Supplementary Materials

Appendix 1. Search terms and search strategies

1.Pubmed (4448)

Search	Query	Items found
#1	Search: ((enterobacteriaceae[MeSH Terms]) OR klebsiella pneumoniae[MeSH Terms]) OR escherichia coli[MeSH Terms]	399348
#2	Search: (((carbapenem resistant) OR (carbapenem resistance)) OR (carbapenem nonsusceptible)) OR (carbapenemase producing)	15576
#3	Search: (((enterobacteriaceae[MeSH Terms]) OR (klebsiella pneumoniae[MeSH Terms])) OR (escherichia coli[MeSH Terms])) AND ((((carbapenem resistant) OR (carbapenem resistance)) OR (carbapenem nonsusceptible)) OR (carbapenemase producing))	5776
#4	Search: (((enterobacteriaceae[MeSH Terms]) OR (klebsiella pneumoniae[MeSH Terms])) OR (escherichia coli[MeSH Terms])) AND ((((carbapenem resistant) OR (carbapenem resistance)) OR (carbapenem nonsusceptible)) OR (carbapenemase producing)) Filters: Humans	4761
#5	Search: (((enterobacteriaceae[MeSH Terms]) OR (klebsiella pneumoniae[MeSH Terms])) OR (escherichia coli[MeSH Terms])) AND ((((carbapenem resistant) OR (carbapenem resistance)) OR (carbapenem nonsusceptible)) OR (carbapenemase producing)) Filters: Humans, from 1994 - 2020	4716
#6	Search: (((enterobacteriaceae[MeSH Terms]) OR (klebsiella pneumoniae[MeSH Terms])) OR (escherichia coli[MeSH Terms])) AND ((((carbapenem resistant) OR (carbapenem resistance)) OR (carbapenem nonsusceptible)) OR (carbapenemase producing)) Filters: Humans, English, from 1994 - 2020	4448

2.Embase(5348)

#	**searches**	**results**
1	Enterobacteriaceae.af.	38034
2	Klebsiella pneumoniae.af.	47767
3	Escherichia coli.af.	425764
4	1 or 2 or 3	470290
5	carbapenem resistant.af.	7442
6	carbapenem resistance.af.	3418
7	carbapenem nonsusceptible.af.	139
8	carbapenemase producing.af.	3413
9	5 or 6 or 7 or 8	11419
10	4 and 9	8235
11	limit 10 to (human and english language and yr="1994 -Current")	5348

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

3.Web of Science(3036)

#	**searches**	**results**
1	TI=(Enterobacteriaceae) Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	6685
2	TI=(Klebsiella pneumoniae) Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	10759
3	TI=(Escherichia coli) Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	102497
4	#3 OR #2 OR #1 Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	118551
5	TI=(carbapenem resistance OR carbapenem resistant OR carbapenem nonsusceptible OR carbapenemase producing) Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	5926
6	#5 AND #4 Databases= WOS, BCI, BIOSIS, CABI, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO, ZOOREC Timespan=1994-2020 Search language=English	3036

4.Cochrane library

ID	Search	Hits
#1	(carbapenem) AND (Enterobacteriaceae) (Limits: Word variations have been searched)	137
#2	(carbapenem) AND (Klebsiella pneumoniae) (Limits: Word variations have been searched)	71
#3	(carbapenem) AND (Escherichia coli) (Limits: Word variations have been searched)	67
#4	#1 OR #2 OR #3 with Cochrane Library publication date Between Jan 1994 and Sep 2020	174

Appendix 2. List of excluded studies with reason for exclusion

First author	Year	Reason for exclusion
Adams[1]	2019	inappropriate control group
Ahn[2]	2014	Not specific to patients with CRE infection
Akgul[3]	2016	Not specific to patients with CRE infection
Balkan[4]	2014	inappropriate control group
Biehle[5]	2015	not a pathogen of interest
Bleumin[6]	2012	No separate data for patients with CRE infection
Bogan[7]	2014	No separate data for patients with CRE infection
Chang[8]	2015	no control group
Cristina[9]	2016	no control group
Dautzenberg[10]	2015	Not specific to patients with CRE infection
de Maio Carrilho[11]	2016	no control group
Debby[12]	2012	Not specific to patients with CRE infection
Diaz[13]	2016	Not specific to patients with CRE infection
Dizbay[14]	2014	not a pathogen of interest
Eser[15]	2019	Not specific to patients with CRE infection
Falcone[16]	2009	not a pathogen of interest
Fang[17]	2019	No separate data for patients with CRE infection
Forde[18]	2017	No separate data for patients with CRE infection
Freire[19]	2015	inappropriate control group
Gao[20]	2019	inappropriate control group
Gasink[21]	2009	No separate data for patients with CRE infection
Gaviria[22]	2011	Letters, comments or reports
Giacobbe[23]	2015	Not the antibiotic resistance of interest
Giannella[24]	2014	Not specific to patients with CRE infection
Girmenia[25]	2015	inappropriate control group
Girometti[26]	2014	no outcomes of interest
Gowda[27]	2014	no outcomes of interest
Grabowsk[28]	2017	No separate data for patients with CRE infection
Hauck[29]	2016	inappropriate control group
Hu[30]	2016	Not specific to patients with CRE infection
Jiao[31]	2015	No separate data for patients with CRE infection
Kang[32]	2019	Not specific to patients with CRE infection
Kofteridis[33]	2014	No separate data for patients with CRE infection
Lai[34]	2013	inappropriate control group
Lee[35]	2013	no outcomes of interest
Lee[36]	2012	inappropriate control group
López-González[37]	2017	inappropriate control group
Lubbert[38]	2014	No separate data for patients with CRE infection
Mantzarlis[39]	2013	inappropriate control group

