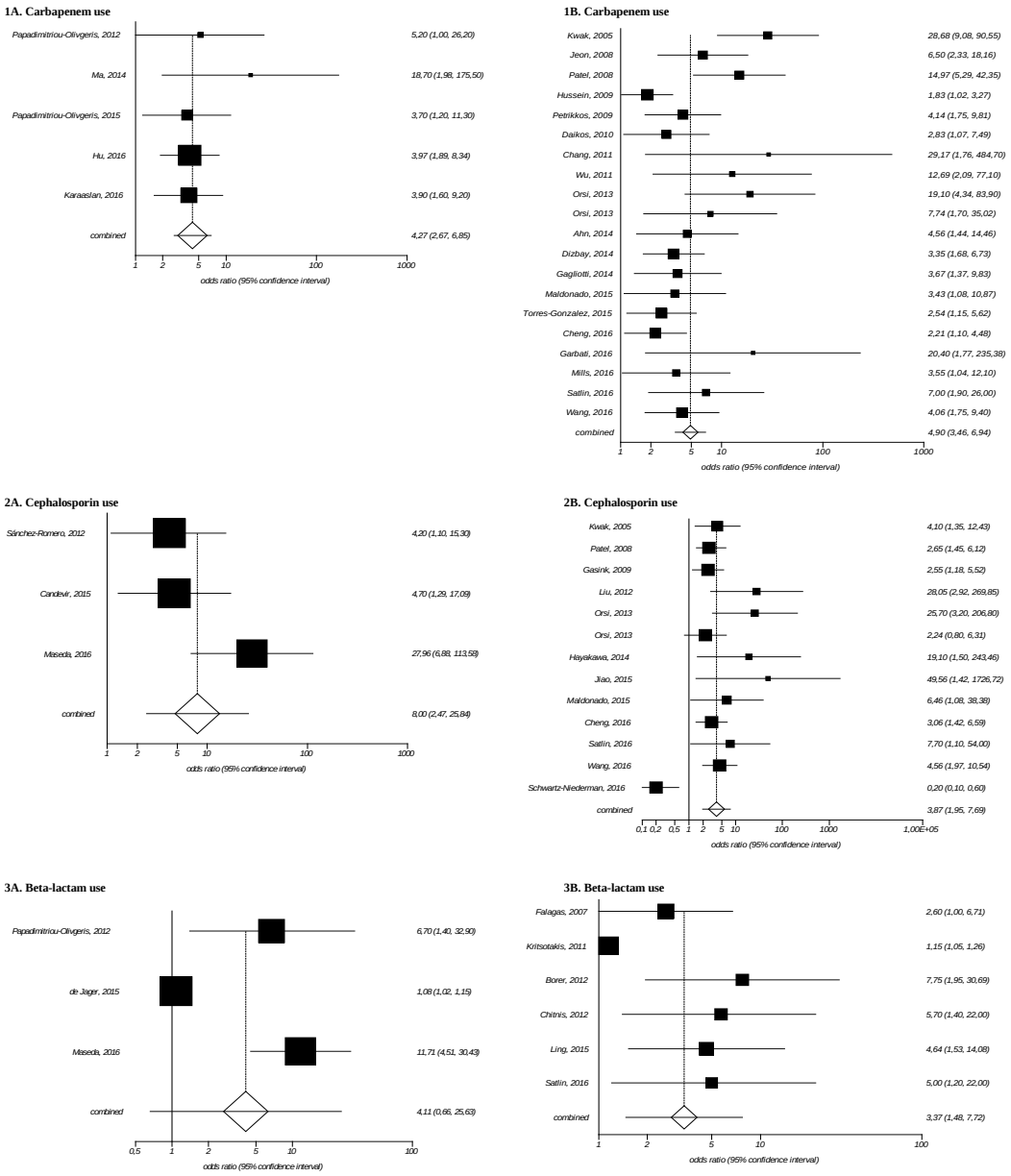


Figure B.The effect of an ICU study design on the overall risk estimate. A) Studies with an ICU setting, B) Studies with a different study setting (e.g. non-ICU, hospital wide).

