

Supplementary Materials

Risk Factors Associated with Antibiotic Exposure Variability in Critically Ill Patients: A Systematic Review

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File S1

Search strategy

To conduct the search, the following keywords were concluded for each section of the PICO question:

- P (PATIENT): Critically ill patients (Critically ill patients OR critical care OR Critical illness OR critically ill OR Intensive care units OR ICU) under antibiotic treatment (Piperacillin OR Piperacillin-tazobactam OR Meropenem OR Linezolid OR Daptomycin OR imipenem OR cefepime OR Beta-lactam OR Beta-lactams OR Fluoroquinolones OR Vancomycin OR Aminoglycosides OR Anti-Bacterial Agents OR antibacterial agents OR Antibacterial OR Anti-Infective Agents OR antibiotic OR antibiotics OR bacterial infections).
- I (INTERVENTION): Described alterations of pharmacokinetic parameters (Target attainment OR Breakpoint of target attainment OR drug concentration OR subtherapeutic OR supratherapeutic OR toxicity OR efficacy OR pharmacokinetics OR pharmacodynamics OR TDM OR Therapeutic drug monitoring Precision dosing OR population pharmacokinetic)
- C (COMPARATOR): Rest of the population admitted to the ICU.
- O (OUTCOME): Variations in pharmacokinetic parameters or subtherapeutic or supratherapeutic plasma concentrations of antibiotics.

Taking into account that we only wanted to include studies with humans, adult patients, and exclude retrospective articles and reviews, the final search was conducted with the following text:

(Critically ill patients OR critical care OR Critical illness OR critically ill OR Intensive care units OR ICU) AND (Piperacillin OR Piperacillin-tazobactam OR Meropenem OR Linezolid OR Daptomycin OR imipenem OR cefepime OR Beta-lactam OR Beta-lactams OR Fluoroquinolones OR Vancomycin OR Aminoglycosides OR Anti-Bacterial Agents OR antibacterial agents OR Antibacterial OR Anti-Infective Agents OR antibiotic OR antibiotics OR bacterial infections) AND (Target attainment OR Breakpoint of target attainment OR drug concentration OR subtherapeutic OR supratherapeutic OR toxicity OR efficacy OR pharmacokinetics OR pharmacodynamics OR TDM OR Therapeutic drug monitoring Precision dosing OR population pharmacokinetic) AND (prospective) NOT (Systematic review OR Meta-analysis OR Review OR Study Protocol) NOT (Pediatric OR Neonates OR Infants OR Children)

File S2

Excluded and Included studies

Excluded for Not accesss

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- Gatti M, Rinaldi M, Laici C, Siniscalchi A, Viale P, Pea F. Role of a Real-Time TDM-Based Expert Clinical Pharmacological Advice Program in Optimizing the Early Pharmacokinetic/Pharmacodynamic Target Attainment of Continuous Infusion Beta-Lactams among Orthotopic Liver Transplant Recipients with Documented or Suspected Gram-Negative Infections. *Antibiotics (Basel)*. 2023 Nov 7;12(11):1599.
- Fan G, Jin L, Bai H, Jiang K, Xie J, Dong Y. Safety and Efficacy of Tigecycline in Intensive Care Unit Patients Based on Therapeutic Drug Monitoring. *Ther Drug Monit*. 2020 Dec;42(6):835-840.
- Gatti M, Rinaldi M, Tonetti T, Siniscalchi A, Viale P, Pea F. Could an Optimized Joint Pharmacokinetic/Pharmacodynamic Target Attainment of Continuous Infusion Piperacillin-Tazobactam Be a Valuable Innovative Approach for Maximizing the Effectiveness of Monotherapy Even in the Treatment of Critically Ill Patients with Documented Extended-Spectrum Beta-

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Excluded for evaluation of adverse events as unique endpoint.

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File S3

Risk of bias analysis

Figure S1. Review authors' judgements about each risk of bias item for each included randomised controlled trial according to Risk of Bias 2 Assessments.

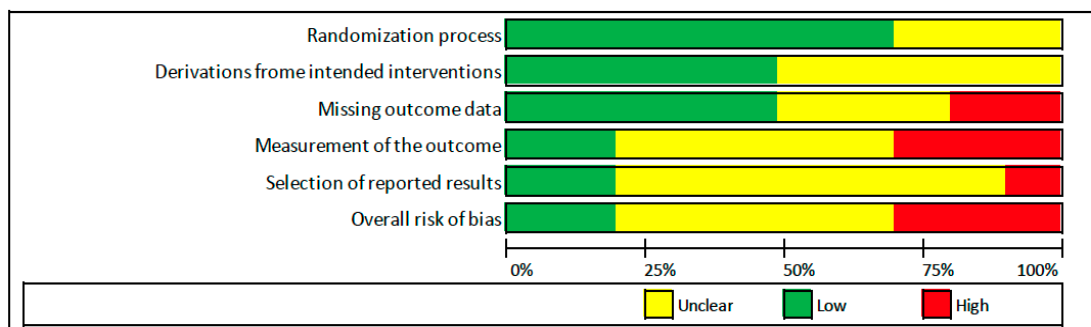


Figure S2. ClinPK reporting quality assessments by study.

