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Global prevalence of cefiderocol non-susceptibility in Enterobacterales, Pseudomonas aeruginosa, Acinetobacter baumannii and Stenotrophomonas maltophilia: a systematic review and meta-analysis

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Abstract

Background: Cefiderocol is a last resort option for carbapenem-resistant (CR) Gram-negative bacteria, especially metallo-β-lactamase (MBL)-producing *Pseudomonas aeruginosa* and CR *Acinetobacter baumannii*. Monitoring global levels of cefiderocol non-susceptibility (CFDC-NS) is important.

Objectives: To systematically collate and examine studies investigating in-vitro CFDC-NS and estimate the global prevalence of CFDC-NS against major Gram-negative pathogens.

Data sources: PubMed and Scopus, up to May 2023.

Study eligibility criteria: Eligible were studies reporting CFDC-NS in Enterobacterales, *P. aeruginosa*, *A. baumannii,* or *Stenotrophomonas maltophilia* clinical isolates.

Methods: Two independent reviewers extracted study data and assessed risk of bias on the population, setting and measurement (susceptibility testing) domains. Binomial-Normal mixed-effects models were applied to estimate CFDC-NS prevalence by species, co-resistance phenotype and breakpoint definition (EUCAST, CLSI, FDA). Sources of heterogeneity were investigated by subgroup and meta-regression analyses.

Results: In all, 78 studies reporting 82,035 clinical isolates were analysed (87% published between 2020 and 2023). CFDC-NS prevalence (EUCAST breakpoints) was low overall, but varied by species [*S. maltophilia* 0.4% (95%CI 0.2-0.7%), Enterobacterales 3.0% (95%CI 1.5-6.0%), *P. aeruginosa* 1.4% (95%CI 0.5-4.0%)] and was highest for *A. baumannii* (8.8%, 95%CI 4.9-15.2%). CFDC-NS was much higher in CR Enterobacterales (12.4%, 95%CI 7.3-20.0%) and CR *A. baumannii* (13.2%, 95%CI 7.8-21.5%), but relatively low for CR *P. aeruginosa* (3.5%, 95%CI 1.6-7.8%). CFDC-NS was exceedingly high in NDM-producing Enterobacterales (38.8%, 95%CI 22.6-58.0%), NDM-producing *A. baumannii* (44.7%, 95%CI 34.5-55.4%), and ceftazidime/avibactam-resistant Enterobacterales (36.6%, 95%CI 22.7-53.1%). CFDC-NS varied considerably with breakpoint definition, predominantly among CR

bacteria. Additional sources of heterogeneity were single-centre investigations and geographical regions.

Conclusions: CFDC-NS prevalence is low overall, but alarmingly high for specific CR phenotypes circulating in some institutions or regions. Continuous surveillance and updating of global CFDC-NS estimates are imperative while cefiderocol is increasingly introduced into clinical practice. The need to harmonize EUCAST and CLSI breakpoints was evident.

Key words:

Cefiderocol; drug resistance; carbapenem-resistant; gram-negative bacteria; prevalence; global epidemiology.

Introduction

Pandrug-resistant Gram-negative bacteria (GNB) are increasingly being reported worldwide [1] and are associated with significant mortality [2] and limited treatment options [3, 4]. Among the currently available antimicrobials, cefiderocol is a last resort option, especially for carbapenem-resistant (CR) *Acinetobacter baumannii* and metallo-β-lactamase (MBL)-producing *Pseudomonas aeruginosa*, since newer β-lactam-β-lactamase inhibitors (including ceftazidime/avibactam ± aztreonam, ceftolozane/tazobactam, meropenem/vaborbactam and imipenem/relebactam) are inactive against these pathogens [3, 5].

However, as with any new drug, resistance to cefiderocol is increasingly being reported and even preceded its clinical use [6, 7]. Notably, cefiderocol heteroresistance is widespread [8] and could potentially result in emergence of resistance in-vivo during treatment [6] and eventually spread of cefiderocol-resistant strains within and across institutions and geographical regions. Furthermore, various β-lactamases have been reported to significantly reduce cefiderocol susceptibility [6]. Among MBLs, New Delhi metallo-β-lactamase (NDM) appears to be the most likely contributing source to cefiderocol resistance [6, 7]. Ceftazidime/avibactam-resistant isolates are also more likely to be cefiderocol-resistant, either due to being MBL-producing or due to *Klebsiella pneumoniae* carbapenemase (KPC) variants conferring cross resistance to cefiderocol [6].

This systematic review and meta-analysis aimed to estimate the global prevalence of cefiderocol non-susceptibility (CFDC-NS) in Enterobacterales, *P. aeruginosa*, *A. baumannii* and *Stenotrophomonas maltophilia*, including subgroups of problematic co-resistance phenotypes (carbapenem-resistant, MBL-producing, NDM-producing, ceftazidime/avibactam-resistant and ceftolozane/tazobactam-resistant). In addition, concurrent analyses of different susceptibility breakpoint thresholds (proposed by CLSI [9], FDA [10], and EUCAST [11]) were preformed, and variation of CFDC-NS prevalence with study-level characteristics was examined.

Methods

Protocol

This review was registered with the International Prospective Register of Systematic Reviews (registration no. CRD42021265927) and complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [12].

Search strategy, information sources and eligibility criteria

PubMed and Scopus were queried from inception to May 27, 2023, with the search term "cefiderocol OR s-649266", without language restriction. After de-duplication, retrieved articles were screened for eligibility by one author using the Rayyan online app for collaborative systematic reviews [13]. A second author validated eligibility of included articles.

Eligible for review were studies of any type of primary research design if they reported cefiderocol susceptibility proportions of clinical isolates of Enterobacterales, *P. aeruginosa*, *A. baumannii* and/or *S. maltophilia*. Exclusion criteria were (in order they were applied): (1) non-primary research articles (e.g. commentaries, editorials, review articles); (2) in vivo infection models in animals; (3) case reports of a single isolate or consecutive isolates from a single patient, (4) studies of selected non-consecutive and/or non-random isolates that could result in selection bias when estimating cefiderocol susceptibility (e.g. isolates selected based on cefiderocol resistance, or studies of patients selected based on receiving treatment with cefiderocol, or series of non-consecutive non-random isolates selected based on specific resistance phenotypes), including experimental studies and randomized controlled trials; (5) irrelevant primary research articles without data of interest to this review (e.g. pharmacokinetic/pharmacodynamic, toxicology studies, non-clinical isolates); and (6) conference abstracts.

Data collection process

Full text papers for all eligible studies were obtained and two reviewers extracted data independently using a purpose-built spreadsheet that had been piloted on two eligible studies by all authors. Data extraction from articles written in languages other than English was done with the aid of Google Translate. The following information was extracted from each paper, when provided: geographical location (country or countries) where the study was conducted, number of participating institutions, breakpoint cut-off used to define resistance, methods of susceptibility testing, numbers and proportions of CFDC-NS isolates for each pathogen species, minimum inhibitor concentration (MIC) range, MIC50 and MIC90. Bacterial subgroups of interest were carbapenem (CAR)-resistant Enterobacterales, MBL-producing Enterobacterales, NDM-producing Enterobacterales, ceftazidime/avibactam (CZA)- and ceftolozane/tazobactam (CTA)- resistant Enterobacterales, CR *P. aeruginosa*, MBL-producing *P. aeruginosa*, NDM-producing *P. aeruginosa*, CZA- and CTA-resistant *P. aeruginosa*, CR *A. baumannii,* MBL-producing *A. baumannii* and NDM-producing *A. baumannii*.

Overlapping studies reporting duplicate isolates were detected by contrasting information on institutions, authors and periods when the studies were conducted. Some studies contributed more than one set of clinical isolates in different periods, at different institutions/regions, and/or for different co-resistance phenotypes. Such subsets were analysed as separate studies in the meta-analyses.

Methods of susceptibility testing

Broth microdilution (BMD) in iron-depleted cation-adjusted Mueller-Hinton broth (ID-CAMHB) (prepared according to recommendations by CLSI [9] or EUCAST [14]) is the currently preferred method for evaluating susceptibility to cefiderocol [9, 11, 15, 16]. ID-CAMHB preparation using human apotransferrin is not recommended due to MIC reproducibility issues [14]. Disk diffusion in standard MH agar (iron-depletion not necessary because iron is bound by the medium) is

an alternative, but not recommended for *A. baumannii* [16] and resistance detected by disk diffusion should ideally be confirmed by broth microdilution [17]. Colonies within zone should be taken into account when measuring the zone diameter [15]. In case of studies reporting more than one method, data extraction was based on the following (in order of preference): broth microdilution, disk diffusion, gradient strip. Susceptibility breakpoints for cefiderocol vary. Contemporary breakpoints proposed by FDA [10], CLSI [9] and EUCAST [11] are summarized in the Supplement (Section 1). With respect to EUCAST, non-species related PK/PD-based breakpoints were applied for *A. baumannii* and *S. maltophilia*. In studies reporting a single criterion, susceptibility percentages for other breakpoint criteria were inferred based on reported MIC ranges or MIC distribution data when available (when maximum MIC was below the susceptibility breakpoint a 0% non-susceptibility was inferred).

Definitions of co-resistance phenotypes

Underlying co-resistance phenotypes were categorized as any phenotype, CR, MBL-producing, NDM-producing, CZA-resistant, or CTA-resistant. “Any phenotype” referred to studies with non-selected isolates of mixed resistance phenotypes. Studies selecting isolates solely based on being CR or CZA-resistant or CTA-resistant or MBL-producing, were reported separately from the “any phenotype” category to avoid overestimating CFDC-NS prevalence, which was expected to be higher for those phenotypes [6]. Similarly, studies selecting isolates solely based on being CZA-resistant, CTA-resistant or MBL-producing isolates were reported separately from the CR category, whereas studies selecting solely NDM-producing isolates were reported separately from the MBL category. Depending on data availability and definitions in the studies, CR was defined, in order of preference, as meropenem MIC>8mg/L, or meropenem resistance or non-susceptibility according to another study-defined breakpoint, or non-susceptibility as defined in the study (not necessarily based on meropenem), or carbapenemase-production.

Risk of bias assessment

Two reviewers examined independently each study for risk of bias concerning two main domains applicable to this review [18]: (a) population and setting and (b) condition measurement (validity and standardization of the susceptibility testing method). Discrepancies in risk of bias assessments were resolved by discussion and consensus. Items for each domain were adapted from the Joanna-Briggs critical appraisal tool for prevalence studies [18, 19]. Items and their interpretation as used in this review are described in the Supplement (Section 2). Studies at moderate or high risk of bias in either domain were categorized as moderate-to-high risk overall, while studies at low risk of bias in both domains were categorized as low risk of bias overall.

Meta-analysis methods

The primary outcome for meta-analysis was CFDC-NS prevalence, stratified by combinations of microorganism species, definition of breakpoints and underlying co-resistance phenotype. Population-averaged proportions were estimated using a random intercept logistic regression model with maximum likelihood estimation [20]. The model assumed a Binomial distribution for the observed number of CFDC-NS isolates in each study and a Normal distribution for the random population-level effects following the logit transformation. This approach correctly handles proportions near 0% or 100% (when variance tends towards zero and classic inverse variance weights are problematic),[21] and maintains the confidence limits of pooled proportions within the zero to one range. The resulting confidence interval (CI) contains highly probable values for the population-averaged (pooled) prevalence proportion of CFDC-NS.

Higgin-Thompson's I^2 statistic was used as a summary index of the amount of variability of CFDC-NS proportions across studies that cannot be attributed to sampling error. Because I^2 is usually high and may not be discriminative for prevalence data [22], we additionally reported between-study variance (τ^2) with respective 95% prediction interval (PI). The PI describes the range CFDC-NS proportions that can be expected in new studies or settings [23]. We used summary forest plots to

present pooled estimates with heterogeneity statistics for each microorganism and each different combination of breakpoint threshold with co-resistance phenotype. Additionally, we constructed forest plots for the study-specific data used in each meta-analysis to illustrate the distributions of CFDC-NS proportions across the studies along with 95% CIs calculated by Wilson's score method (presented in the Supplement).

To examine potential sources of variation in CFDC-NS prevalence, we conducted a series of univariate meta-regressions with the Binomial-Normal mixed-effects model. We applied this to carbapenem-resistant *Enterobacterales*, *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* based on the CLSI breakpoints, as this was the most frequent combination of breakpoints with co-resistance phenotype with a minimum of 15 studies available for each meta-regression. Odds ratios (ORs) with respective 95% CI were calculated to summarise the strength and direction of associations between study-level covariates and CFDC-NS prevalence. A covariate-specific R^2 was calculated as the portion of between-study variance that was reduced after the inclusion of that covariate in a null model. Moreover, for each covariate level we calculated pooled estimates of CFDC-NS prevalence based on subgroup analysis. Candidate covariates were decided a priori in our study protocol. The following study-level variables were examined: year when data collection ended, geographical region (WHO classification), multinational setting (yes/no), multicentre setting (yes/no), and risk of bias (classified as either low or moderate-to-high). Despite our protocol plans, we were unable to examine substantive characteristics related to clinical setting (such as type and level of care, age of the patients, clinical specialty, and type of infection), which were largely unreported in the studies. The number of retrieved studies was inadequate to justify multivariable meta-regression.

All analyses were carried out in STATA (Version 17; Statcorp, College Station, TX, USA).

Results

Study characteristics

The flow chart of the review is depicted in Figure 1. A total of 78 studies were eligible for review [8, 16, 21, 24-98], which contributed 86 independent sets of data for analysis and reported 82,035 clinical isolates in total. Main characteristics of the studies are summarized in the Supplement, Sections 3-6. Several studies were identified as having overlapping collections of isolates as a result of the SIDERO-WT surveillance study being conducted yearly (2014-2019) in several countries in North America and Europe [25, 26, 55, 56, 58, 99-105]. Only non-overlapping data were collected for meta-analysis (see Supplement, Section 7). Most studies (87%) were published in the last four years (2020-2023). Regions most represented were Europe (50% of data sets), the Americas (33%), and the Western Pacific Region (17%) (Supplement, Section 5). Data for Enterobacterales were reported in 53 studies [8, 16, 26-31, 33, 34, 36-38, 41-48, 51, 54, 56, 57, 59, 60, 62, 64-69, 72, 75-85, 87, 91, 92, 95, 96], *P. aeruginosa* in 41 studies [7, 8, 16, 26, 28, 33, 34, 36, 39, 41-43, 45-49, 52-54, 56, 57, 61, 63, 66, 70, 71, 73-75, 78, 79, 83, 85, 86, 88, 89, 91, 94, 97, 106], *A. baumannii* in 35 studies [8, 16, 24, 26, 28, 30, 33-36, 39, 41-43, 45-48, 50, 52-54, 56, 57, 61, 66, 75, 78, 79, 85, 86, 90, 91, 93, 107] and *S. maltophilia* in 19 studies [8, 16, 26, 28, 30, 33, 40-42, 48, 52-54, 61, 74, 75, 78, 79, 85].

Risk of bias assessment

Overall risk of bias was moderate-to-high in most (94%) study sets of data, predominantly concerning moderate or high risks in the population and setting domains (86% of data sets). The latter was mostly due to inadequate descriptions of the characteristics of the study populations and insufficient sample sizes in individual studies of the pathogen populations of interest (Supplement, Section 6). About half (n=46; 54%) of the study sets were classified as moderate-to-high risk of bias in the domain of condition measurement. In about half of the cases (n=44, 51%), the studies lacked a clear definition or citation of the method for interpreting trailing (broth microdilution) or colonies within zone (disk diffusion). There were 14 data sets for which a method other than broth

240 microdilution was used (n=9 disk diffusion [8, 36, 37, 51, 65, 72, 75, 88, 92, 95], n=5 gradient strip
241 [36, 68, 69, 94, 97]). Apotransferrin for medium preparation was reported on 4 data sets (2 studies
242 [60, 61]).
243
244 **Cefiderocol activity against Enterobacterales**
245 Figure 2 is a summary forest plot of CFDC-NS prevalence estimates in Enterobacterales for
246 different combinations of breakpoints definition and co-resistance phenotype. The respective forest
247 plots for each separate meta-analysis and a summary table are available in the Supplement (Section
248 8). Data on CFDC-NS against the various Enterobacterales species (*Klebsiella* spp, *E. coli*,
249 *Enterobacter* spp, *Serratia* spp, *Citrobacter* spp, *Proteus* spp, *Morganella morganii*) are also available
250 in the Supplement (Section 9).
251 Using the EUCAST breakpoint thresholds, the pooled CFDC-NS prevalence was generally low
252 (3.0%, 95% CI 1.5-6.0%), but much higher in CR Enterobacterales (12.4%, 95% CI 7.3-20.0%), and
253 exceedingly high in MBL-producing (24.9%, 95% CI 16.6-35.5%), NDM-producing (38.8%, 95% CI
254 22.6-58.0%) and CZA-resistant (36.6%, 95% CI 22.7-53.1%) Enterobacterales. Notable differences in
255 CFDC-NS percentages were evident when contrasting the results between the EUCAST breakpoints
256 and the CLSI breakpoints in Figure 2. Pooled CFDC-NS percentages based on the former were much
257 greater than the latter, especially among CR (12.4% vs 3.8%), MBL-producing (24.9% vs 13.0%),
258 NDM-producing (38.7% vs 18.7%) and CZA-resistant (36.6% vs 8.3%) Enterobacterales.
259
260 **Cefiderocol activity against *P. aeruginosa***
261 As seen in Figure 3, CFDC-NS prevalence (EUCAST breakpoints) was generally low (1.4%, 95%
262 CI 0.5-4.0%), even among CR (3.5%, 95% CI 1.6-7.8%,) and MBL-producing (1.8%, 95% CI 0.3-10.4%),
263 CZA-resistant (6.8%, 95% CI 3.1-14.6%) and CTA-resistant (8.3%, 95% CI 4.1-16.0%) isolates. CFDR-NS
264 proportion was highest among NDM-producing isolates (22.9%, 95% CI 8.1-49.7%) but this estimate
265 was based on few isolates (n=51). Notable differences in CFDC-NS prevalence estimates were

observed comparing CLSI to EUCAST and FDA definitions of breakpoints among the CR *P. aeruginosa* isolates (0.8% vs 3.5% vs 14.6%), especially for the MBL-producers (1.6% vs 1.8% vs 23.3%), NDM-producers (19.5% vs 22.9% vs 58.7%), CZA-resistant (1.7% vs 6.8% vs 19.5%) and CTA-resistant (2.2% vs 8.3% vs 15.1%) isolates. The respective forest plots for each meta-analysis of each combination of breakpoint criterion and co-resistance phenotype, together with a summary table, are available in the Supplement (Section 10).

Cefiderocol activity against *A. baumannii*

The summary forest plot of subgroup-averaged proportions of CFDC-NS against *A. baumannii*, by co-resistance phenotype and breakpoints definition, is depicted in Figure 4. Respective forest plots for each meta-analysis and summary table are available in the Supplement (Section 11). Overall CFDC-NS prevalence in *A. baumannii* was higher compared to other species. CFDC-NS proportions (EUCAST breakpoints) were similar in the "any phenotype" (8.8%, 95% CI 4.9-15.2%,) and the CR (13.2%, 95% CI 7.8-21.5%) groups of *A. baumannii*, reflecting the high burden of carbapenem-resistance in this organism (i.e. sets of non-selected isolates classified as any/mixed phenotype included large portions of CR isolates). CFDC-NS prevalence was much higher among MBL-producing (40.9%, 95% CI 31.4-51.1%) and NDM-producing (44.7%, 95% CI 34.5-55.4%) *A. baumannii* isolates, with the majority of MBL-producing isolates being NDM-producers. Similar to other species, CFDC-NS prevalence was much lower when CLSI breakpoints were used as opposed to the EUCAST and FDA cut-offs among CR *A. baumannii* isolates (8.5% vs 13.2% vs 26.6%, respectively), especially for the MBL-producers (20.4% vs 40.9% vs 53.1%) and the NDM-producers (23.0% vs 44.7% vs 71.3%, respectively).

Cefiderocol activity against *S. maltophilia*

Cefiderocol non-susceptibility against *S. maltophilia* was very low, irrespective of the breakpoint definition used. CFDC-NS prevalence was 0.2% (95% CI 0.1-0.4%) where earlier CLSI

breakpoint criteria were used, 0.1% (95% CI 0.0-3.7%) when the new CLSI criteria were used, and 0.4% (95% CI 0.2-0.7%) with EUCAST breakpoints. In the largest study contributing the majority of data for *S. maltophilia*, the prevalence of CFDC-NS was 2.4% based on the new CLSI breakpoints, compared to 0.4% based on EUCAST and 0.2% based on prior CLSI breakpoints. A summary forest plot and respective forest plots for each meta-analysis are available in the Supplement (Section 12).

Heterogeneity

As evident from the heterogeneity statistics and prediction intervals in Figures 2-4, the data were characterised by considerable variability, even within the subgroups defined by combinations of co-resistance phenotype and breakpoint definition. Potential sources of variation in CFDC-NS prevalence were examined among CR isolates (CLSI breakpoints) by a series of univariate meta-regressions and the results are presented in the Supplement (Section 13). Indicatively, we present the results of the investigation for Enterobacterales in Table 1. These investigations revealed that single-centre study designs were associated with higher CFDC-NS prevalence, explaining a large portion of the variance among Enterobacterales (R^2 28%) and *A. baumannii* (R^2 21%). Regional variation was also observed. The results also suggested, albeit with a high degree of uncertainty, that CFDC-NS prevalence was higher in the Americas than elsewhere for CR *K. pneumoniae* (OR 1.9; 95% CI 0.2 - 17.4), higher in the Western Pacific Region than elsewhere for CR Enterobacterales (OR 3.3; 95% CI 0.4 – 27.0) and higher in Europe than elsewhere for CR *P. aeruginosa* (OR 1.6; 95% CI 0.3 – 9.6). Consistently in all meta-regressions, there was no evidence of variation in CFDC-NS prevalence according to risk of bias assessments.

Discussion

This systematic review and meta-analysis revealed differential pathogen-specific variation in the global prevalence of CFDC-NS, which was seen to be low for Enterobacterales, *P. aeruginosa*, and *S. maltophilia* but much higher against *A. baumannii*. Significant variability was also observed within each species, depending on the underlying antimicrobial co-resistance phenotype. Overall, cefiderocol appeared to retain relatively good activity against CR bacteria (especially CR *S. maltophilia* and *P. aeruginosa*), but for certain phenotypes (MBL/NDM-producing Enterobacterales and *A. baumannii*, and CZA-resistant Enterobacterales) CFDC-NS is exceedingly high.

Substantial heterogeneity of CFDC-NS prevalence among the studies was highlighted in this review and was found to persist even within presumably homogeneous subgroups of isolates defined by different combinations of co-resistance phenotype and CFDC breakpoint threshold. There was some evidence of regional variation, which might reflect differences in the epidemiology of carbapanemases between the regions, with selected carbapanemases having conferred cross-resistance to CFDC [6]. In addition, antimicrobial resistance might vary significantly among different clinical settings, but despite our initial plans, relevant data were largely unreported in the studies. Therefore, the population-averaged susceptibility estimates reported in this study are probably not generalizable to individual institutions and/or specific clinical settings (as indicated by wide prediction intervals), but serve to illustrate that despite high susceptibility to cefiderocol overall, there are settings where high non-susceptibility has been reported. Notably, the meta-regression models consistently attributed higher odds of CFDC-NS to single-centre studies. This might reflect clonal spreads or outbreaks of CR clones, possibly associated with β-lactamases, that have resulted in decreased cefiderocol susceptibility locally in some institutions or regions. Nevertheless, the lower prediction limits of CFDC-NS prevalence were considerably higher than zero for several co-resistance phenotypes examined in this review; thereby a high index of suspicion should be maintained when empirically administering cefiderocol, particularly in settings of aggravated antimicrobial resistance, or when *A. baumannii* is implicated.

Cefiderocol, exhibiting greater stability against β-lactamases (ESBL, AmpC, and all classes of carbapanemases including MBLs) can inhibit (especially based on CLSI breakpoints) the vast majority of Gram-negative isolates that are not-susceptible to carbapenems, ceftazidime/avibactam, ceftolozane/tazobactam and colistin [54, 58, 108, 109]. However, despite very high susceptibility rates in initial reports worldwide, non-susceptibility to cefiderocol appears to be more common in CR Gram-negative pathogens when applying the more stringent breakpoints proposed by EUCAST or FDA (the latter for non-fermenting Gram-negative bacteria) [16, 47]. In line with the current meta-analysis, a prior systematic review on mechanisms of CFDC-NS by the same authors, identified several β-lactamases (and various other mechanisms) that may result in higher MIC of cefiderocol, notably NDM and KPC variants conferring resistance for CZA [6]. Of interest, combination of cefiderocol with β-lactamases may be able to overcome resistance [6, 110].

Significant differences in the levels of CFDC-NS prevalence were noted when different proposed thresholds for antimicrobial breakpoints were used, which were pronounced among the CR phenotypes, especially MBL/NDM-producing isolates, similar to a previous report [111]. This has important clinical implications as the greatest clinical utility of cefiderocol is against infections by CR Gram-negative bacteria, particularly the MBL-producing isolates, which are associated with limited treatment options [3]. Therefore, harmonization of breakpoints is urgently needed, as well development of accurate in vitro susceptibility testing considering limitations of current methods [17].

Between-study variability is a main source of uncertainty for any meta-analysis and we attempted to account for heterogeneity by using a random effects model when pooling prevalence data and identify main sources of heterogeneity by subgroup and meta-regression analyses. Nevertheless, there are other important limitations to our investigation that should be mentioned. First, comparisons between CFDC-NS prevalence rates for different breakpoint criteria proposed by CLSI, FDA, and EUCAST were partly indirect because not all studies reported susceptibility data using all breakpoint definitions. Second, for a number of studies we inferred the susceptibility percentages

based on the maximum MICs being below the breakpoints. For example, in studies reporting susceptibilities based on CLSI breakpoints (MIC ≤4 mg /L) without reporting detailed MIC distribution data, the susceptibility proportions based on EUCAST breakpoints or FDA breakpoints were estimable only when the maximum MIC was lower than or equal to the EUCAST or FDA breakpoint respectively (i.e. 100% susceptible). Bias from this approach would most likely be towards underestimating CFDC-NS prevalence. Third, data on cefiderocol susceptibility for specific CR phenotypes (MBL, NDM) were limited, and reporting bias is possible. Finally, cefiderocol susceptibility testing has limitations including poor reproducibility of broth microdilution and disk diffusion for *A. baumannii*, difficulties in interpretation due to trailing in broth microdilution and colonies within zones of inhibition in disk diffusion, and inoculum-dependent MIC [17]. In our review, most (84%) studies used broth microdilution, but about half were considered at moderate or high risk of bias for not clearly reporting interpretation of trailing in broth microdilution. Nevertheless, such lack of reporting does not necessarily mean that interpretation of trailing was inappropriate. Moreover, meta-regression analyses did not detect variation in CFDC-NS prevalence according to risk of bias assessments in the condition measurement domain.

In conclusion, cefiderocol currently maintains a good level of activity against major Gram-negative pathogens and CFDC-NS prevalence is low overall. However, CFDC-NS prevalence proportions were alarmingly high in specific CR phenotypes circulating in some institutions or regions. A high index of suspicion for CFDC-NS is required concerning MBL- (predominantly NDM-) producing Enterobacterales and *A. baumannii*, NDM-producing *P. aeruginosa*, as well as CZA-resistant Enterobacterales, due to the possibility of emergence and spread of isolates with β-lactamases that may significantly increase cefiderocol's MIC. Antimicrobial stewardship, infection control and continued surveillance at the local level, as well as regular updating and reporting of global CFDC-NS estimates, are imperative for preventing or delaying emerging resistance against cefiderocol. Harmonization of EUCAST and CLSI breakpoints would help such efforts.

Transparency declaration

Conflict of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] S. Karakonstantis, E.I. Kritsotakis, A. Gikas, Pandrug-resistant Gram-negative bacteria: a systematic review of current epidemiology, prognosis and treatment options, J Antimicrob Chemother 75(2) (2019) 271–282.

[2] S. Karakonstantis, A. Gikas, E. Astrinaki, E.I. Kritsotakis, Excess mortality due to pandrug-resistant Acinetobacter baumannii infections in hospitalized patients, Journal of Hospital Infection 106(3) (2020) 447-453.

[3] S. Karakonstantis, E. Kritsotakis, A. Gikas, Treatment Options for K. pneumoniae, P. aeruginosa and A. baumannii Co-resistant to Carbapenems, Aminoglycosides, Polymyxins and Tigecycline. An Approach Based on the Mechanisms of Resistance to Carbapenems., Infection 48(6) (2020) 835-851.