Marimuthu[40]	2013	Letters, comments or reports
Mazza[41]	2017	inappropriate control group
Miller[42]	2016	no outcomes of interest
Mouloudi[43]	2014	inappropriate control group
Muggeo[44]	2017	No separate data for patients with CRE infection
Nouvenne[45]	2014	No separate data for patients with CRE infection
Orsi[46]	2011	inappropriate control group
Papadimitriou-Olivgeris[47]	2013	Not specific to patients with CRE infection
Patel[48]	2015	inappropriate control group
Porwal[49]	2014	Letters, comments or reports
Qureshi[50]	2014	inappropriate control group
Rodrigues[51]	2016	inappropriate control group
Salsano[52]	2016	inappropriate control group
Segagni Lusignani[53]	2020	No separate data for patients with CRE infection
Shankar[54]	2018	no control group
Taminato[55]	2019	inappropriate control group
Tamma[56]	2017	inappropriate control group
Tascini[57]	2015	Not specific to patients with CRE infection
Tsereteli[58]	2018	no outcomes of interest
Tumbarello[59]	2015	inappropriate control group
Tumbarello[60]	2014	inappropriate control group
Tuon[61]	2017	no outcomes of interest
Jamal[62]	2016	no outcomes of interest
Wang[63]	2016	No separate data for patients with CRE infection

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

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Appendix 3. Descriptive details of the 50 included studies

Table S1 Descriptive details of the 50 included studies

First Author	Year	Country	Region	Economic status	Infection type	Pathogen	Resistance type	Sample size (n)		Mortality measurements	Mortality (%)	
								CRE	CSE		CRE	CSE
Alicino	2015	Italy	Europe	High income	bloodstream infection	Klebsiella pneumoniae	NA	349	162	30d mortality	36.1	23.5
Balkhair	2019	Oman	Asia	High income	bloodstream infection	Klebsiella pneumoniae	NA	69	305	30d mortality	63.8	24.3
Ben-David	2012	Israel	Asia	High income	bloodstream infection	Klebsiella pneumoniae	KPC-producing	42	85	in-hospital mortality	69	24
										mortality attributable to infection	48	17
Brizendine	2015	USA	America	High income	urinary tract infection	Klebsiella pneumoniae	NA	22	64	in-hospital mortality	18	2
Chang	2019	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	46	239	28d mortality	50	14.6
										7d mortality	37	10.5
										in-hospital mortality	58.7	15.9
Chang	2011	China	Asia	Lower middle income	bloodstream infection	Escherichia. coli	NA	17	34	in-hospital mortality	94.12	50
										28d hospital mortality	70.59	47.06
										14d hospital mortality	47.06	38.24
Chiotos	2018	USA	America	High income	mixed	Mixed Enterobacteriaceae	NA	31	144	30d mortality	6.5	1.4

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Cienfuegos-Gallet	2019	Colombia	America	Upper middle income	mixed	Klebsiella pneumoniae	KPC-producing	49	289	30d mortality	32.65	15.92
Correa	2013	Brazil	America	Upper middle income	mixed	Klebsiella pneumoniae	NA	20	40	in-hospital mortality	50	27.5
Cubero	2015	Spain	Europe	High income	mixed	Klebsiella pneumoniae	OXA-producing	20	9	in-hospital mortality	35	11.1
Daikos	2009	Greece	Europe	High income	bloodstream infection	Klebsiella pneumoniae	VIM-producing	14	148	14d mortality	42.9	16.9
Fraenkel-Wandel	2016	Israel	Asia	High income	bloodstream infection	Klebsiella pneumoniae	KPC-producing	68	136	in-hospital mortality	65	40
Gallagher	2014	USA	America	High income	bloodstream infection	Klebsiella pneumoniae	NA	43	111	in-hospital mortality	45	32
Garbati	2016	Saudi Arabia	Asia	High income	mixed	Mixed Enterobacteriaceae	NA	29	58	in-hospital mortality	31	12.1
Gomez Rueda	2014	Colombia	America	Upper middle income	mixed	Klebsiella pneumoniae	NA	61	61	in-hospital mortality	50.8	32.7
Hoxha	2016	Italy	Europe	High income	mixed	Klebsiella pneumoniae	NA	49	49	30d mortality	61	20
										6d mortality	24	8
Huang	2018	China	Asia	Upper middle income	mixed	Klebsiella pneumoniae	NA	267	1328	in-hospital mortality	14.61	5.65

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Hussein	2013	Israel	Asia	High income	bloodstream infection	Klebsiella pneumoniae	NA	103	214	30d mortality	43.7	29
Kotb	2020	Egypt	Africa	Lower middle income	mixed	Mixed Enterobacteriaceae	NA	871	727	mortality in ICU	61.1	51.7
Lee	2016	Korea	Asia	High income	mixed	Mixed Enterobacteriaceae	NA	37	37	in-hospital mortality	10.8	10.8
										28d mortality	27	21.6
Li	2019	China	Asia	Upper middle income	mixed	Klebsiella pneumoniae	NA	244	263	30d mortality in ICU	28.9	11
Liu	2019	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	20	69	30d mortality	55	15.9
Liu	2012	China	Asia	Lower middle incom	bloodstream infection	Klebsiella pneumoniae	NA	25	50	in-hospital mortality	60	40
										28d mortality	52	30
										14d mortality	44	22
Mclaughlin	2014	USA	America	High income	bloodstream infection	Klebsiella pneumoniae	KPC-producing	15	60	in-hospital mortality	33.3	11.7
Meng	2017	China	Asia	Upper middle income	mixed	Escherichia. coli	not focusing on a particular type of carbapenemase-producing strains	49	96	in-hospital mortality	12	1
Mouloudi	2010	Greece	Europe	High income	bloodstream infection	Klebsiella pneumoniae	KPC-producing	37	22	in-hospital mortality	68	41
										mortality attributable to infection	27	14