Author / Year	Checklist Item																								Overall
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
Abdul-Aziz 2015	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Abdul-Aziz 2016	1	1	1	1	1	1		1	1	1	0	1	1	0	0	0		1	1			1	1		78,9%
Abdulla 2020	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	0		1	1	1	85,7%
Abdulla 2020	0	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	0		1	1	1	81,0%
Adnan 2013	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Akers 2014	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Alihodzic 2022	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1	1		1	1	1	95,2%
Allou 2016	1	1	1	1	1	1		1	1	1	0	1	1	1	1	0		1	1	0		1	1	1	85,7%
Alobaid 2016	1	1	1	1	1	1		0	1	1	1	1	1	1	1	0		1	1			1	1	1	90,0%
Alobaid 2017	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Alshaer 2022	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1			1	1	1	90,0%
Alsultan 2022	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
An 2023	1	1	1	1	1	1		0	0	1	1	1	1	1	1	0		1	1	0		1	1	1	81,0%
An 2023	1	1	1	1	1	1		0	1	1	1	1	1	1	0	0		1	1	0		1	1	1	81,0%
Areskog Lejbman 2024	0	1	1	1	1	1		1	1	1	0	1	1	0	1	0		1	1	0		1	1	1	76,2%
Asín-Prieto 2014	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1	1		1	1	1	95,2%
Aubron 2011	1	1	1	1	1	1		1	1	1	0	1	1	0	1	0		1	1			1	1	1	85,0%
Awissi 2015	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1	0		1	1	1	90,5%
Bai 2023	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Bakke 2017	1	1	1	1	1	1		1	1	1	0	1	1	0	1	0		1	1	0		1	1	1	81,0%
Baptista 2012	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Barletta 2000	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Barrasa 2019	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	1		1	1	1	90,5%
Barreto 2023	1	1	1	1	1	1		1	1	1	1	1	0	0	1	0		1	1			1	1	1	85,0%
Beckhouse 1988	0	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	90,0%
Belzberg 2004	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Beumier 2013	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1	1		1	1	1	95,2%
Bilal 2023	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Bilgrami 2010	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	1		1	1	1	90,5%
Binder 2013	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Blackman 2021	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Blassmann 2016	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1			1	1	1	90,0%
Borsuk-De Moor 2018	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	0		1	1	1	85,7%
Bos 2018	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Boucher 2016	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	1		1	1	1	90,5%
Bougle 2019	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Bracco 2008	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Braune 2018	1	1	1	1	1	0		1	1	1	1	1	1	0	1	0		1	1	1		1	1	1	85,7%
Breilh 2019	0	0	1	1	1	1		1	1	1	1	1	1	1	1	0	0	1	1	1		1	1	1	81,8%
Brink 2009	1	1	1	1	1	1		1	1	1	1	1	1	1	1	0		1	1			1	1	1	95,0%
Bue 2020	1	1	1	1	1	1		1	1	1	1	1	0	0	1	0		1	1	1		1	1	1	85,7%
Burger 2018	1	1	1	1	1	0		0	1	1	1	1	1	0	1	0		1	1	1		1	1	1	81,0%
Burkhardt 2006	1	1	1	1	1	1		1	1	1	1	1	1	0	0	0		0	1			1	1	1	80,0%
Burkhardt 2009	1	1	1	1	1	1		1	1	1	1	1	1	0	1	0		1	1	1		1	1	1	90,5%

Busse 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,2%
Calov 2023	1	1	1	1	1	1	1	1	0	1	0				1	1		1	90,0%
Campassi 2014	1	1	1	1	1	1	1	1	1	1	0				1	1		1	95,0%
Carlier 2013	1	1	1	1	1	1	1	1	0	0	0				1	1		1	85,0%
Carlier 2014	1	1	1	1	1	1	1	1	0	0	0				1	1		1	85,0%
Carlier 2014	1	1	1	1	1	1	1	1	0	0	0				1	1		1	85,0%
Carrie 2017	0	0	1	1	1	1	1	1	1	1	0				1	1	1	1	81,0%
Černá Pařízková 2021	1	1	1	1	1	1	1	1	1	1	0				1	1		1	95,0%
Chapuis 2010	1	1	1	1	1	1	1	1	1	1	0				1	1		1	95,0%
Cheng 2021	1	1	1	1	1	1	0	1	1	1	1	1	0		1	1		1	90,0%
Cheng 2022	1	1	1	1	1	1	0	1	1	1	0	1	0		1	1	1	1	85,7%
Chung 2011	1	1	1	1	1	1	0	1	1	1	1	1	0		1	1	0	1	85,7%
Corcione 2020	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Corcione 2021	1	1	1	1	1	1	1	1	0	1	0	1	0		1	1		1	85,0%
Cornwell 1997	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Correia 2023	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Corti 2013	1	1	1	1	1	1	1	1	0	1	0				1	1	1	1	90,5%
Costea 2020	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Couffignal 2014	1	1	1	1	1	1	1	0	1	1	1	0	1		1	1		0	85,0%
Cristallini 2016	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
D'Arcy 2012	1	1	1	1	1	1	1	1	1	0	1	0			1	1	1	1	90,5%
Dailly 2013	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
De Corte 2023	1	1	1	1	1	1	1	0	1	1	0	1	0		1	1	0	1	81,0%
de Montmollin 2014	1	1	1	1	1	1	1	0	1	1	1	1	0		1	1	0	1	85,7%
De Winter 2021	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Dedkaew 2015	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Del Bono 2017	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Deshpande 2010	1	1	1	1	1	1	1	0	1	1	0	1	0		1	1	1	1	85,7%
Dhaese 2019	1	1	1	1	1	1	1	1	1	1	0	1	0		1	1		1	90,0%
Dimski 2020	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	90,9%
Dreesen 2022	1	1	1	1	1	1	1	1	1	0	1	1			1	1		1	95,0%
Ehmann 2017	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Ehmann 2019	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1		1	100,0%
El-Haffaf 2024	1	1	1	1	1	1	1	0	1	1	0	1	0		1	1	0	1	81,0%
Ernest 1992	1	1	1	1	1	1	1	1	0	1	0	0	0	1	1	1	0	1	81,8%
Escobar 2014	1	1	1	1	1	1	1	1	1	0	1	0			1	1	1	1	90,5%
Esteve-Pitarch 2021	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Facca 1998	1	1	1	1	1	1	1	1	1	0	0	0			1	1		1	85,0%
Farkas 2022	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Fiaccadori 2004	1	1	1	1	1	1	1	1	1	0	1	0			1	1	1	1	90,5%
Fillâtre 2021	1	1	1	1	1	1	1	1	1	0	0	0			1	1	0	1	81,0%
Fish 2005	1	1	1	1	1	1	1	1	0	1	0				1	1	1	1	90,5%
Fournier 2018	1	1	1	1	1	1	0	1	0	0	0	0	1	0	1	1	0	1	68,2%
Fournier 2018	1	1	1	1	1	1	0	1	0	0	0	0	1		1	1		1	80,0%
Frame 1999	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Frazee 2017	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Fukumoto 2023	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Galar 2019	1	1	1	1	1	1	1	0	1	1	0	1	0		1	1	1	1	85,7%
Gieling 2020	1	1	1	1	1	1	1	1	1	1	1	0			1	1		1	95,0%
Gijsen 2021	1	1	1	1	1	1	0	1	1	1	1	1	0		1	1		1	90,0%

[illegible]