[4] S. Karakonstantis, P. Ioannou, G. Samonis, D.P. Kofteridis, Systematic review of antimicrobial combination options for pandrug-resistant Acinetobacter baumannii, Antibiotics (Basel, Switzerland) (2021).

[5] Y. Doi, Treatment Options for Carbapenem-resistant Gram-negative Bacterial Infections, Clinical Infectious Diseases 69(Supplement_7) (2019) S565-S575.

[6] S. Karakonstantis, M. Rousaki, E.I. Kritsotakis, Cefiderocol: Systematic Review of Mechanisms of Resistance, Heteroresistance and In Vivo Emergence of Resistance, Antibiotics 11(6) (2022) 723.

[7] C. Wang, D. Yang, Y. Wang, W. Ni, Cefiderocol for the Treatment of Multidrug-Resistant Gram-Negative Bacteria: A Systematic Review of Currently Available Evidence, Frontiers in pharmacology 13 (2022) 896971.

[8] J.E. Choby, T. Ozturk, S.W. Satola, J.T. Jacob, D.S. Weiss, Widespread cefiderocol heteroresistance in carbapenem-resistant Gram-negative pathogens, The Lancet Infectious Diseases 21(5) (2021) 597-598.

[9] CLSI, Performance Standards for Antimicrobial Susceptibility Testing. 32st ed. CLSI supplement M100., Clinical Laboratory Standards Institute, Wayne, 2022.

[10] FDA, Cefiderocol Injection. FDA Identified Breakpoints. <https://www.fda.gov/drugs/development-resources/cefiderocol-injection>, 2020 (accessed 22/12/2022.2022).

[11] The European Committee on Antimicrobial Susceptibility Testing, Breakpoint tables for interpretation of MICs and zone diameters. Version 12.0. <http://www.eucast.org/>, 2023 (accessed 2023-03-24.2023).

[12] M.J. Page, D. Moher, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shamseer, J.M. Tetzlaff, E.A. Akl, S.E. Brennan, R. Chou, J. Glanville, J.M. Grimshaw, A. Hróbjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, L.A. Stewart, J. Thomas, A.C. Tricco, V.A. Welch, P. Whiting, J.E. McKenzie, PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews, BMJ 372 (2021) n160.

[13] M. Ouzzani, H. Hammady, Z. Fedorowicz, A. Elmagarmid, Rayyan—a web and mobile app for systematic reviews, Systematic Reviews 5(1) (2016) 210.

[14] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth, Diagnostic microbiology and infectious disease 94(4) (2019) 321-325.

[15] P.J. Simner, R. Patel, Cefiderocol Antimicrobial Susceptibility Testing Considerations: the Achilles' Heel of the Trojan Horse?, Journal of clinical microbiology 59(1) (2020).

[16] C.P. Morris, Y. Bergman, T. Tekle, J.A. Fissel, P.D. Tamma, P.J. Simner, Cefiderocol Antimicrobial Susceptibility Testing against Multidrug-Resistant Gram-Negative Bacilli: a Comparison of Disk Diffusion to Broth Microdilution, Journal of clinical microbiology 59(1) (2020).

[17] P.J. Simner, E.L. Palavecino, M.J. Satlin, A.J. Mathers, M.P. Weinstein, J.S. Lewis, 2nd, R. Humphries, Potential of Inaccurate Cefiderocol Susceptibility Results: a CLSI AST Subcommittee Advisory, Journal of clinical microbiology 61(4) (2023) e0160022.
[18] C.B. Migliavaca, C. Stein, V. Colpani, Z. Munn, M. Falavigna, Quality assessment of prevalence studies: a systematic review, Journal of clinical epidemiology 127 (2020) 59-68.
[19] Z. Munn, S. Moola, K. Lisy, D. Riitano, C. Tufanaru, Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data, International journal of evidence-based healthcare 13(3) (2015) 147-53.
[20] L. Lin, H. Chu, Meta-analysis of Proportions Using Generalized Linear Mixed Models, Epidemiology 31(5) (2020) 713-717.
[21] J. Xu, H. Guo, L. Li, F. He, Molecular epidemiology and genomic insights into the transmission of carbapenem-resistant NDM-producing Escherichia coli, Computational and structural biotechnology journal 21 (2023) 847-855.
[22] C.B. Migliavaca, C. Stein, V. Colpani, T.H. Barker, P.K. Ziegelmann, Z. Munn, M. Falavigna, Meta-analysis of prevalence: I(2) statistic and how to deal with heterogeneity, Res Synth Methods 13(3) (2022) 363-367.
[23] J. IntHout, J.P.A. Ioannidis, M.M. Rovers, J.J. Goeman, Plea for routinely presenting prediction intervals in meta-analysis, BMJ open 6(7) (2016) e010247.
[24] C. Ballesté-Delpierre, Á. Ramírez, L. Muñoz, C. Longshaw, I. Roca, J. Vila, Assessment of In Vitro Cefiderocol Susceptibility and Comparators against an Epidemiologically Diverse Collection of Acinetobacter baumannii Clinical Isolates, Antibiotics (Basel, Switzerland) 11(2) (2022).
[25] F.J. Candel, A. Santerre Henriksen, C. Longshaw, Y. Yamano, A. Oliver, In vitro activity of the novel siderophore cephalosporin, cefiderocol, in Gram-negative pathogens in Europe by site of infection, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 28(3) (2022) 447.e1-447.e6.
[26] J.A. Karlowsky, M.A. Hackel, M. Takemura, Y. Yamano, R. Echols, D.F. Sahm, In Vitro Susceptibility of Gram-Negative Pathogens to Cefiderocol in Five Consecutive Annual Multinational SIDERO-WT Surveillance Studies, 2014 to 2019, Antimicrobial agents and chemotherapy 66(2) (2022) e0199021.
[27] P. Lan, Y. Lu, Z. Chen, X. Wu, X. Hua, Y. Jiang, J. Zhou, Y. Yu, Emergence of High-Level Cefiderocol Resistance in Carbapenem-Resistant Klebsiella pneumoniae from Bloodstream Infections in Patients with Hematologic Malignancies in China, Microbiology spectrum 10(2) (2022) e0008422.
[28] D. Shortridge, J.M. Streit, R. Mendes, M. Castanheira, In Vitro Activity of Cefiderocol against U.S. and European Gram-Negative Clinical Isolates Collected in 2020 as Part of the SENTRY Antimicrobial Surveillance Program, Microbiology spectrum 10(2) (2022) e0271221.
[29] Q. Wang, L. Jin, S. Sun, Y. Yin, R. Wang, F. Chen, X. Wang, Y. Zhang, J. Hou, Y. Zhang, Z. Zhang, L. Luo, Z. Guo, Z. Li, X. Lin, L. Bi, H. Wang, Occurrence of High Levels of Cefiderocol Resistance in Carbapenem-Resistant Escherichia coli before Its Approval in China: a Report from China CRE-Network, Microbiology spectrum (2022) e0267021.
[30] Q. Wang, L. Jin, S. Sun, Y. Yin, R. Wang, F. Chen, X. Wang, Y. Zhang, J. Hou, Y. Zhang, Z. Zhang, L. Luo, Z. Guo, Z. Li, X. Lin, L. Bi, H. Wang, Occurrence of High Levels of Cefiderocol Resistance in Carbapenem-Resistant Escherichia coli before Its Approval in China: a Report from China CRE-Network, Microbiology spectrum 10(3) (2022) e0267021.
[31] Q. Zhang, N. Neidig, T.Y. Chu, C. Divoky, J. Carpenter, C. Lee-Hsiao, H. Threatt, R. Sultana, K. Bush, In vitro antibacterial activity of cefiderocol against recent multidrug-resistant carbapenem-nonsusceptible Enterobacterales isolates, Diagnostic microbiology and infectious disease 103(1) (2022) 115651.
[32] J.C. Abdul-Mutakabbir, L. Nguyen, P.T. Maassen, K.C. Stamper, R. Kebriaei, K.S. Kaye, M. Castanheira, M.J. Rybak, In Vitro Antibacterial Activity of Cefiderocol against Multidrug-Resistant Acinetobacter baumannii, Antimicrobial agents and chemotherapy 65(9) (2021) e0264620.

[33] M. Albano, M.J. Karau, A.N. Schuetz, R. Patel, Comparison of Agar Dilution to Broth Microdilution for Testing In Vitro Activity of Cefiderocol against Gram-Negative Bacilli, Journal of clinical microbiology 59(1) (2020).
[34] S.S. Bhagwat, N.J. Legakis, T. Skalidis, A. Loannidis, C. Goumenopoulos, P.R. Joshi, R. Shrivastava, S.R. Palwe, H. Periasamy, M.V. Patel, S. Chatzipanagiotou, In vitro activity of cefepime/zidebactam (WCK 5222) against recent Gram-negative isolates collected from high resistance settings of Greek hospitals, Diagnostic microbiology and infectious disease 100(3) (2021) 115327.
[35] D. Carcione, C. Siracusa, A. Sulejmani, R. Migliavacca, A. Mercato, A. Piazza, L. Principe, N. Clementi, N. Mancini, V. Leoni, J. Intra, In Vitro Antimicrobial Activity of the Siderophore Cephalosporin Cefiderocol against Acinetobacter baumannii Strains Recovered from Clinical Samples, Antibiotics (Basel, Switzerland) 10(11) (2021).
[36] B. Ghebremedhin, P. Ahmad-Nejad, In-Vitro Efficacy of Cefiderocol in Carbapenem-Non-Susceptible Gram-Negative Bacilli of Different Genotypes in Sub-Region of North Rhine Westphalia, Germany, Pathogens 10(10) (2021).
[37] A.S. Jacob, G.L. Chong, K. Lagrou, M. Depypere, S. Desmet, No in vitro activity of cefiderocol against OXA-427-producing Enterobacterales, J Antimicrob Chemother 76(12) (2021) 3317-3318.
[38] Y.L. Lee, W.C. Ko, W.S. Lee, P.L. Lu, Y.H. Chen, S.H. Cheng, M.C. Lu, C.Y. Lin, T.S. Wu, M.Y. Yen, L.S. Wang, C.P. Liu, P.L. Shao, Z.Y. Shi, Y.S. Chen, F.D. Wang, S.H. Tseng, C.N. Lin, Y.H. Chen, W.H. Sheng, C.M. Lee, H.J. Tang, P.R. Hsueh, In-vitro activity of cefiderocol, cefepime/zidebactam, cefepime/enmetazobactam, omadacycline, eravacycline and other comparative agents against carbapenem-nonsusceptible Enterobacterales: results from the Surveillance of Multicenter Antimicrobial Resistance in Taiwan (SMART) in 2017-2020, International journal of antimicrobial agents 58(3) (2021) 106377.
[39] P.Y. Liu, W.C. Ko, W.S. Lee, P.L. Lu, Y.H. Chen, S.H. Cheng, M.C. Lu, C.Y. Lin, T.S. Wu, M.Y. Yen, L.S. Wang, C.P. Liu, P.L. Shao, Y.L. Lee, Z.Y. Shi, Y.S. Chen, F.D. Wang, S.H. Tseng, C.N. Lin, Y.H. Chen, W.H. Sheng, C.M. Lee, H.J. Tang, P.R. Hsueh, In vitro activity of cefiderocol, cefepime/enmetazobactam, cefepime/zidebactam, eravacycline, omadacycline, and other comparative agents against carbapenem-non-susceptible Pseudomonas aeruginosa and Acinetobacter baumannii isolates associated from bloodstream infection in Taiwan between 2018-2020, Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi (2021).
[40] M. Biagi, A. Vialichka, M. Jurkovic, T. Wu, A. Shajee, M. Lee, S. Patel, R.E. Mendes, E. Wenzler, Activity of Cefiderocol Alone and in Combination with Levofloxacin, Minocycline, Polymyxin B, or Trimethoprim-Sulfamethoxazole against Multidrug-Resistant Stenotrophomonas maltophilia, Antimicrob Agents Chemother 64(9) (2020).
[41] M. Delgado-Valverde, M.D.C. Conejo, L. Serrano, F. Fernández-Cuenca, Á. Pascual, Activity of cefiderocol against high-risk clones of multidrug-resistant Enterobacterales, Acinetobacter baumannii, Pseudomonas aeruginosa and Stenotrophomonas maltophilia, J Antimicrob Chemother 75(7) (2020) 1840-1849.
[42] A.R. Golden, H.J. Adam, M. Baxter, A. Walkty, P. Lagacé-Wiens, J.A. Karlowsky, G.G. Zhanel, In Vitro Activity of Cefiderocol, a Novel Siderophore Cephalosporin, against Gram-Negative Bacilli Isolated from Patients in Canadian Intensive Care Units, Diagnostic microbiology and infectious disease 97(1) (2020) 115012.
[43] A. Iregui, Z. Khan, D. Landman, J. Quale, Activity of Cefiderocol Against Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter baumannii Endemic to Medical Centers in New York City, Microbial drug resistance (Larchmont, N.Y.) 26(7) (2020) 722-726.
[44] B.D. Johnston, P. Thuras, S.B. Porter, M. Anacker, B. VonBank, P. Snippes Vagnone, M. Witwer, M. Castanheira, J.R. Johnson, Activity of Cefiderocol, Ceftazidime-Avibactam, and Eravacycline against Carbapenem-Resistant Escherichia coli Isolates from the United States and International Sites in Relation to Clonal Background, Resistance Genes, Coresistance, and Region, Antimicrobial agents and chemotherapy 64(10) (2020).

[45] M. Kresken, M. Korte-Berwanger, S.G. Gatermann, Y. Pfeifer, N. Pfennigwerth, H. Seifert, G. Werner, In vitro activity of cefiderocol against aerobic Gram-negative bacterial pathogens from Germany, International journal of antimicrobial agents 56(4) (2020) 106128.
[46] C. Longshaw, D. Manissero, M. Tsuji, R. Echols, Y. Yamano, In vitro activity of the siderophore cephalosporin, cefiderocol, against molecularly characterized, carbapenem-non-susceptible Gram-negative bacteria from Europe, JAC-antimicrobial resistance 2(3) (2020).
[47] S. Mushtaq, Z. Sadouki, A. Vickers, D.M. Livermore, N. Woodford, In Vitro Activity of Cefiderocol, a Siderophore Cephalosporin, against Multidrug-Resistant Gram-Negative Bacteria, Antimicrobial agents and chemotherapy 64(12) (2020).
[48] K.V.I. Rolston, B. Gerges, S. Shelburne, S.L. Aitken, I. Raad, R.A. Prince, Activity of Cefiderocol and Comparators against Isolates from Cancer Patients, Antimicrobial agents and chemotherapy 64(5) (2020).
[49] D.A. Talan, S.S. Takhar, A. Krishnadasan, W.R. Mower, D.J. Pallin, M. Garg, J. Femling, R.E. Rothman, J.C. Moore, A.E. Jones, F. Lovecchio, J. Jui, M.T. Steele, A.M. Stubbs, W.K. Chiang, G.J. Moran, Emergence of Extended-Spectrum β-Lactamase Urinary Tract Infections Among Hospitalized Emergency Department Patients in the United States, Ann Emerg Med 77(1) (2021) 32-43.
[50] V. Trebosc, B. Schellhorn, J. Schill, V. Lucchini, J. Bühler, M. Bourotte, J.J. Butcher, M. Gitzinger, S. Lociuro, C. Kemmer, G.E. Dale, In vitro activity of rifabutin against 293 contemporary carbapenem-resistant Acinetobacter baumannii clinical isolates and characterization of rifabutin mode of action and resistance mechanisms, J Antimicrob Chemother (2020).
[51] O. Xie, K. Cisera, L. Taylor, C. Hughes, B. Rogers, Clinical syndromes and treatment location predict utility of carbapenem sparing therapies in ceftriaxone-non-susceptible Escherichia coli bloodstream infection, Annals of clinical microbiology and antimicrobials 19(1) (2020) 57.
[52] S.C. Hsueh, Y.J. Lee, Y.T. Huang, C.H. Liao, M. Tsuji, P.R. Hsueh, In vitro activities of cefiderocol, ceftolozane/tazobactam, ceftazidime/avibactam and other comparative drugs against imipenem-resistant Pseudomonas aeruginosa and Acinetobacter baumannii, and Stenotrophomonas maltophilia, all associated with bloodstream infections in Taiwan, The Journal of antimicrobial chemotherapy 74(2) (2019) 380-386.
[53] M.R. Jacobs, A.M. Abdelhamed, C.E. Good, D.D. Rhoads, K.M. Hujer, A.M. Hujer, T.N. Domitrovic, S.D. Rudin, S.S. Richter, D. van Duin, B.N. Kreiswirth, C. Greco, D.E. Fouts, R.A. Bonomo, ARGONAUT-I: Activity of Cefiderocol (S-649266), a Siderophore Cephalosporin, against Gram-Negative Bacteria, Including Carbapenem-Resistant Nonfermenters and Enterobacteriaceae with Defined Extended-Spectrum β-Lactamases and Carbapenemases, Antimicrobial agents and chemotherapy 63(1) (2019).
[54] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, In Vitro Activity of the Siderophore Cephalosporin, Cefiderocol, against Carbapenem-Nonsusceptible and Multidrug-Resistant Isolates of Gram-Negative Bacilli Collected Worldwide in 2014 to 2016, Antimicrobial agents and chemotherapy 62(2) (2018).
[55] J.A. Karlowsky, M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, D.F. Sahm, In Vitro Activity of Cefiderocol, a Siderophore Cephalosporin, Against Gram-Negative Bacilli Isolated by Clinical Laboratories in North America and Europe in 2015-2016: SIDERO-WT-2015, International journal of antimicrobial agents (2018).
[56] K.M. Kazmierczak, M. Tsuji, M.G. Wise, M. Hackel, Y. Yamano, R. Echols, D.F. Sahm, In vitro activity of cefiderocol, a siderophore cephalosporin, against a recent collection of clinically relevant carbapenem-non-susceptible Gram-negative bacilli, including serine carbapenemase- and metallo-β-lactamase-producing isolates (SIDERO-WT-2014 Study), International journal of antimicrobial agents 53(2) (2019) 177-184.
[57] M.E. Falagas, T. Skalidis, K.Z. Vardakas, N.J. Legakis, Activity of cefiderocol (S-649266) against carbapenem-resistant Gram-negative bacteria collected from inpatients in Greek hospitals, The Journal of antimicrobial chemotherapy 72(6) (2017) 1704-1708.

[58] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, In Vitro Activity of the Siderophore Cephalosporin, Cefiderocol, against a Recent Collection of Clinically Relevant Gram-Negative Bacilli from North America and Europe, Including Carbapenem-Nonsusceptible Isolates (SIDERO-WT-2014 Study), Antimicrobial agents and chemotherapy 61(9) (2017).
[59] S. Kanazawa, T. Sato, N. Kohira, T. Ito-Horiyama, M. Tsuji, Y. Yamano, Susceptibility of Imipenem-Susceptible but Meropenem-Resistant bla(IMP-6)-Carrying Enterobacteriaceae to Various Antibacterials, Including the Siderophore Cephalosporin Cefiderocol, Antimicrobial agents and chemotherapy 61(7) (2017).
[60] N. Kohira, J. West, A. Ito, T. Ito-Horiyama, R. Nakamura, T. Sato, S. Rittenhouse, M. Tsuji, Y. Yamano, In Vitro Antimicrobial Activity of a Siderophore Cephalosporin, S-649266, against Enterobacteriaceae Clinical Isolates, Including Carbapenem-Resistant Strains, Antimicrobial agents and chemotherapy 60(2) (2016) 729-34.
[61] A. Ito, N. Kohira, S.K. Bouchillon, J. West, S. Rittenhouse, H.S. Sader, P.R. Rhomberg, R.N. Jones, H. Yoshizawa, R. Nakamura, M. Tsuji, Y. Yamano, In vitro antimicrobial activity of S-649266, a catechol-substituted siderophore cephalosporin, when tested against non-fermenting Gram-negative bacteria, J Antimicrob Chemother 71(3) (2016) 670-7.
[62] B.D. Johnston, P. Thuras, S.B. Porter, C. Clabots, J.R. Johnsona, Activity of cefiderocol, ceftazidime-avibactam, and eravacycline against extended-spectrum cephalosporin-resistant Escherichia coli clinical isolates (2012-20017) in relation to phylogenetic background, sequence type 131 subclones, bla(CTX-M) genotype, and coresistance, Diagnostic microbiology and infectious disease 100(1) (2021) 115314.
[63] B. Ihssane, E.O. Fatima, K. Aboubakr, B. Fatna, T. Mohammed, B. Pierre, H. Te-Din, N. Kaotar, First report of Pseudomonas aeruginosa strains co-harboring bla(NDM)-bla(VIM) and bla(VIM)-bla(IMP) metallo-β-lactamase genes in Morocco, Journal of global antimicrobial resistance 33 (2023) 42-43.
[64] P. Perez-Palacios, D. Girlich, N. Soraa, A. Lamrani, F.M.R. Maoulainine, F. Bennaoui, H. Amri, N.S. El Idrissi, M. Bouskraoui, A. Birer, A.B. Jousset, S. Oueslati, J. Raymond, T. Naas, Multidrug-resistant Enterobacterales responsible for septicaemia in a neonatal intensive care unit in Morocco, Journal of global antimicrobial resistance 33 (2023) 208-217.
[65] S.G. Badran, M.M. Malek, R.M. Ateya, A.H. Afifi, M.M. Magdy, E.S. Elgharabawy, Susceptibility of carbapenem-resistant Enterobacterales isolates to new antibiotics from a tertiary care hospital, Egypt: A matter of hope, Journal of infection in developing countries 16(12) (2022) 1852-1859.
[66] M. Alzayer, M.F. Alghoribi, B. Alalwan, A. Alreheli, S. Aljohani, M. Bosaeed, M. Doumith, In vitro activity of cefiderocol against clinically important carbapenem non-susceptible Gram-negative bacteria from Saudi Arabia, Journal of global antimicrobial resistance 32 (2023) 176-180.
[67] Y.D. Bakthavatchalam, A. Shankar, Y. Manokaran, K. Walia, B. Veeraraghavan, Can fosfomycin be an alternative therapy for infections caused by E. coli harbouring dual resistance: NDM and four-amino acid insertion in PBP3?, JAC-antimicrobial resistance 5(2) (2023) dlad016.
[68] J.E. Cañada-García, E. Ramírez de Arellano, M. Jiménez-Orellana, E. Viedma, A. Sánchez, A. Alhambra, J. Villa, A. Delgado-Iribarren, V. Bautista, N. Lara, S. García-Cobos, B. Aracil, E. Cercenado, M. Pérez-Vázquez, J. Oteo-Iglesias, Carbapenemase-Producing Klebsiella pneumoniae in COVID-19 Intensive Care Patients: Identification of IncL-VIM-1 Plasmid in Previously Non-Predominant Sequence Types, Antibiotics (Basel, Switzerland) 12(1) (2023).
[69] J.E. Cañada-García, Z. Moure, P.J. Sola-Campoy, M. Delgado-Valverde, M.E. Cano, D. Gijón, M. González, I. Gracia-Ahufinger, N. Larrosa, X. Mulet, C. Pitart, A. Rivera, G. Bou, J. Calvo, R. Cantón, J.J. González-López, L. Martínez-Martínez, F. Navarro, A. Oliver, Z.R. Palacios-Baena, Á. Pascual, G. Ruiz-Carrascoso, J. Vila, B. Aracil, M. Pérez-Vázquez, J. Oteo-Iglesias, CARB-ES-19 Multicenter Study of Carbapenemase-Producing Klebsiella pneumoniae and Escherichia coli From All Spanish Provinces Reveals Interregional Spread of High-Risk Clones Such as ST307/OXA-48 and ST512/KPC-3, Front Microbiol 13 (2022) 918362.

[70] C. Lasarte-Monterrubio, P.A. Fraile-Ribot, J.C. Vázquez-Ucha, G. Cabot, P. Guijarro-Sánchez, I. Alonso-García, S. Rumbo-Feal, F. Galán-Sánchez, A. Beceiro, J. Arca-Suárez, A. Oliver, G. Bou, Activity of cefiderocol, imipenem/relebactam, cefepime/taniborbactam and cefepime/zidebactam against ceftolozane/tazobactam- and ceftazidime/avibactam-resistant Pseudomonas aeruginosa, J Antimicrob Chemother 77(10) (2022) 2809-2815.
[71] G. Morroni, L. Brescini, A. Antonelli, V. Di Pilato, S. Castelletti, A. Brenciani, G. D'Achille, M. Mingoia, E. Giovanetti, S. Fioriti, A. Masucci, T. Giani, A. Giacometti, G.M. Rossolini, O. Cirioni, Clinical and microbiological features of ceftolozane/tazobactam-resistant Pseudomonas aeruginosa isolates in a university hospital in central Italy, Journal of global antimicrobial resistance 30 (2022) 377-383.
[72] P. Zalas-Więcek, K. Płachta, E. Gospodarek-Komkowska, Cefiderocol against Multi-Drug and Extensively Drug-Resistant Escherichia coli: An In Vitro Study in Poland, Pathogens 11(12) (2022).
[73] L. Devoos, A. Biguenet, J. Rousselot, M. Bour, P. Plésiat, D. Fournier, K. Jeannot, Performance of discs, sensititre EUMDROXF microplates and MTS gradient strips for the determination of the susceptibility of multidrug-resistant Pseudomonas aeruginosa to cefiderocol, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 29(5) (2023) 652.e1-652.e8.
[74] N. Kohira, M.A. Hackel, M. Oota, M. Takemura, F. Hu, H. Mizuno, D.F. Sahm, Y. Yamano, In vitro antibacterial activities of cefiderocol against Gram-negative clinical strains isolated from China in 2020, Journal of global antimicrobial resistance 32 (2023) 181-186.
[75] G. Bianco, M. Boattini, S. Comini, G. Banche, R. Cavallo, C. Costa, Disc Diffusion and ComASP(®) Cefiderocol Microdilution Panel to Overcome the Challenge of Cefiderocol Susceptibility Testing in Clinical Laboratory Routine, Antibiotics (Basel, Switzerland) 12(3) (2023).
[76] Y.S. Huang, P.Y. Chen, P.C. Chou, J.T. Wang, In Vitro Activities and Inoculum Effects of Cefiderocol and Aztreonam-Avibactam against Metallo-β-Lactamase-Producing Enterobacteriaceae, Microbiology spectrum 11(3) (2023) e0056923.
[77] C. Lasarte-Monterrubio, P. Guijarro-Sánchez, J.C. Vázquez-Ucha, I. Alonso-Garcia, L. Alvarez-Fraga, M. Outeda, M. Martinez-Guitian, A. Peña-Escolano, R. Maceiras, E. Lence, C. González-Bello, J. Arca-Suárez, G. Bou, A. Beceiro, Antimicrobial Activity of Cefiderocol against the Carbapenemase-Producing Enterobacter cloacae Complex and Characterization of Reduced Susceptibility Associated with Metallo-β-Lactamase VIM-1, Antimicrobial agents and chemotherapy 67(5) (2023) e0150522.
[78] M. Padovani, A. Bertelli, S. Corbellini, G. Piccinelli, F. Gurrieri, M.A. De Francesco, In Vitro Activity of Cefiderocol on Multiresistant Bacterial Strains and Genomic Analysis of Two Cefiderocol Resistant Strains, Antibiotics (Basel, Switzerland) 12(4) (2023).
[79] R.F. Potter, M.A. Wallace, C.E. Muenks, K. Alvarado, M.L. Yarbrough, C.D. Burnham, Evaluation of Variability in Interpretation of Disk Diffusion Testing for Cefiderocol Using Different Brands of Mueller-Hinton Agar, The journal of applied laboratory medicine 8(3) (2023) 523-534.
[80] P.D. Tamma, Y. Bergman, E.B. Jacobs, J.H. Lee, S. Lewis, S.E. Cosgrove, P.J. Simner, Comparing the activity of novel antibiotic agents against carbapenem-resistant Enterobacterales clinical isolates, Infection control and hospital epidemiology 44(5) (2023) 762-767.
[81] V. Di Pilato, L. Henrici De Angelis, N. Aiezza, I. Baccani, C. Niccolai, E.M. Parisio, C. Giordano, G. Camarlinghi, S. Barnini, S. Forni, L. Righi, M.T. Mechi, T. Giani, A. Antonelli, G.M. Rossolini, Resistome and virulome accretion in an NDM-1-producing ST147 sublineage of Klebsiella pneumoniae associated with an outbreak in Tuscany, Italy: a genotypic and phenotypic characterisation, The Lancet. Microbe 3(3) (2022) e224-e234.
[82] L. Daoud, F. Al-Marzooq, C.A. Moubareck, A. Ghazawi, T. Collyns, Elucidating the effect of iron acquisition systems in Klebsiella pneumoniae on susceptibility to the novel siderophore-cephalosporin cefiderocol, PloS one 17(12) (2022) e0277946.
[83] C. Le Terrier, P. Nordmann, L. Poirel, In vitro activity of aztreonam in combination with newly developed β-lactamase inhibitors against MDR Enterobacterales and Pseudomonas aeruginosa producing metallo-β-lactamases, Journal of Antimicrobial Chemotherapy 78(1) (2022) 101-107.