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

										mortality in ICU	57	41
Ny	2015	USA	America	High income	mixed	Klebsiella pneumoniae	NA	48	48	in-hospital mortality	14.6	10.4
Orsi	2013	Italy	Europe	High income	mixed	Klebsiella pneumoniae	KPC-producing	36	43	in-hospital mortality	38.9	27.9
Pan	2019	China	Asia	Upper middle income	mixed	Klebsiella pneumoniae	KPC-producing	66	132	in-hospital mortality	57.6	18.2
										28d mortality	18.18	11.36
Patel	2008	USA	America	High income	mixed	Klebsiella pneumoniae	NA	99	99	in-hospital mortality	48	20
										mortality attributable to infection	38	12
Pereira	2015	USA	America	High income	mixed	Klebsiella pneumoniae	NA	20	36	in-hospital mortality	45	28
Pouch	2015	USA	America	High income	urinary tract infection	Mixed Enterobacteriaceae	NA	20	80	in-hospital mortality	30	10
Qureshi	2012	USA	America	High income	bloodstream infection	Klebsiella pneumoniae	NA	19	51	28d mortality	47.4	27.5
Sánchez-Romero	2011	Spain	Europe	High income	mixed	Klebsiella pneumoniae	VIM-producing	28	55	14d mortality	46.4	30.9
Schwaber	2008	Israel	Asia	High income	mixed	Klebsiella pneumoniae	NA	48	56	in-hospital mortality	44	12.5

Shilo	2013	Israel	Asia	High income	urinary tract infection	Klebsiella pneumoniae	NA	135	127	in-hospital mortality	29	25
Simkins	2014	USA	America	High income	mixed	Klebsiella pneumoniae	NA	13	39	in-hospital mortality	46	8
Tian	2016	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	33	81	in-hospital mortality	42.4	19.8
										mortality attributable to infection	42.4	24.6
										28d mortality	33.3	18.5
Torres-Gonzalez	2016	Mexico	America	Upper middle income	mixed	Mixed Enterobacteriaceae	OXA-producing	27	108	mortality attributable to infection	11.1	7.4
Trecarichi	2016	Italy	Europe	High income	bloodstream infection	Klebsiella pneumoniae	NA	161	117	21d mortality	52.2	14.5
Ulu	2015	Turkey	Asia	Upper middle income	mixed	Klebsiella pneumoniae	NA	47	51	mortality in ICU	44.7	51
Vardakas	2015	Greece	Europe	High income	mixed	Klebsiella pneumoniae	NA	80	24	mortality in ICU	72.5	58.3
Wang	2018	China	Asia	Upper middle income	mixed	Klebsiella pneumoniae	NA	48	48	in-hospital mortality	47.9	4.2
Xiao	2018	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	135	293	30d mortality	58.5	15.4

Zhang	2018	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	54	84	in-hospital mortality	18.5	8.3
										7d mortality	16.7	1.2
										28d mortality	18.5	2.4
Zheng	2018	China	Asia	Upper middle income	bloodstream infection	Klebsiella pneumoniae	NA	59	230	28d mortality	54.2	19.6
Zheng	2020	China	Asia	Upper middle income	neurosurgical infection	Mixed Enterobacteriaceae	NA	26	107	mortality attributable to infection	69.2	12.1
Zuo	2020	China	Asia	Upper middle income	pneumonia	Klebsiella pneumoniae	NA	74	74	in-hospital mortality	35.1	20.3
										mortality attributable to infection	25.7	9.5
Villegas	2016	7 countries in Latin America	America	Upper middle income	bloodstream infection	Mixed Enterobacteriaceae	NA	53	202	in-hospital mortality	64	30
										mortality attributable to infection	85	43
Stewardson	2019	10 countries	Asia, Africa, America	low and middle income countries	bloodstream infection	Mixed Enterobacteriaceae	NA	123	174	in-hospital mortality	35	20

OXA,oxacillinase; KPC, Klebsiella pneumoniae carbapenemase; VIM, Verona integron-encoded MBL; NA, Not Applicable i.e. include non-carbapenemase-producing strains or not focusing on a particular type of carbapenemase-producing strains

Appendix 4. Risk of bias assessed with the Newcastle-Ottawa Assessment Scale.

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability. In this version of NOS, we define the exposure as carbapenem resistance and the outcome as death in hospital and the target population is patients infected with *Enterobacteriaceae*.

