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Deaths Attributable to Carbapenem-Resistant *Enterobacteriaceae* Infections

Technical Appendix

Technical Appendix Table. Characteristics and outcomes of studies included in a systematic review and metaanalysis of deaths attributable to carbapenem-resistant *Enterobacteriaceae* infections*

Study first author, year (reference)	Study design, year(s), country	No. patients, characteristic	Type of infection	Concurrent condition or severity of disease score on admission (CRE vs. CSE)	Type/location of death reported	Deaths		Attributable deaths (%)†	Independent predictors of death‡
						No. CRE-associated/ no. total (%)	No. CSE-associated/ no. total (%)		
Ben-David, 2012 (*1*)	Retrospective cohort, 2006, Israel	192	BSI	Pitt bacteremia score, median: 4 vs. 2 (CSE) and 3 (ESBL-producing)§	In hospital	29/42 (69)	45/150 (30)	39	Carbapenem resistance, Charlson comorbidity index, Pitt bacteremia score
Chang, 2011 (*2*)	Retrospective matched (1:1 by sex, age, year of hospital admission, LOS up to the isolation of *Escherichia coli*) case-control, 2006–2008, Taiwan	51	BSI	Pitt bacteremia score, mean ± SD: 5.6 ± 4.4 vs. 2.5 ± 2.6	In hospital	16/17 (94)	17/34 (50)	44	NR
Gaviria, 2011 (*3*)	Retrospective matched (1:1 by age, date of specimen collection) case-control, 2009–2011, USA	57	Undetermined infections	Charlson comorbidity index score, median: 2 vs. 1.1	NR	1/19 (5)	3/38 (8)	–3	NR
Mouloudi, 2010 (*4*)	Retrospective nested case-control study, 2007–2008, Greece	59, ICU patients	BSI	APACHE II score, median: 26 (KPC-producing) and 20 (MBL-producing) vs. 17.5	In hospital	25/37 (68)	9/22 (41)	27	KPC-production, SOFA score, solid organ transplantation, age
Daikos, 2009 (*5*)	Multicenter prospective cohort, 2004–2006, Greece	162, 33% ICU patients	BSI	NR	All-cause 14-d	6/14 (43)	25/148 (17)	26	MIC of carbapenems >4 μg/mL, age, rapidly fatal underlying disease (McCabe and Jackson classification). After adjustment for inappropriate empirical or definitive antibiotic treatment: age, rapidly fatal underlying disease

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Patel, 2008 (*6*)	Retrospective matched (1:1 by site of infection) case-control, 2004–2006, USA	198	72% BSI (primary and secondary), 34% intra-abdominal infection, 2% urosepsis, 2% ventriculitis, 2% osteomyelitis, 2% empyema, 1% deep sinus infection	NR	In hospital	48/99 (48)	20/99 (20)	28	Heart disease, liver disease, ICU admission, carbapenem resistance
Schwaber, 2008 (*7*)	Retrospective cohort, 2003–2006, Israel	104	Various infections#	NR	In hospital	21/48 (44)	7/56 (13)	31	Carbapenem resistance, malignancy, mechanical ventilation
Daikos, 2007 (*8*)	2-center retrospective case-control, 2003–2004, Greece	56, 46% ICU-patients	BSI	NR	All-cause 14-d	7/13 (54)	5/43 (12)	42	Imipenem resistance, APACHE II score
Falagas, 2007 (*9*)	2-center retrospective matched (1:1 by site of infection) case-control, 2000–2006, Greece	106, 60% ICU patients	26% BSI, 23% pneumonia, 23% UTIs, 15% surgical site infection, 8% catheter-related infection, 6% genital tract infections	APACHE II score, mean ± SD: 14.4 ± 8.8 vs. 12.4 ± 6.1	In hospital	16/53 (30)	18/53 (34)	–4	APACHE II score