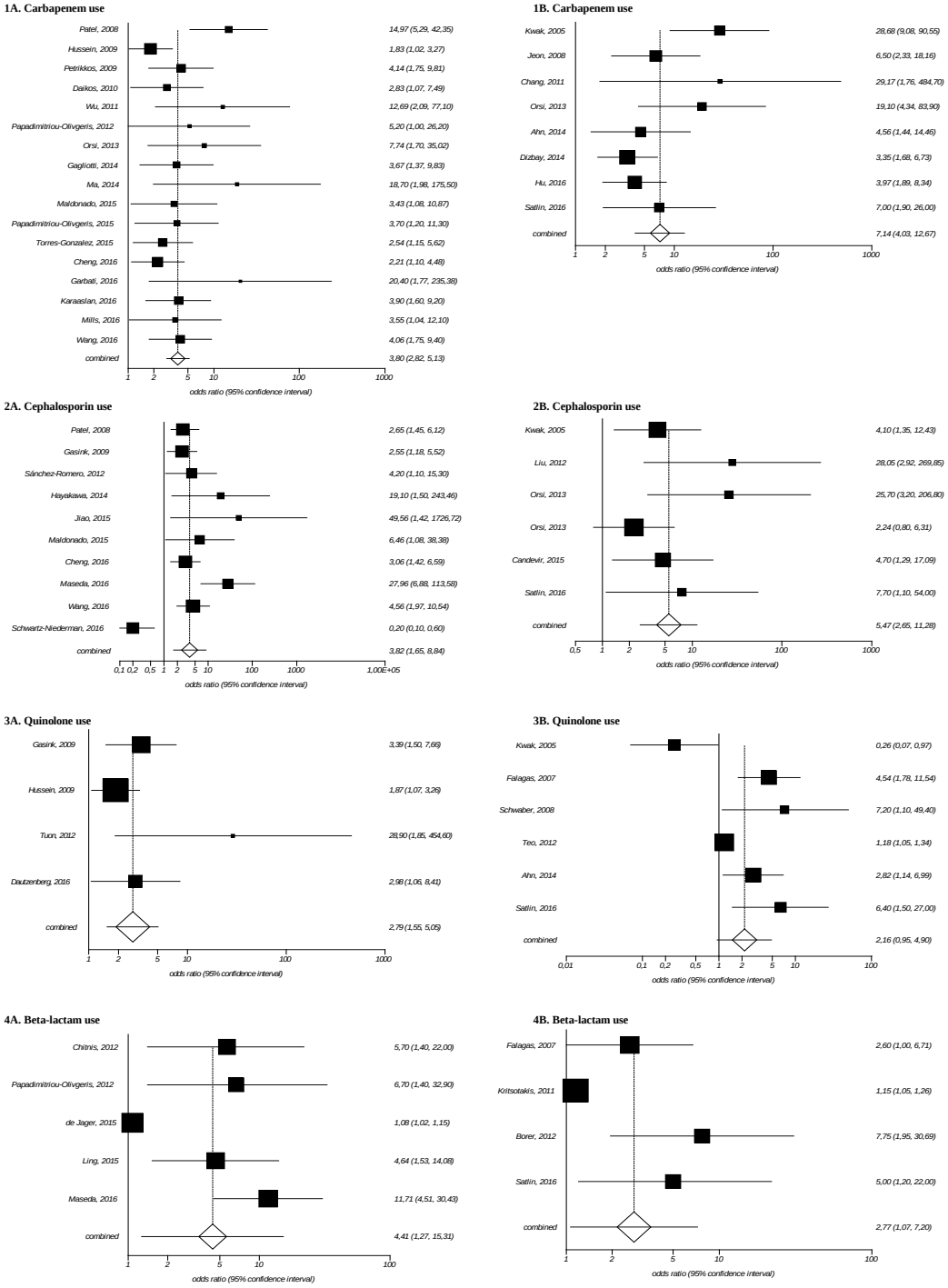


Figure C.The effect of carbapenem resistance mechanism on the overall risk estimate. A) Studies only describing carbapenemase production as carbapenem resistance mechanism, B) Studies describing another resistance mechanism or did not investigate the resistance mechanism involved.