Selection: (Maximum 4 stars)

1) Representativeness of the exposed cohort
   a) truly representative of the average carbapenem resistance in patients infected with *Enterobacteriaceae*. ✵
   b) somewhat representative of the average carbapenem resistance in patients infected with *Enterobacteriaceae* ✵
   c) selected group of users (e.g. organ transplant recipients, onco-hematological patients)
   d) no description of the derivation of the cohort
2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort
3) Ascertainment of exposure
   a) secure record (e.g. medical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description
4) Demonstration that outcome of interest was not present at start of study

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

a) yes ✵

b) no

Comparability: (Maximum 2 stars)

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for age✵

b) study controls for comorbidity✵

Outcome: (Maximum 3 stars)

1) Assessment of outcome

a) independent blind assessment ✵

b) record linkage ✵

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (adequate if >14 days) ✵

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ✵

b) subjects lost to follow up unlikely to introduce bias - small number lost - > 80 % follow up, or description provided of those lost ✵

c) follow up rate < 80% and no description of those lost

d) no statement

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

First Author	Year	selection(1)	selection(2)	selection(3)	selection(4)	comparability(1)	outcome(1)	outcome(2)	outcome(3)	Total score	Risk of bias
Alicino	2015	1	1	1	1	0	1	1	1	7	Low
Balkhair	2019	1	1	1	1	0	1	1	1	7	Low
Ben-David	2012	1	1	1	1	1	1	1	1	8	Low
Brizendine	2015	0	1	1	1	1	1	1	1	7	Low
Chang	2019	1	1	1	1	0	1	1	1	7	Low
Chang	2011	1	1	1	1	1	1	1	1	8	Low
Chiotos	2018	0	1	1	1	1	1	1	1	7	Low
Cienfuegos-Gallet	2019	1	1	1	1	1	1	1	1	8	Low
Correa	2013	1	1	1	1	1	1	1	1	8	Low
Cubero	2015	1	1	1	1	0	1	1	1	7	Low
Daikos	2009	1	1	1	1	0	1	0	1	6	Moderate
Fraenkel-Wandel	2016	1	1	1	1	1	1	1	1	8	Low
Gallagher	2014	1	1	1	1	0	1	1	1	7	Low
Garbati	2016	1	1	1	1	0	1	1	1	7	Low
Gomez Rueda	2014	1	1	1	1	0	1	1	1	7	Low
Hoxha	2016	1	1	1	1	1	1	1	0	7	Low
Huang	2018	1	1	1	1	2	1	1	1	9	Low
Hussein	2013	1	1	1	1	1	1	1	1	8	Low
Kotb	2020	1	1	1	1	0	1	1	1	7	Low
Lee	2016	1	1	1	1	1	1	1	1	8	Low
Li	2019	0	1	1	1	1	1	1	1	7	Low
Liu	2019	0	1	1	1	1	1	1	1	7	Low

Liu	2012	1	1	1	1	1	1	1	1	8	Low
Mclaughlin	2014	1	1	1	1	1	1	1	1	8	Low
Meng	2017	1	1	1	1	1	1	1	1	8	Low
Mouloudi	2010	0	1	1	1	1	1	1	1	7	Low
Ny	2015	1	1	1	1	1	1	1	1	8	Low
Orsi	2013	1	1	1	1	1	1	1	1	8	Low
Pan	2019	1	1	1	1	1	1	1	1	8	Low
Patel	2008	1	1	1	1	1	1	1	1	8	Low
Pereira	2015	0	1	1	1	1	1	1	1	7	Low
Pouch	2015	0	1	1	1	1	1	1	1	7	Low
Qureshi	2012	1	1	1	1	0	1	1	1	7	Low
Sánchez-Romero	2011	1	1	1	1	0	1	0	1	6	Moderate
Schwaber	2008	1	1	1	1	0	1	1	1	7	Low
Shilo	2013	1	1	1	1	1	1	1	1	8	Low
Simkins	2014	0	1	1	1	1	1	1	1	7	Low
Tian	2016	1	1	1	1	1	1	1	1	8	Low
Torres-Gonzalez	2016	1	1	1	1	0	1	1	1	7	Low
Trecarichi	2016	0	1	1	1	0	1	1	1	6	Moderate
Ulu	2015	0	1	1	1	1	1	1	1	7	Low
Vardakas	2015	0	1	1	1	1	1	1	1	7	Low
Wang	2018	1	1	1	1	1	1	1	1	8	Low
Xiao	2018	1	1	1	1	1	1	1	1	8	Low
Zhang, Y.	2018	0	1	1	1	0	1	1	1	6	Mod
Zheng, Si-Han	2018	1	1	1	1	1	1	1	1	8	Low
Zheng,Guanghui	2020	0	1	1	1	1	1	1	1	7	Low

Zuo	2020	1	1	1	1	1	1	1	1	8	Low
Villegas	2016	1	1	1	1	1	1	1	1	8	Low
Stewardson	2019	1	1	1	1	2	1	1	1	9	Low

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Appendix 5. The results from stratified analysis and meta-regression for different mortality outcome type

Table S2 Subgroup analysis of the effect of carbapenem resistance on in-hospital mortality for patients infected with Enterobacteriaceae