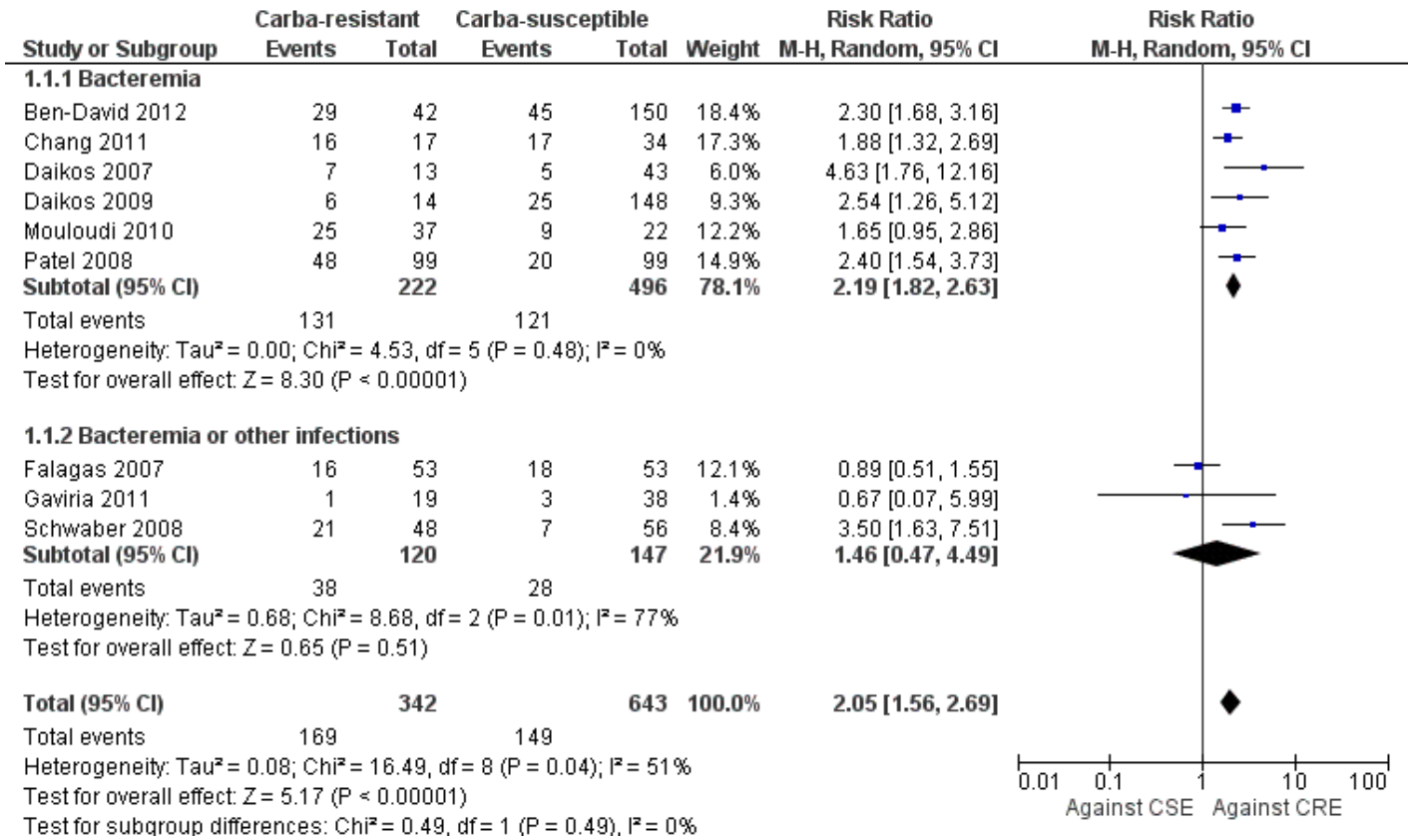
*Except for the causative pathogen (*Escherichia coli*) in the 2011 study by Chang et al., the causative pathogen in all studies was *Klebsiella pneumoniae*. CRE, carbapenem-resistant *Enterobacteriaceae*; CSE, carbapenem-susceptible *Enterobacteriaceae*; BSI, bloodstream infection; ESBL, extended-spectrum β-lactamase; LOS,: length of stay; NR, not reported; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation; KPC, *K. pneumoniae* carbapenemase; MBL, metallo-β-lactamase; SOFA, Sequential Organ Failure Assessment; UTIs, urinary tract infections

†Attributable death was calculated by the authors of this review as the difference in all-cause death between the 2 compared groups.

‡Only the results of multivariable analyses reported on the total study population and not on each patient group (CRE and CSE) separately were extracted.

§ESBL-producing bacteria were considered as carbapenem-susceptible.

#Carbapenem-resistant group: 40% UTIs, 19% wound/skin/soft tissue infections, 13% blood/intravenous line–related infections; carbapenem-susceptible group: 55% UTIs, 15% wound/skin/soft tissue infections, 15% blood/intravenous line–related infections



Technical Appendix Figure. Death risk ratios (RRs) for patients infected with carbapenem-resistant Enterobacteriaceae (CRE) versus carbapenem-susceptible *Enterobacteriaceae* (CSE). Vertical line represents the point of no difference between carbapenem-resistant and carbapenem-susceptible pathogens; squares represent RRs; diamonds represent pooled RRs for all studies; horizontal lines represent 95% CIs. RRs were determined by using a Mantel-Haenszel (M-H) random effects model. Carba-resistant, CRE; Carba-susceptible, CSE. References: Ben-David 2012 (*1*); Chang 2011 (*2*); Daikos 2007 (*8*); Daikos 2009 (*5*); Mouloudi 2010 (*4*); Patel 2008 (*6*); Falagas 2007 (*9*); Gaviria 2011 (*3*); Schwaber 2008 (*7*).

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