Malone 2001	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	90,5%
Martin 1991	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Martínez-Casanova 2023	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Masich 2020	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Mattioli 2016	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Meenks 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0		1	90,5%
Meenks 2023	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Messiano 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Meyer 2005	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Mimoz 2006	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Mitton 2022	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1			1	90,0%
Mokline 2018	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Moni 2020	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Morbitzer 2019	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Moreira de Freitas 2020	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1		1	90,5%
Moser 2021	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Naik 2017	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Nakamura 2015	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0		1	85,7%
Nicolau 2021	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Niibe 2020	1	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1		1	81,0%
Niibe 2022	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1		1	90,5%
O’brink-Hansen 2015	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1			1	90,0%
Obara 2016	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Obara 2016	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Olbrisch 2019	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Oliveira 2020	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,5%
Onichimowski 2020	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1		1	90,5%
Padulles Zamora 2019	1	1	0	1	1	1	1	1	1	1	0	1	0	1	1	1		1	85,7%
Petejova 2012	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1		1	90,5%
Petersson 2021	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Poli 2019	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Pressiat 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Rahbar 2016	1	1	1	1	1	1	0	0	0	1	0	1	1	1	1			1	80,0%
Ram 2021	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Rebuck 2002	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Ren 2021	1	1	1	1	1	1	1	0	1	1	0	1	0	1	1	0		1	81,0%
Roberts 2010	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0		1	85,7%
Roberts 2012	0	1	1	1	1	1	1	0	1	1	0	1	0	1	1	1		1	81,0%
Roberts 2015	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	90,9%
Roberts 2015	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Roberts 2021	0	1	1	1	1	1	1	0	1	1	0	1	0	1	1	0		1	76,2%
Roger 2016	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Roger 2016	1	1	1	1	1	1	1	1	1	1	0	1	0	0	1	1	1	1	86,4%
Roger 2017	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Roos 2007	1	1	1	1	1	1	0	1	1	1	0	0	0	1	1			1	75,0%
Ruiz-Ramos 2018	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1		1	95,2%
Ruiz-ramos 2018	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%
Ruiz-Ramos 2020	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0		1	85,7%
Sanchez-Navarro 2005	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1			1	95,0%

Scharf 2022	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	90,5%
Schmidt 2019	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Seo 2023	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Seyler 2011	0	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	85,7%
Shahrami 2020	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Shekar 2023	1	1	1	1	0	1	0	1	1	1	0	1	1	0	1	1	76,2%
Shi 2022	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Shikuma 1990	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Sima 2021	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	90,5%
Šima 2022	1	1	1	1	1	1	0	1	1	0	1	0	1	1		1	85,0%
Sime 2015	1	1	1	1	1	1	0	1	1	0	1	0	1	1	1	1	85,7%
Sime 2017	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Sime 2019	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	90,5%
Sime 2019	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Simon 2021	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	90,5%
Singhan 2019	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Sinnollareddy 2018	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Sjovall 2018	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Smeets 2023	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Smit 2020	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Soraluce 2018	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	90,5%
Soraluce 2020	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	90,5%
Stain 2019	1	1	1	1	1	1	1	1	0	1	1	0	1	1		0	85,0%
Sturm 2013	1	1	1	1	1	1	0	0	0	1	0	0	1	1		1	75,0%
Sukarnjanaset 2019	1	1	1	1	1	1	1	1	1	1	0	0	1	1		1	90,0%
Taccone 2010	0	1	1	1	1	1	1	1	1	1	1	0	1	1		1	90,0%
Tang 1999	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Tang 2023	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Taubert 2016	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	90,5%
Tikiso 2023	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Traunmüller 2002	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Triginer 1990	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Tsai 2016	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Tsai 2018	0	1	1	1	1	1	1	1	1	1	1	0	1	1		1	90,0%
Turner 2018	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Uchino 2002	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Ulldemolins 2015	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Ulldemolins 2016	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Ulldemolins 2021	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Van der Starre 2010	1	1	1	1	1	1	0	1	1	1	1	0	1	1		1	90,0%
Van Zanten 2008	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Veillette 2021	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Villa 2015	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	90,5%
Wang 2018	1	1	1	1	1	1	1	1	1	1	1	0	1	1		1	95,0%
Wang 2021	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0	1	85,7%
Wang 2021	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	95,2%
Wang 2023	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0	1	85,7%
Wen 2016	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	90,5%
Whitehouse 2005	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	0	86,4%
Wicha 2017	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0	1	85,7%

Wong 2018	1	1	1	1	1	1	1	1	1	0	1	1	0	1	0	1	1	1	85,0%
Wu 2019	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	90,0%
Wu 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,0%
Wulkersdorfer 2024	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,0%
Xie 2017	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,0%
You 2024	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	0	1	1	81,0%
Zander 2016	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0	1	1	85,7%
Zeitlinger 2007	0	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	85,0%
Zeng 2024	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,0%
Zhao 2022	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	95,0%
Zhao 2022	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	90,0%
Zheng 2020	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	90,5%
Zoller 2014	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	0	1	1	85,7%
Zoller 2022	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	90,0%

File S4

Risk factors that were studied without finding any impact were (indicating the number of studies whenever more than one:

Platelets (8), ethnicity (7), red blood cell count (6), prothrombin time (4), heart rate (4), respiratory rate (2), interleukin-6 (3), cerebrospinal fluid (CSF) drainage (3), Protein in CSF (2), Interleukin-6 in CSF (2), Cells in CSF (2), lactate, pyruvate, glycerol or glutamate in CSF, other drainage, Injury Severity Score, PEEP, PAFI, ASA classification, allogeneic blood products, carbamide, Glucose, Creatine phosphokinase (CPK), potassium, vancomycin manufacturer, uric acid, anesthesia duration, intra-anesthetic or post-anesthetic peritoneal membrane transporter status, cholinesterase, factor V, CD64, Pitt bacteremia score, post-surgical drainage, hypothermia, emergent surgery, Glasgow Coma Scale, SaO₂, Simplified Septic Shock Score (SSS), Complete SSS, SIRS, ARCTIC score, ICDSC and drug characteristics like protein plasmatic union percentage.