Sub-groups	No. of studies	No. of CRE patients	No. of CSE patients	unweighted means of mortality among CRE patients	unweighted means of mortality among CSE patients	RR(95%CI)	*P* value (significance tests of RR=1)	I²(%)	*P* value between groups	RD(95%CI)	*P* value (significance tests of RD=0)	I²(%)	*P* value beteen groups
Pathogens													
Klebsiella pneumoniae	24	1340	3072	43.10%	20.26%	2.12(1.77, 2.53)	0.000	57.4		0.22(0.16, 0.28)	0.000	72.3	
Mixed Enterobacteriaceae pathogens	5	262	551	34.16%	16.58%	2.01(1.62, 2.49)	0.000	0.0	**0.161**	0.17(0.06, 0.29)	0.003	65.8	**0.591**
Escherichia. coli	2	66	130	53.06%	25.50%	3.83(0.46, 31.78)	0.214	76.2		0.27(-0.06, 0.59)	0.115	88.6	
Geographical region													
America	11	414	840	40.43%	19.30%	1.97(1.60, 2.43)	0.000	22.2		0.20(0.14, 0.27)	0.000	28.2	
Europe	3	93	74	47.30%	26.67%	1.58(1.06, 2.38)	0.026	0.0	**0.781**	0.19(0.05, 0.33)	0.009	0.0	**0.832**
Asia	16	1038	2665	43.11%	19.23%	2.28(1.81, 2.85)	0.000	65.4		0.23(0.15, 0.31)	0.000	82.7	
Economic status													
High income	17	732	1110	39.45%	19.21%	1.94(1.57, 2.40)	0.000	42.5	**0.494**	0.19(0.13, 0.26)	0.000	57.8	**0.263**
Upper middle income	13	813	2469	46.59%	21.04%	2.29(1.85, 2.82)	0.000	55.2		0.25(0.16, 0.34)	0.000	81.8	
Infection type													
Bloodstream infections	12	556	1278	54.42%	27.73%	2.01(1.68, 2.41)	0.000	50.7	**0.323**	0.26(0.19, 0.34)	0.000	61.7	**0.355**

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Urinary tract infection	3	177	271	25.67%	12.33%	2.40(0.82, 7.03)	0.110	72.5		0.11(0.00, 0.21)	0.044	29.7	
Pneumonia	1	74	74	35.10%	20.30%	1.73(1.00, 3.00)	0.049	NA		0.15(0.01, 0.29)	0.040	NA	
Mixed	15	861	2130	36.41%	15.34%	2.34(1.83, 2.97)	0.000	40.8		0.20(0.13, 0.28)	0.000	74.7	
Resistance type													
KPC-producing Enterobacteriaceae	6	264	478	55.30%	27.13%	2.13(1.56, 2.89)	0.000	58.7		0.30(0.20, 0.40)	0.000	46.2	
OXA-producing Enterobacteriaceae	1	20	9	35.00%	11.10%	3.15(0.45, 21.96)	0.247	NA		0.24(-0.05, 0.53)	0.110	NA	
include non-carbapenemase-producing strains or multiple resistance types	24	1384	3266	39.36%	18.59%	2.08(1.75, 2.47)	0.000	51.5	**0.716**	0.20(0.14, 0.25)	0.000	69.8	**0.450**
Sample size													
<100	14	387	588	42.33%	20.34%	1.96(1.52, 2.53)	0.000	30.6		0.21(0.13, 0.30)	0.000	58.3	
100-200	11	589	959	41.13%	18.07%	2.26(1.80, 2.84)	0.000	41.7	**0.641**	0.23(0.15, 0.30)	0.000	64.8	**0.974**
>200	6	692	2206	44.39%	22.76%	2.02(1.49, 2.72)	0.000	78.4		0.21(0.09, 0.32)	0.000	85.5	
Range of publication year													
2008-2010	3	184	177	53.33%	24.50%	2.28(1.57, 3.31)	0.000	24.7		0.29(0.20, 0.38)	0.000	0.0	
2011-2013	6	275	379	56.84%	32.40%	1.71(1.29, 2.28)	0.000	54.7	**0.278**	0.24(0.08, 0.41)	0.004	79.3	**0.658**
2014-2016	14	482	1022	37.92%	18.47%	1.86(1.57, 2.20)	0.000	11.5		0.18(0.12, 0.24)	0.000	35.1	
2017-2020	8	727	2175	34.93%	11.69%	2.74(2.00, 3.75)	0.000	60.0		0.22(0.12, 0.32)	0.000	86.1	
Total	**31**	1668	3753	42.30%	20.00%	2.09(1.81, 2.42)	0.000	49.8		**0.22(0.17, 0.26)**	0.000	**71.0**	

OXA,oxacillinase; KPC, Klebsiella pneumoniae carbapenemase

Table S3 Subgroup analysis of the effect of carbapenem resistance on 28d or 30d mortality for patients infected with Enterobacteriaceae

Sub-groups	**No. of studies**	**No. of CRE patients**	**No. of CSE patients**	**unweighted means of mortality among CRE patients**	**unweighted means of mortality among CSE patients**	**RR(95%CI)**	***P* value (significance tests of RR=1)**	**I²(%)**	***P* value between groups**	**RD(95%CI)**	***P* value (significance tests of RD=0)**	**I²(%)**	***P* value beteen groups**
Pathogens													
Klebsiella pneumoniae	14	1076	2248	44.60%	19.14%	2.34(1.90, 2.88)	0.000	65.9	**0.761**	0.25(0.18, 0.32)	0.000	76.9	**0.124**
Mixed Enterobacteriaceae pathogens	2	68	181	16.75%	11.50%	1.78(0.57, 5.60)	0.321	34.3		0.05(-0.03, 0.13)	0.213	0.0	
Escherichia. coli	1	17	34	70.59%	47.06%	1.50(0.94, 2.40)	0.091	NA		0.24(-0.04, 0.51)	0.092	NA	
Geographical region													
America	3	99	484	28.85%	14.94%	2.00(1.37, 2.92)	0.000	0.0	**0.927**	0.12(-0.00, 0.23)	0.055	50.1	**0.441**
Europe	2	398	211	48.55%	21.75%	2.04(1.07, 3.90)	0.030	73.6		0.26(-0.02, 0.53)	0.068	87.5	
Asia	12	664	1768	45.40%	20.81%	2.31(1.81, 2.94)	0.000	68.4		0.25(0.16, 0.34)	0.000	77.0	
Economic status													
High income	7	657	962	40.79%	21.04%	1.92(1.46, 2.52)	0.000	57.6	**0.427**	0.19(0.08, 0.30)	0.001	80.6	**0.414**
Upper middle income	10	504	1501	44.29%	19.07%	2.48(1.92, 3.20)	0.000	58.9		0.25(0.16, 0.35)	0.000	75.7	
Infection type													
Bloodstream infections	12	929	1812	48.59%	22.31%	2.29(1.81, 2.90)	0.000	72.0	**0.746**	0.26(0.18, 0.34)	0.000	73.2	**0.108**
Mixed	5	232	651	29.07%	14.06%	2.05(1.50, 2.81)	0.000	4.2		0.14(0.02, 0.26)	0.019	74.5	