[84] S. Maraki, V.E. Mavromanolaki, D. Stafylaki, E. Scoulica, In vitro activity of newer β-lactam/β-lactamase inhibitor combinations, cefiderocol, plazomicin and comparators against carbapenemase-producing Klebsiella pneumoniae isolates, Journal of chemotherapy (Florence, Italy) (2023) 1-5.
[85] S. Oueslati, P. Bogaerts, L. Dortet, S. Bernabeu, H. Ben Lakhal, C. Longshaw, Y. Glupczynski, T. Naas, In vitro Activity of Cefiderocol and Comparators against Carbapenem-Resistant Gram-Negative Pathogens from France and Belgium, Antibiotics (Basel, Switzerland) 11(10) (2022).
[86] T. Sewunet, D. Asrat, Y. Woldeamanuel, A. Aseffa, C.G. Giske, Molecular epidemiology and antimicrobial susceptibility of Pseudomonas spp. and Acinetobacter spp. from clinical samples at Jimma medical center, Ethiopia, Frontiers in microbiology 13 (2022) 951857.
[87] R.A. Bonnin, C. Emeraud, A.B. Jousset, T. Naas, L. Dortet, Comparison of disk diffusion, MIC test strip and broth microdilution methods for cefiderocol susceptibility testing on carbapenem-resistant enterobacterales, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 28(8) (2022) 1156.e1-1156.e5.
[88] H.C. Mİrza, G. İnce Cevİz, Comparison of in vitro activities of cefiderocol, imipenem/relebactam and other antibiotics against carbapenem-resistant Pseudomonas aeruginosa isolates, Turk Hij Den Biyol Derg 79(3) (2022) 433-442.
[89] A. Ruedas-López, I. Alonso-García, C. Lasarte-Monterrubio, P. Guijarro-Sánchez, E. Gato, J.C. Vázquez-Ucha, J.A. Vallejo, P.A. Fraile-Ribot, B. Fernández-Pérez, D. Velasco, J.M. Gutiérrez-Urbón, M. Oviaño, A. Beceiro, C. González-Bello, A. Oliver, J. Arca-Suárez, G. Bou, Selection of AmpC β-Lactamase Variants and Metallo-β-Lactamases Leading to Ceftolozane/Tazobactam and Ceftazidime/Avibactam Resistance during Treatment of MDR/XDR Pseudomonas aeruginosa Infections, Antimicrob Agents Chemother 66(2) (2022) e0206721.
[90] A. Iovleva, M.M. Mustapha, M.P. Griffith, L. Komarow, C. Luterbach, D.R. Evans, E. Cober, S.S. Richter, K. Rydell, C.A. Arias, J.T. Jacob, R.A. Salata, M.J. Satlin, D. Wong, R.A. Bonomo, D. van Duin, V.S. Cooper, D. Van Tyne, Y. Doi, Carbapenem-Resistant Acinetobacter baumannii in U.S. Hospitals: Diversification of Circulating Lineages and Antimicrobial Resistance, mBio 13(2) (2022) e0275921.
[91] G. Nayak, B. Behera, S. Mohanty, P. Kar, J. Jena, Analysis of In Vitro Activity of Cefiderocol Against Carbapenem-Resistant Gram-Negative Bacilli by Broth Microdilution and Disk Diffusion Method: A Single-Center Study in Odisha, India, Infection and drug resistance 15 (2022) 5887-5897.
[92] R.A. Ramadan, A.M. Bedawy, E.M. Negm, T.H. Hassan, D.A. Ibrahim, S.M. ElSheikh, R.M. Amer, Carbapenem-Resistant Klebsiella pneumoniae Among Patients with Ventilator-Associated Pneumonia: Evaluation of Antibiotic Combinations and Susceptibility to New Antibiotics, Infection and drug resistance 15 (2022) 3537-3548.
[93] I. Galani, V. Papoutsaki, I. Karaiskos, N. Moustakas, L. Galani, S. Maraki, V.E. Mavromanolaki, O. Legga, K. Fountoulis, E.D. Platsouka, P. Giannopoulou, H. Papadogeorgaki, M. Damala, E. Chinou, A. Pasxali, I. Deliolanis, H. Vagiakou, E. Petinaki, A. Chli, E. Vagdatli, P. Kazila, V. Papaioannou, K. Kontopoulou, A.N. Ferke, E. Moraitou, A. Antoniadou, H. Giamarellou, In vitro activities of omadacycline, eravacycline, cefiderocol, apramycin, and comparator antibiotics against Acinetobacter baumannii causing bloodstream infections in Greece, 2020-2021: a multicenter study, European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology 42(7) (2023) 843-852.
[94] M. Marner, L. Kolberg, J. Horst, N. Böhringer, J. Hübner, I.D.M. Kresna, Y. Liu, U. Mettal, L. Wang, M. Meyer-Bühn, S. Mihajlovic, M. Kappler, T.F. Schäberle, U. von Both, Antimicrobial Activity of Ceftazidime-Avibactam, Ceftolozane-Tazobactam, Cefiderocol, and Novel Darobactin Analogs against Multidrug-Resistant Pseudomonas aeruginosa Isolates from Pediatric and Adolescent Cystic Fibrosis Patients, Microbiology spectrum 11(1) (2023) e0443722.
[95] O.K. Ozyurt, P. Tufanoglu, O. Cetinkaya, B. Ozhak, H. Yazisiz, G. Ongut, O. Turhan, D. Ogunc, In vitro Activity of Cefiderocol and Ceftazidime-Avibactam, Against Carbapenemase-Producing Enterobacterales, Clinical laboratory 69(1) (2023).
[96] Karpova E.V., T. D.V., Activity of Cefiderocol and Other New Antibiotics Against Extensively Drug-Resistant Klebsiella pneumoniae Strains. , Antibiotics and Chemotherapy. 67(11) (2022) 16-21.

[97] C. Weber, T. Schultze, S. Göttig, J. Kessel, A. Schröder, M. Tietgen, S. Besier, T. Burbach, S. Häussler, T.A. Wichelhaus, D. Hack, V.A.J. Kempf, M. Hogardt, Antimicrobial Activity of Ceftolozane-Tazobactam, Ceftazidime-Avibactam, and Cefiderocol against Multidrug-Resistant Pseudomonas aeruginosa Recovered at a German University Hospital, Microbiology spectrum 10(5) (2022) e0169722.
[98] Y. Wang, Y. Li, J. Zhao, J. Guan, W. Ni, Z. Gao, Susceptibility of cefiderocol and other antibiotics against carbapenem-resistant, Gram-negative bacteria, Ann Transl Med 10(5) (2022) 261.
[99] N. Kohira, M.A. Hackel, Y. Ishioka, M. Kuroiwa, D.F. Sahm, T. Sato, H. Maki, Y. Yamano, Reduced susceptibility mechanism to cefiderocol, a siderophore cephalosporin, among clinical isolates from a global surveillance programme (SIDERO-WT-2014), Journal of global antimicrobial resistance 22 (2020) 738-741.
[100] T. Sato, A. Ito, Y. Ishioka, S. Matsumoto, M. Rokushima, K.M. Kazmierczak, M. Hackel, D.F. Sahm, Y. Yamano, Escherichia coli strains possessing a four amino acid YRIN insertion in PBP3 identified as part of the SIDERO-WT-2014 surveillance study, JAC-antimicrobial resistance 2(3) (2020) dlaa081.
[101] S. Stracquadanio, E. Torti, C. Longshaw, A.S. Henriksen, S. Stefani, In vitro activity of cefiderocol and comparators against isolates of Gram-negative pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in Italy, Journal of global antimicrobial resistance 25 (2021) 390-398.
[102] E. Cercenado, L. Cardenoso, R. Penin, C. Longshaw, A.S. Henriksen, A. Pascual, In vitro activity of cefiderocol and comparators against isolates of Gram-negative bacterial pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in Spain, Journal of global antimicrobial resistance 26 (2021) 292-300.
[103] T. Naas, G. Lina, A. Santerre Henriksen, C. Longshaw, F. Jehl, In vitro activity of cefiderocol and comparators against isolates of Gram-negative pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in France, JAC-antimicrobial resistance 3(2) (2021) dlab081.
[104] V. Gant, A. Hussain, M. Bain, C. Longshaw, A.S. Henriksen, In vitro activity of cefiderocol and comparators against Gram-negative bacterial isolates from a series of surveillance studies in England: 2014-2018, Journal of global antimicrobial resistance 27 (2021) 1-11.
[105] P. Thelen, A.S. Henriksen, C. Longshaw, Y. Yamano, B. Caldwell, A. Hamprecht, In vitro activity of cefiderocol against Gram-negative bacterial pathogens in Germany, Journal of global antimicrobial resistance 28 (2022) 12-17.
[106] J.A. Karlowsky, A.J. Walkty, M.R. Baxter, H.J. Adam, P.R.S. Lagacé-Wiens, F. Schweizer, D. Bay, J.P. Lynch, 3rd, M.R. Mulvey, G.G. Zhanel, In Vitro Activity of Cefiderocol against Extensively Drug-Resistant Pseudomonas aeruginosa: CANWARD, 2007 to 2019, Microbiology spectrum 10(4) (2022) e0172422.
[107] J.C. Abdul-Mutakabbir, L. Nguyen, P.T. Maassen, K.C. Stamper, R. Kebriaei, K.S. Kaye, M. Castanheira, M.J. Rybak, In Vitro Antibacterial Activity of Cefiderocol against Multidrug-Resistant Acinetobacter baumannii, Antimicrob Agents Chemother 65(9) (2021) e0264620-e0264620.
[108] J.A. Karlowsky, S.H. Lob, K.M. Kazmierczak, S.P. Hawser, S. Magnet, K. Young, M.R. Motyl, D.F. Sahm, In vitro activity of imipenem/relebactam against Gram-negative ESKAPE pathogens isolated in 17 European countries: 2015 SMART surveillance programme, Journal of Antimicrobial Chemotherapy 73(7) (2018) 1872-1879.
[109] K.M. Kazmierczak, P.A. Bradford, G.G. Stone, B.L.M. de Jonge, D.F. Sahm, In Vitro Activity of Ceftazidime-Avibactam and Aztreonam-Avibactam against OXA-48-Carrying Enterobacteriaceae Isolated as Part of the International Network for Optimal Resistance Monitoring (INFORM) Global Surveillance Program from 2012 to 2015, Antimicrobial agents and chemotherapy 62(12) (2018) e00592-18.
[110] G. Bianco, P. Gaibani, S. Comini, M. Boattini, G. Banche, C. Costa, R. Cavallo, P. Nordmann, Synergistic Effect of Clinically Available Beta-Lactamase Inhibitors Combined with Cefiderocol against Carbapenemase-Producing Gram-Negative Organisms, Antibiotics (Basel, Switzerland) 11(12) (2022).

[111] Y. Yamano, M. Takemura, C. Longshaw, R. Echols, 1269. Differences in Interpretative Breakpoints Between CLSI, FDA and EUCAST Impact Reporting of Susceptibility and Resistance to Cefiderocol, Open Forum Infect Dis. 2020 Dec 31;7(Suppl 1):S651. doi: 10.1093/ofid/ofaa439.1453. eCollection 2020 Oct.

TABLES

Table 1. Univariate meta-regression analysis of the associations between study-level characteristics and prevalence of cefiderocol non-susceptible carbapenem-resistant Enterobacterales based on CLSI breakpoints.

Study characteristic	Level	S	Predicted CFDC-NS % (CI)	Odds ratio (CI)	*P* value	R^2
Year	2015-2019	5	5.4 (0.0 - 16.3)	Ref.	0.718	0.9%
	2020-2023	31	3.6 (0.5 - 6.7)	0.66 (0.07 - 6.46)		
Region[1]	EUR	12	3.1 (0.0 - 7.2)	0.72 (0.13 - 3.88)	0.700	6.8%
	AMR	8	1.1 (0.0 - 3.3)	0.21 (0.03 - 1.63)	0.136	
	WPR	6	9.6 (0.0 - 26.2)	3.27 (0.40 - 27.02)	0.272	
	Multi-regional	10	6.1 (0.0 - 15.1)	2.05 (0.33 - 12.64)	0.440	
Multinational	No	30	4.1 (0.5 - 7.7)	Ref.	0.662	1.5%
	Yes	6	2.6 (0.0 - 7.7)	0.61 (0.07 - 5.59)		
Multicenter	No	8	27.9 (0.0 - 57.9)	Ref.	0.001	28.1%
	Yes	28	2.2 (0.3 - 4.1)	0.06 (0.01 - 0.33)		

RoB, population and setting	Moderate/High risk	33	4.3 (0.7 - 7.8)	Ref.	0.337	3.1%
	Low risk	3	1.1 (0.0 - 4.1)	0.25 (0.01 - 4.23)		
RoB, condition measurement	Moderate/High risk	19	3.8 (0.0 - 7.9)	Ref.	0.992	0.0%
	Low risk	17	3.8 (0.0 - 8.2)	1.01 (0.20 - 5.06)		

S, the number of independent data sets in the analysis; CFDC-NS, Cefiderocol non-susceptible; CI, 95% confidence interval; EUR, European region; AMR, Region of the Americas; WPR, Western Pacific Region; RoB, risk of bias.

[1] Region defined by the WHO grouping. The odds ratio for each region compares that region to all other regions combined (e.g. EUR vs.. elsewhere).

FIGURE CAPTIONS

Figure 2. Summary forest plot of cefiderocol non-susceptibility against Enterobacterales

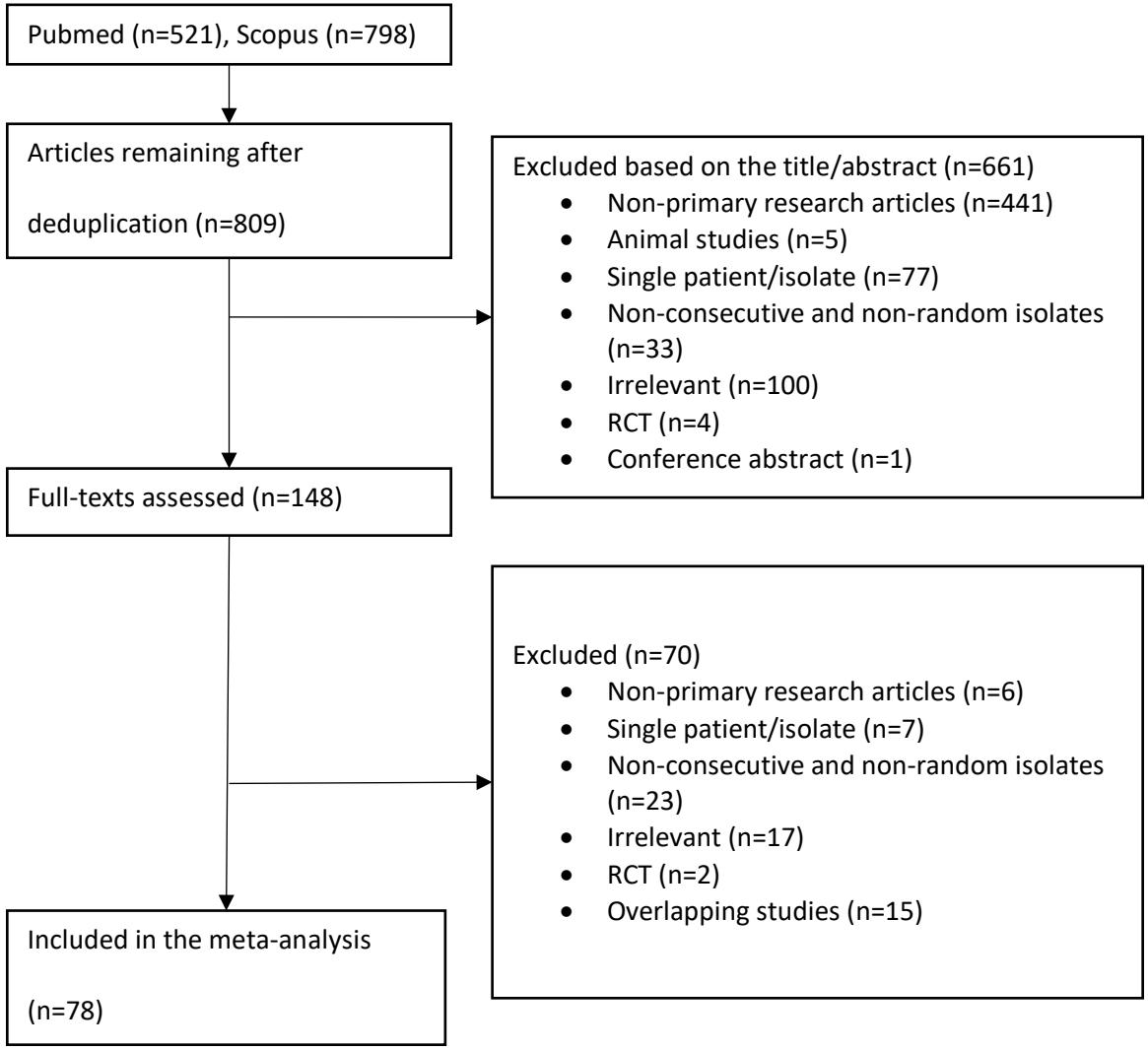
S is the number of independent sets of data in the analysis. **n / N** is the ratio of the cumulative number of isolates that were non-susceptible to cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. The centre of the diamond is the population-averaged (pooled estimate) prevalence of CFDC-NS isolates. The length of the diamond indicates the 95% confidence interval (**CI**) for the pooled estimate. The horizontal thick lines extending from the diamond represent the 95% prediction interval (**PI**) for the prevalence of CFDC-NS isolates in new studies. **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**, ceftolozane/tazobactam

Figure 3. Summary forest plot of cefiderocol non-susceptibility against *P. aeruginosa*

S is the number of independent sets of data in the analysis. **n / N** is the ratio of the cumulative number of isolates that were non-susceptible to Cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. The centre of the diamond is the population-averaged (pooled estimate) prevalence of CFDC-NS isolates. The length of the diamond indicates the 95% confidence interval (**CI**) for the pooled estimate. The horizontal thick lines extending from the diamond represent the 95% prediction interval (**PI**) for the prevalence of CFDC-NS isolates

836 in new studies. **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**,
837 ceftolozane/tazobactam
838
839 **Figure 4.** Summary forest plot of cefiderocol non-susceptibility against *A. baumannii*
840 **S** is the number of independent sets of data in the analysis. **n / N** is the ratio of the cumulative number of isolates that were non-susceptible to Cefiderocol
841 (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. The centre of the diamond is
842 the population-averaged (pooled estimate) prevalence of CFDC-NS isolates. The length of the diamond indicates the 95% confidence interval (**CI**) for the
843 pooled estimate. The horizontal thick lines extending from the diamond represent the 95% prediction interval (**PI**) for the prevalence of CFDC-NS isolates
844 in new studies. **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**,
845 ceftolozane/tazobactam
846

847 **Figure 1. Flow chart of the review**



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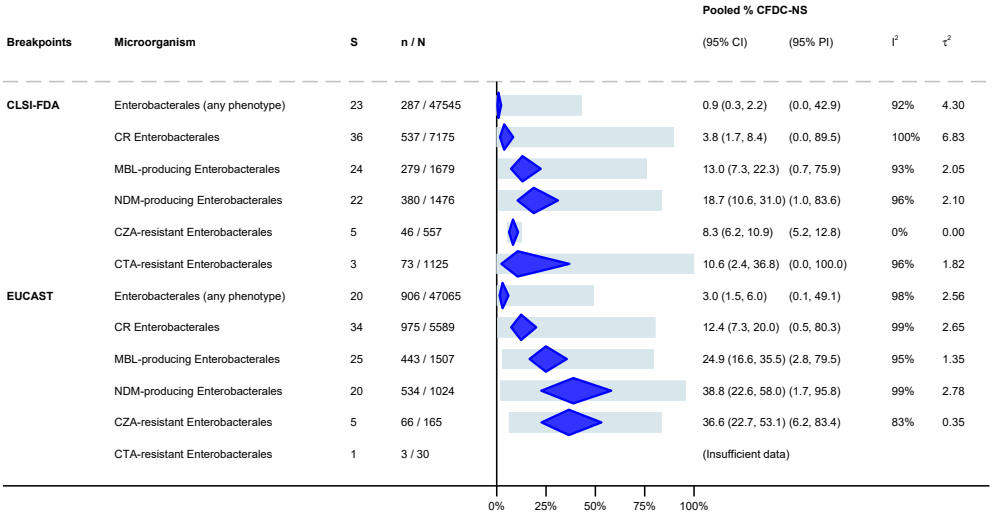
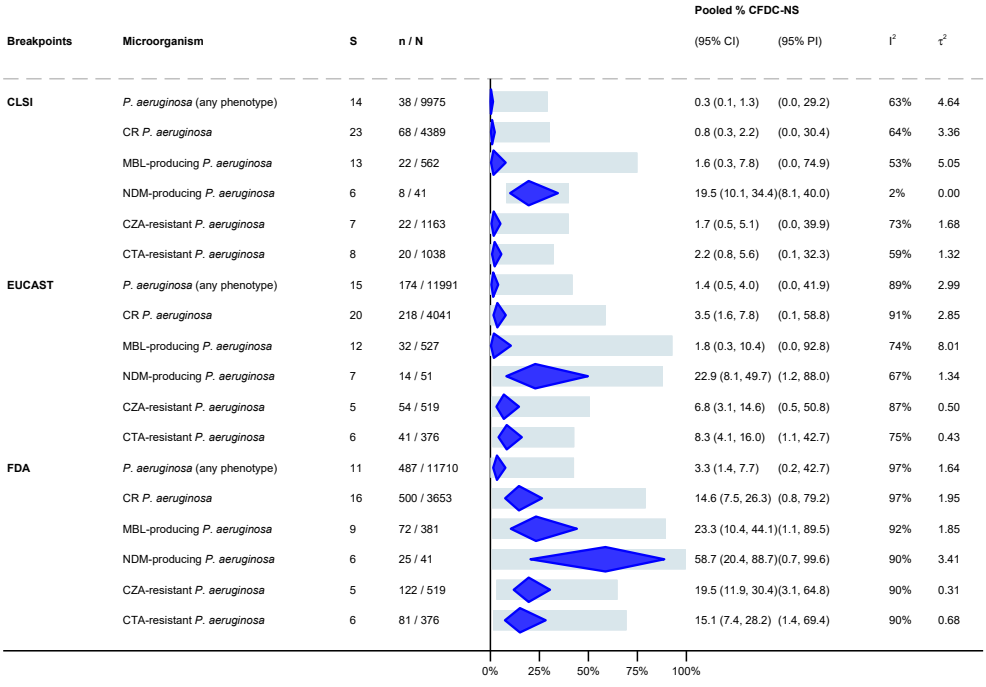
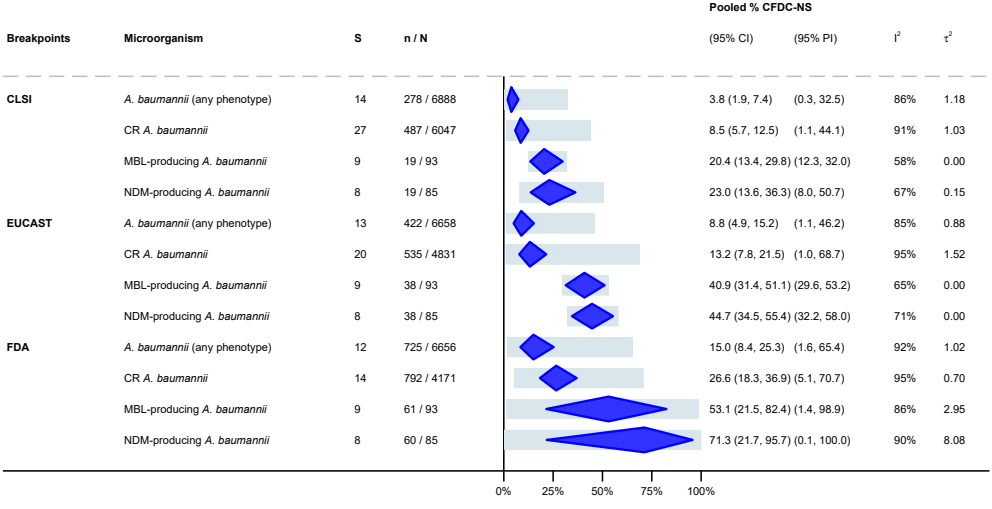

Pooled % CFDC-NS
Breakpoints
Microorganism
S
n / N
(95% CI)
(95% PI)
I²
τ²
CLSI-FDA
Enterobacterales (any phenotype) 23 287 / 47545 0.9 (0.3, 2.2) (0.0, 42.9) 92% 4.30
CR Enterobacterales 36 537 / 7175 3.8 (1.7, 8.4) (0.0, 89.5) 100% 6.83
MBL-producing Enterobacterales 24 279 / 1679 13.0 (7.3, 22.3) (0.7, 75.9) 93% 2.05
NDM-producing Enterobacterales 22 380 / 1476 18.7 (10.6, 31.0) (1.0, 83.6) 96% 2.10
CZA-resistant Enterobacterales 5 46 / 557 8.3 (6.2, 10.9) (5.2, 12.8) 0% 0.00
CTA-resistant Enterobacterales 3 73 / 1125 10.6 (2.4, 36.8) (0.0, 100.0) 96% 1.82
EUCAST
Enterobacterales (any phenotype) 20 906 / 47065 3.0 (1.5, 6.0) (0.1, 49.1) 98% 2.56
CR Enterobacterales 34 975 / 5589 12.4 (7.3, 20.0) (0.5, 80.3) 99% 2.65
MBL-producing Enterobacterales 25 443 / 1507 24.9 (16.6, 35.5) (2.8, 79.5) 95% 1.35
NDM-producing Enterobacterales 20 534 / 1024 38.8 (22.6, 58.0) (1.7, 95.8) 99% 2.78
CZA-resistant Enterobacterales 5 66 / 165 36.6 (22.7, 53.1) (6.2, 83.4) 83% 0.35
CTA-resistant Enterobacterales 1 3 / 30 (Insufficient data)
0%
25%
50%
75%
100%


Pooled % CFDC-NS
Breakpoints
Microorganism
S
n / N
(95% CI)
(95% PI)
I²
τ²
CLSI
P. aeruginosa (any phenotype) 14 38 / 9975 0.3 (0.1, 1.3) (0.0, 29.2) 63% 4.64
CR P. aeruginosa 23 68 / 4389 0.8 (0.3, 2.2) (0.0, 30.4) 64% 3.36
MBL-producing P. aeruginosa 13 22 / 562 1.6 (0.3, 7.8) (0.0, 74.9) 53% 5.05
NDM-producing P. aeruginosa 6 8 / 41 19.5 (10.1, 34.4) (8.1, 40.0) 2% 0.00
CZA-resistant P. aeruginosa 7 22 / 1163 1.7 (0.5, 5.1) (0.0, 39.9) 73% 1.68
CTA-resistant P. aeruginosa 8 20 / 1038 2.2 (0.8, 5.6) (0.1, 32.3) 59% 1.32
EUCAST
P. aeruginosa (any phenotype) 15 174 / 11991 1.4 (0.5, 4.0) (0.0, 41.9) 89% 2.99
CR P. aeruginosa 20 218 / 4041 3.5 (1.6, 7.8) (0.1, 58.8) 91% 2.85
MBL-producing P. aeruginosa 12 32 / 527 1.8 (0.3, 10.4) (0.0, 92.8) 74% 8.01
NDM-producing P. aeruginosa 7 14 / 51 22.9 (8.1, 49.7) (1.2, 88.0) 67% 1.34
CZA-resistant P. aeruginosa 5 54 / 519 6.8 (3.1, 14.6) (0.5, 50.8) 87% 0.50
CTA-resistant P. aeruginosa 6 41 / 376 8.3 (4.1, 16.0) (1.1, 42.7) 75% 0.43
FDA
P. aeruginosa (any phenotype) 11 487 / 11710 3.3 (1.4, 7.7) (0.2, 42.7) 97% 1.64
CR P. aeruginosa 16 500 / 3653 14.6 (7.5, 26.3) (0.8, 79.2) 97% 1.95
MBL-producing P. aeruginosa 9 72 / 381 23.3 (10.4, 44.1) (1.1, 89.5) 92% 1.85
NDM-producing P. aeruginosa 6 25 / 41 58.7 (20.4, 88.7) (0.7, 99.6) 90% 3.41
CZA-resistant P. aeruginosa 5 122 / 519 19.5 (11.9, 30.4) (3.1, 64.8) 90% 0.31
CTA-resistant P. aeruginosa 6 81 / 376 15.1 (7.4, 28.2) (1.4, 69.4) 90% 0.68
0%
25%
50%
75%
100%


Pooled % CFDC-NS
Breakpoints
Microorganism
S
n / N
(95% CI)
(95% PI)
I²
τ²
CLSI
A. baumannii (any phenotype) 14 278 / 6888 3.8 (1.9, 7.4) (0.3, 32.5) 86% 1.18
CR A. baumannii 27 487 / 6047 8.5 (5.7, 12.5) (1.1, 44.1) 91% 1.03
MBL-producing A. baumannii 9 19 / 93 20.4 (13.4, 29.8) (12.3, 32.0) 58% 0.00
NDM-producing A. baumannii 8 19 / 85 23.0 (13.6, 36.3) (8.0, 50.7) 67% 0.15
EUCAST
A. baumannii (any phenotype) 13 422 / 6658 8.8 (4.9, 15.2) (1.1, 46.2) 85% 0.88
CR A. baumannii 20 535 / 4831 13.2 (7.8, 21.5) (1.0, 68.7) 95% 1.52
MBL-producing A. baumannii 9 38 / 93 40.9 (31.4, 51.1) (29.6, 53.2) 65% 0.00
NDM-producing A. baumannii 8 38 / 85 44.7 (34.5, 55.4) (32.2, 58.0) 71% 0.00
FDA
A. baumannii (any phenotype) 12 725 / 6656 15.0 (8.4, 25.3) (1.6, 65.4) 92% 1.02
CR A. baumannii 14 792 / 4171 26.6 (18.3, 36.9) (5.1, 70.7) 95% 0.70
MBL-producing A. baumannii 9 61 / 93 53.1 (21.5, 82.4) (1.4, 98.9) 86% 2.95
NDM-producing A. baumannii 8 60 / 85 71.3 (21.7, 95.7) (0.1, 100.0) 90% 8.08
0%
25%
50%
75%
100%

Supplementary material

Global prevalence of cefiderocol non-susceptibility in Enterobacterales, *P. aeruginosa*, *A. baumannii* and *S. maltophilia*: a systematic review and meta-analysis

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Abbreviations

EUCAST	European Committee on Antimicrobial Susceptibility Testing
CAR	carbapenem
CLSI	Clinical and Laboratory Standards Institute
CTA	ceftolozane/tazobactam
CZA	ceftazidime/avibactam
MBL	metallo-β lactamase
NDM	New Delhi metallo-β lactamase,

1 Breakpoints for cefiderocol by FDA, CLSI and EUCAST

	FDA [1]				CLSI [2]				EUCAST [3]				
	MIC (mg/L)		Zone diameter in disk diffusion (mm)		MIC (mg/L)		Zone diameter in disk diffusion (mm)		MIC (mg/L)		Zone diameter in disk diffusion (mm)		
	S ≤	R >	S ≥	R <	S ≤	R >	S ≥	R <	S ≤	R >	S ≥	R <	ATU
Enterobacterales	4	8*	16	9*	4	8*	16	12*	2	2	22	22	18-22
P .aeruginosa	1	2*	22	13*	4	8*	18	13*	2	2	22	22	14-22
A. baumannii	1	2*	19	11*	4	8*	15	11*	2[#]	2[#]	17[#]	ND[#]	ND
S. maltophilia	ND	ND	ND	ND	1	1[$]	17	13*	2[#]	2[#]	20[#]	ND[#]	ND

Abbreviations: **ATU**= area of technical uncertainty, **ND**= not defined, **R**= resistant, **S**= susceptible

* MICs or diameters between the S and R breakpoints are defined as intermediate.