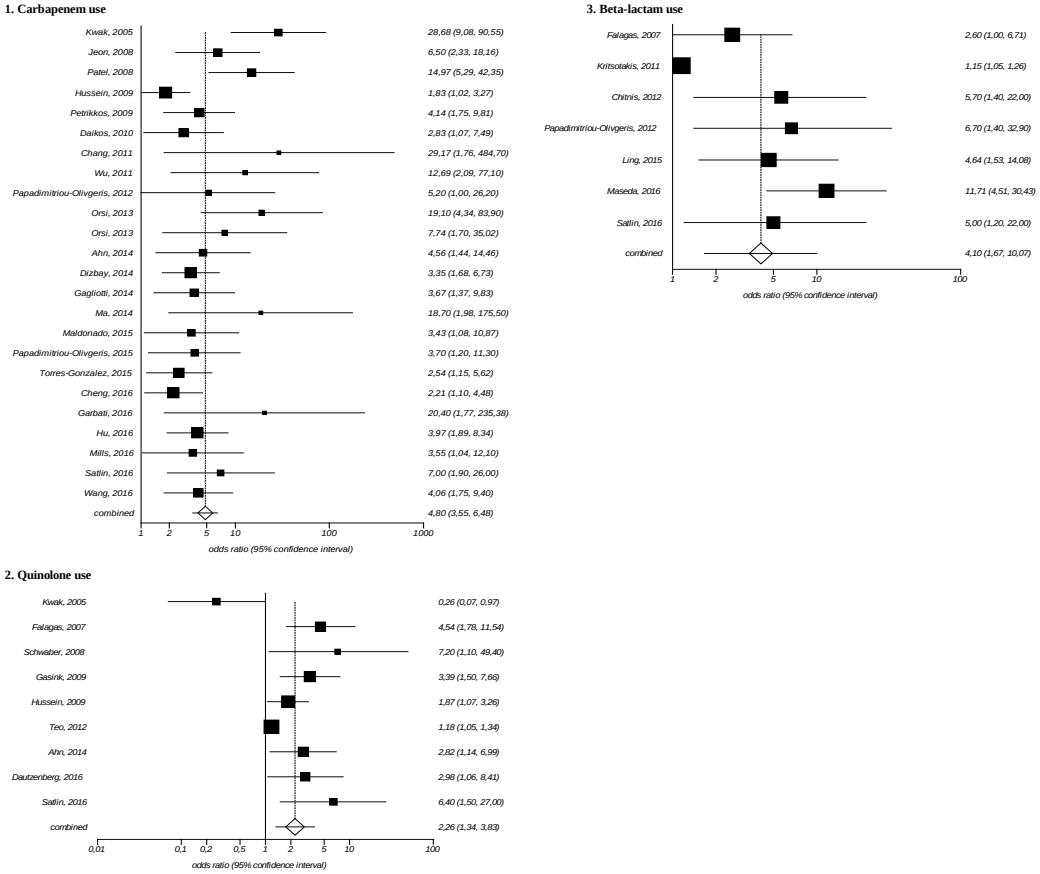
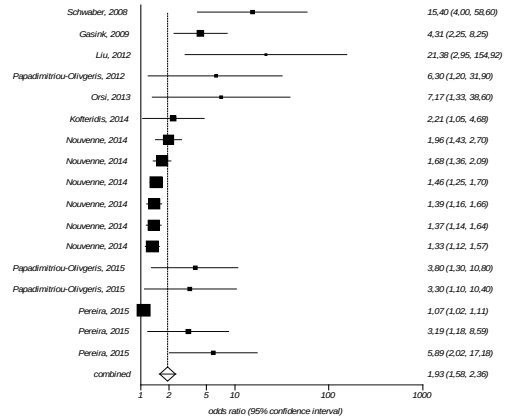


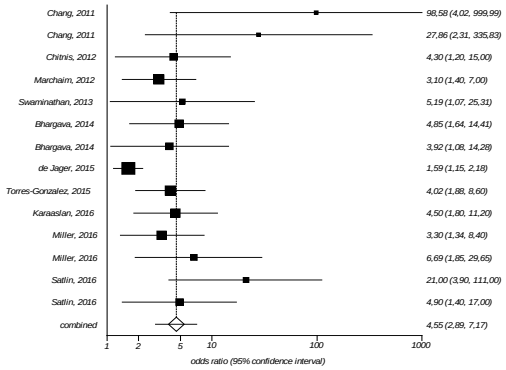
Figure D.The effect of study quality on the overall risk estimate; only studies with a moderate/high study quality (>15).

S5 file. Forest plots of additional meta-analyses of other risk factors and/or protective factors for the acquisition of carbapenem-resistant Enterobacteriaceae.