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Resistance type													
KPC-producing Enterobacteriaceae	2	115	421	25.42%	13.64%	1.89(1.27, 2.82)	0.002	0.0	**0.428**	0.11(0.01, 0.21)	0.030	22.9	**0.211**
include non-carbapenemase-producing strains or multiple resistance types	15	1046	2042	45.17%	20.72%	2.29(1.84, 2.84)	0.000	67.2		0.24(0.16, 0.32)	0.000	79.5	
Sample size													
<100	6	167	290	52.17%	27.01%	1.97(1.45, 2.67)	0.000	33.6		0.25(0.14, 0.37)	0.000	41.3	
100-200	4	184	441	19.12%	8.42%	2.30(1.25, 4.24)	0.008	34.6	**0.207**	0.09(0.04, 0.15)	0.001	3.7	**0.088**
>200	7	810	1732	48.42%	20.33%	2.39(1.80, 3.18)	0.000	80.1		0.28(0.17, 0.39)	0.000	83.5	
Range of publication year													
2011-2013	4	164	329	53.42%	33.39%	1.56(1.25, 1.94)	0.000	0.0		0.17(0.08, 0.26)	0.000	0.0	
2014-2016	4	468	349	39.35%	20.90%	1.79(1.28, 2.49)	0.001	32.6	**0.060**	0.18(0.05, 0.32)	0.009	67.9	**0.568**
2017-2020	9	529	1785	39.70%	13.43%	2.91(2.41, 3.51)	0.000	29.1		0.26(0.14, 0.37)	0.000	88.0	
Total	**17**	1161	2463	42.85%	19.88%	**2.23(1.83, 2.72)**	**0.000**	**63.6**		**0.23(0.15, 0.30)**	**0.000**	**79.1**	

KPC, Klebsiella pneumoniae carbapenemase

Table S4 Subgroup analysis of the effect of carbapenem resistance on mortality attributable to infection for patients infected with Enterobacteriaceae

Sub-groups	**No. of studies**	**No. of CRE patients**	**No. of CSE patients**	**unweighted means of mortality among CRE patients**	**unweighted means of mortality among CSE patients**	**RR(95%CI)**	***P* value (significance tests of RR=1)**	**I²(%)**	***P* value between groups**	**RD(95%CI)**	***P* value (significance tests of RD=0)**	**I²(%)**	***P* value beteen groups**
Pathogens													
Klebsiella pneumoniae	5	285	361	36.22%	15.42%	2.81(2.06, 3.82)	0.000	0.0	**0.739**	0.23(0.16, 0.29)	0.000	0.0	**0.388**
Mixed Enterobacteriaceae pathogens	3	106	417	55.10%	20.83%	2.72(1.17, 6.32)	0.020	84.6		0.34(0.02, 0.65)	0.036	93.3	
Geographical region													
America	3	179	409	44.70%	20.80%	2.27(1.41, 3.68)	0.001	52.4	**0.484**	0.24(0.03, 0.46)	0.026	89.5	**0.641**
Europe	1	37	22	27.00%	14.00%	1.98(0.61, 6.43)	0.255	NA		0.13(-0.07, 0.34)	0.195	NA	
Asia	4	175	347	46.33%	15.80%	3.32(2.22, 4.97)	0.000	38.8		0.32(0.14, 0.49)	0.000	77.4	
Economic status													
High income	3	178	206	37.67%	14.33%	2.99(2.01, 4.43)	0.000	0.0	**0.932**	0.26(0.17, 0.34)	0.000	0.0	**0.725**
Upper middle income	5	213	572	46.68%	19.32%	2.68(1.66, 4.32)	0.000	70.4		0.28(0.10, 0.47)	0.002	87.7	
Infection type													
Bloodstream infections	4	165	390	50.60%	24.65%	2.08(1.75, 2.48)	0.000	0.0	**0.075**	0.30(0.18, 0.42)	0.000	53.4	**0.203**
Pneumonia	1	74	74	25.70%	9.50%	2.71(1.21, 6.07)	0.015	NA		0.16(0.04, 0.28)	0.008	NA	
Neurosurgical infection	1	26	107	69.20%	12.10%	5.70(3.22, 10.08)	0.000	NA		0.57(0.38, 0.76)	0.000	NA	