[#] Not species related PK/PD breakpoints proposed by EUCAST [3] and disk correlates [4]

[$] CLSI susceptibility breakpoint for *S. maltophilia* have been recently modified to ≤1 mg/L.

In studies reporting only one set of criteria susceptibility percentages for other breakpoint criteria were inferred based on MIC distribution data when available or reported MIC ranges (when maximum MIC was below the susceptibility breakpoint a 0% non-susceptibility was inferred). Below are 3 examples to further clarify this approach:

In the study of "Falagas ME, 2017", the breakpoints were not defined. However, based on reported MIC ranges for *P. aeruginosa* (≤0.03–1), all *P. aeruginosa* isolates were susceptible to cefiderocol according to all three breakpoint cutoffs (CLSI, EUCAST, FDA). On the contrary, based on reported MIC ranges for *K. pneumoniae* (≤0.03–4) only susceptibility based on CLSI breakpoints (susceptible if MIC≤4mg/L) was estimable (0% non-susceptible), while susceptibility based on EUCAST breakpoints (MIC≤2mg/L) could not be estimated (>0% to 10% non-susceptible based on max MIC 4mg/L and MIC90 1mg/L). In the study "Wang Y 2022" cefiderocol susceptibility was evaluated based on CLSI breakpoints (susceptible if MIC≤4mg/L). Nevertheless, MIC ranges were also reported. For example, cefiderocol's MIC range against CR *K. pneumoniae* was <0.03 to 2mg/L. Therefore, all CR *K. pneumoniae* isolates were also susceptible by EUCAST breakpoints (MIC≤2mg/L). On the contrary, in the study "Jacobs MR, 2018", also applying CLSI breakpoints, the MIC range for Enterobacterales was ≤0.03 to >64mg/L and detailed MIC distribution data

were not available. Therefore, susceptibility proportion based on EUCAST breakpoints was not estimable in this study (but >10% based on MIC90 4mg/L). In other words, in studies using CLSI breakpoints and not reporting detailed MIC distribution data, cefiderocol susceptibility proportion based on EUCAST breakpoints was estimable only when 100%.

2 Tool for risk of bias assessment

Domains/items assessed	Risk of bias assessment
Domain 1: Population and setting	**Low risk of bias**: Answer is "Yes" to at least 3 of 4 items **Moderate/high risk of bias**: Answer is "No" or "Unclear" to 2 or more items
○ Were study participants sampled in an appropriate way?	**Yes:** Inclusion of all consecutive isolates (as eligible per study inclusion criteria) or random sample of all consecutive isolates, and exclusion of duplicates (same pathogen isolated >1 time from the same patient) **No**: Convenience sampling or inclusion of duplicates **Unclear**: Above information not clearly reported
○ Was the sample size adequate?	**Yes**: Study has conducted a sample size calculation. If a sample size calculation was not provided a sample size was considered adequate if >1000 for each pathogen of interest (hypothesizing a prevalence of resistance of 1% ± 0.5%) **No:** Study does not report any sample size calculation and sample size (for each pathogen of interest) was less than 1000.
○ Were the study subjects and the setting described in detail?	**Yes:** Clear description of the characteristics of the study population, including patients' age, setting (inpatients/outpatient/mixed), type of inpatients (ICU/non-IUC/mixed), antimicrobial resistance phenotype included (any/carbapenem-resistant/MDR/XDR/PDR), origin of the infection (healthcare-onset, community-onset) **No**: Any of the above information missing/ not clearly reported
○ Was the data analysis conducted with sufficient coverage of the identified sample?	**Yes**: No missing data on susceptibility to antimicrobials of interest or missing data unlikely to introduce coverage bias **No:** Missing data on susceptibility to antimicrobials of interest likely to introduce coverage bias (e.g. selective rather than universal susceptibility testing to antimicrobial of interest)
Domain 2: Condition measurement (susceptibility testing method) *	**Low risk of bias**: Answer is "Yes" to both items **Moderate/high risk of bias**: Answer is "No" or "Unclear" to either of the 2 items
○ Were valid methods used for the identification of the condition?	• Yes: BMD in iron-depleted cation-adjusted Mueller-Hinton broth or the Sensititer lyophilized BMD panel • No: Disk diffusion or gradient strip (acceptable, but less preferrable methods [5])
○ Was the condition measured in a standard, reliable way for all participants?	• Yes: Clear definition of how trailing (BMD) or colonies within zone (disk diffusion) were interpreted (or appropriate citations of the correct method). • No: Lack of reporting of the above
Overall risk of bias assessment	**Low risk**: Study at low risk of bias in both domains **Moderate/high risk**: Study at moderate/high risk of bias in either domain

Tool adapted from the Joann-Briggs tool for quality assessment of prevalence studies [6, 7].
BMD= broth microdilution

* Studies referencing CLSI guidelines, EUCAST guidance [8] or prior publications describing the correct methodology for assessing susceptibility of cefiderocol [9-11] were considered at low risk of bias.

3 Characteristics of included studies

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Alzayer M, 2023 [12] **set 1**	Surveillance study	Saudi Arabia (NA)	2015-2019	• Moderate/high • Moderate/high • Moderate/high	• *K. pneumoniae* • *E. coli* • CR *K. pneumoniae* • CR *E. coli*	• Breakpoints: CLSI, MIC distributions available • CR not defined. Isolates selected based on production of VIM/NDM/KPC or OXA-48-like
Alzayer M, 2023 [12] **set 2**	Surveillance study	Saudi Arabia (NA)	2018-2019	• Moderate/high • Moderate/high • Moderate/high	• CR *A. baumannii* • CR *P. aeruginosa*	• MIC distributions available • CR not defined
Bakthavatchalam YD, 2023 [13]	Descriptive cohort	India (1)	2020-2022	• Moderate/high • Moderate/High • Moderate/high	• NDM E.coli	• Breakpoints: CLSI, MIC distribution available • NDM *E.coli* co-harbouring a PBP3 insert
Bianco G, 2023 [14]	Descriptive cohort	Italy (3)	2019-2022	• Moderate/high • Low risk • Moderate/high	• CP Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: EUCAST
Cañada-García JE, 2023 [15]	Descriptive cohort	Spain (5)	2020-2021	• Moderate/high • Moderate/High • Moderate/high	• CP *K. pneumoniae*	• Breakpoints: EUCAST

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Galani I, 2023 [16]	Descriptive cohort	Greece (19)	2020-2021	• Moderate/high • Moderate/High • Moderate/high	• CR *A. baumannii*	• Breakpoints: CLSI, EUCAST. Distribution of inhibition zones available. • 98.9% of isolates had MEM MIC≥4 mg/L
Devoos L, 2023 [17]	Descriptive cohort	France (78)	2015-2022	• Moderate/high • Low risk • Moderate/high	• MDR CR *P. aeruginosa*	• Breakpoints: EUCAST, MIC distribution available • *P. aeruginosa* resistant to ceftazidime (MIC > 8 mg/L), imipenem (MIC> 4 mg/L) and ceftolozane/tazobactam (MIC> 4/4 mg/L)
Huang YS, 2023 [18]	Descriptive cohort	Taiwan (1)	2016-2021	• Moderate/high • Low risk • Moderate/high	• MBL-producing CR Enterobacterales	• Breakpoints: CLSI. EUCAST non-susceptibility estimated based on Figure 1A. • CR= MEM MIC≥4 mg/L. Dual carbapenemase isolates excluded.
Ihssane B, 2023 [19]	Surveillance study	Morocco (NA)	2021	• Moderate/high • Moderate/high • Moderate/high	• MBL *P. aeruginosa*	• Breakpoints: EUCAST (exact MICs reported) • Isolates selected based on co-harboring NDM-VIM or VIM-IMP MBLs

First author, publication year	**Study type**	**Countries (number of institutions)**	**Period of isolate collection**	**Risk of bias assessment:** • **Overall** • **population and setting** • **condition measurement**	**Susceptibility data for;**	**Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates**
Kohira N, 2023 [20]	Surveillance study	China (5)	2020	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: EUCAST + CLSI • CR= MEM non-susceptible based on CLSI
Lasarte-Monterrubio C, 2023 [21]	Descriptive cohort	Spain (NA)	NA	• Moderate/high • Moderate/high • Moderate/high	• CP E. cloacae	• Breakpoints: EUCAST, MIC distribution available
Le Terrier C, 2023 [22]	Surveillance	Switzerland (NA)	NA	• Moderate/high • Low risk • Moderate/high	• MBL Enterobacterales • MBL *P. aeruginosa*	• Breakpoints: EUCAST, MIC distribution available
Maraki S, 2023 [23]	Descriptive cohort	Greece (1)	2021	• Low risk • Low risk • Low risk	• CP *K. pneumoniae*	• Breakpoints: EUCAST • CR= CP *K. pneumoniae*. All were also resistant to IMI and MEM.
Marner M, 2023 [24]	Descriptive cohort	Germany (1)	2006-2018	• Moderate/high • Moderate/high • Moderate/high	• MDR *P. aeruginosa*	• Breakpoints: EUCAST. MIC distribution available. • MDR= resistant to the lead compounds of 3 or 4 of the following antibiotic classes: acyl ureidopenicillins (piperacillin or piperacillin-tazobactam), third- or

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
						fourth-generation cephalosporins (ceftazidime and cefepime), fluoroquinolones (ciprofloxacin), and carbapenems (meropenem and imipenem)
Padovani M, 2023 [25]	Descriptive cohort	Italy (1)	2021-2022	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: EUCAST
Pérez-Palacios P, 2023 [26]	Descriptive cohort	Morocco (1)	2019	• Low risk • Moderate/high • Moderate/high	• MDR Enterobacterales (all *K. pneumoniae* or *E. hormaechei*)	• Breakpoints: EUCAST. • MDR= "resistance to at least three families of antibiotics compared to the wild-type phenotype" • CR if MEM MIC>8mg/L
Potter RF, 2023 [27]	Descriptive cohort	USA (1)	2018-2020	• Moderate/high • Moderate/high • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI, EUCAST, FDA

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Ruedas-López A, 2023 [28]	Descriptive cohort	Spain (1)	2020	• Low risk • Moderate/high • Moderate/high	• CTA-resistant, CZA-resistant *P. aeruginosa*	• Breakpoints: MIC distribution available.
Sewunet T, 2023 [29]	Descriptive cohort	Ethiopia (1)	2016	• Low risk • Moderate/high • Moderate/high	• CZA/MEM-resistant *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: EUCAST • CR= MEM MIC>8mg/L
Tamma PD, 2023 [30]	Descriptive cohort	USA (3)	2016-2021	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales	• Breakpoints: CLSI • CR= resistant to at least 1 carbapenem or carrying at least 1 carbapenemase gene
Xu J, 2023 [31]	Descriptive cohort	China (1)	2016-2017	• Moderate/high • Moderate/high • Moderate/high	• NDM CR *E. coli*	• Breakpoints: CLSI, MIC distribution available
Badran SG, 2022 [32]	Descriptive cohort	Egypt (1)	2021	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales • MBL Enterobacterales	• Breakpoints: CLSI (only resistance proportion reported, non-susceptibility data not available) • CR defined as resistance (by disk diffusion) to any of MEM, IMP, DOR, ETP
Ballesté-Delpierre C, 2022 [33]	Surveillance study	Argentina, Azerbaijan,	NA	• Moderate/high • Moderate/high	• *A. baumannii*	• Breakpoints: CLSI, MIC distribution available

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
		Croatia, Greece, Italy, Morocco, Mozambique, Peru, Spain (NA)		• Moderate/high		• CR defined as MEM MIC>8 mg/L
Bonnin RA, 2022 [5]	Descriptive cohort	France (NA)	2021	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales	• Breakpoints: EUCAST, MIC distribution available • CR= MEM>8mg/L
Cañada-García JE, 2022 [34]	Descriptive cohort	Spain (62)	2019-2019	• Moderate/high • Moderate/High • Moderate/high	• CP *E. coli* and *K. pneumoniae*	• Breakpoints: EUCAST
Candel FJ, 2022 [35]	Surveillance study (SIDERO-WT*)	Europe (145)	2013-2018	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii*	• Breakpoints: EUCAST • CR defined as MEM MIC>8 mg/L
Di Pilato V, 2022 [36]	Descriptive cohort	Italy (11)	2018-2019	• Moderate/high • Moderate/high • Moderate/high	• NDM-1 producing *K. pneumoniae*	• Breakpoints: EUCAST, MIC distribution available
Daoud L, 2022[37]	Descriptive cohort	United Arab Emirates (3)	NA	• Moderate/high • Moderate/high • Moderate/high	• *K. pneumoniae*	• Breakpoints: CLSI, MIC distribution available • CR= MEM MIC>8mg/L
Iovleva A, 2022 [38]	Descriptive cohort	USA (23)	2017-2018	• Low risk • Moderate/high • Moderate/high	• CR *A. baumannii*	• Breakpoints: CLSI • CR= MEM or IMI MIC ≥4mg/L
Karlowsky JA, 2022 [39]	Surveillance study	USA, Canada, Europe (205)	2014-2019	• Low risk • Low risk	• Enterobacterales • *P. aeruginosa*	• Breakpoints: CLSI, MIC distribution available

First author, publication year	**Study type**	**Countries (number of institutions)**	**Period of isolate collection**	**Risk of bias assessment:** • **Overall** • **population and setting** • **condition measurement**	**Susceptibility data for;**	**Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates**
	(SIDERO-WT*)			• Low risk	• *A. baumannii* • *S. maltophilia*	• MEM-nonsusceptible (MIC ≥2 mg/L)
Karlowsky JA, 2022 [40]	Surveillance study (CANWARD)	Canada (NA)	2007	• Moderate/high • Low risk • Moderate/high	• MDR/XDR *P. aeruginosa*	• Breakpoints: CLSI, MIC distribution available • MDR/XDR or not susceptible to any of the antipseudomonal agents tested. • CR=meronement non-susceptible by CLSI 2022
Karpova EV, 2022 [41]	Descriptive cohort	Russia	2016-2021	• Moderate/high • Moderate/high • Moderate/high	• XDR *K. pneumoniae*	• Breakpoints: EUCAST
Lan P, 2022 [42]	Descriptive cohort	China (15)	2018-2020	• Low risk • Low risk • Low risk	• CR *K. pneumoniae*	• Breakpoints: CLSI, MIC distribution available • CR not defined
Lasarte-Monterrubio C, 2022 [43]	Descriptive cohort	Spain (3)	NA	• Moderate/high • Moderate/high • Moderate/high	• CZA-R and CTA-R *P. aeruginosa*	• Breakpoints: EUCAST, MIC distribution available • CZA-R and CTA-R *P. aeruginosa* following cephalosporin treatment

First author, publication year	**Study type**	**Countries (number of institutions)**	**Period of isolate collection**	**Risk of bias assessment:** • **Overall** • **population and setting** • **condition measurement**	**Susceptibility data for;**	**Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates**
Mİrza HC, 2022 [44]	Descriptive cohort	Turkey (1)	2014-2018	• Moderate/high • Moderate/high • Moderate/high	• *CR P. aeruginosa*	• Breakpoints: EUCAST and CLSI • CR= IMI-resistant by CLSI and EUCAST
Morroni G, 2022 [45]	Descriptive cohort	Italy (1)	2018-2019	• Low risk • Low risk • Low risk	• CTA-R *P. aeruginosa*	• Breakpoints: EUCAST, MIC distribution available
Nayak G, 2022 [46]	Descriptive cohort	India (1)	2020-2021	• Moderate/high • Low risk • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: CLSI, MICI distribution available • CR= resistance to any carbapenem (MEM, IMI, ETP, DOR)
Ramadan RA, 2022 [47]	Descriptive cohort	Egypt (1)	2020-2021	• Low risk • Moderate/high • Moderate/high	• CR *K. pneumoniae*	• Breakpoints: CLSI • CR= non-susceptibility to at least one carbapenem (MEM, IMI, ETP, DOR)
Oueslati S, 2022 [48]	Surveillance study	France, Belgium (NA)	2012-2019	• Moderate/high • Low risk • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: EUCAST, MIC distribution available • CR= carbapenemase-producing or CR by other mechanisms (but CR not-defined)

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Shortridge D, 2022 [49]	Surveillance study (SENTRY)	Europe (35), USA (31)	2020	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI, EUCAST, FDA. CR defined as MEM/IMP MIC>2mg/L
Wang Q, 2022 [50]	Surveillance study (China CRE-Network)	China (48)	2018-2019	• Moderate/high • Low risk • Moderate/high	• CR *E. coli* • CR *K. pneumoniae* • CR *Enterobacter cloacae*	• Breakpoints: CLSI • CR defined as resistance to at least 1 carbapenem or at least 1 carbapenemase production
Wang Y, 2022 [51]	Descriptive cohort	China (4)	2012-2018	• Low risk • Low risk • Low risk	• CR *K. pneumoniae* • CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI • All isolates had MEM and IMP MIC ≥8mg/L
Weber C, 2022 [52]	Descriptive cohort	Germany (1)	2013-2017	• Moderate/high • Moderate/high • Moderate/high	• CR *P. aeruginosa*	• Breakpoints: EUCAST • CR= MDR nonsusceptible for at least piperacillin-tazobactam, ceftazidime, cefepime, imipenem, meropenem, and ciprofloxacin. Species
Zalas-Więcek P, 2022 [53]	Descriptive cohort	Poland (2)	2016-2022	• Moderate/high • Moderate/high • Moderate/high	• MDR *E. coli*	• Breakpoints: EUCAST, MIC distribution available

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Zhang Q, 2022 [54]	Descriptive cohort	USA (14)	2011-2018	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales	• Breakpoints: CLSI, MIC distribution available • CR defined as NS to at least 1 carbapenem (based on CLSI breakpoints)
Abdul-Mutakabbir JC, 2021 [55]	Surveillance study	USA (1)	NA	• Moderate/high • Low risk • Moderate/high	• CR *A. baumannii*	• Breakpoints: CLSI • CR not defined (all isolates had MEM MIC >4mg/L)
Albano M, 2021 [56]	Surveillance studies	USA, Canada, Singapore (NA)	NA	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI, MIC distribution available • Isolates selected for cefiderocol-resistance were excluded
Bhagwat SS, 2021 [57]	Surveillance study	Greece (15)	2014-2018	• Moderate/high • Moderate/high • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii*	• Breakpoints: EUCST, FDA • CR defined as MEM MIC >8 mg/L and IMP MIC>4 mg/L
Carcione D, 2021 [58]	Surveillance study	Italy (1)	2020-2021	• Moderate/high • Moderate/high • Moderate/high	• CR *A. baumannii*	• Breakpoints: EUCAST, MIC distribution available • 17 of 20 isolates had MEM MIC>8mg/ml. Included only in the

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
						CR/CNS/CP subgroup meta-analysis
Choby JE, 2021 [59]	Surveillance study (Georgia EIP)	USA (NA)	Different ranges per pathogen	• Moderate/high • Moderate/high • Moderate high	• CR *Klebsiella* spp (2011-2015) • CR *P. aeruginosa* (2015-2016) • CR *A. baumannii* (2012-2015) • *S. maltophilia* (2018-2021)	• Breakpoints: CLSI • CR not defined
Ghebremedhin B, 2021 [60]	Surveillance studies	Germany (1)	2014-2021	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: EUCAST, MIC distribution available • CR not defined
Jacob A, 2021 [61]	Descriptive cohort	Belgium (1)	2015-2020	• Moderate/high • Moderate/high • Moderate/high	• Enterobacterales	• Breakpoints: EUCAST, CLSI, FDA • Selected for OXA-427 production
Johnston BD, 2021, [62]	Descriptive cohort	USA (1)	2012-2017	• Moderate/high • Moderate/high • Moderate/high	• ESBL *E. coli*	• Breakpoints: EUCAST, MIC distribution data available
Lee YL, 2021 [63]	Surveillance (SMART)	Taiwan (16)	2017-2020	• Moderate/high • Low risk • Moderate/high	• *E. coli* • *K. pneumoniae*	• Breakpoints: CLSI, MIC distribution available • For the CR subgroup in the meta-analysis only

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
						the CP isolates were considered
Liu PY, 2021 [64]	Surveillance study (SMART)	Taiwan (16)	2018-2020	• Moderate/high • Low • Moderate/high	• CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: CLSI • IMP MIC >2 mg/dl
Morris CP, 2021 [4]	Descriptive cohort	USA (1)	2017	• Moderate/high • Low • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI, EUCAST • ETP MIC ≥ 2mg/dl for Enterobacterales • MEM MIC ≥ 8mg/dl for *P. aeruginosa* and *A baumannii*.
Biagi M, 2020 [65]	Surveillance study (SENTRY)	Multinational (detailed data not available)	2017-2018	• Moderate/high • Low • Moderate/high	• *S. maltophilia*	• Breakpoints: CLSI
Delgado-Valverde, 2020 [66]	Surveillance (PIRASOA programme)	Spain (27)	2014-2018	• Moderate/high • Low • Moderate/high	• CP *K. pneumoniae* • CP *E. clocae* • CP *P. aeruginosa* • CP-*A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI • ESBL and/or CP isolates selected. 112 of 125 Enterobacterales, all *A.baumannii* and all *P. aeruginosa* were CP
Golden RA, 2020 [67]	Surveillance study (CANWARD)	Canada (14)	2015-2017	• Moderate/high • Low risk • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI, MIC distribution available • CR Enterobacterales and *P. aeruginosa* defined based on

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
						ertapenem- and meropenem non-susceptibility, respectively
Iregui A, 2020 [68], **set 1**	Surveillance study	USA (7)	2017	• Moderate/high • Low • Moderate/high	• *E. coli* • *Enterobacter* spp • *K. pneumoniae*	• Breakpoints: CLSI ("S" if MIC≤4mg/L)
Iregui A, 2020 [68], **set 2**	Surveillance study	USA (7)	2013-2014	• Moderate/high • Low • Moderate/high	• CR *K. pneumoniae* • CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: CLSI ("S" if MIC≤4mg/L) • CR not defined
Iregui A, 2020 [68], **set 3**	Descriptive cohort	USA (NA)	NA	• Moderate/high • Low • Moderate/high	• *K. pneumoniae* • *P. aeruginosa* • *A. baumannii*	• Breakpoints: CLSI ("S" if MIC≤4mg/L). MIC distribution data available. • Isolates well-characterized for presence of b-lactamase and porin/efflux resistance mechanisms
Johnston BD, 2020 [69]	Surveillance study (MDH, SENTRY)	USA, China, India, Taiwan, Philippines, Thailand, Korea, Vietnam, Turkey,	MDH 2009-2017 SENTRY 2003-2017	• Moderate/high • Moderate/high • Moderate/high	• CR *E. coli*	• Breakpoints: EUCAST • "non-susceptible to ≥ 1 carbapenems" (CLSI M100-S27 cited)

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
		Italy, Russia, Spain, UK, Israel, Belarus, Belgium, Germany, Greece, Poland, Chile, Argentina, Brazil, Mexico, Ecuador, Venezuela. (NA)				
Kresken M, 2020 [70], **set 1**	Surveillance study (Paul-Ehrlich society)	Germany (12)	2013-2014	• Low risk • Low risk • Low risk	• Enterobacterales • *P. aeruginosa* • *A. baumannii*	• Breakpoints: EUCAST, MIC distribution available
Kresken M, 2020 [70], **set 2**	Surveillance studies	Germany	2010-2017	• Moderate/high • Low risk • Moderate/high	• CP Enterobacterales • CP *P. aeruginosa* • CP *A. baumannii*	• Breakpoints: EUCAST, MIC distribution available • Isolates selected for carbapenemase production
Longshaw C, 2020 [71]	Surveillance study (SIDERO-CR)	Europe (110); predominantly Italy, Greece, Russia	2014-2016	• Moderate/high • Low risk • Moderate/high	• CP Enterobacterales • CP *P. aeruginosa* • CP *A. baumannii*	• Breakpoints: EUCAST, MIC distribution available • CR defined as MEM MIC ≥2mg/L. Overlap with Hackel MA, 2018 [72].