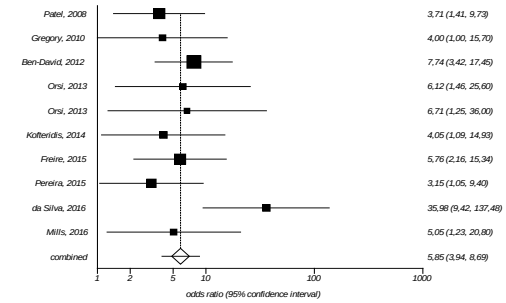
1A. Underlying disease or condition



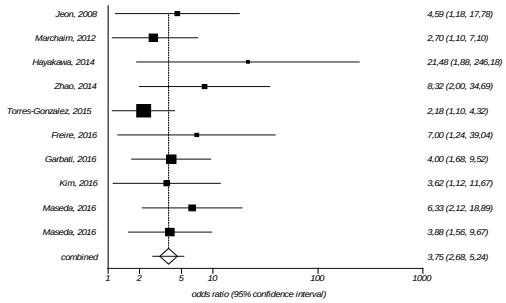
1B. Underlying disease or condition



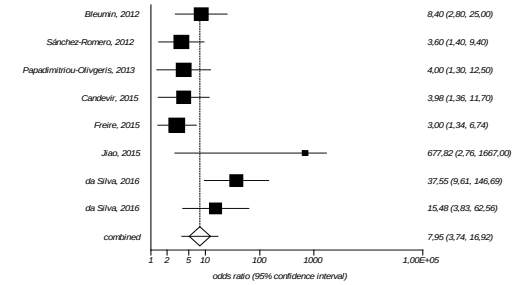
2A. Invasive procedures



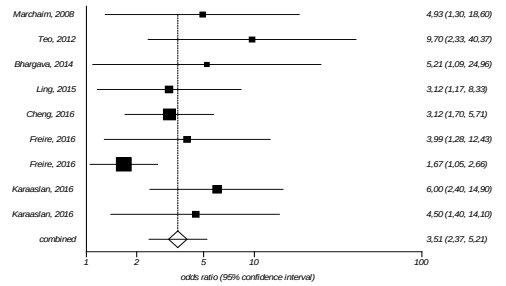
2B. Invasive procedures



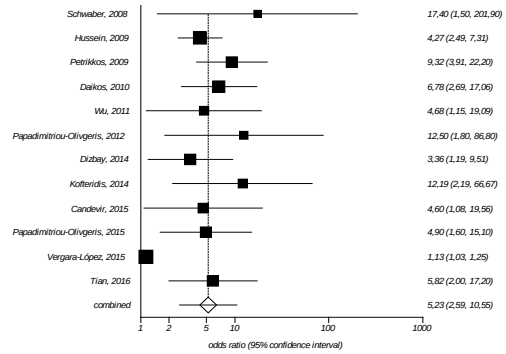
3A. Medical devices



3B. Medical devices



4A. ICU admission



4B. ICU admission

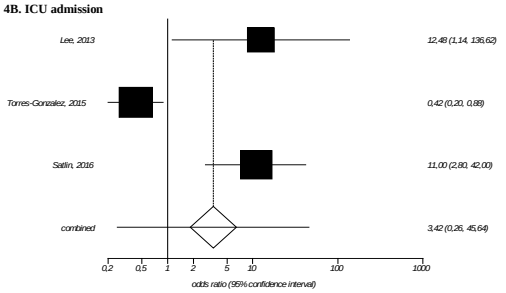
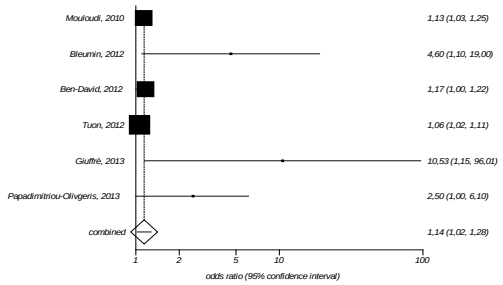
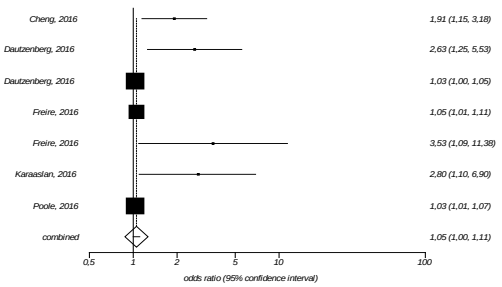


Figure A.The effect of studied Enterobacteriaceae species on the overall risk estimate. A)Studies only including *K. pneumoniae* isolates, B) other studies (e.g. all CRE, *Enterobacter* spp.)