Mixed	2	126	207	24.55%	9.70%	2.75(1.32, 5.71)	0.007	27.2		0.16(-0.08, 0.40)	0.200	87.2	
Resistance type													
KPC-producing Enterobacteriaceae	2	79	107	37.50%	15.50%	2.69(1.61, 4.51)	0.000	0.0		0.23(0.06, 0.41)	0.010	43.8	
OXA-producing Enterobacteriaceae	1	27	108	11.10%	7.40%	1.50(0.43, 5.28)	0.528	NA		0.04(-0.09, 0.17)	0.572	NA	
include non-carbapenemase-producing strains or multiple resistance types	5	285	563	52.06%	20.24%	2.96(1.87, 4.70)	0.000	75.4	**0.488**	0.33(0.20, 0.46)	0.000	76.9	**0.277**
Sample size													
<100	1	37	22	27.00%	14.00%	1.98(0.61, 6.43)	0.255	NA		0.13(-0.07, 0.34)	0.195	NA	
100-200	6	301	554	39.07%	13.77%	3.21(2.35, 4.39)	0.000	22.0	**0.641**	0.26(0.13, 0.39)	0.000	80.0	**0.566**
>200	1	53	202	85.00%	43.00%	1.97(1.62, 2.40)	0.000	NA		0.42(0.30, 0.54)	0.000	NA	
Range of publication year													
2008-2010	2	136	121	32.50%	13.00%	3.07(1.79, 5.28)	0.000	0.0		0.23(0.10, 0.36)	0.000	27.2	
2011-2013	1	42	85	48.00%	17.00%	2.89(1.63, 5.13)	0.000	NA		0.31(0.14, 0.48)	0.000	NA	
2014-2016	3	113	391	46.17%	25.00%	2.00(1.66, 2.40)	0.000	0.0	**0.380**	0.24(-0.02, 0.49)	0.067	89.5	**0.849**
2017-2020	2	100	181	47.45%	10.80%	4.14(1.94, 8.82)	0.000	58.4		0.36(-0.05, 0.77)	0.082	92.5	
Total		391	778	43.30%	17.45%	**2.74(1.97, 3.81)**	**0.000**	**58.3**		**0.27(0.15, 0.38)**	**0.000**	**79.5**	

OXA,oxacillinase;KPC, Klebsiella pneumoniae carbapenemase

Table S5 Univariate meta-regression of the potential variables on risk difference of in-hospital mortality for patients with CRE versus CSE

Variables	Sub-categories	No. of studies	No. of CRE patients	No. of CSE patients	coefficient	standard error	95% confidence interval		*P* value from meta-regression
Pathogens	Klebsiella pneumoniae	24	1340	3072	-0.199	0.187	-0.583	0.184	0.296
	Mixed Enterobacteriaceae pathogens	5	262	551	-0.178	0.210	-0.608	0.252	0.404
	Escherichia. coli	2	66	130	reference	-	-	-	-
Geographical region	America	11	414	840	-0.025	0.105	-0.241	0.190	0.810
	Europe	3	93	74	-0.067	0.216	-0.510	0.375	0.757
	Asia	16	1038	2665					
Economic status	High income	17	732	1110	-0.068	0.097	-0.267	0.131	0.490
	Upper middle income	13	813	2469	reference	-	-	-	-
Infection type	Bloodstream infections	12	556	1278	0.228	0.195	-0.171	0.627	0.252
	Urinary tract infection	3	177	271	reference	-	-	-	-
	pneumonia	1	74	74	0.084	0.335	-0.604	0.771	0.805
	Mixed	15	861	2130	0.150	0.203	-0.267	0.567	0.468
Resistance type	KPC-producing Enterobacteriaceae	6	264	478	0.062	0.995	-1.977	2.100	0.951
	OXA-producing Enterobacteriaceae	1	20	9	reference	-	-	-	-
	include non-carbapenemase-producing strains or multiple resistance types	24	1384	3266	-0.007	0.992	-2.040	2.025	0.994
Sample size	<100	14	387	588	0.006	0.128	-0.255	0.268	0.962
	100-200	11	589	959	reference	-	-	-	-
	>200	6	692	2206	-0.029	0.109	-0.253	0.194	0.789
Range of publication year	2008-2010	3	184	177	0.042	0.183	-0.335	0.418	0.823
	2011-2013	6	275	379	0.031	0.131	-0.238	0.299	0.816
	2014-2016	14	482	1022	-0.005	0.117	-0.245	0.234	0.964
	2017-2020	8	727	2175	reference	-	-	-	-
Sample size	-	31	1668	3753	-0.00012	0.00013	-0.00039	0.00015	0.380
Year of publication	-	31	1668	3753	-0.005	0.015	-0.035	0.025	0.751

OXA,oxacillinase;KPC, Klebsiella pneumoniae carbapenemase

Zhou R, *et al. BMJ Open* 2021; 11:e054971. doi: 10.1136/bmjopen-2021-054971

Table S6 Univariate meta-regression of the potential variables on risk difference of 28d or 30d mortality for patients with CRE versus CSE

Variables	Sub-groups	No. of studies	No. of CRE patients	No. of CSE patients	coefficient	standard error	95% confidence interval		P value from meta-regression
Pathogens	Klebsiella pneumoniae	14	1076	2248	reference	-	-	-	-
	Mixed Enterobacteriaceae pathogens	2	68	181	-0.228	0.385	-1.055	0.598	0.563
	Escherichia. coli	1	17	34	-0.047	0.247	-0.576	0.483	0.853
Geographical region	America	3	99	484	-0.129	0.204	-0.566	0.307	0.536
	Europe	2	398	211	-0.116	0.154	-0.447	0.215	0.464
	Asia	12	664	1768	reference	-	-	-	-
Economic status	High income	7	657	962	-0.066	0.110	-0.301	0.169	0.558
	Upper middle income	10	504	1501	reference	-	-	-	-
Infection type	Bloodstream infections	12	929	1812	reference	-	-	-	-
	Mixed	5	232	651	-0.095	0.165	-0.446	0.257	0.575
Resistance type	KPC-producing Enterobacteriaceae	2	115	421	-0.150	0.210	-0.599	0.298	0.486
	include non-carbapenemase-producing strains or multiple resistance types	15	1046	2042	reference	-	-	-	-
Sample size	<100	6	167	290	-0.030	0.141	-0.332	0.272	0.833
	100-200	4	184	441	-0.179	0.236	-0.686	0.327	0.460
	>200	7	810	1732	reference	-	-	-	-
Range of publication year	2011-2013	4	164	329	-0.168	0.134	-0.455	0.119	0.229
	2014-2016	4	468	349	-0.182	0.144	-0.491	0.128	0.228
	2017-2020	9	529	1785	reference	-	-	-	-
Sample size	-	17	1161	2463	0.00009	0.00039	-0.00075	0.00092	0.827
Year of publication	-	17	1161	2463	0.027	0.020	-0.017	0.070	0.207