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
						Useful for MBL data + for EUCAST breakpoints
Mushtaq S, 2020 [73]	Surveillance study (PHE-AMRHAI)	United Kingdom (NA)	2008-2018	• Moderate/high • Moderate/high • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: CLSI, FDA, EUCAST • CR not defined. Isolates selected based on carbapenemase production or CR associated with other mechanisms
Rolston KVI, 2020 [74]		USA (1)	2014-2017	• Moderate/high • Moderate/high • Moderate/high	• Enterobacterales (including ESBL and CR subgroups) • MDR *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI ("S" if MIC≤4mg/L), MIC distribution data available • CR and MDR not defined
Talan DA, 2020 [75]	Descriptive cohort	USA (11)	2018-2019	• Low risk • Moderate/high • Moderate/high	• Enterobacterales	• Breakpoints: CLSI • ESBL
Trebosc V, 2020 [76]	Surveillance study (JMI laboratories)	Europe (144), USA (99), Asia-West Pacific (50)	2017-2019	• Moderate/high • Moderate/high • Moderate/high	• CR *A. baumannii*	• Breakpoints: CLSI • CR not defined (all isolates had MEM MIC>8mg/L)
Xie O, 2020 [77]	Descriptive cohort	Australia (1)	2015-2016	• Low risk • Moderate/high • Moderate/high	• *E. coli*	• Breakpoints: CLSI • ceftriaxone-non-susceptible

First author, publication year	**Study type**	**Countries (number of institutions)**	**Period of isolate collection**	**Risk of bias assessment:** • **Overall** • **population and setting** • **condition measurement**	**Susceptibility data for;**	**Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates**
Hsueh SC, 2019 [78]	Descriptive cohort	Taiwan (1)	2016-2017	• Moderate/high • Low • Moderate/high	• CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI ("S" if MIC≤4mg/L) • IMP MIC ≥ 8mg/dl
Jacobs MR, 2018 [79]	Surveillance (ARGONAUT)	USA (NA)	NA	• Moderate/high • Low • Moderate/high	• Enterobacterales • *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI ("S" if MIC≤4mg/L) • Carbapenem-resistance defined as MEM MIC>1mg/L for Enterobacterales, >2mg/L for *Acinetobacter* and *Pseudomonas*
Hackel MA, 2018 [72]	Surveillance study (IHMA)	24 countries in Europe, 10 countries in Latin America, 2 countries in North America, 8 countries in Asia, 3 countries in South Pacific, 2 countries in Africa, 3 countries in Middle East. (NA)	2014-2016	• Moderate/high • Low • Moderate/high	• CR Enterobacterales • CR *P. aeruginosa* • CR *A. baumannii* • *S. maltophilia*	• Breakpoints: CLSI ("S" if MIC≤4mg/L) • MEM MIC ≥ 2mg/dl for Enterobacterales • MEM MIC ≥ 16 mg/dl for *P. aeruginosa* and *A baumannii*.
Karlowsky JA, 2018 [10], **set 1**	Surveillance study	North America (45); USA, Canada	2015-2016	• Moderate/high • Low risk	• Klebsiella spp • E. coli	• Breakpoints: CLSI

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
	(SIDERO-WT*)			• Moderate/high	• Serratia spp • Enterobacter spp • Citrobacter spp	
Karlowsky JA, 2018 [10], **set 2**	Surveillance study (SIDERO-WT*)	Europe (55)	2015-2016	• Moderate/high • Low risk • Moderate/high	• Klebsiella spp • E. coli • Serratia spp • Enterobacter spp • Citrobacter spp	• Breakpoints: CLSI
Kazmierczak KM 2018 [80]	Surveillance study (SIDERO-WT*)	Canada, United States, Czech Republic, France, Germany, Greece, Hungary, Italy, Russia, Spain, Sweden, Turkey, United Kingdom (99 hospitals total)	2014	• Moderate/high • Low • Moderate/high	• MBL Enterobacterales • MBL *P. aeruginosa* • MBL *A. baumannii*	• Breakpoints: CLSI ("S" if MIC≤4mg/L) • Data extracted only for MBL producers*
Falagas ME, 2017 [81]	Descriptive cohort	Greece (18)	2010-2016	• Moderate/high • Moderate/high • Moderate/high	• CR *K. pneumoniae* • CR *E. cloacae* • CR *P. stuartii* • CR *P. aeruginosa* • CR *A. baumannii*	• Breakpoints: not defined. MIC range, MIC_{50} and MIC_{90} reported. • MEM MIC >1mg/dl for Enterobacterales • MEM MIC > 2mg/dl for *P. aeruginosa* and *A. baumannii*

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Hackel MA, 2017 [11], **set 1**	Surveillance study (SIDERO-WT*)	North America (50); USA, Canada	2014-2015	• Moderate/high • Low risk • Moderate/high	• Klebsiella spp • E. coli • Serratia spp • Enterobacter spp • Citrobacter spp	• Breakpoints: CLSI
Hackel MA, 2017 [11], **set 2**	Surveillance study (SIDERO-WT*)	Europe (49)	2014-2015	• Moderate/high • Low risk • Moderate/high	• Klebsiella spp • E. coli • Serratia spp • Enterobacter spp • Citrobacter spp	• Breakpoints: CLSI
Kanazawa S, 2017 [82]	Surveillance study	Japan (1)	2010-2014	• Moderate/high • Low risk • Moderate/high	• Enterobacterales	• Breakpoints: CLSI, MIC distribution available • IMP-Susceptible (≤1mg/L) but MEM-Resistant (≥4mg/L) blaIMP-6
Ito A, 2016 [83], **set 1**	Descriptive cohort	Worldwide (NA)	2009-2011	• Moderate/high • Moderate/high • Moderate/high	• *P. aeruginosa* • *A. baumannii* • *S. maltophilia*	• Breakpoints: Not defined. MIC distribution data available
Ito A, 2016 [83], **set 2**	Descriptive cohort	Worldwide (NA)	2000-2009	• Moderate/high • Moderate/high • Moderate/high	• *P. aeruginosa* • *A. baumannii*	• Breakpoints: Not defined. MIC distribution data available • "β-lactam-resistant" isolates

First author, publication year	Study type	Countries (number of institutions)	Period of isolate collection	Risk of bias assessment: • Overall • population and setting • condition measurement	Susceptibility data for;	Breakpoints used by the study, availability of MIC distribution data and definition of resistance phenotypes of included isolates
Kohira N, 2016 [84]¸**set 1**	Surveillance study (IHMA)	North America, Europe, Africa, Asia, Latin America, South Pacific, Middle East (NA)	2009-2011	• Moderate/high • Moderate/high • Moderate/high	• *E. coli* • *K pneumoniae* • *S marcescens* • *C freundii* • *E aerogenes* • E cloacae	• Breakpoints: Not defined • CR defined as meropenem MIC>4
Kohira N, 2016 [84], **set 2**	Surveillance study (JMI Laboratories)	North America, Europe, Asia-Pacific, and Latin America (NA)	2000-2009	• Moderate/high • Moderate/high • Moderate/high	• *K pneumoniae* • *S marcescens* • *C freundii* • E cloacae	• Breakpoints: Not defined, MIC distribution available • Well-characterized for β-lactamases

Abbreviations: **ARGONAUT**= Antibacterial Resistance Leadership Group [ARLG] Reference Group for the testing of Novel Therapeutics, **CP**= carbapenemase-producing, **CR**= carbapenem-resistant (including carbapenem-nonsusceptible), **DOR**= doripenem **EIP**= Emerging Infections Program, ESBL= extended-spectrum β-lactamase, **ETP**= ertapenem, **IHMA**= International Health Management Associates, **IMP**= imipenem, **MBL**= metallo-β-lactamase producing, **MDH**= Minessota Department of Health, **MEM**= meropenem, **MIC**= minimum inhibitory concentration, **NA**= not available, **NS**= non-susceptible, **PHE-AMRHAI**= Public Health England's Antimicrobial Resistance and Healthcare Associated Infections, **PIRASOA**= Institutional Programme for the Prevention and Control of Healthcare-Associated Infections and Appropriate Use of Antimicrobials (Andalusia), **RCT**= randomized controlled trial, **SMART**= Surveillance of Multicenter Antimicrobial Resistance in Taiwan

* See prior Table for data extracted from each SIDERO-WT publication

4 Summary table of study characteristics

Variable	Statistics[1,2]
Year of publication	
2015-2019	10 (13%)
2020-2023	68 (87%)
Region	
Europe	34 (40%)
Americas	18 (21%)
Western Pacific region	11 (13%)
Other region	10 (11%)
Multiple regions	13 (15%)
Multinational study	20 (24%)
Median number of countries (IQR)	1 (1-1)
Multicentre study	59 (69%)
Median number of hospitals (IQR)	4.5 (1-19)
Age group of patients	
Adults	5 (6%)
All ages	8 (9%)
Pediatric	1 (1%)
Not reported	72 (84%)
Type of patients	
Inpatients	12 (14%)
Outpatients	1 (1%)
Mixed	8 (9%)
Not reported	65 (76%)
Broth microdilution for CFDC susceptibility test	72 (84%)
MIC distribution reported	38 (44%)
Population and setting risk of bias	
Low	12 (14%)
Moderate-to-high	74 (86%)
Condition measurement risk of bias	
Low	40 (47%)
Moderate-to-high	46 (53%)
Overall risk of bias	
Low	5 (6%)
Moderate-to-high	81 (94%)

CFDC= cefiderocol

[1] Summary statistics are median (interquartile range) for continuous variables, and n (%) for categorical variables.

[2] 78 publications contributed 86 independent sets of data. Summary statistics for all variables, except the year of publication, were calculated over the 86 independent sets of data.

5 WHO regions

WHO-regions		Number of independent study sets*	%
Americas		**28**	**33%**
	Only in America	18	26%
	As part of multi-regional study	10**	12%
European region		**43**	**50%**
	Only in Europe	34	28%
	As part of multi-regional study	9**	11%
Western Pacific region		**15**	**17%**
	Only in Western Pacific region	11	13%
	As part of multi-regional study	4	5%
South-East Asia region		**6**	**7%**
	Only in South-East Asia region	2	2%
	As part of multi-regional study	4	5%
Africa		**4**	**5%**
	Only in Africa	1	1%
	As part of multi-regional study	3	4%
Eastern Mediterranean region		**10**	**12%**
	Only in Eastern Mediterranean region	7	8%
	As part of multi-regional study	3	4%
Not reported (multiple regions)		**3**	**4%**
Multiregional		**13 ****	**15%**

* n=78 studies contributing to n=86 independent data sets

**Including n=3 AMR, EUR, n=1 AMR, WPR, n=1 AMR, EUR, WPR, n=1 AMR, EUR, WPR, SEAR, n=1 AMR, EUR, EMR, AFR, n=1 AMR, UR, EMR, SEAR, n=1 AMR, EUR, EMR, SEAR, AFR, n=1 AMR, EUR, WPR, AFR, SEAR, n=3 multiple regions but regions not specified n=3

6 Critical appraisal of risk of bias of reviewed studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	PS	CM	Overall
Abdul-Mutakabbir JC, 2021	U	N	N	Y	Y	Y	MH	L	MH
Albano M (excl IHMA set), 2021	U	N	N	Y	Y	Y	MH	L	MH
Alzayer M, set 1, 2023	Y	N	N	Y	Y	N	MH	MH	MH
Alzayer M, set2, 2023	Y	N	N	Y	Y	N	MH	MH	MH
Badran SG, 2022	U	N	Y	Y	N	N	MH	MH	MH
Bakthavatchalam YD, 2023	U	N	N	Y	N	N	MH	MH	MH
Ballesté-Delpierre C, 2022	U	N	N	N	Y	N	MH	MH	MH
Bhagwat SS, 2021	Y	N	N	Y	Y	N	MH	MH	MH
Biagi M, 2020	U	N	N	Y	Y	Y	MH	L	MH
Bianco G, 2023	U	N	N	Y	Y	Y	MH	L	MH
Bonnin RA, 2022	U	N	N	Y	Y	N	MH	MH	MH
Candel FJ, 2022	Y	N	N	Y	Y	Y	MH	L	MH
Carcione D, 2021	U	N	N	Y	Y	N	MH	MH	MH
Cañada-García JE, 2022	Y	N	N	Y	N	N	MH	MH	MH
Cañada-García JE, 2023	Y	N	N	Y	N	N	MH	MH	MH
Choby JE, 2021	U	N	N	Y	N	Y	MH	MH	MH
Daoud L, 2022	U	N	N	Y	Y	N	MH	MH	MH
Delgado-Valverde M, 2020	U	N	N	Y	Y	Y	MH	L	MH
Devoos L, 2023	U	N	N	Y	Y	Y	MH	L	MH
Di Pilato V, 2022	N	N	Y	Y	N	N	MH	MH	MH
Falagas ME, 2017	Y	N	N	Y	Y	N	MH	MH	MH
Galani I, 2023	Y	N	N	Y	N	N	MH	MH	MH
Ghebremedhin B, 2021	U	N	N	Y	N	N	MH	MH	MH
Golden RA, 2020	U	N	N	Y	Y	Y	MH	L	MH
Hackel MA, 2018	U	N	N	Y	Y	Y	MH	L	MH
Hackel MA, Europe, 2017	U	N	N	Y	Y	Y	MH	L	MH
Hackel MA, North America, 2017	U	N	N	Y	Y	Y	MH	L	MH
Hsueh SC, 2019	U	N	N	Y	Y	Y	MH	L	MH
Huang YS, 2023	Y	N	N	Y	Y	Y	MH	L	MH
Ihssane B, 2023	U	N	N	Y	Y	N	MH	MH	MH
Iovleva A, 2022	Y	N	Y	Y	Y	N	L	MH	MH
Iregui A, set 1, 2020	U	N	N	Y	Y	Y	MH	L	MH
Iregui A, set 2, 2020	U	N	N	Y	Y	Y	MH	L	MH
Iregui A, set 3, 2020	N	N	N	Y	Y	Y	MH	L	MH
Ito A, set 1, 2015	Y	N	N	Y	N	N	MH	MH	MH
Ito A, set 2, 2015	Y	N	N	Y	N	N	MH	MH	MH
Jacob A, 2021	Y	N	N	Y	Y	N	MH	MH	MH
Jacobs MR, 2018	U	N	N	Y	Y	Y	MH	L	MH
Johnston BD, 2020	U	N	N	Y	Y	N	MH	MH	MH
Johnston BD, 2021	Y	N	N	Y	Y	N	MH	MH	MH
Kanazawa S, 2017	U	N	N	Y	Y	Y	MH	L	MH
Karlowsky JA (1), 2022	Y	N	N	Y	Y	Y	MH	L	MH
Karlowsky JA (2), 2022	Y	N	N	Y	Y	Y	MH	L	MH
Karlowsky JA, Europe, 2018	Y	N	N	Y	Y	Y	MH	L	MH
Karlowsky JA, North America, 2018	Y	N	N	Y	Y	Y	MH	L	MH
Karpova EV, 2022	U	N	N	Y	Y	N	MH	MH	MH
Kazmierczak KM, 2019	U	N	N	Y	Y	Y	MH	L	MH
Kohira N, 2023	U	N	N	Y	Y	Y	MH	L	MH
Kohira N, set 1, 2016	Y	N	N	Y	N	N	MH	MH	MH
Kohira N, set 2, 2016	U	N	N	Y	N	N	MH	MH	MH

Kresken M, set 1, 2020	Y	N	Y	Y	Y	Y	L	L	L
Kresken M, set 2, 2020	Y	N	N	Y	Y	Y	MH	L	MH
Lan P, 2022	Y	N	Y	Y	Y	Y	L	L	L
Lasarte-Monterrubio C, 2022	U	N	Y	Y	Y	N	MH	MH	MH
Lasarte-Monterrubio C, 2023	U	N	N	Y	Y	N	MH	MH	MH
Le Terrier C, 2023	U	N	N	Y	Y	Y	MH	L	MH
Lee YL, 2021	U	N	N	Y	Y	Y	MH	L	MH
Liu PY, 2021	U	N	N	Y	Y	Y	MH	L	MH
Longshaw C, 2020	U	N	N	Y	Y	Y	MH	L	MH
Maraki S, 2023	Y	N	Y	Y	Y	Y	L	L	L
Marner M, 2023	U	N	Y	Y	N	Y	MH	MH	MH
Morris CP, 2021	Y	N	N	Y	Y	Y	MH	L	MH
Morroni G, 2022	Y	N	Y	Y	Y	Y	L	L	L
Mushtaq S, 2020	Y	N	N	Y	Y	N	MH	MH	MH
Mİrza HC, 2022	Y	N	N	Y	N	N	MH	MH	MH
Nayak G, 2022	Y	N	N	Y	Y	Y	MH	L	MH
Oueslati S, 2022	U	N	N	Y	Y	Y	MH	L	MH
Ozyurt OK, 2023	U	N	N	Y	N	N	MH	MH	MH
Padovani M, 2023	Y	N	N	Y	Y	Y	MH	L	MH
Potter RF, 2023	U	N	N	Y	Y	N	MH	MH	MH
Pérez-Palacios P, 2023	Y	N	Y	Y	Y	N	L	MH	MH
Ramadan RA, 2022	Y	N	Y	Y	N	N	L	MH	MH
Rolston KVI, 2020	U	N	N	Y	Y	N	MH	MH	MH
Ruedas-López A, 2023	Y	N	Y	Y	Y	N	L	MH	MH
Sewunet T, 2023	Y	N	Y	Y	N	N	L	MH	MH
Shortridge D, 2022	Y	N	N	Y	Y	Y	MH	L	MH
Talan DA, 2020	Y	N	Y	Y	N	N	L	MH	MH
Tamma PD, 2023	Y	N	N	Y	Y	N	MH	MH	MH
Trebosc V, 2020	U	N	N	Y	Y	N	MH	MH	MH
Wang Q, 2022	U	N	N	Y	Y	Y	MH	L	MH
Wang Y, 2022	Y	N	Y	Y	Y	Y	L	L	L
Weber C, 2022	U	N	N	Y	N	N	MH	MH	MH
Xie O, 2020	Y	N	Y	Y	N	N	L	MH	MH
Xu J, 2023	Y	N	N	N	Y	N	MH	MH	MH
Zalas-Więcek P, 2022	U	N	N	Y	N	N	MH	MH	MH
Zhang Q, 2022	U	N	N	Y	Y	N	MH	MH	MH

Notes.

PS, population and setting domain; **CM**, condition measurement domain, **Y/U/N**, yes/unclear/no; **L**; low risk of bias; **MH**, moderate-to-high risk of bias.

Q1: Were study participants sampled in an appropriate way?

Q2: Was the sample size adequate?

Q3: Were the study subjects and the setting described in detail?

Q4: Was the data analysis conducted with sufficient coverage of the identified sample?

Q5: Were valid methods used for the identification of the condition?

Q6: Was the condition measured in a standard, reliable way for all participants?

7 Overview of SIDERO-WT publications

First author, publication year	Study period	Countries-isolates involved	Notes regarding overlap	Included/ excluded in the meta-analysis
Karlowsky, 2022 [39]	2014-2019	Total* all isolates	Overlap with all prior SIDERO-WT publications (but no separate data for different Enterobacterales spp)	Included
Candel FJ, 2022 [35]	2014-2019	Europe all isolates	Overlap with Karlowsky 2022 but additional data for each Enterobacterales spp and from SIDERO-Proteeae	Included in meta-analyses for specific Enterobacterales spp (EUCAST breakpoints)
Thelen P, 2022 [85]	2014-2018	Germany all isolates	Overlap with Karlowsky 2022, Candel 2022, Karlowsky 2018 and Hackel 2017	Excluded
Stracquadanio S, 2021 [86]	2014-2018	Italy all isolates	Overlap with Karlowsky 2022, Candel 2022, Karlowsky 2018 and Hackel 2017	Excluded
Cercenado E, 2021 [87]	2014-2018	Spain all isolates	Overlap with Karlowsky 2022, Candel 2022, Karlowsky 2018 and Hackel 2017	Excluded
Naas T, 2021 [88]	2014-2018	France all isolates	Overlap with Karlowsky 2022, Candel 2022, Karlowsky 2018 and Hackel 2017	Excluded
Gant V, 2021 [89]	2014-2018	England all isolates	Overlap with Karlowsky 2022, Candel 2022, Karlowsky 2018 and Hackel 2017	Excluded
Karlowsky et al 2018 [10]	2015-2016	Total* all isolates	Overlap with Karlowsky	Included in meta-analyses for specific Enterobacterales spp (CLSI breakpoints)
Sato T, 2020 [90]	2014	Total* E. coli isolates with four	Selection of isolates from SIDERO-WT 2014	Excluded

		aminoacid insertion in PBP-3		
Kohira et al 2020 [91]	2014	Total* isolates with cefiderocol MIC>4 mg/L	Subgroup of isolates from SIDERO-WT 2014	Excluded (no data of interest for meta-analysis)
Kazmierczak KM 2018 [80]	2014	Total* carbapenem NS isolates	Subgroup of isolates from SIDERO-WT 2014	Included for meta-analysis of MBL-producers subgroups.
Hackel MA, 2017 [11]	2014-2015	Total*- all isolates	Subroups of isolates reported in Kazmierczak 2018 and Kohira 2020)	Included in meta-analyses for specific Enterobacterales spp (CLSI breakpoints)

Abbreviations: **MIC**= minimum inhibitory concentration, **NS**= non-susceptible

* USA, Canada, Europe (Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Netherlands, Poland, Portugal, Romania, Russia, Serbia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom)

8 Meta-analysis of cefiderocol non-susceptibility in Enterobacterales

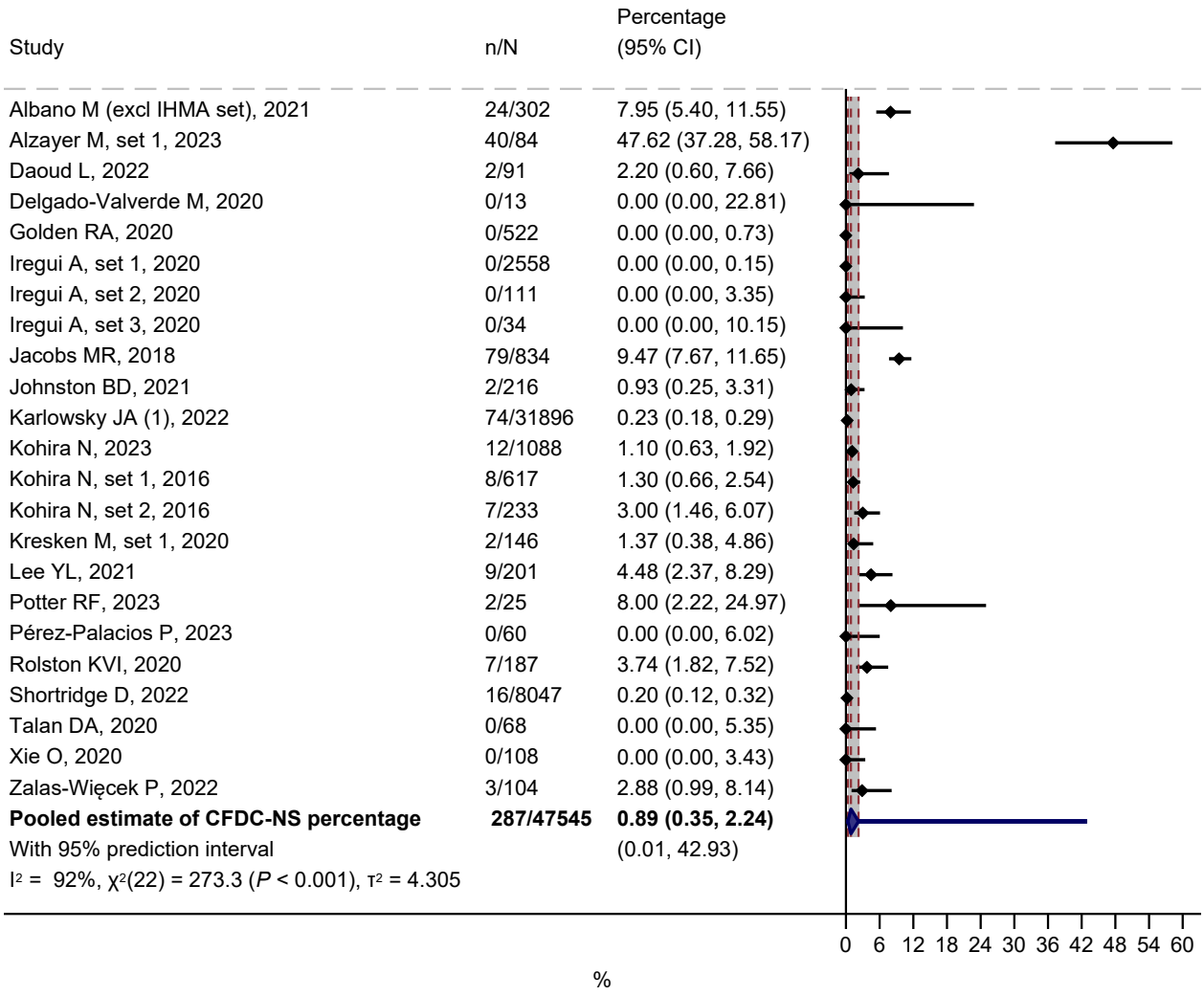
8.1 Summary table

Enterobacterales	Breakpoints	S	n/N	CFDC -NS %	Lower CL, %	Upper CL, %	I^2, %	τ^2	Lower PL, %	Upper PL, %
Any phenotype	CLSI-FDA	23	287/47545	0.9	0.3	2.2	92	4.305	0.0	42.9
	EUCAST	20	906/47065	3.0	1.5	6.0	98	2.561	0.1	49.1
CR	CLSI-FDA	36	537/7175	3.8	1.7	8.4	100	6.827	0.0	89.5
	EUCAST	34	975/5589	12.4	7.3	20.0	99	2.646	0.5	80.3
MBL-producing	CLSI-FDA	24	279/1679	13.0	7.3	22.3	93	2.047	0.7	75.9
	EUCAST	25	443/1507	24.9	16.6	35.5	95	1.347	2.8	79.5
NDM-producing	CLSI-FDA	22	380/1476	18.7	10.6	31.0	96	2.099	1.0	83.6
	EUCAST	20	534/1024	38.8	22.6	58.0	99	2.778	1.7	95.8
CZA-resistant	CLSI-FDA	5	46/557	8.3	6.2	10.9	0	0.000	5.2	12.8
	EUCAST	5	66/165	36.6	22.7	53.1	83	0.345	6.2	83.4
CTA-resistant	CLSI-FDA	3	73/1125	10.6	2.4	36.8	96	1.816	0.0	100.0
	EUCAST	1	3/30	.	.	.	.	.	.	.