File S5

Main characteristics of studies included:

Author and year	Study type	Drugs	N^a Centers	Country	N^a Patients	Primary endpoint
Whitehouse 2005	RCT	Linezolid, Teicoplanin	Unicentric	UK	54	PK/PKPOP
Burkhardt 2006	Prospective observational	Ertapenem	Unicentric	Germany	17	PK/PKPOP
Roos 2007	Prospective observational	Cefpirome	Unicentric	Australia	12	PK/PKPOP
Roberts 2010	Prospective observational	Genatmicin	Multicentric	Australia	14	PK/PKPOP
Asín-Prieto 2014	Prospective observational	PTZ	Unicentric	Spain	16	PK/PKPOP

<i>Escobar 2014</i>	Prospective observational	Vancomycin	Unicentric	Chile	9	PK/PKPOP
<i>Couffignal 2014</i>	Prospective observational	Imipenem	Multicentric	France	63	PK/PKPOP
<i>Carlier 2014</i>	Prospective observational	Cefuroxima	Unicentric	Belgium	160	PK/PKPOP
<i>Zoller 2014</i>	Prospective observational	Linezolid	Unicentric	Germany	30	Exposure
<i>Luque 2014</i>	Prospective observational	PTZ	Unicentric	Spain	11	PK/PKPOP
<i>Ulldemolins 2015</i>	Prospective observational	Meropenem	Multicentric	Spain	30	Exposure
<i>Kees 2015</i>	Prospective observational	Meropenem	Unicentric	Germany	32	PK/PKPOP
<i>Abdul-Aziz 2015</i>	Prospective observational	Doripenem	Unicentric	Malaysia	12	PK/PKPOP
<i>Roger 2016</i>	Prospective observational	Linezolid	Unicentric	France	13	PK/PKPOP
<i>Roberts 2015</i>	Prospective observational	Linezolid	Unicentric	Australia	35	PK/PKPOP
<i>Ulldemolins 2016</i>	Prospective observational	Piperacillin	Multicentric	Spain	19	PK/PKPOP
<i>Roger 2016</i>	RCT	Ciprofloxacin	Unicentric	France	11	PK/PKPOP
<i>Alobaid 2016</i>	Prospective observational	Meropenem	Unicentric	Australia	19	PK/PKPOP
<i>Taubert 2016</i>	Prospective observational	Linezolid	Unicentric	Germany	52	PK/PKPOP
<i>Tsai 2016</i>	Prospective observational	Meropenem	Unicentric	Australia	11	PK/PKPOP
<i>Blassmann 2016</i>	Prospective observational	Meropenem	Unicentric	Germany	21	PK/PKPOP
<i>Rahbar 2016</i>	Prospective observational	Doripenem	Unicentric	USA	30	PK/PKPOP
<i>Naik 2017</i>	RCT	Cefazolina	Unicentric	USA	20	PK/PKPOP
<i>Xie 2017</i>	Prospective observational	Tigecycline	Unicentric	China	10	PK/PKPOP
<i>Wicha 2017</i>	Prospective observational	Linezolid	Unicentric	Germany	28	PK/PKPOP
<i>Sime 2017</i>	Prospective observational	PTZ	Unicentric	Australia	37	PK/PKPOP
<i>Sjovall 2018</i>	Prospective observational	Meropenem	Unicentric	Denmark	51	PK/PKPOP
<i>Borsuk-De Moor 2018</i>	Prospective observational	Tigecycline	Multicentric	Poland	37	PK/PKPOP
<i>Braune 2018</i>	Prospective observational	Meropenem	Unicentric	Germany	19	PK/PKPOP
<i>Bos 2018</i>	Prospective observational	Ceftriaxone, cefazolin, Meropenem, ampicillin, benzylpenicillin, flucloxacillin and piperacillin	Unicentric	Mozambique	88	PK/PKPOP
<i>Hanberg 2018</i>	Prospective observational	Meropenem	Unicentric	Denmark	10	PK/PKPOP
<i>Soraluce 2018</i>	Prospective observational	Daptomycin	Multicentric	Spain	16	PK/PKPOP
<i>Kanji 2018</i>	Prospective observational	PTZ	Unicentric	Canada	34	PK/PKPOP
<i>Fournier 2018</i>	Prospective observational	Amoxicillin	Unicentric	Switzerland	21	PK/PKPOP
<i>Tsai 2018</i>	Prospective observational	Vancomycin	Unicentric	Australia	15	PK/PKPOP
<i>Turner 2018</i>	Prospective observational	Vancomycin	Unicentric	USA	19	PK/PKPOP
<i>Wong 2018</i>	Prospective observational	Ceftriaxone, cefazolin, Meropenem, ampicillin, benzylpenicillin, flucloxacillin and piperacillin	Unicentric	Australia	330	Exposure