KPC, Klebsiella pneumoniae carbapenemase

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Table S7 Univariate meta-regression of the potential variables on risk ratio of in-hospital mortality for patients with CRE versus CSE

Variables	Sub-categories	No. of studies	No. of CRE patients	No. of CSE patients	coefficient	standard error	95% confidence interval		*P* value from meta-regression
Pathogens	Klebsiella pneumoniae	24	1340	3072	-0.040	0.344	-0.744	0.664	0.908
	Mixed Enterobacteriaceae pathogens	5	262	551	-0.080	0.387	-0.872	0.713	0.838
	Escherichia. coli	2	66	130	reference	-	-	-	-
Geographical region	America	11	414	840	-0.108	0.173	-0.463	0.247	0.537
	Europe	3	93	74	-0.334	0.306	-0.962	0.293	0.284
	Asia	16	1038	2665					
Economic status	High income	17	732	1110	-0.165	0.156	-0.485	0.154	0.299
	Upper middle income	13	813	2469	reference	-	-	-	-
Infection type	Bloodstream infections	12	556	1278	0.194	0.308	-0.437	0.825	0.533
	Urinary tract infection	3	177	271	reference	-	-	-	-
	pneumonia	1	74	74	0.044	0.495	-0.972	1.061	0.929
	Mixed	15	861	2130	0.339	0.315	-0.307	0.985	0.291
Resistance type	KPC-producing Enterobacteriaceae	6	264	478	-0.394	1.108	-2.664	1.875	0.725
	OXA-producing Enterobacteriaceae	1	20	9	reference	-	-	-	-
	include non-carbapenemase-producing strains or multiple resistance types	24	1384	3266	-0.419	1.100	-2.672	1.835	0.707
Sample size	<100	14	387	588	-0.142	0.189	-0.529	0.246	0.460
	100-200	11	589	959	reference	-	-	-	-
	>200	6	692	2206	-0.119	0.187	-0.502	0.265	0.532
Range of publication year	2008-2010	3	184	177	-0.157	0.254	-0.677	0.364	0.541
	2011-2013	6	275	379	-0.447	0.192	-0.840	-0.054	0.027
	2014-2016	14	482	1022	-0.343	0.175	-0.702	0.017	0.061
	2017-2020	8	727	2175	reference	-	-	-	-
Sample size	-	31	1668	3753	0.00016	0.00023	-0.00031	0.00062	0.503
Year of publication	-	31	1668	3753	0.023	0.023	-0.024	0.070	0.316

OXA,oxacillinase;KPC, Klebsiella pneumoniae carbapenemase

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Table S8 Univariate meta-regression of the potential variables on risk ratio of 28-30d mortality for patients with CRE versus CSE

Variables	Sub-groups	No. of studies	No. of CRE patients	No. of CSE patients	coefficient	standard error	95% confidence interval		*P* value from meta-regression
Pathogens	Klebsiella pneumoniae	14	1076	2248	reference	-	-	-	-
	Mixed Enterobacteriaceae pathogens	2	68	181	-0.370	0.464	-1.364	0.625	0.439
	Escherichia. coli	1	17	34	-0.443	0.388	-1.275	0.389	0.272
Geographical region	America	3	99	484	-0.125	0.313	-0.796	0.545	0.695
	Europe	2	398	211	-0.146	0.299	-0.787	0.495	0.633
	Asia	12	664	1768	reference	-	-	-	-
Economic status	High income	7	657	962	-0.262	0.189	-0.664	0.141	0.186
	Upper middle income	10	504	1501	reference	-	-	-	-
Infection type	Bloodstream infections	12	929	1812	reference	-	-	-	-
	Mixed	5	232	651	-0.117	0.244	-0.636	0.402	0.637
Resistance type	KPC-producing Enterobacteriaceae	2	115	421	-0.209	0.316	-0.882	0.465	0.519
	include non-carbapenemase-producing strains or multiple resistance types	15	1046	2042	reference	-	-	-	-
Sample size	<100	6	167	290	-0.191	0.224	-0.672	0.290	0.408
	100-200	4	184	441	-0.064	0.322	-0.754	0.625	0.845
	>200	7	810	1732	reference	-	-	-	-
Range of publication year	2011-2013	4	164	329	-0.621	0.149	-0.939	-0.302	0.001
	2014-2016	4	468	349	-0.514	0.160	-0.856	-0.171	0.006
	2017-2020	9	529	1785	reference	-	-	-	-
Sample size	-	17	1161	2463	0.00039	0.00067	-0.00104	0.00182	0.572
Year of publication	-	17	1161	2463	0.093	0.025	0.038	0.147	0.002

KPC, Klebsiella pneumoniae carbapenemase