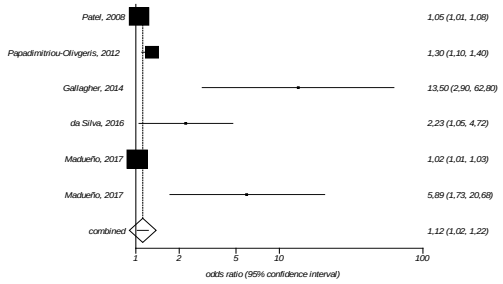
5A. Demographic patient characteristics



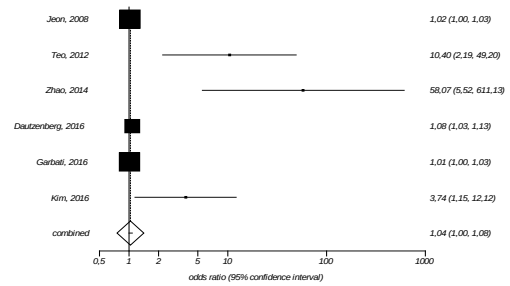
5B. Demographic patient characteristics



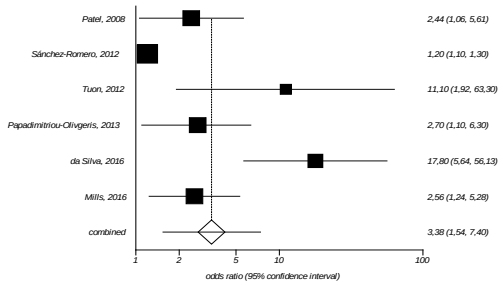
6A. Exposure to hospital care



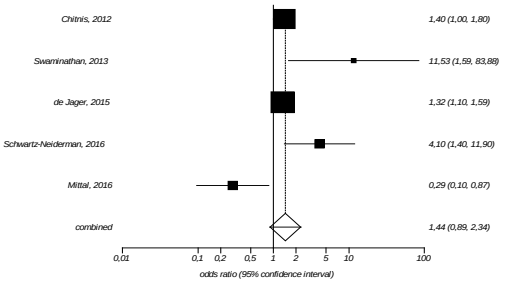
6B. Exposure to hospital care



7A. Mechanical ventilation



7B. Mechanical ventilation



8B. CRE exposure

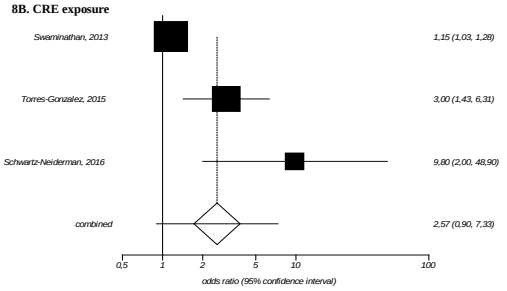


Figure A.Continued.

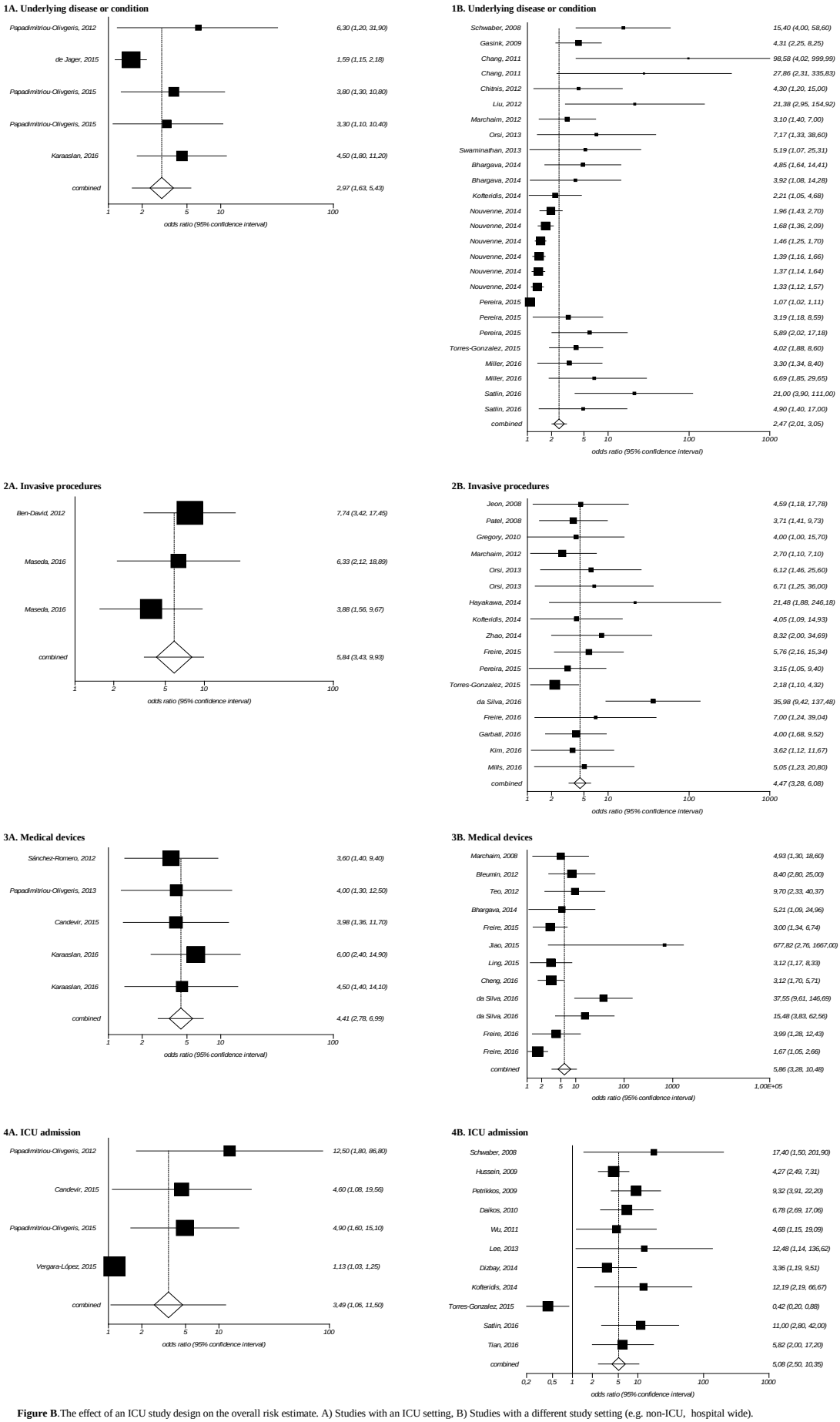
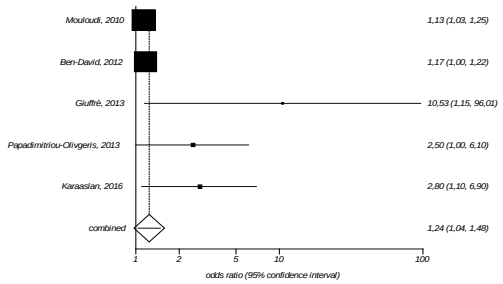
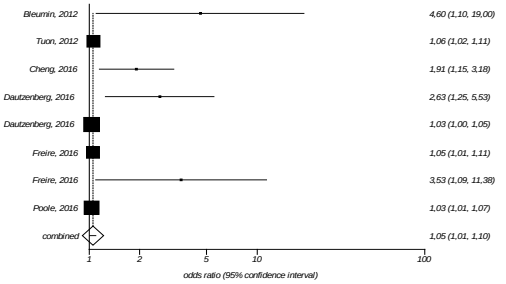