S is the number of independent datasets in the analysis (a single study may have contributed more than one sets of data). n/N is the ratio of the cumulative number of Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. CFDC-NS, cefiderocol non-susceptible; CL, 95% confidence limit; PL, 95% prediction limit; CAR, carbapenem; MBL, metallo-β-lactamase; NDM, New Delhi metallo-β-lactamase; CZA, ceftazidime/avibactam; CTA, ceftolozane/tazobactam

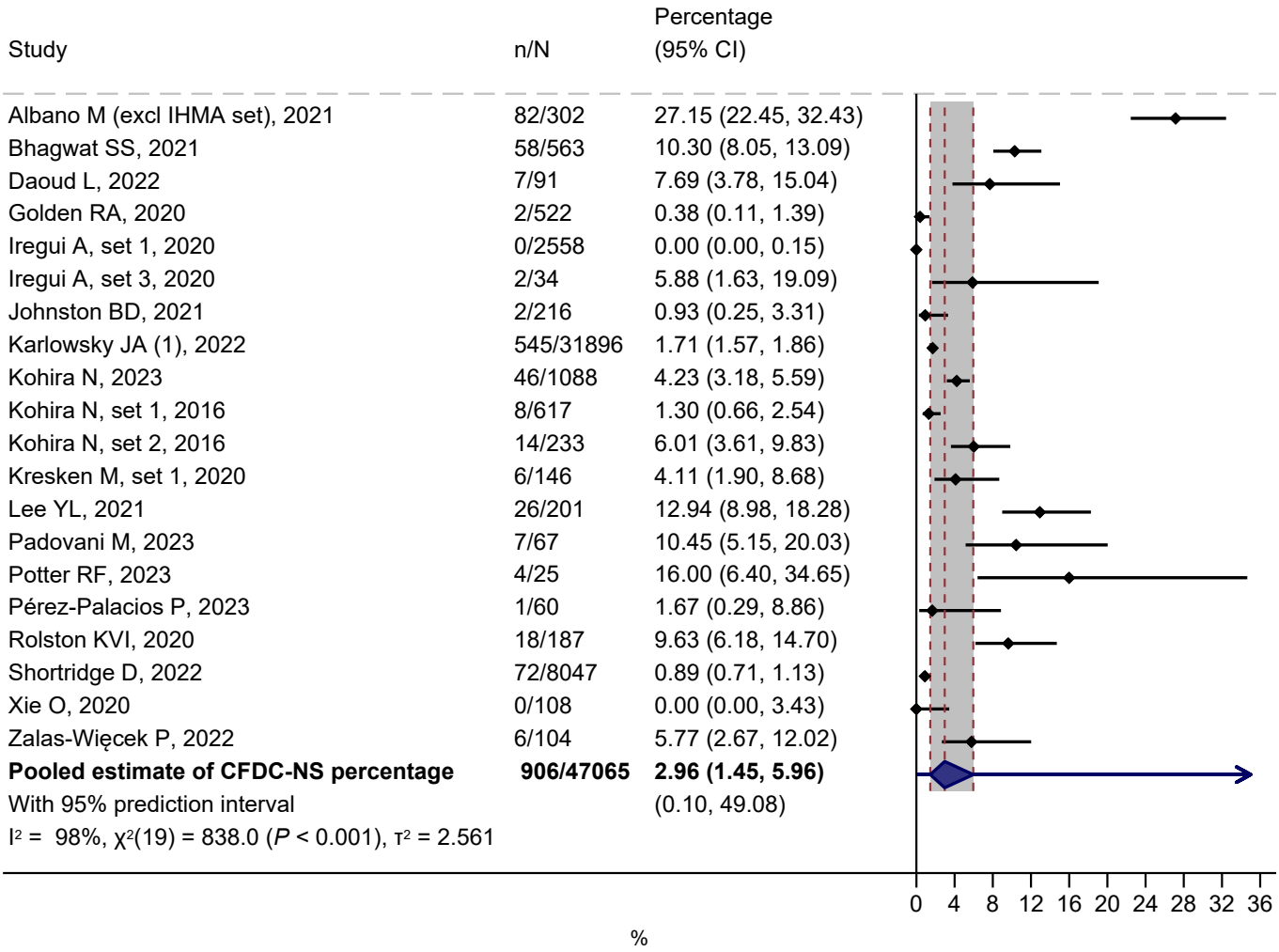
8.2 Forest plots

8.2.1 Enterobacterales, any phenotype; CLSI-FDA



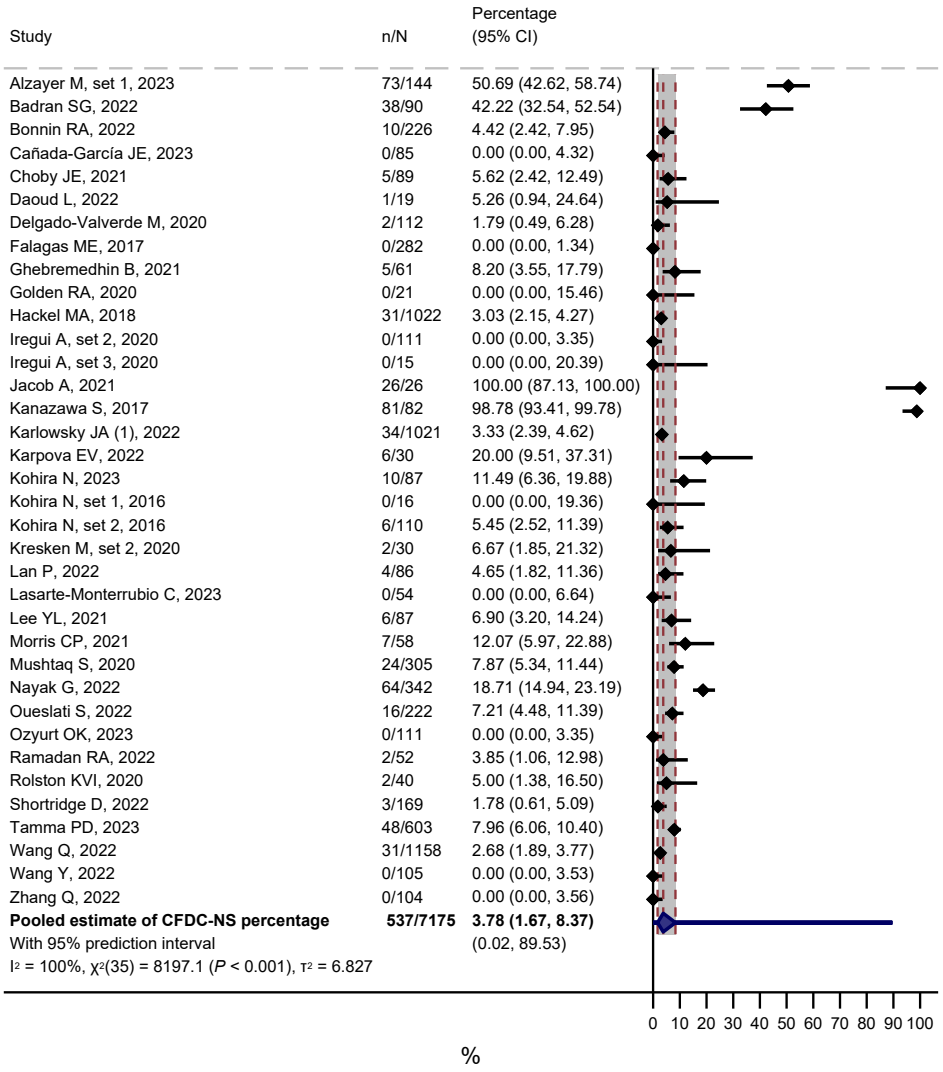
Note. n is the number of Enterobacterales (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of Enterobacterales (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.2 Enterobacterales, any phenotype; EUCAST



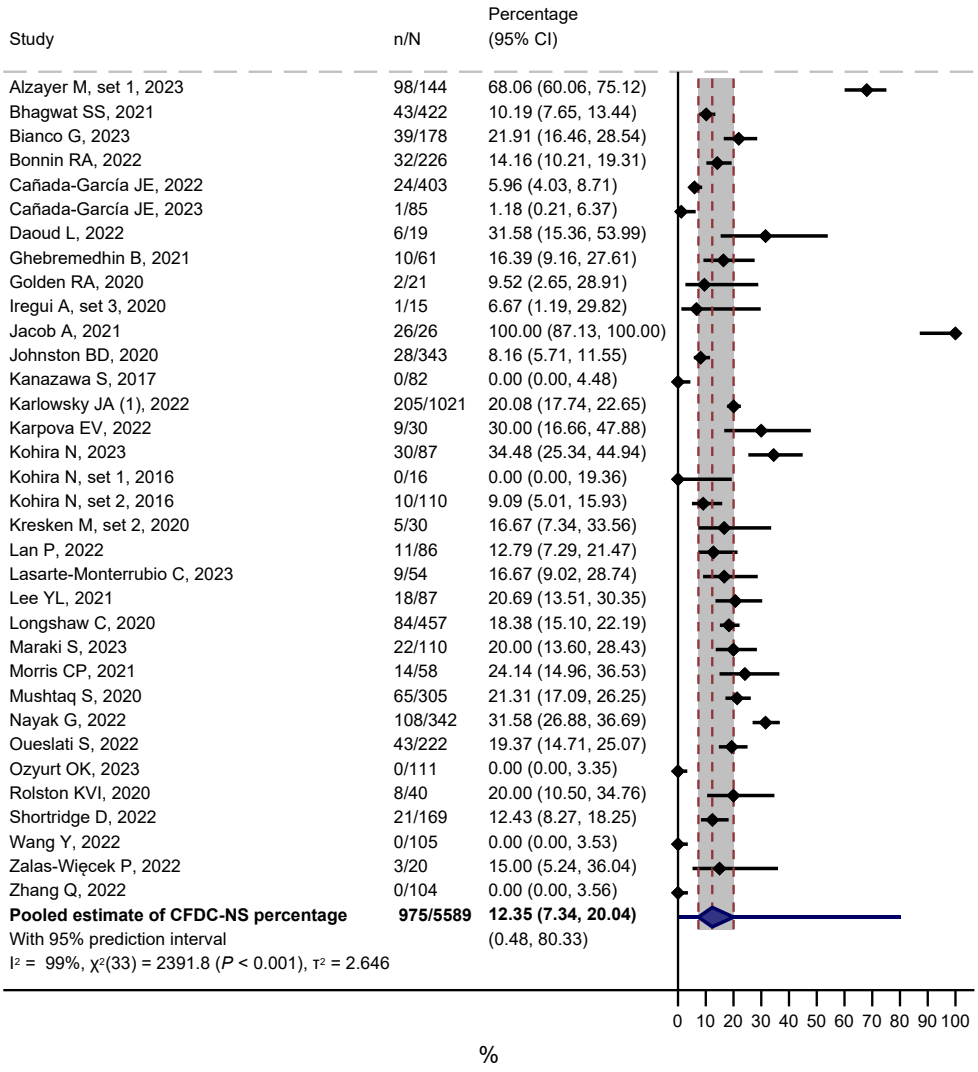
Note. n is the number of Enterobacterales (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of Enterobacterales (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.3 Enterobacterales, carbapenem-resistant; CLSI-FDA



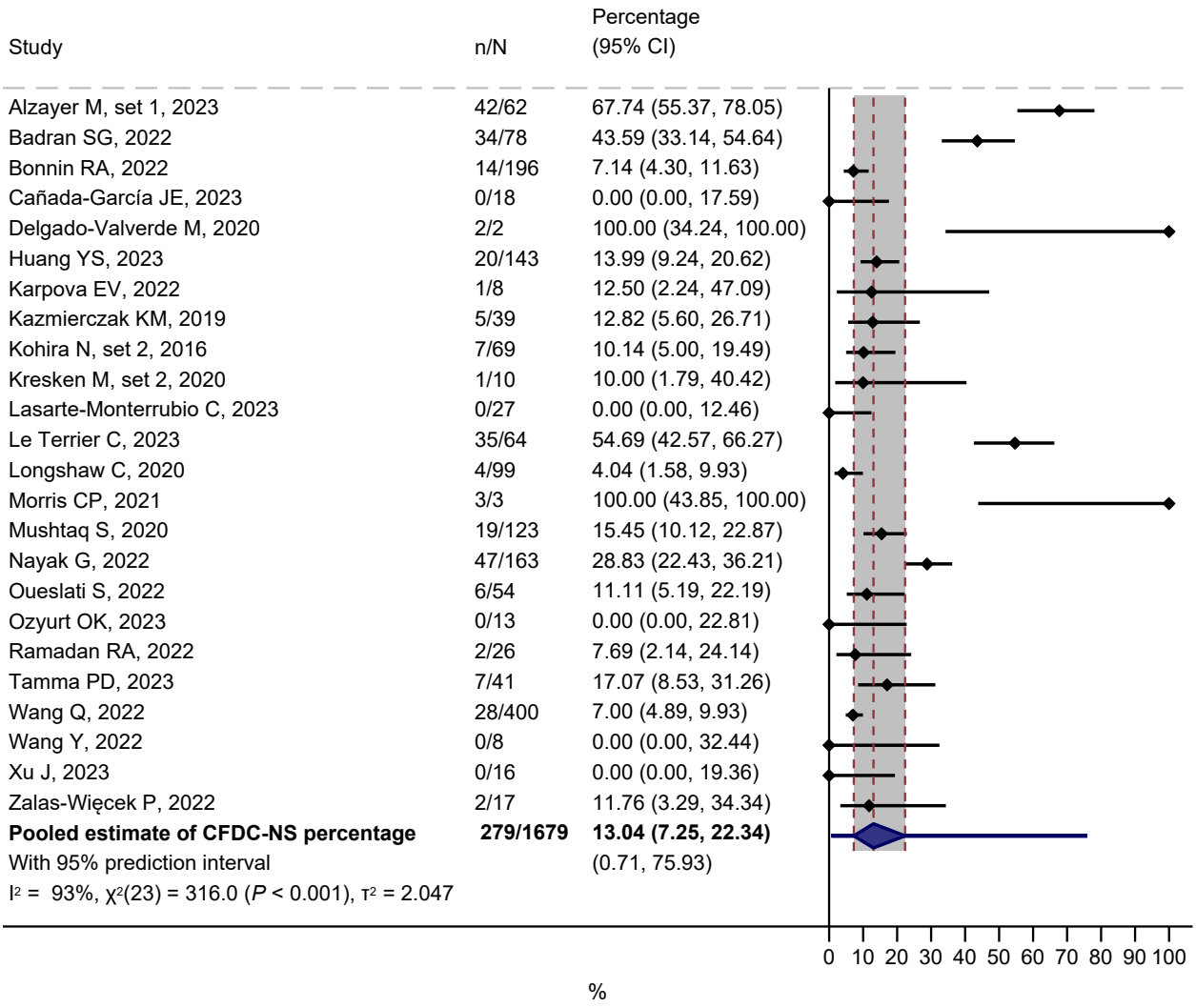
Note. n is the number of CR Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of CR Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.4 Enterobacterales, carbapenem-resistant; EUCAST



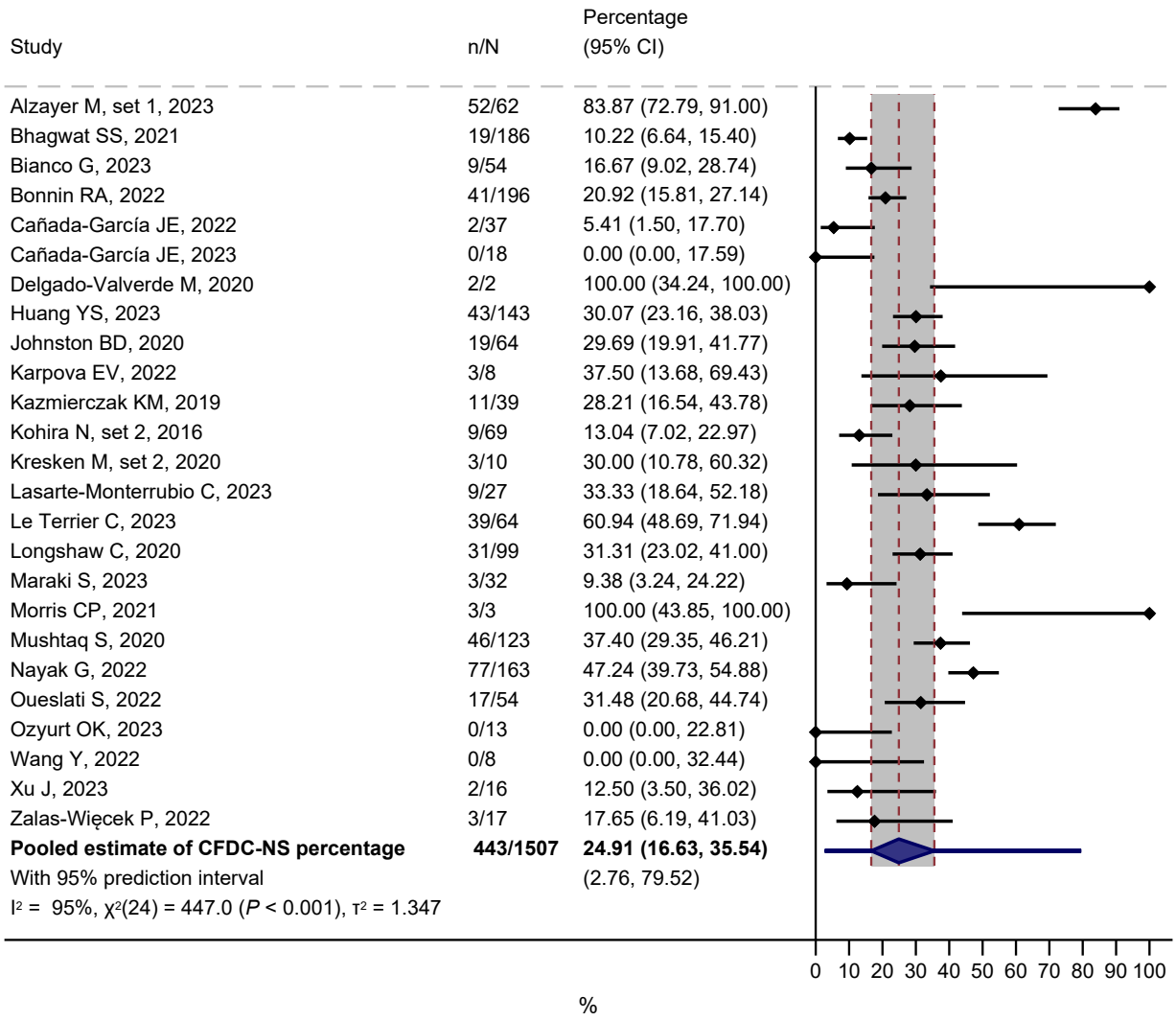
Note. n is the number of CR Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CR Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.5 Enterobacterales, MBL-producing; CLSI-FDA



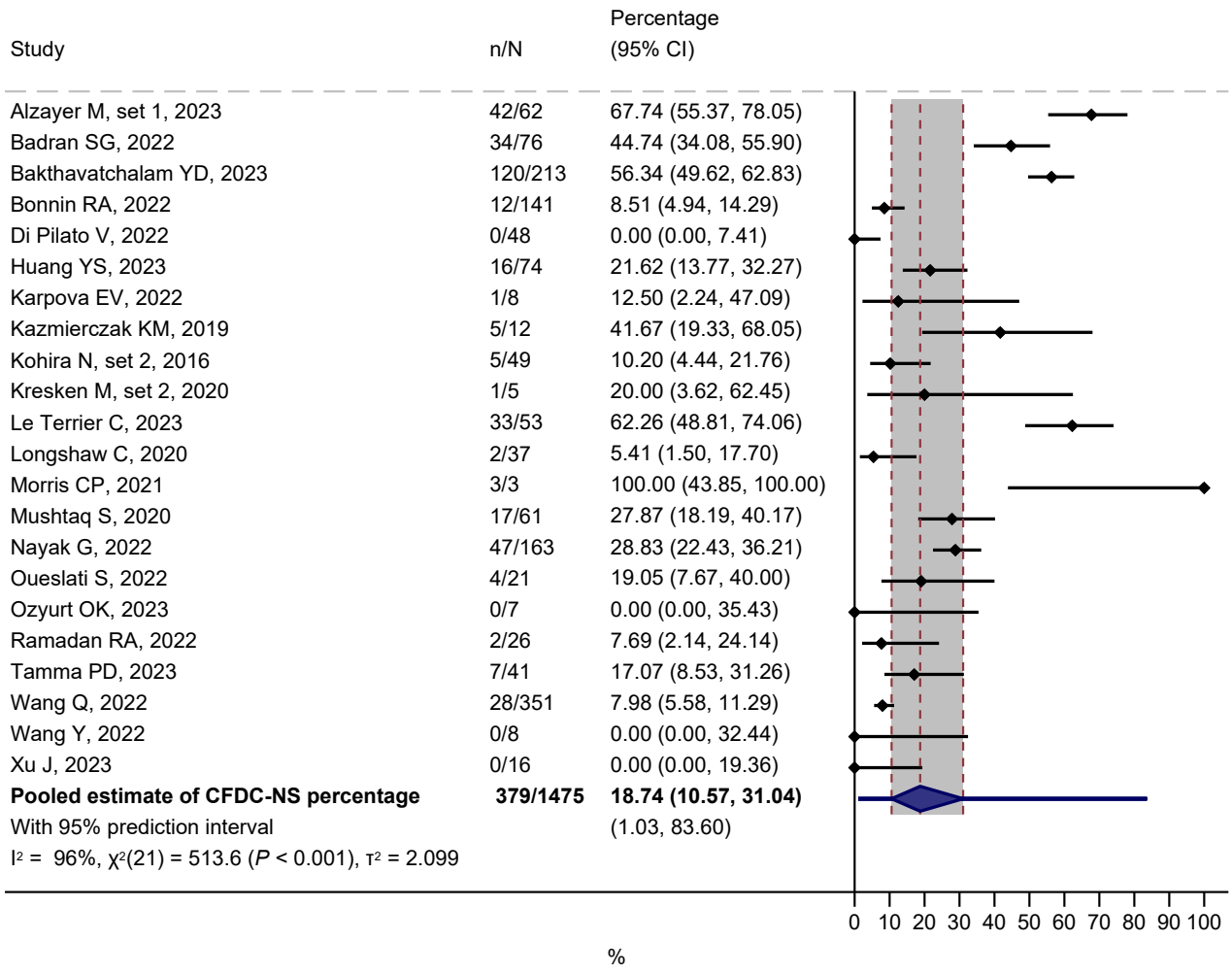
Note. n is the number of MBL-producing Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of MBL-producing Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.6 Enterobacterales, MBL-producing; EUCAST



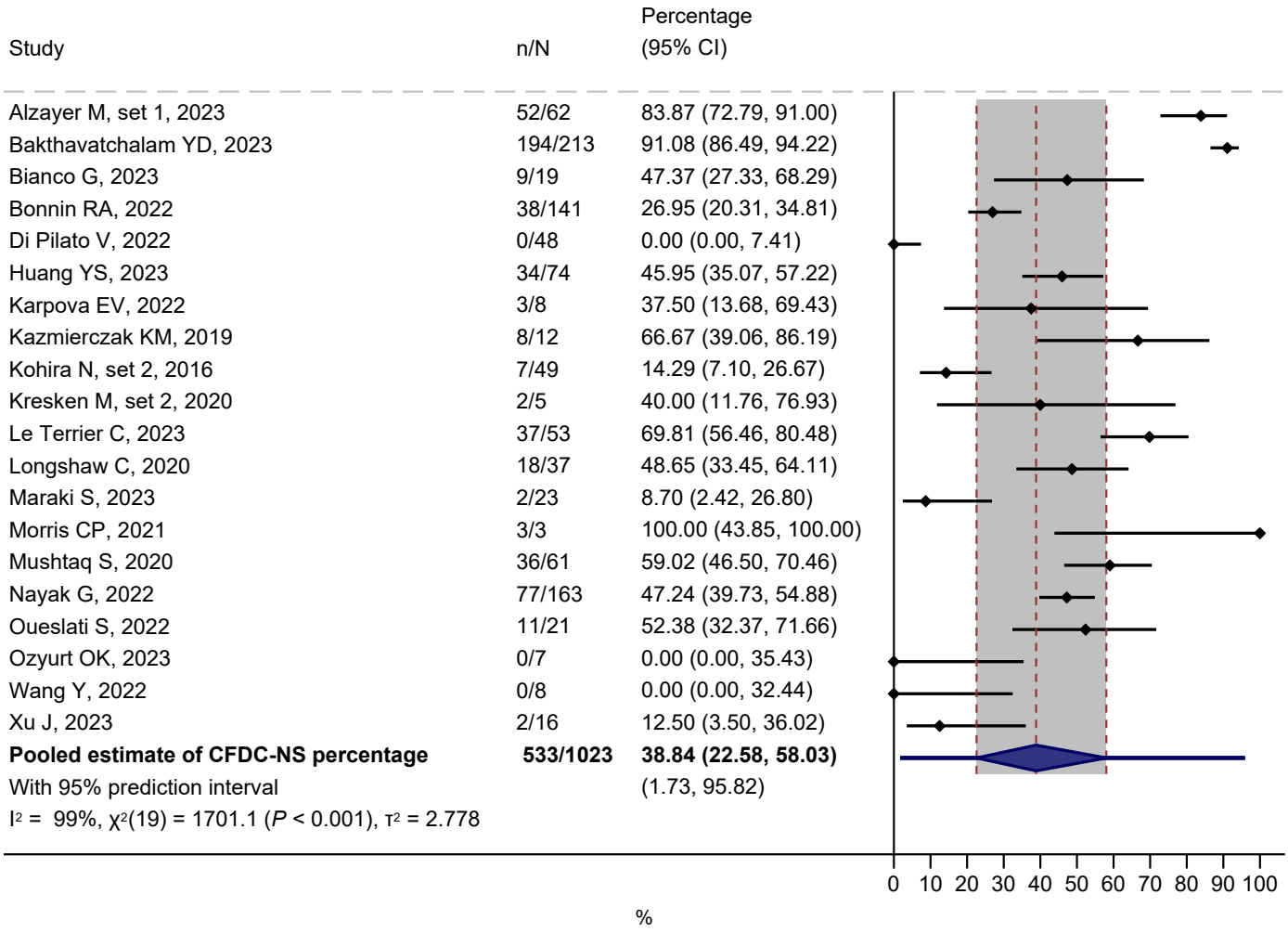
Note. n is the number of MBL-producing Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of MBL-producing Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.7 Enterobacterales, NDM-producing; CLSI-FDA



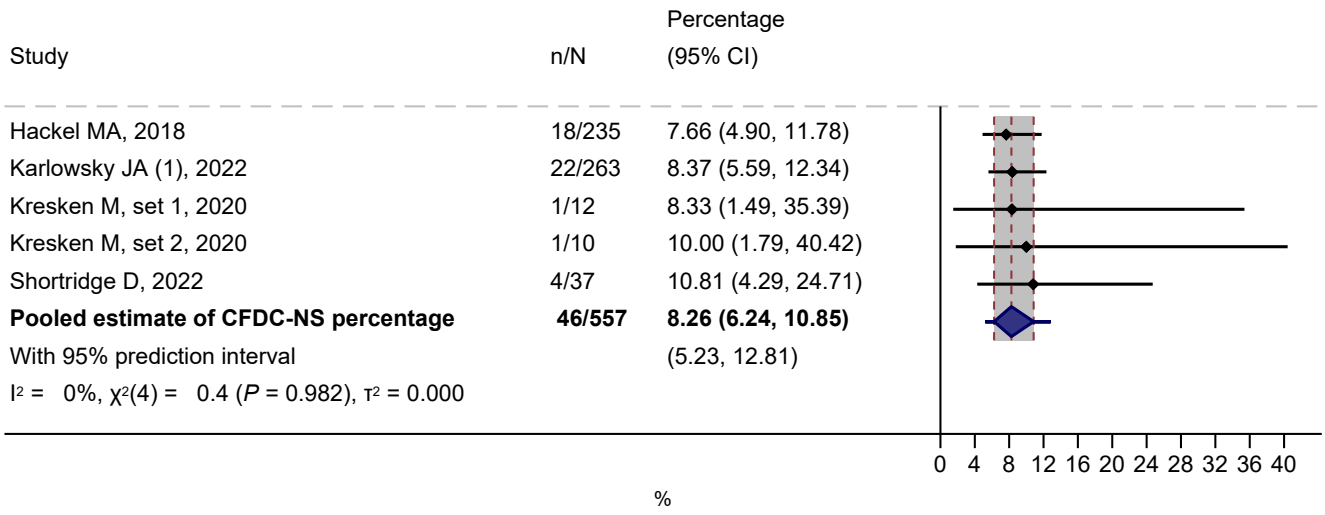
Note. n is the number of NDM-producing Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of NDM-producing Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.8 Enterobacterales, NDM-producing; EUCAST



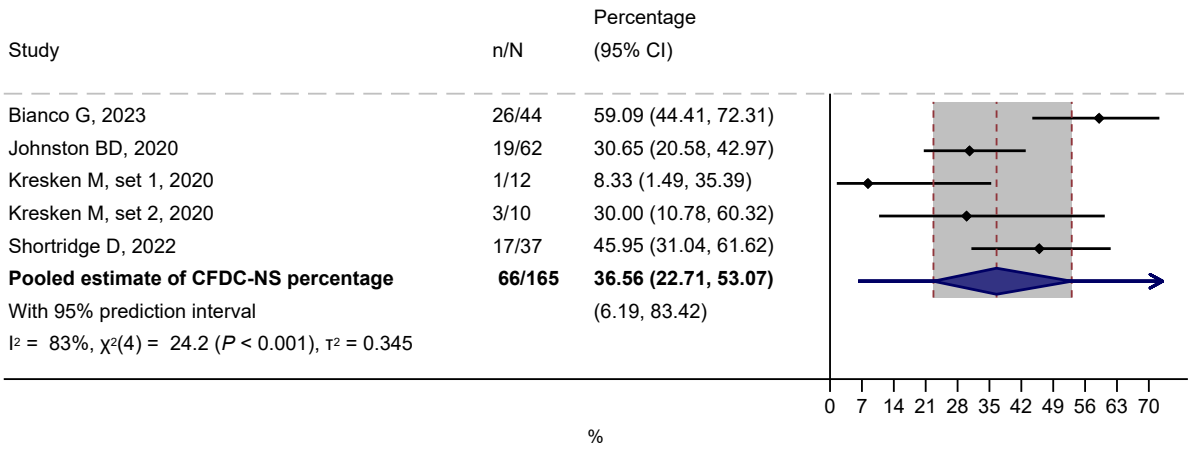
Note. n is the number of NDM-producing Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of NDM-producing Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.9 Enterobacterales, CZA-resistant; CLSI-FDA