<i>Stain 2019</i>	Prospective observational	Ceftazidime/avibactam	Unicentric	USA	10	PK/PKPOP
<i>Leuppi-Taegtmeyer 2019</i>	Prospective observational	Colistin	Multicentric	Switzerland	10	PK/PKPOP
<i>Sukarnjanaset 2019</i>	Prospective observational	Piperacillin	Unicentric	Thailand	48	PK/PKPOP
<i>Padulles Zamora 2019</i>	Prospective observational	Meropenem	Unicentric	Spain	12	PK/PKPOP
<i>Sime 2019</i>	Prospective observational	Ceftolozane/tazobactam	Unicentric	Australia	12	PK/PKPOP
<i>Kanji 2019</i>	Prospective observational	Vancomycin	Unicentric	Canada	31	PK/PKPOP
<i>Sime 2019</i>	Prospective observational	Ceftolozane/tazobactam	Unicentric	Australia	6	PK/PKPOP
<i>Kovacevic 2019</i>	Prospective observational	Vancomycin	Unicentric	Bosnia and Herzegovina	73	PK/PKPOP
<i>Kalaria 2020</i>	Prospective observational	Tazobactam	Unicentric	USA	18	PK/PKPOP
<i>Masich 2020</i>	Prospective observational	Vancomycin	Unicentric	USA	16	PK/PKPOP
<i>Bue 2020</i>	Prospective observational	Piperacillin	Unicentric	Denmark	10	PK/PKPOP
<i>Niibe 2020</i>	Prospective observational	Meropenem	Unicentric	Japan	21	PK/PKPOP
<i>Zheng 2020</i>	Prospective observational	Linezolid	Unicentric	China	20	PK/PKPOP
<i>Onichimowski 2020</i>	Prospective observational	Meropenem	Unicentric	Poland	19	PK/PKPOP
<i>Li 2020</i>	Prospective observational	Imipenem	Unicentric	China	30	PK/PKPOP
<i>Smit 2020</i>	Prospective observational	Genatmicin	Multicentric	Dutch	542	PK/PKPOP
<i>Blackman 2021</i>	Prospective observational	Linezolid	Unicentric	USA	11	PK/PKPOP
<i>Ulldemolins 2021</i>	Prospective observational	Ceftriaxone	Multicentric	Spain	8	PK/PKPOP
<i>Wang 2021</i>	Prospective observational	Linezolid	Multicentric	China	117	PK/PKPOP
<i>De Winter 2021</i>	Prospective observational	Amikacin	Unicentric	Belgium	97	PK/PKPOP
<i>Cheng 2021</i>	Prospective observational	Cefepime	Multicentric	New Zealand	6	PK/PKPOP
<i>Lan 2022</i>	Prospective observational	Meropenem	Unicentric	China	48	PK/PKPOP
<i>Dreesen 2022</i>	Prospective observational	Ceftriaxone	Unicentric	Belgium	33	PK/PKPOP
<i>Meenks 2022</i>	Prospective observational	Ceftriaxone	Unicentric	Netherlands	91	PK/PKPOP
<i>Alshaer 2022</i>	Prospective observational	Meropenem	Unicentric	Austria	12	PK/PKPOP
<i>Kumta 2022</i>	Prospective observational	Meropenem	Multicentric	China y Australia	8	PK/PKPOP
<i>Fukumoto 2023</i>	Prospective observational	Meropenem	Unicentric	Japan	32	PK/PKPOP
<i>Meenks 2023</i>	Prospective observational	Flucloxacillin	Multicentric	Netherlands	31	PK/PKPOP
<i>Tang 2023</i>	Prospective observational	Polimixina B	Unicentric	China	105	PK/PKPOP
<i>Wang 2023</i>	Prospective observational	Teicoplanin	Unicentric	China	151	PK/PKPOP
<i>Barreto 2023</i>	Prospective observational	Cefepime	Unicentric	USA	120	PK/PKPOP
<i>Facca 1998</i>	Prospective observational	ceftizoxime	Unicentric	USA	72	PK/PKPOP
<i>Frame 1999</i>	Prospective observational	Ceftazidime	Unicentric	USA	39	PK/PKPOP
<i>Dailly 2013</i>	Prospective observational	Ertapenem	Unicentric	France	8	PK/PKPOP
<i>Beumier 2013</i>	Prospective observational	Vancomycin	Unicentric	Belgium	32	PK/PKPOP

<i>O'brink-Hansen 2015</i>	Prospective observational	Piperacillin	Unicentric	Denmark	15	PK/PKPOP
<i>Lin 2016</i>	Prospective observational	Vancomycin	Unicentric	China	100	PK/PKPOP
<i>Ide 2018</i>	Prospective observational	Linezolid	Unicentric	Japan	27	PK/PKPOP
<i>Kang 2020</i>	Prospective observational	Cefpirome	Unicentric	South Korea	15	PK/PKPOP
<i>Grensemann 2020</i>	Prospective observational	Meropenem	Unicentric	Germany	19	PK/PKPOP
<i>Liu 2020</i>	Prospective observational	Vancomycin	Unicentric	China	25	PK/PKPOP
<i>Ruiz-Ramos 2020</i>	Prospective observational	Tigecycline	Unicentric	Spain	25	PK/PKPOP
<i>Lin 2021</i>	Prospective observational	Vancomycin	Unicentric	China	374	PK/PKPOP
<i>Sima 2021</i>	Prospective observational	Ciprofloxacin	Unicentric	Czech Republic	29	PK/PKPOP
<i>Zhao 2022</i>	Prospective observational	Meropenem	Unicentric	China	64	PK/PKPOP
<i>Alsultan 2022</i>	Prospective observational	Meropenem	Unicentric	Saudi Arabia	43	Exposure
<i>Wang 2021</i>	Prospective observational	Vancomycin	Unicentric	China	11	PK/PKPOP
<i>Busse 2022</i>	RCT	Meropenem	Unicentric	Germany	30	PK/PKPOP
<i>Farkas 2022</i>	Prospective observational	Genatmicin	Unicentric	USA	24	PK/PKPOP
<i>Hahn 2021</i>	Prospective observational	PTZ	Unicentric	South Korea	26	PK/PKPOP
<i>Gijsen 2022</i>	Prospective observational	Meropenem	Unicentric	Belgium	58	PK/PKPOP
<i>Pressiat 2022</i>	Prospective observational	Amikacin	Unicentric	France	39	PK/PKPOP
<i>Alihodzic 2022</i>	Prospective observational	Ciprofloxacin	Unicentric	Germany	17	PK/PKPOP
<i>Šima 2022</i>	Prospective observational	Ciprofloxacin	Unicentric	Czech Republic	29	Exposure
<i>Kang 2022</i>	Prospective observational	Meropenem	Unicentric	Korea	13	PK/PKPOP
<i>An 2023</i>	Prospective observational	Meropenem	Unicentric	USA	130	PK/PKPOP
<i>Bai 2023</i>	Prospective observational	Imipenem	Unicentric	China	51	PK/PKPOP
<i>Martínez-Casanova 2023</i>	Prospective observational	PTZ	Unicentric	Spain	106	PK/PKPOP
<i>An 2023</i>	Prospective observational	Cefepime	Unicentric	USA	130	PK/PKPOP
<i>Bilal 2023</i>	Prospective observational	cefepime	Unicentric	Germany	14	PK/PKPOP
<i>Ehmann 2019</i>	Prospective observational	Meropenem	Unicentric	Germany	48	PK/PKPOP
<i>Soraluce 2020</i>	Prospective observational	Linezolid	Multicentric	Spain	40	PK/PKPOP
<i>Lee 2021</i>	Prospective observational	Meropenem	Unicentric	South Korea	30	PK/PKPOP
<i>Dedkaew 2015</i>	Prospective observational	Vancomycin	Unicentric	Thailand	138	PK/PKPOP
<i>Seo 2023</i>	Prospective observational	Cefepime	Unicentric	Korea	21	PK/PKPOP
<i>Mattioli 2016</i>	Prospective observational	Meropenem	Unicentric	Italy	27	PK/PKPOP
<i>Abdulla 2020</i>	Prospective observational	Ciprofloxacin	Multicentric	Netherlands Australia, New Zealand, South Korea, and Switzerland	42	PK/PKPOP
<i>Cheng 2022</i>	Prospective observational	Ciprofloxacin	Multicentric	Spain	8	PK/PKPOP
<i>Isla 2008</i>	Prospective observational	Meropenem	Multicentric	Spain	20	PK/PKPOP