Figure B.The effect of an ICU study design on the overall risk estimate. A) Studies with an ICU setting, B) Studies with a different study setting (e.g. non-ICU, hospital wide).

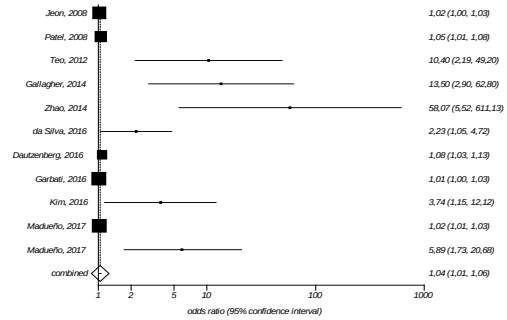
5A. Demographic patient characteristics



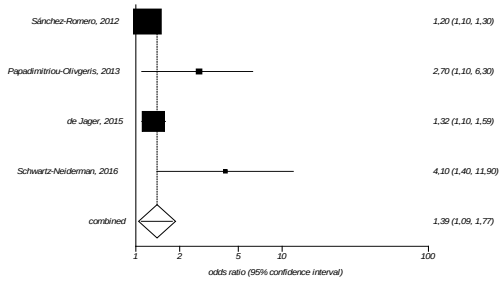
5B. Demographic patient characteristics



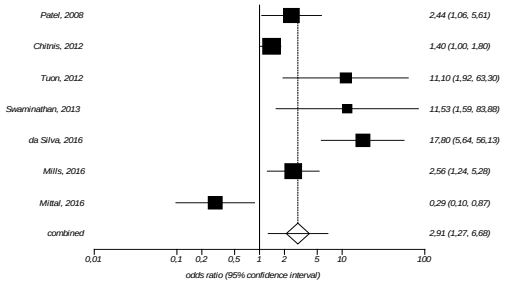
6B. Exposure to hospital care



7A. Mechanical ventilation



7B. Mechanical ventilation



8B. CRE exposure

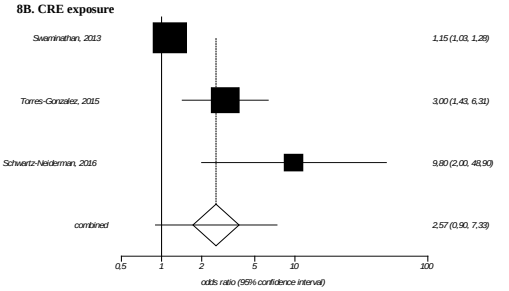
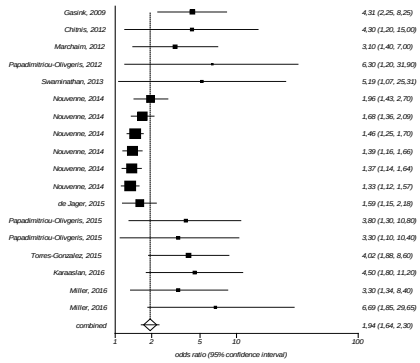
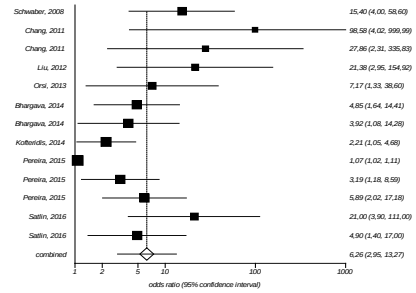


Figure B.Continued.