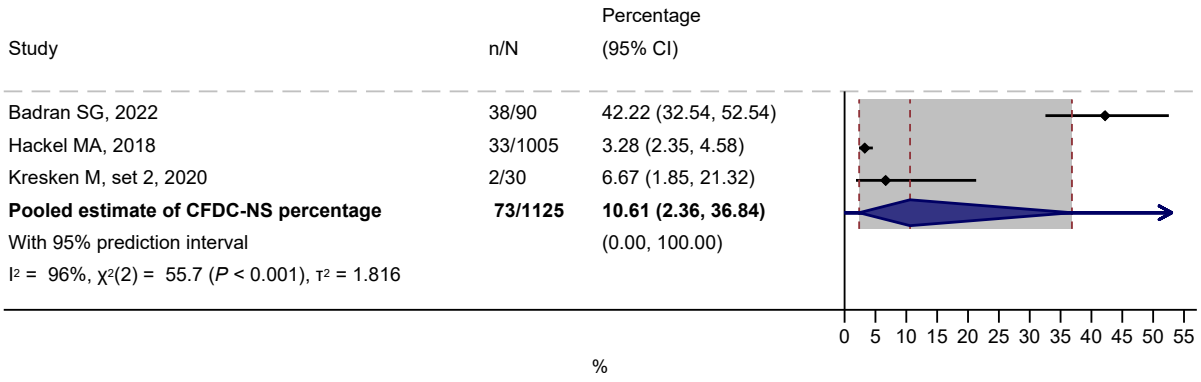
Note. n is the number of CZA-resistant Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of CZA-resistant Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.10 Enterobacterales, CZA-resistant; EUCAST



Note. n is the number of CZA-resistant Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CZA-resistant Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

8.2.11 Enterobacterales, CTA-resistant; CLSI-FDA



Note. n is the number of CTA-resistant Enterobacterales isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI-FDA breakpoints. N is the overall number of CTA-resistant Enterobacterales clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

9 Meta-analysis of cefiderocol non-susceptibility in different Enterobacterales species

Klebsiella spp.	Breakpoints	S	n/N	CFDC-NS %	Lower CL, %	Upper CL, %	I^2, %	τ^2	Lower PL, %	Upper PL, %
Any phenotype	CLSI-FDA	20	47/6121	0.1	0.0	0.9	66	10.769	0.0	64.0
	EUCAST	13	286/6600	2.7	1.0	7.0	96	2.731	0.1	55.5
CR	CLSI-FDA	24	131/3320	1.8	0.7	4.3	86	3.843	0.0	54.0
	EUCAST	20	379/2114	10.6	5.2	20.3	96	2.524	0.4	78.7
MBL-producing	CLSI-FDA	11	34/269	4.1	1.1	14.4	85	2.878	0.1	72.9
	EUCAST	11	54/272	8.9	2.6	26.4	92	3.273	0.1	88.4
E. coli										
Any phenotype	CLSI-FDA	16	32/6658	0.3	0.1	1.2	56	6.897	0.0	50.1
	EUCAST	13	79/7498	1.0	0.3	3.6	85	5.584	0.0	69.0
CR	CLSI-FDA	15	107/763	4.3	1.3	12.8	90	2.930	0.1	69.2
	EUCAST	15	147/793	10.8	4.8	22.9	91	1.863	0.5	73.1
MBL-producing	CLSI-FDA	9	62/233	14.0	3.4	42.8	96	4.185	0.1	96.6
	EUCAST	9	96/231	36.3	15.3	64.3	96	2.588	1.0	97.0
Enterobacter spp.										
Any phenotype	CLSI-FDA	14	16/2620	0.3	0.1	1.7	21	5.712	0.0	45.2
	EUCAST	9	66/1644	3.0	0.6	12.9	86	3.802	0.0	81.9
CR	CLSI-FDA	15	44/626	6.5	3.2	12.8	70	0.940	0.7	39.8
	EUCAST	11	51/233	22.6	15.6	31.6	66	0.173	9.0	46.2
MBL-producing	CLSI-FDA	7	22/152	15.7	3.9	45.9	85	3.027	0.1	96.1
	EUCAST	6	28/108	30.6	16.6	49.4	78	0.310	6.1	74.9
Proteus spp.										
Any phenotype	CLSI-FDA	3	2/66	3.0	0.8	11.3	0	0.000	0.1	40.7
	EUCAST	4	6/664	2.1	0.2	16.1	0	4.234	0.0	97.4
CR	CLSI-FDA	3	1/25	4.0	0.6	23.5	0	0.000	0.0	100.0
	EUCAST	2	0/17	0.0	.	.	0	0.542	.	.

Serratia spp.	Breakpoints	S	n/N	CFDC-NS %	Lower CL, %	Upper CL, %	I^2, %	τ^2	Lower PL, %	Upper PL, %
Any phenotype	CLSI-FDA	10	10/2009	0.4	0.1	1.6	0	2.701	0.0	19.4
	EUCAST	7	10/1851	0.5	0.3	1.0	15	0.000	0.2	1.2
CR	CLSI-FDA	1	5/5	.	.	.	.	.	.	.
	EUCAST	3	3/16	18.8	6.2	44.8	15	0.000	1.4	78.4
Citrobacter spp.										
Any phenotype	CLSI-FDA	9	5/1160	0.4	0.2	1.0	0	0.000	0.1	1.2
	EUCAST	4	11/899	1.9	0.5	6.6	0	0.441	0.0	52.0
Morganella spp.										
Any phenotype	CLSI-FDA	3	0/24	0.0	.	.	0	0.542	.	.
	EUCAST	4	0/302	0.0	.	.	0	1.000	.	.

S is the number of independent datasets in the analysis (a single study may have contributed more than one sets of data). **n/N** is the ratio of the cumulative number of *Klebsiella* spp. isolates that were non-susceptible to Cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. **CFDC-NS**, cefiderocol non-susceptible; **CL**, 95% confidence limit; **PL**, 95% prediction limit; **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**, ceftolozane/tazobactam

10 Meta-analysis of cefiderocol non-susceptibility in *P. aeruginosa*

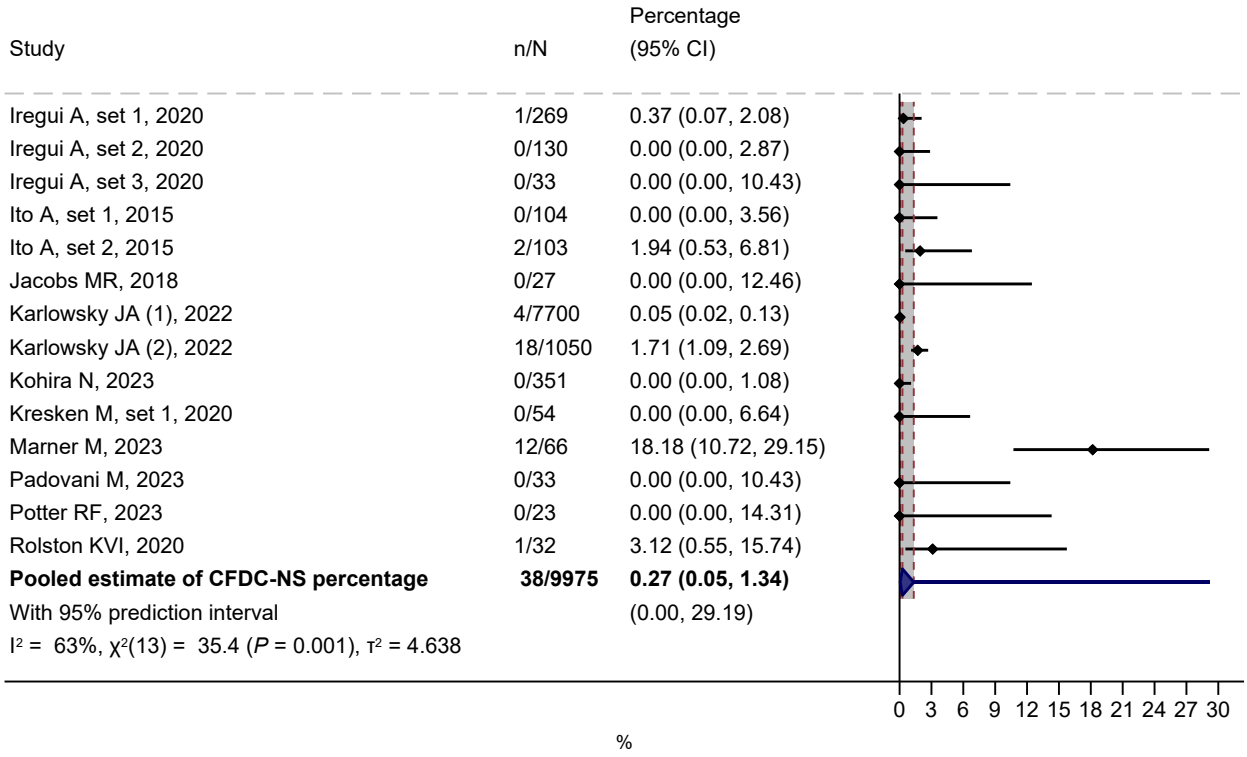
10.1 Summary table

P. aeruginosa	Breakpoints	S	n/N	CFDC-NS %	Lower CL, %	Upper CL, %	I^2, %	τ^2	Lower PL, %	Upper PL, %
Any phenotype	CLSI	14	38/9975	0.3	0.1	1.3	63	4.638	0.0	29.2
	EUCAST	15	174/11991	1.4	0.5	4.0	89	2.986	0.0	41.9
	FDA	11	487/11710	3.3	1.4	7.7	97	1.639	0.2	42.7
CR	CLSI	23	68/4389	0.8	0.3	2.2	64	3.361	0.0	30.4
	EUCAST	20	218/4041	3.5	1.6	7.8	91	2.849	0.1	58.8
	FDA	16	500/3653	14.6	7.5	26.3	97	1.954	0.8	79.2
MBL-producing	CLSI	13	22/562	1.6	0.3	7.8	53	5.045	0.0	74.9
	EUCAST	12	32/527	1.8	0.3	10.4	74	8.010	0.0	92.8
	FDA	9	72/381	23.3	10.4	44.1	92	1.854	1.1	89.5
NDM-producing	CLSI	6	8/41	19.5	10.1	34.4	2	0.000	8.1	40.0
	EUCAST	7	14/51	22.9	8.1	49.7	67	1.339	1.2	88.0
	FDA	6	25/41	58.7	20.4	88.7	90	3.413	0.7	99.6
CZA-resistant	CLSI	7	22/1163	1.7	0.5	5.1	73	1.682	0.0	39.9
	EUCAST	5	54/519	6.8	3.1	14.6	87	0.505	0.5	50.8
	FDA	5	122/519	19.5	11.9	30.4	90	0.315	3.1	64.8
CTA-resistant	CLSI	8	20/1038	2.2	0.8	5.6	59	1.322	0.1	32.3
	EUCAST	6	41/376	8.3	4.1	16.0	75	0.432	1.1	42.7
	FDA	6	81/376	15.1	7.4	28.2	90	0.678	1.4	69.4

S is the number of independent datasets in the analysis (a single study may have contributed more than one sets of data). **n/N** is the ratio of the cumulative number of *Klebsiella* spp. isolates that were non-susceptible to Cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. **CFDC-NS**, cefiderocol non-susceptible; **CL**, 95% confidence limit; **PL**, 95% prediction limit; **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**, ceftolozane/tazobactam

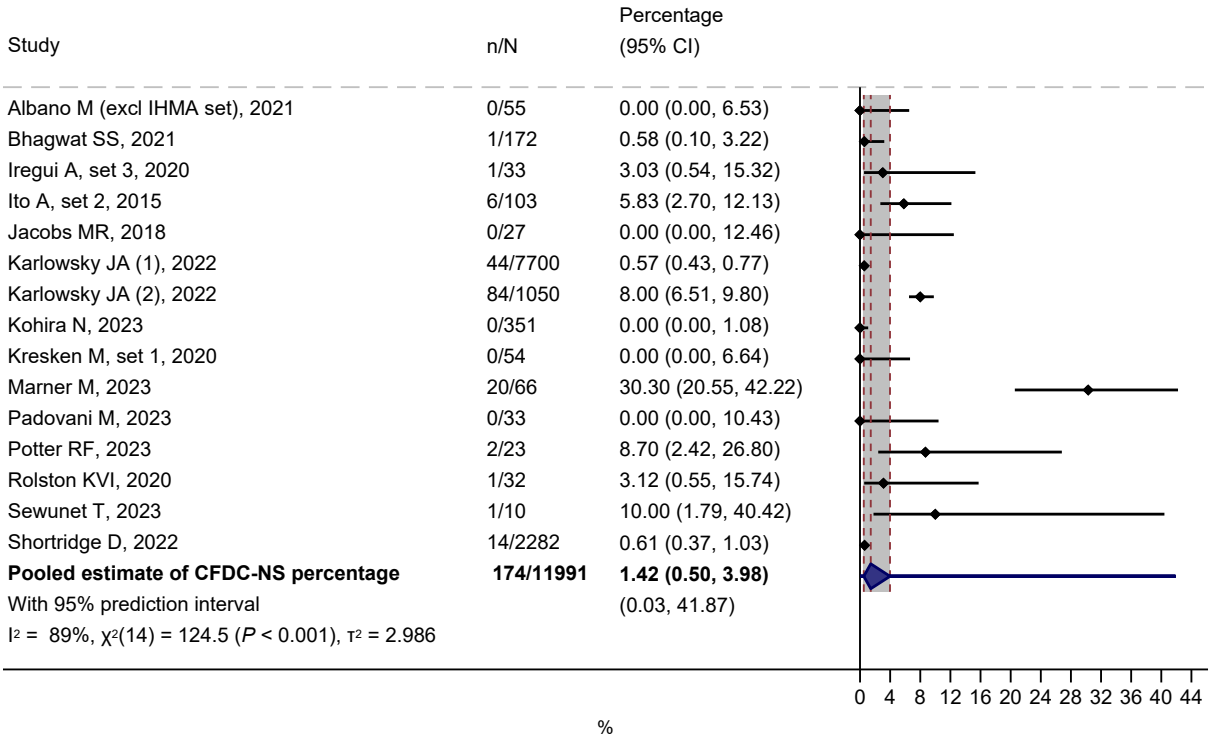
10.2 Forest plots

10.2.1 P. aeruginosa, any phenotype; CLSI



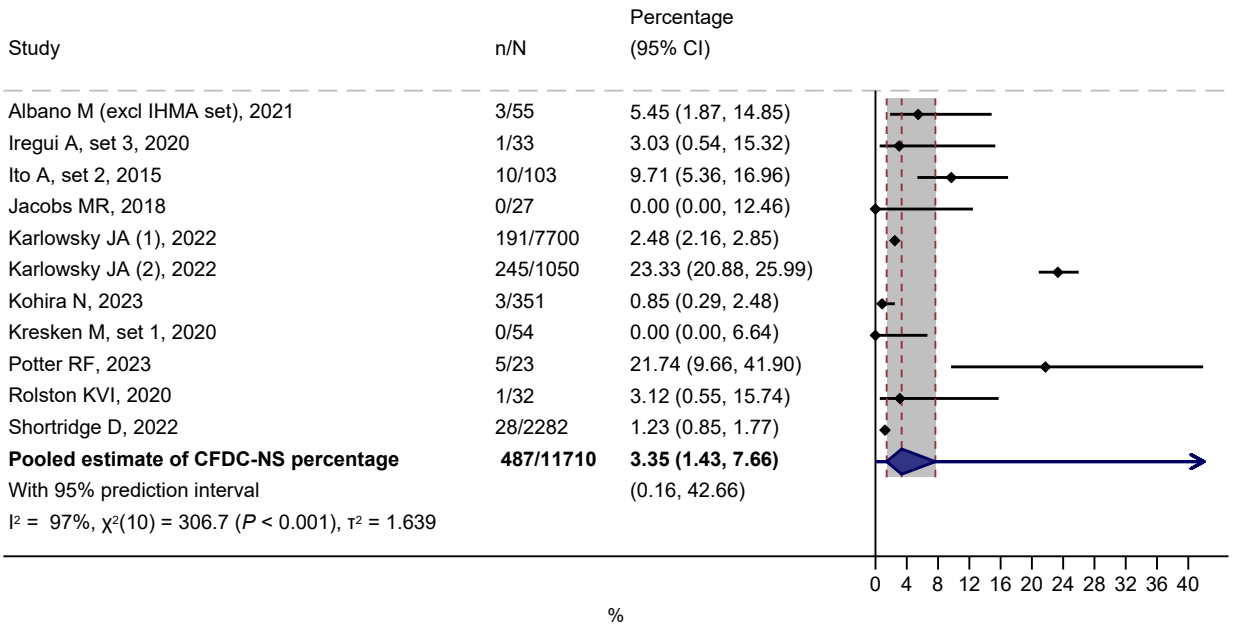
Note. n is the number of *P. aeruginosa* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of *P. aeruginosa* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.2 P. aeruginosa, any phenotype; EUCAST



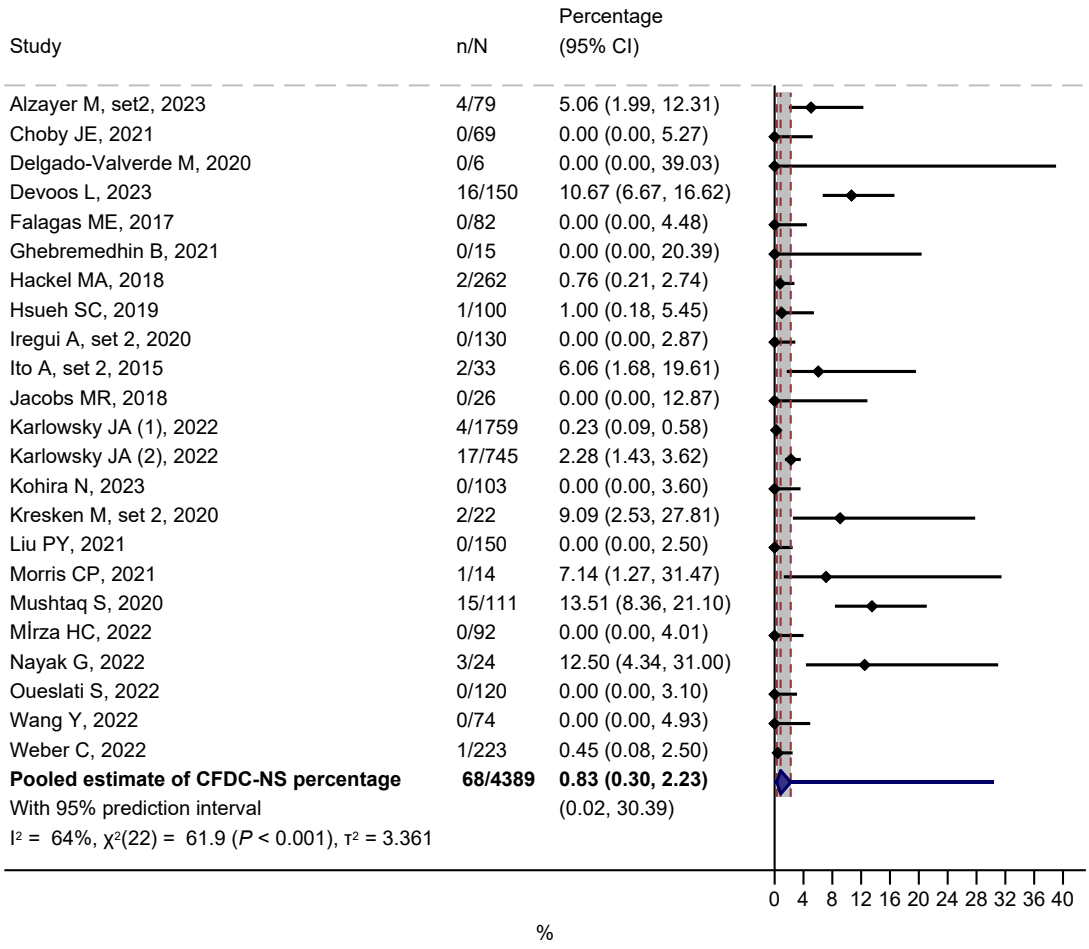
Note. n is the number of *P. aeruginosa* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of *P. aeruginosa* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.3 P. aeruginosa, any phenotype; FDA



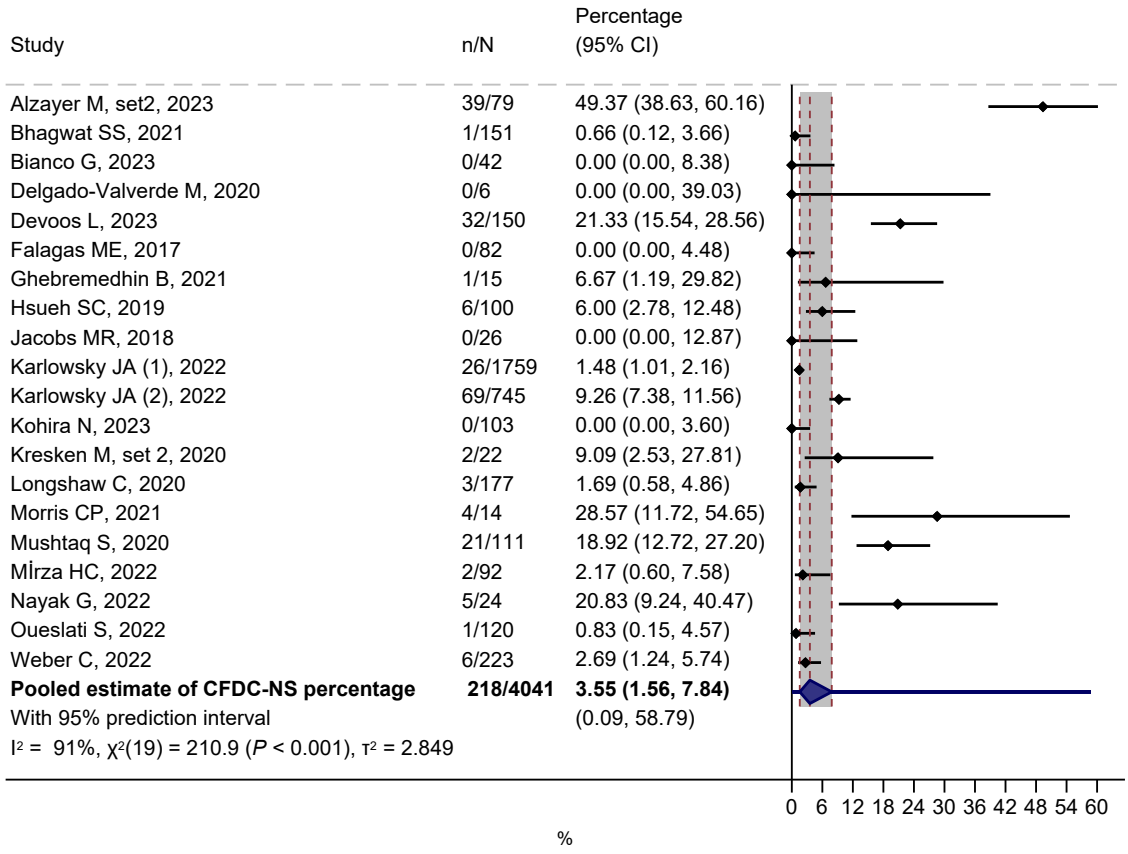
Note. n is the number of *P. aeruginosa* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of *P. aeruginosa* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.4 *P. aeruginosa*, carbapenem-resistant; CLSI



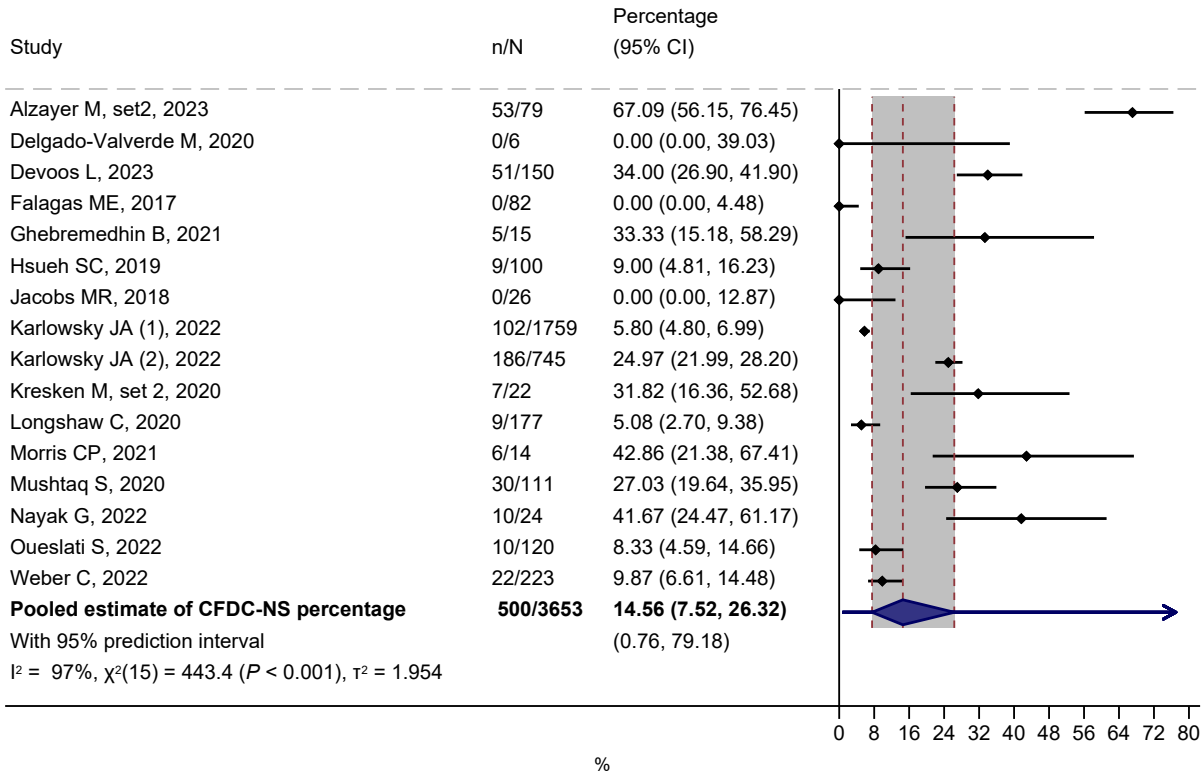
Note. n is the number of CR *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of CR *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.5 *P. aeruginosa*, carbapenem-resistant; EUCAST



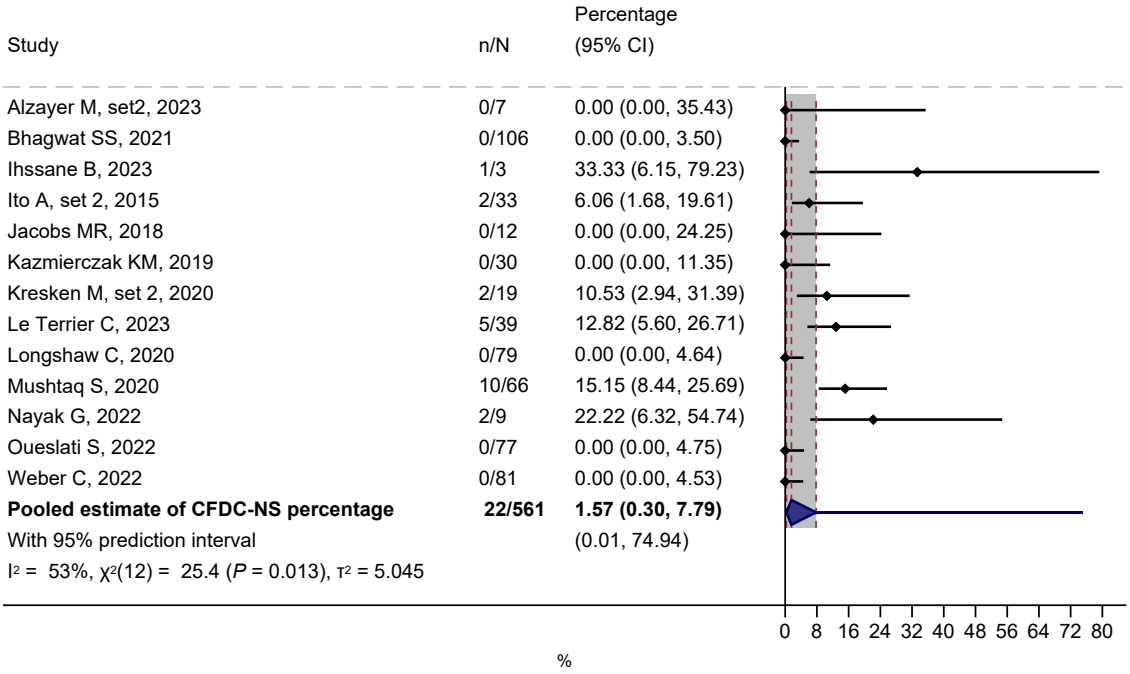
Note. n is the number of CR *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CR *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.6 *P. aeruginosa*, carbapenem-resistant; FDA