<i>Alobaid 2017</i>	Prospective observational	Piperacillin	Unicentric	Australia	37	Exposure
<i>Kim 2022</i>	Prospective observational	PTZ	Unicentric	South Korea	38	PK/PKPOP
<i>Ernest 1992</i>	Prospective observational	Genatmicin	Unicentric	Australia	5	PK/PKPOP
<i>Shikuma 1990</i>	Prospective observational	Piperacillin	Unicentric	USA	11	PK/PKPOP
<i>Cornwell 1997</i>	Prospective observational	Aztreonam	Unicentric	USA	28	PK/PKPOP
<i>Giles 2000</i>	Prospective observational	Meropenem	Unicentric	UK	10	Exposure
<i>Barletta 2000</i>	Prospective observational	Genatamicin, tobramicin	Unicentric	USA	19	Exposure
<i>Malone 2001</i>	Prospective observational	Cefepime	Unicentric	USA	12	PK/PKPOP
<i>Traunmüller 2002</i>	Prospective observational	Ceftazidime	Unicentric	Austria	12	PK/PKPOP
<i>Uchino 2002</i>	Prospective observational	Vancomycin	Unicentric	Australia	7	PK/PKPOP
<i>Fiaccadori 2004</i>	Prospective observational	Linezolid	Unicentric	Italy	15	Exposure
<i>Meyer 2005</i>	Prospective observational	Linezolid	Unicentric	Austria	20	PK/PKPOP
<i>Fish 2005</i>	Prospective observational	Imipenem	Unicentric	USA	12	Exposure
<i>Kielstein 2006</i>	Prospective observational	Vancomycin, Meropenem	Unicentric	Germany	10	PK/PKPOP
<i>Mimoz 2006</i>	Prospective observational	Vancomycin	Unicentric	Thailand	20	PK/PKPOP
<i>Bracco 2008</i>	Prospective observational	Tobramicina	Unicentric	Canada	287	PK/PKPOP
<i>Burkhardt 2009</i>	Prospective observational	Ertapenem	Unicentric	Germany	6	Exposure
<i>Golestaneh 2009</i>	Prospective observational	Vancomycin	Unicentric	USA	10	Exposure
<i>Deshpande 2010</i>	Prospective observational	Meropenem	Unicentric	USA	10	Exposure
<i>Bilgrami 2010</i>	Prospective observational	Meropenem	Unicentric	Australia	10	PK/PKPOP
<i>Taccone 2010</i>	Prospective observational	Piperacillin-tazobactam (n = 27), ceftazidime (n = 18), cefepime (n = 19) or Meropenem (n = 16).	Multicentric	Belgium	80	Exposure
<i>Seyler 2011</i>	Prospective observational	Meropenem, PTZ, cefepime, ceftazidime	Unicentric	Belgium	53	Exposure
<i>Baptista 2012</i>	Prospective observational	Vancomycin	Unicentric	Portugal	93	Exposure
<i>Roberts 2012</i>	Prospective observational	Ciprofloxacin, Meropenem, piperacillin/tazobactam , or vancomycin	Multicentric	Australia	24	Exposure
<i>Petejova 2012</i>	Prospective observational	Vancomycin	Unicentric	Czech Republic	17	PK/PKPOP
<i>D'Arcy 2012</i>	Prospective observational	Amikacin	Unicentric	Ireland	5	PK/PKPOP
<i>Binder 2013</i>	Prospective observational	Meropenem	Unicentric	Germany	25	PK/PKPOP
<i>Adnan 2013</i>	Prospective observational	Meropenem, Piperacillin	Unicentric	Australia	10	Exposure
<i>Carlier 2013</i>	Prospective observational	Meropenem, Piperacillin	Unicentric	Belgium	61	Exposure
<i>Sturm 2013</i>	Prospective observational	PTZ	Unicentric	USA	9	Exposure
<i>Carlier 2014</i>	Prospective observational	PTZ	Unicentric	Belgium	11	Exposure
<i>Huttner 2015</i>	Prospective observational	imipenem, Meropenem, PTZ, cefepime	Unicentric	Switzerland	100	Exposure
<i>Sime 2015</i>	RCT	Piperacillin	Unicentric	Australia	32	Exposure

<i>Awissi 2015</i>	Prospective observational	PTZ	Unicentric	Canada	22	PK/PKPOP
<i>Villa 2015</i>	Prospective observational	Linezolid	Unicentric	Italy	3	PK/PKPOP
<i>Wen 2016</i>	Prospective observational	Imipenem	Unicentric	China	10	Exposure
<i>Boucher 2016</i>	Prospective observational	imipenem	Unicentric	USA	10	Exposure
<i>Jung 2017</i>	Prospective observational	PTZ	Unicentric	France	23	PK/PKPOP
<i>Roger 2017</i>	Prospective observational	PTZ	Unicentric	France	12	PK/PKPOP
<i>Carrie 2017</i>	Prospective observational	cefazolin, cefotaxime, PTZ, cefepime, ceftazidime y Meropenem	Unicentric	France	79	Exposure
<i>Ruiz-Ramos 2018</i>	Prospective observational	Amikacin	Unicentric	Spain	30	Exposure
<i>Fournier 2018</i>	RCT	Amoxicillin, Meropenem, Flucloxacillin, piperacillin-tazobactam, Ceftriaxone, Imipenem/cilastatin, Ceftazidime, Ertapenem, Cefazolin.	Unicentric	Switzerland	45	Exposure
<i>Sinnollareddy 2018</i>	Prospective observational	Piperacillin	Unicentric	Australia	6	PK/PKPOP
<i>Wang 2018</i>	Prospective observational	Teicoplanin	Unicentric	China	18	Exposure
<i>Kassel 2018</i>	Prospective observational	Vancomycin, cefepime	Unicentric	USA	20	Exposure
<i>Olbrisch 2019</i>	Prospective observational	Piperacillin	Unicentric	Germany	36	Exposure
<i>Barrassa 2019</i>	Prospective observational	Linezolid	Multicentric	Spain	21	Exposure
<i>Schmidt 2019</i>	Prospective observational	Colistina	Unicentric	Germany	4	Exposure
<i>Singhan 2019</i>	Prospective observational	Meropenem	Unicentric	Thailand	15	PK/PKPOP
<i>Bougle 2019</i>	Prospective observational	Amoxicillin Piperacillin Cefotaxime Ceftazidine Cefepime Meropenem Imipenem Vancomycin Ciprofloxacin Genatmicin Tobramicina Amikacin	Unicentric	France	44	Exposure
<i>Dhaese 2019</i>	Prospective observational	PTZ, Meropenem	Unicentric	Belgium	253	Exposure
<i>Leon 2020</i>	Prospective observational	PTZ, Meropenem, imipenem, Ceftriaxone, cefotaxima	Unicentric	France	48	Exposure
<i>Roberts 2021</i>	Prospective observational	Meropenem, piperacillin/tazobactam , vancomycin	Multicentric	14 paises	381	Exposure
<i>Gieling 2020</i>	Prospective observational	Ciprofloxacin	Multicentric	Netherlands	39	Exposure
<i>Moni 2020</i>	Prospective observational	Colistina	Unicentric	India	20	Exposure
<i>Lin 2021</i>	Prospective observational	Vancomycin	Unicentric	Taiwan	17	Exposure
<i>Abdulla 2020</i>	Prospective observational	Amoxicillin, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, meropenem.	Multicentric	Netherlands	147	Exposure
<i>Moreira de Freitas 2020</i>	Prospective observational	Vancomycin	Unicentric	Brazil	55	Exposure