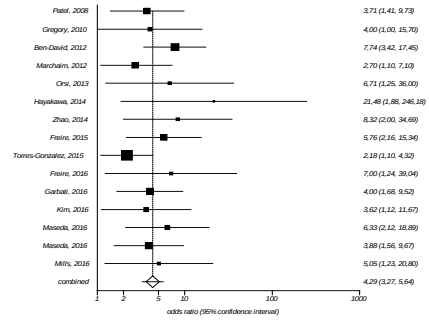
1A. Underlying disease or condition



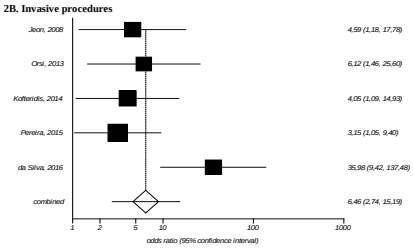
1B. Underlying disease or condition



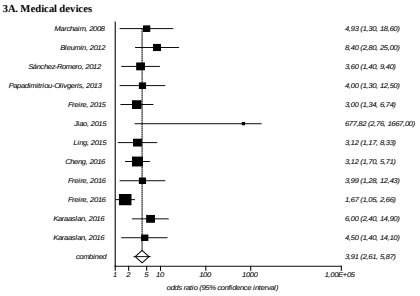
2A. Invasive procedures



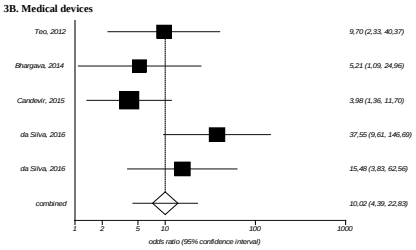
2B. Invasive procedures



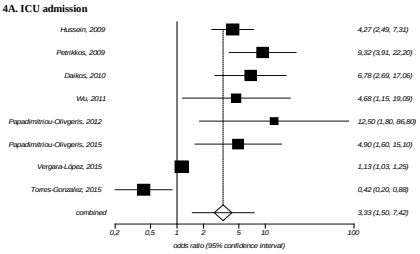
3A. Medical devices



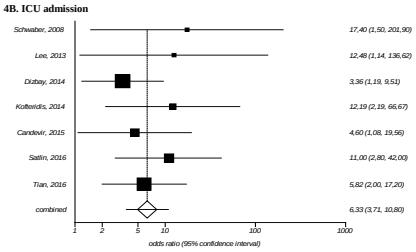
3B. Medical devices



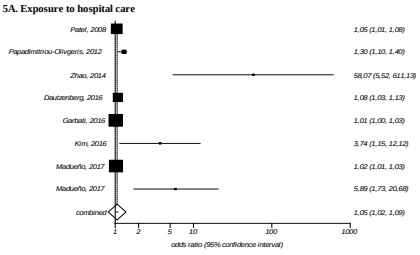
4A. ICU admission



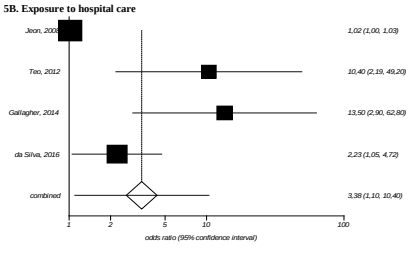
4B. ICU admission



5A. Exposure to hospital care



5B. Exposure to hospital care



6A. Mechanical ventilation

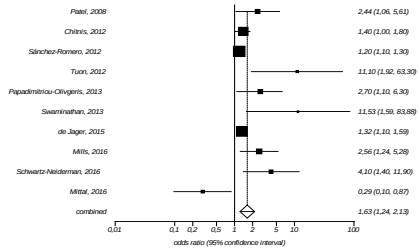
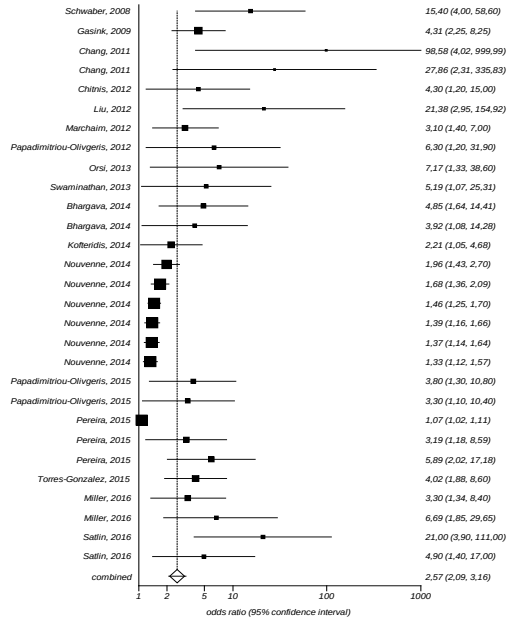
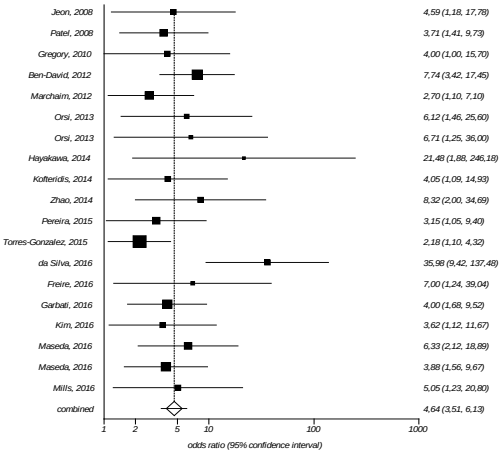


Figure C. The effect of carbapenem resistance mechanism on the overall risk estimate. A) Studies only describing carbapenemase production as carbapenem resistance mechanism, B) Studies describing another resistance mechanism or did not investigate the resistance mechanism involved.

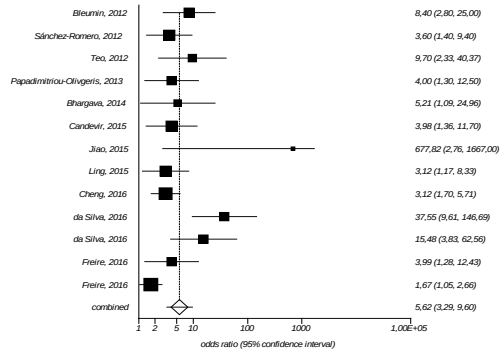
1A. Underlying disease or condition



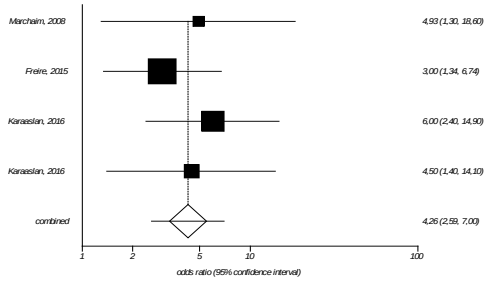
2A. Invasive procedures



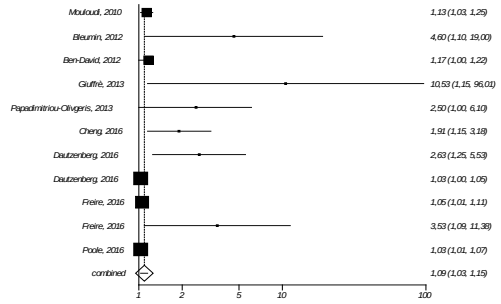
3A. Medical devices



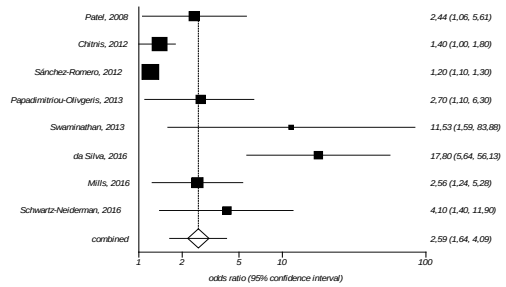
3B. Medical devices



4A. Demographic patient characteristics



5A. Mechanical ventilation



5B. Mechanical ventilation

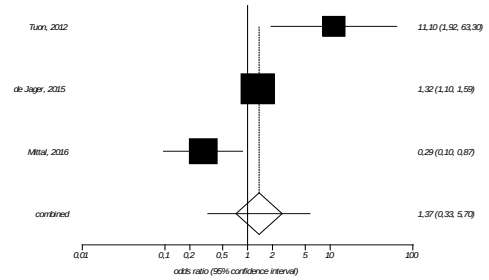


Figure D.The effect of study quality on the overall risk estimate. A) only studies with a moderate/high study quality (>15), B) only studies with a low study quality (≤15).

References

1. **Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D.** 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. Bmj **339**.
2. **von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S.** 2007. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Bmj **335:**806-808.