<i>Kühn 2020</i>	Prospective observational	Piperacillin, ceftazidime, meropenem, linezolid	Unicentric	Germany	86	Exposure
<i>Corcione 2021</i>	Prospective observational	Amikacin, Genatmicin	Unicentric	Italy	8	Exposure
<i>Petersson 2021</i>	Prospective observational	Meropenem, Piperacillin	Unicentric	Sweden	135	Exposure
<i>Nicolau 2021</i>	Prospective observational	Ceftolozane/tazobactam	Multicentric	Europe and USA	11	Exposure
<i>Fillâtre 2021</i>	Prospective observational	Piperacillin	Unicentric	France	42	Exposure
<i>Moser 2021</i>	Prospective observational	Flucloxacillin	Unicentric	Switzerland	50	Exposure
<i>Esteve-Pitarch 2021</i>	Prospective observational	PTZ, Meropenem	Unicentric	Spain	118	Exposure
<i>Černá Pařízková 2021</i>	Prospective observational	Meropenem	Unicentric	Czech Republic	25	Exposure
<i>Liebchen 2022</i>	Prospective observational	Piperacillin, Meropenem	Unicentric	Germany	17	Exposure
<i>Messiano 2022</i>	Prospective observational	Meropenem	Unicentric	Brazil	15	Exposure
<i>Zoller 2022</i>	Prospective observational	Linezolid	Unicentric	Germany	68	Exposure
<i>Shekar 2023</i>	Prospective observational	Caspofungin, cefepime, ceftriaxone, ciprofloxacin, linezolid, meropenem, piperacillin, vancomycin	Multicentric	New Zealand and Switzerland	85	Exposure
<i>Smeets 2023</i>	Prospective observational	Vancomycin	Unicentric	Netherlands	20	Exposure
<i>Correia 2023</i>	Prospective observational	Ceftazidime	Multicentric	France	98	Exposure
<i>Martin 1991</i>	Prospective observational	Ofloxacin	Unicentric	France	12	PK/PKPOP
<i>Akers 2014</i>	Prospective observational	PTZ	Unicentric	USA	13	PK/PKPOP
<i>Gomez 2015</i>	Prospective observational	Imipenem	Unicentric	Brazil	51	PK/PKPOP
<i>Ko 2016</i>	Prospective observational	Vancomycin	Unicentric	USA	263	Exposure
<i>Mokline 2018</i>	Prospective observational	Linezolid	Unicentric	Tunisia	13	Exposure
<i>Lim 2019</i>	Prospective observational	Teicoplanin	Unicentric	South Korea	8	PK/PKPOP
<i>Kovacevic 2019</i>	Prospective observational	Vancomycin	Unicentric	Bosnia and Herzegovina	61	Exposure
<i>Wu 2019</i>	Prospective observational	Piperacillin/tazobactam, cefepime, and Meropenem	Unicentric	Taiwan	100	Exposure
<i>Morbitzer 2019</i>	Prospective observational	Vancomycin	Unicentric	USA	17	Exposure
<i>Breilh 2019</i>	RCT	PTZ, Meropenem, ertapenem, imipenem, doripenem, Ceftriaxone, ofloxacin, linezolid, daptomycin, metronidazol	Multicentric	Belgium and the Netherlands	45	PK/PKPOP
<i>Oliveira 2020</i>	Prospective observational	Meropenem, Vancomycin	Unicentric	Brazil	30	Exposure
<i>Mahmoud 2020</i>	Prospective observational	Vancomycin	Unicentric	USA	8	Exposure
<i>Veillette 2021</i>	Prospective observational	PTZ	Unicentric	USA	29	Exposure
<i>Gijsen 2021</i>	Prospective observational	Ceftriaxone	Unicentric	Belgium	31	Exposure
<i>Shi 2022</i>	Prospective observational	Teicoplanin	Unicentric	China	106	Exposure
<i>Zhao 2022</i>	Prospective observational	Vancomycin	Multicentric	China	414	Exposure

<i>Calov 2023</i>	Prospective observational	Daptomycin	Unicentric	Germany	13	Exposure
<i>Tikiso 2023</i>	Prospective observational	Linezolid	Unicentric	Germany	18	PK/PKPOP
<i>Roberts 2015</i>	RCT	Ciprofloxacin, meropenem, PTZ, vancomycin	Multicentric	Australia	24	PK/PKPOP
<i>Scharf 2022</i>	Prospective observational	Vancomycin	Unicentric	Germany	7	Exposure
<i>Wulkersdorfer 2024</i>	Prospective observational	PTZ	Unicentric	Austria	7	PK/PKPOP
<i>Shahrami 2020</i>	Prospective observational	Amikacin	Unicentric	Iran	37	PK/PKPOP
<i>Simon 2021</i>	RCT	Linezolid	Unicentric	Germany	30	Exposure
<i>Del Bono 2017</i>	Prospective observational	Meropenem	Unicentric	Italy	19	Exposure
<i>Wu 2022</i>	Prospective observational	Linezolid	Unicentric	China	23	Exposure
<i>Corti 2013</i>	Prospective observational	Daptomycin	Unicentric	Switzerland	9	PK/PKPOP
<i>Corcione 2020</i>	Prospective observational	Meropenem	Unicentric	Italy	17	Exposure
<i>Lyu 2018</i>	RCT	PTZ	Unicentric	China	120	Exposure
<i>Van der Starre 2010</i>	Prospective observational	Vancomycin PPX	Unicentric	USA	24	Exposure
<i>Triginer 1990</i>	Prospective observational	Genatmicin	Unicentric	Spain	40	PK/PKPOP
<i>Tang 1999</i>	Prospective observational	Genatmicin	Unicentric	Taiwan	52	PK/PKPOP
<i>Rebuck 2002</i>	Prospective observational	Levofloxacin	Unicentric	USA	30	PK/PKPOP
<i>Belzberg 2004</i>	Prospective observational	Imipenem	Unicentric	USA	54	PK/PKPOP
<i>Sanchez-Navarro 2005</i>	Prospective observational	Levofloxacin	Unicentric	Spain	9	PK/PKPOP
<i>Van Zanten 2008</i>	Prospective observational	Ciprofloxacin	Unicentric	Netherlands	32	Exposure
<i>Brink 2009</i>	Prospective observational	Ertapenem	Unicentric	South Africa	8	Exposure
<i>Chapuis 2010</i>	Prospective observational	Cefepime	Unicentric	Switzerland	21	PK/PKPOP
<i>Aubron 2011</i>	Prospective observational	Vancomycin	Unicentric	Australia	48	PK/PKPOP
<i>Chung 2011</i>	Prospective observational	Vancomycin	Unicentric	Korea	141	Exposure
<i>Karnik 2013</i>	Prospective observational	Colistin	Unicentric	India	15	PK/PKPOP
<i>Koegelenberg 2013</i>	Prospective observational	Rifampicin, isoniazide, etambutol	Unicentric	South Africa	10	Exposure
<i>de Montmollin 2014</i>	Prospective observational	Amikacin	Unicentric	France	146	Exposure
<i>Nakamura 2015</i>	Prospective observational	Teicoplanin	Unicentric	Japan	106	Exposure
<i>Abdul-Aziz 2016</i>	Prospective observational	Meropenem, PTZ	Multicentric	Spain	211	Exposure
<i>Zander 2016</i>	Prospective observational	Piperacillin	Unicentric	Germany	60	Exposure
<i>Allou 2016</i>	Prospective observational	Genatmicin	Unicentric	France	57	Exposure
<i>Obara 2016</i>	Prospective observational	Vancomycin	Unicentric	Brazil	83	Exposure
<i>Bakke 2017</i>	Prospective observational	Vancomycin	Multicentric	Norway	83	Exposure
<i>Ruiz-ramos 2018</i>	Prospective observational	Amikacin	Unicentric	Spain	85	Exposure
<i>Burger 2018</i>	Prospective observational	Meropenem	Unicentric	Switzerland	101	Exposure
<i>Huang 2020</i>	Prospective observational	Imipenem	Unicentric	China	25	PK/PKPOP

<i>Helset 2020</i>	Prospective observational	Vancomycin	Unicentric	Norway	83	Exposure
<i>Ram 2021</i>	Prospective observational	Colistina	Unicentric	India	30	Exposure
<i>Ren 2021</i>	Prospective observational	Vancomycin	Multicentric	USA	7220	Exposure
<i>Niibe 2022</i>	Prospective observational	Meropenem	Unicentric	Japan	12	PK/PKPOP
<i>Mitton 2022</i>	Prospective observational	Imipenem	Unicentric	South Africa	68	Exposure
<i>Helset 2024</i>	Prospective observational	Meropenem	Unicentric	Norway	87	Exposure
<i>Areskog Lejbman 2024</i>	Prospective observational	Cefotaxime, PTZ, Meropenem	Unicentric	Sweden	102	Exposure
<i>Beckhouse 1988</i>	Prospective observational	Gentamicin, tobramycin, amikacin	Unicentric	USA	49	PK/PKPOP
<i>Zeitlinger 2007</i>	Prospective observational	Levofloxacin, fosfomycin, cefpirome	Unicentric	Austria	34	Exposure
<i>Cristallini 2016</i>	Prospective observational	Vancomycin	Unicentric	Belgium	107	Exposure
<i>Ehmann 2017</i>	Prospective observational	Meropenem	Unicentric	Germany	48	Exposure
<i>Costea 2020</i>	Prospective observational	Amikacin, Genatmicin	Unicentric	France	138	Exposure
<i>Logre 2020</i>	Prospective observational	Amikacin	Multicentric	France	93	Exposure
<i>De Corte 2023</i>	Prospective observational	Meropenem, PTZ	Unicentric	Belgium	781	Exposure
<i>Guilhaumou 2023</i>	Prospective observational	Cefepime, cefotaxime, ceftazidime, meropenem	Multicentric	France	170	Exposure
<i>El-Haffaf 2024</i>	Prospective observational	PTZ	Unicentric	Canada	43	Exposure
<i>Campassi 2014</i>	Prospective observational	Vancomycin	Unicentric	Argentina	363	Exposure
<i>Zeng 2024</i>	Prospective observational	Polimixina B	Unicentric	China	23	Exposure
<i>Galar 2019</i>	Prospective observational	Daptomycin	Unicentric	Spain	63	Exposure
<i>Obara 2016</i>	Prospective observational	Vancomycin	Unicentric	Brazil	83	Exposure
<i>Fraze 2017</i>	Prospective observational	Vancomycin	Unicentric	USA	399	Exposure
<i>You 2024</i>	Prospective observational	Imipenem, meropenem	Unicentric	China	186	Exposure
<i>Huang 2023</i>	Prospective observational	Tigecycline	Unicentric	China	17	Exposure
<i>Poli 2019</i>	Prospective observational	Clindamycin	Unicentric	Switzerland	1	Exposure
<i>Liebchen 2021</i>	Prospective observational	Vancomycin, Teicoplanin	Unicentric	Germany	3	Exposure
<i>Köhler 2022</i>	Prospective observational	Linezolid	Unicentric	Germany	1	Exposure
<i>Dimski 2020</i>	Prospective observational	Meropenem	Unicentric	Germany	25	Exposure
BMI: Body mass index; CrCl: Creatinine clearance; EGFR: Estimated glomerular filtration rate; PK/PKPOP: Population pharmacokinetic model (PKPOP); PTZ: Piperacillin-Tazobactam; RRT: Renal replacement therapy; TBW: Total body weight						