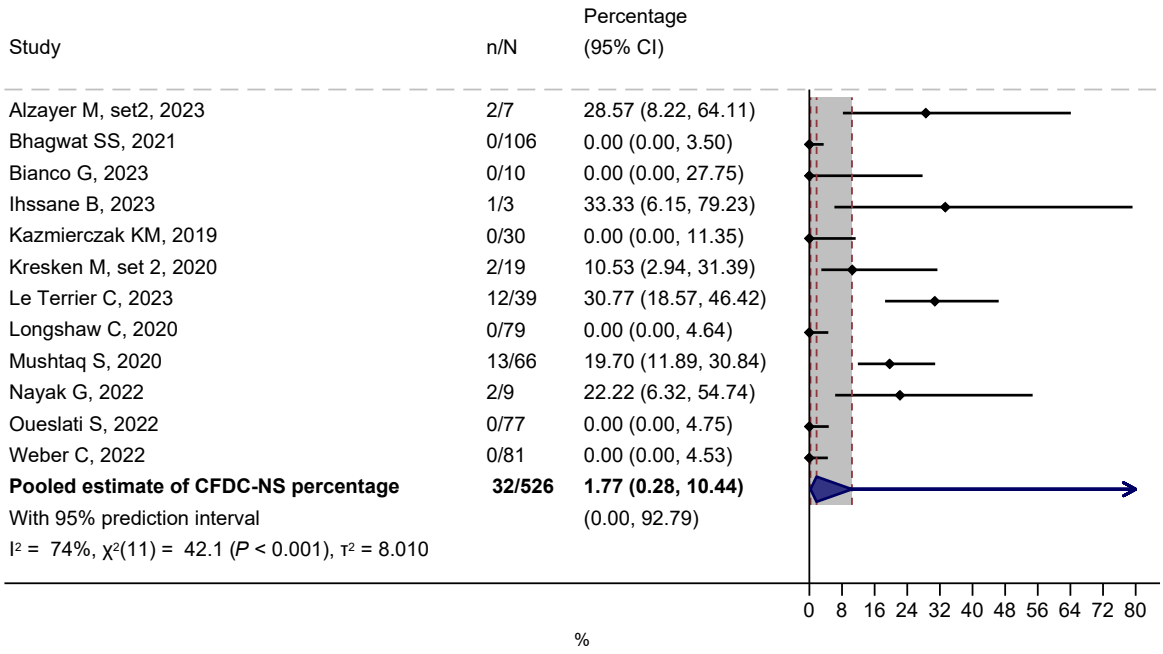
Note. n is the number of CR *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of CR *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.7 *P. aeruginosa*, MBL-producing; CLSI



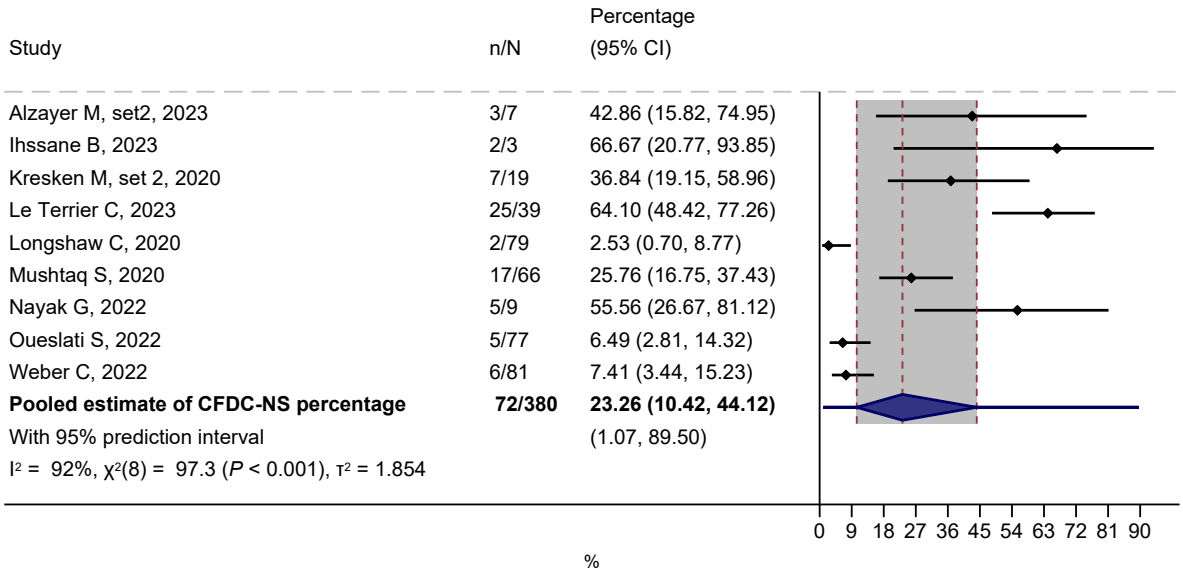
Note. n is the number of MBL-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of MBL-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.8 *P. aeruginosa*, MBL-producing; EUCAST



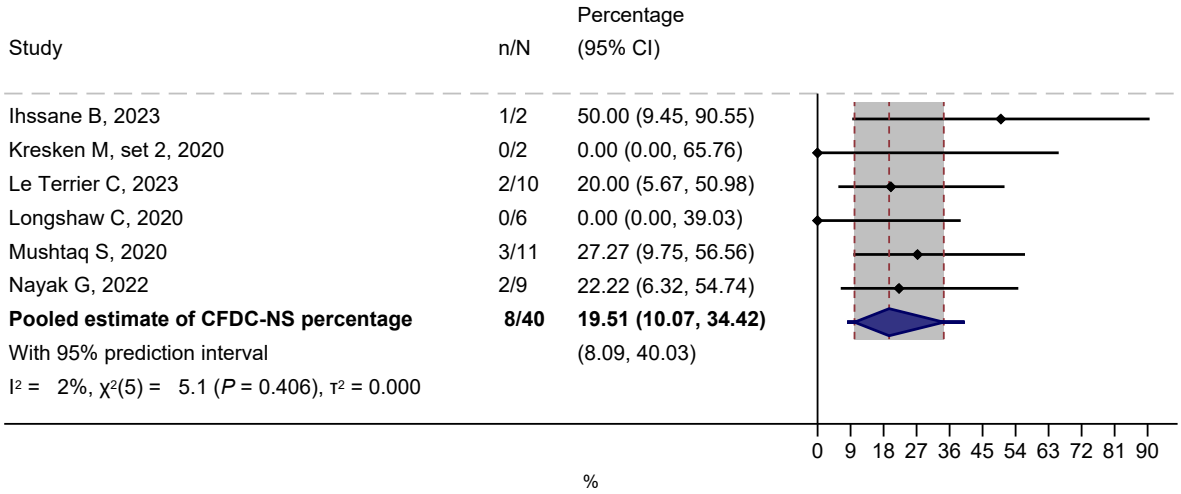
Note. n is the number of MBL-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of MBL-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.9 *P. aeruginosa*, MBL-producing; FDA



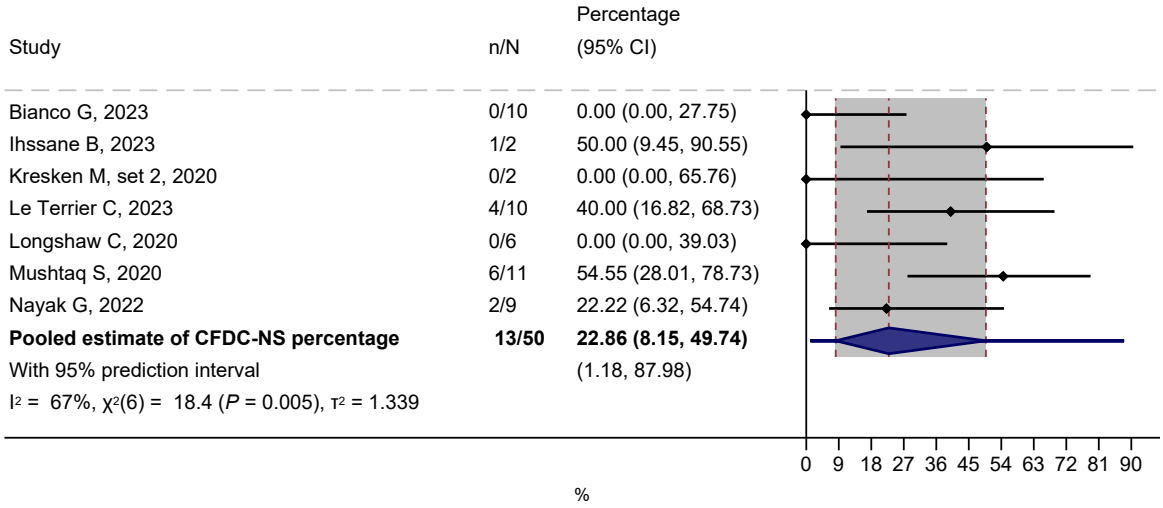
Note. n is the number of MBL-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of MBL-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.10 *P. aeruginosa*, NDM-producing; CLSI



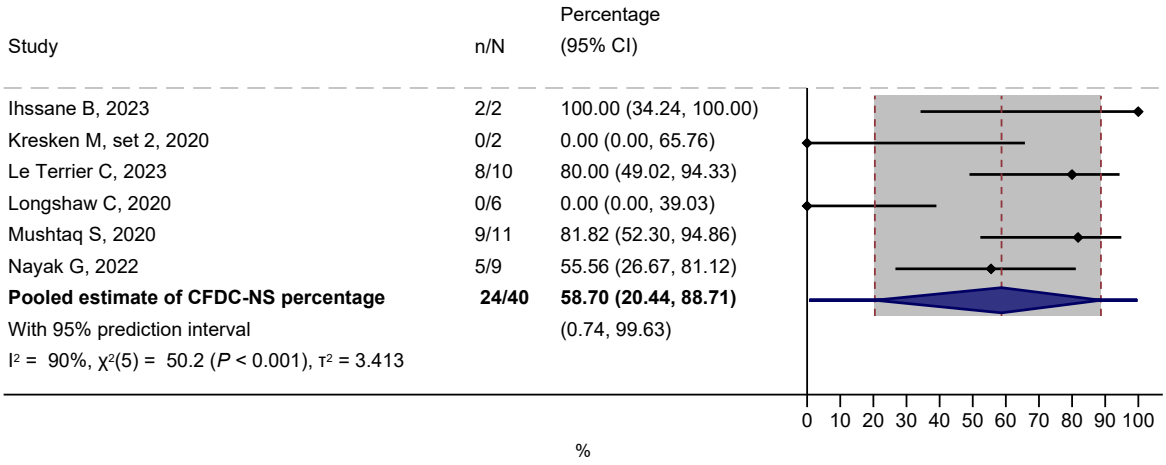
Note. n is the number of NDM-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of NDM-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.11 *P. aeruginosa*, NDM-producing; EUCAST



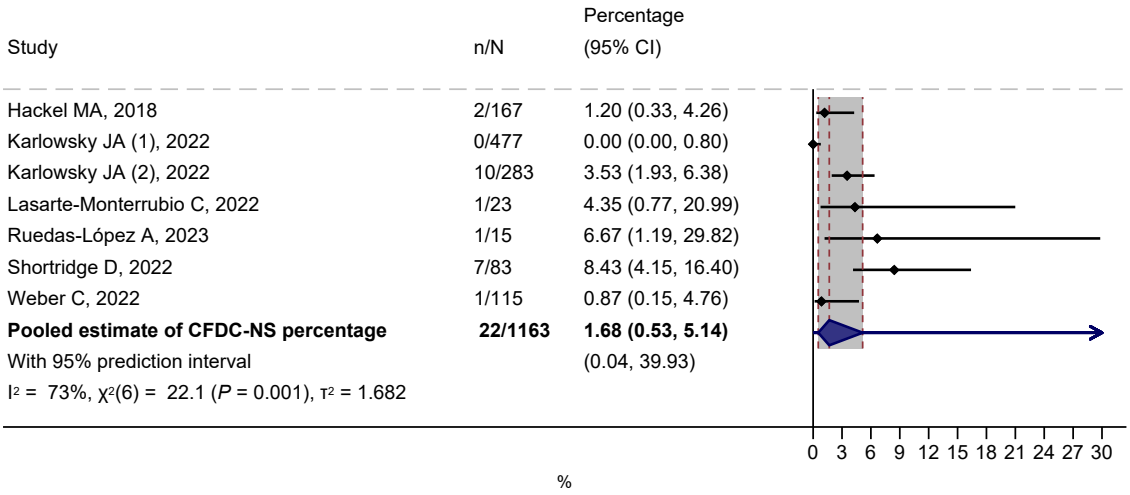
Note. n is the number of NDM-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of NDM-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.12 *P. aeruginosa*, NDM-producing; FDA



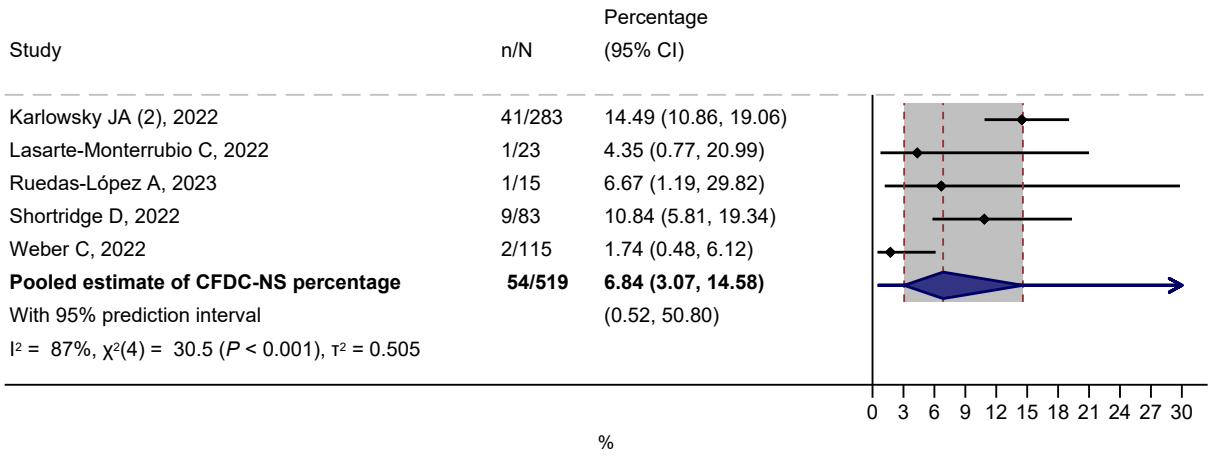
Note. n is the number of NDM-producing *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of NDM-producing *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.13 *P. aeruginosa*, CZA-resistant; CLSI



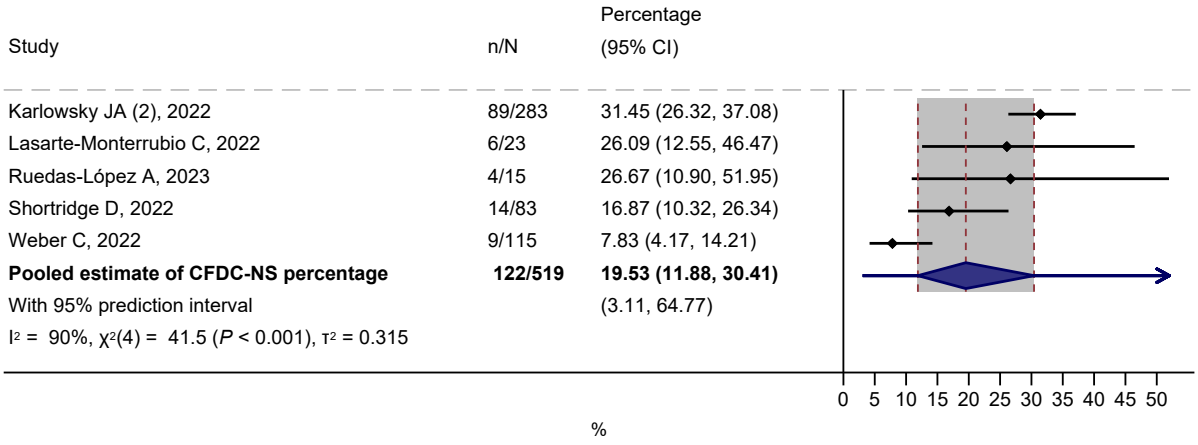
Note. n is the number of CZA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of CZA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.14 *P. aeruginosa*, CZA-resistant; EUCAST



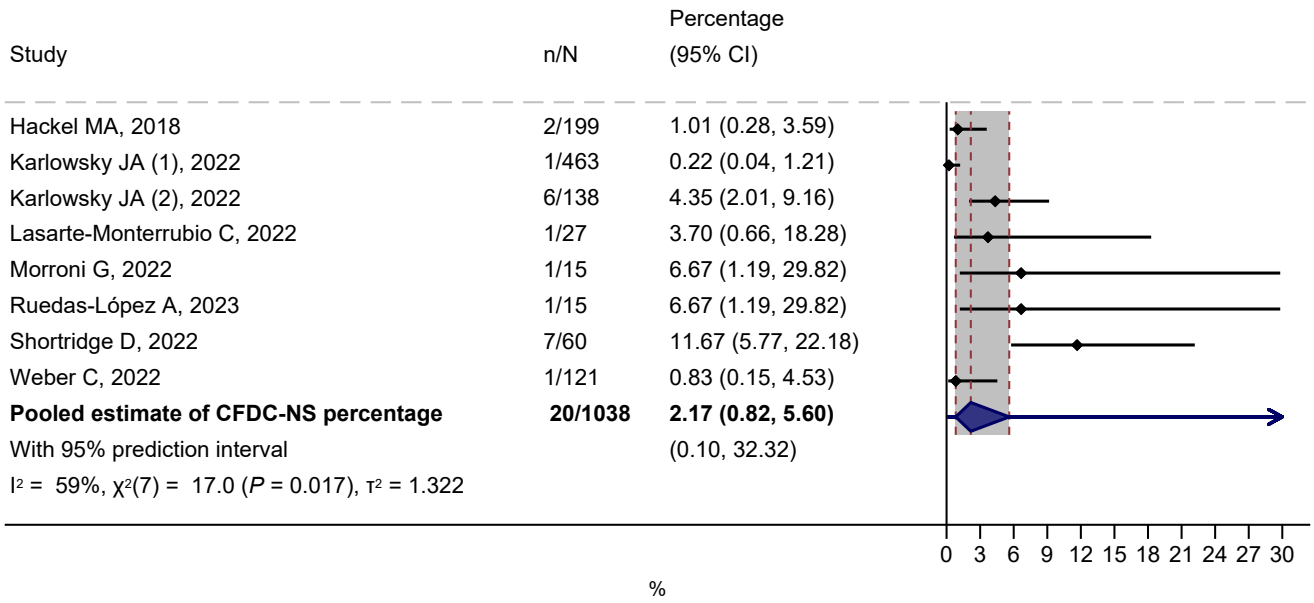
Note. n is the number of CZA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CZA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.15 *P. aeruginosa*, CZA-resistant; FDA



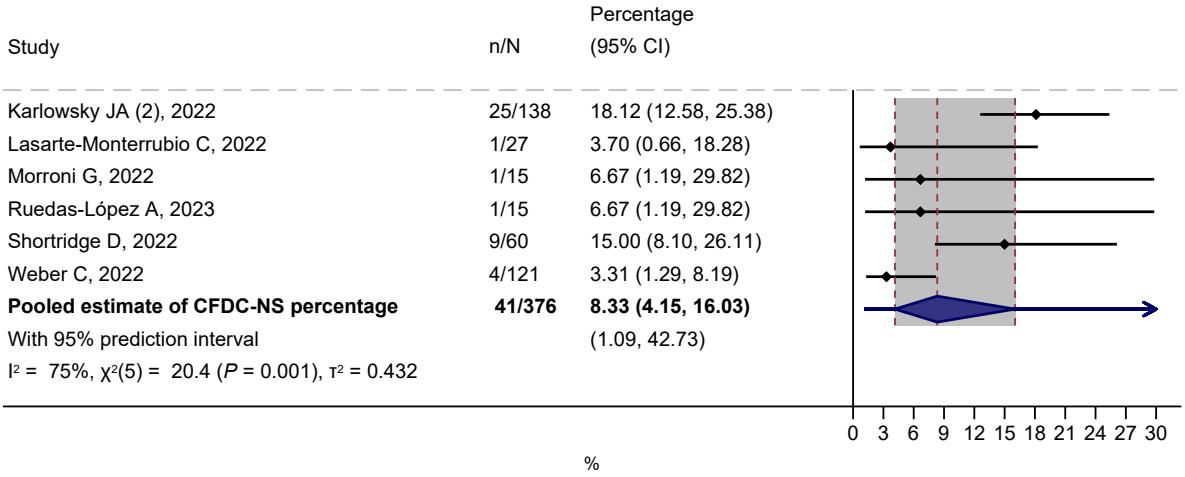
Note. n is the number of CZA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of CZA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.16 *P. aeruginosa*, CTA-resistant; CLSI



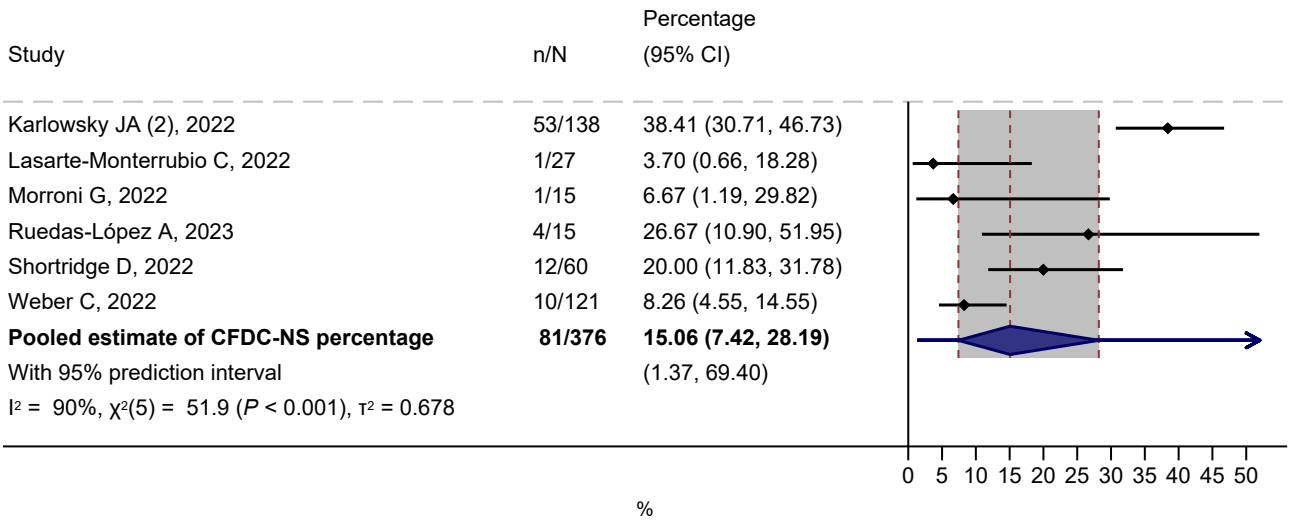
Note. n is the number of CTA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of CTA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.17 *P. aeruginosa*, CTA-resistant; EUCAST



Note. n is the number of CTA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CTA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

10.2.18 *P. aeruginosa*, CTA-resistant; FDA



Note. n is the number of CTA-resistant *P. aeruginosa* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of CTA-resistant *P. aeruginosa* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11 Meta-analysis of cefiderocol non-susceptibility in *A. baumannii*

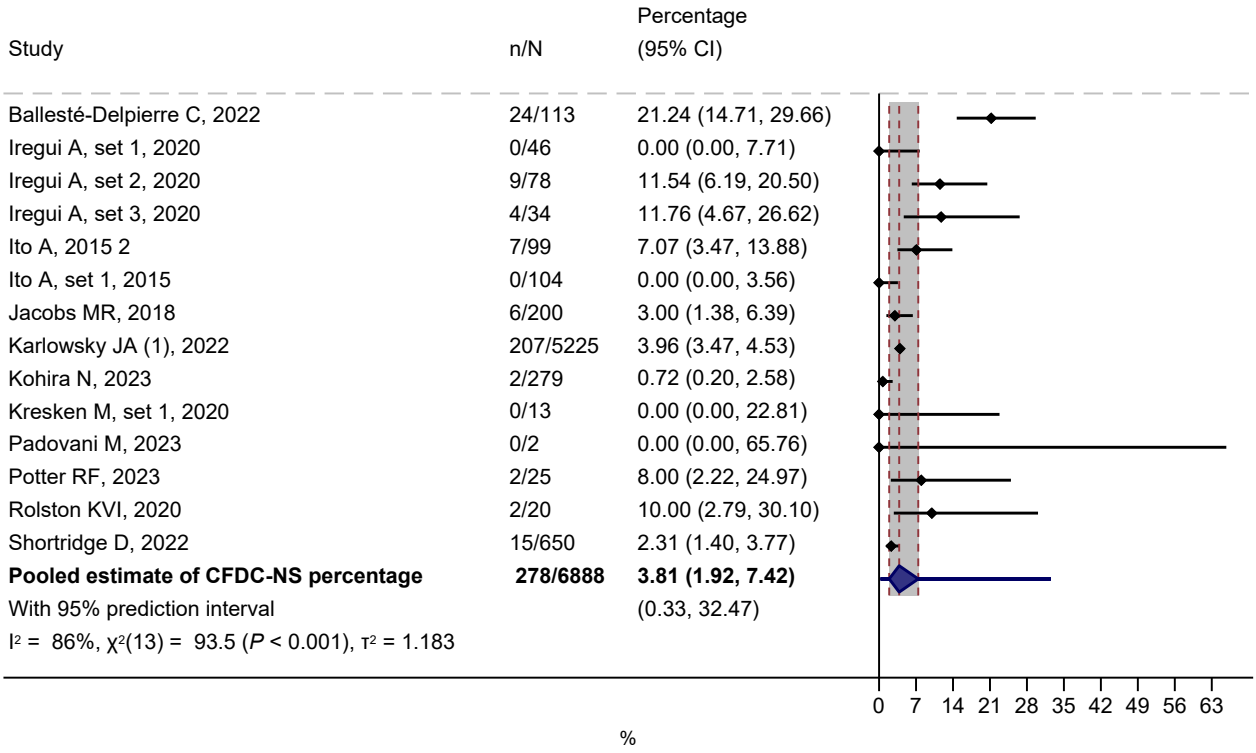
11.1 Summary table

A. baumannii	**Breakpoints**	**S**	**n/N**	**CFDC-NS %**	**Lower CL, %**	**Upper CL, %**	**I^2, %**	**τ^2**	**Lower PL, %**	**Upper PL, %**
Any phenotype	CLSI	14	278/6888	3.8	1.9	7.4	86	1.183	0.3	32.5
	EUCAST	13	422/6658	8.8	4.9	15.2	85	0.882	1.1	46.2
	FDA	12	725/6656	15.0	8.4	25.3	92	1.025	1.6	65.4
CR	CLSI	27	487/6047	8.5	5.7	12.5	91	1.027	1.1	44.1
	EUCAST	20	535/4831	13.2	7.8	21.5	95	1.524	1.0	68.7
	FDA	14	792/4171	26.6	18.3	36.9	95	0.698	5.1	70.7
MBL-producing	CLSI	9	19/93	20.4	13.4	29.8	58	0.000	12.3	32.0
	EUCAST	9	38/93	40.9	31.4	51.1	65	0.000	29.6	53.2
	FDA	9	61/93	53.1	21.5	82.4	86	2.953	1.4	98.9
NDM-producing	CLSI	8	19/85	23.0	13.6	36.3	67	0.146	8.0	50.7
	EUCAST	8	38/85	44.7	34.5	55.4	71	0.000	32.2	58.0
	FDA	8	60/85	71.3	21.7	95.7	90	8.076	0.1	100.0

S is the number of independent datasets in the analysis (a single study may have contributed more than one sets of data). **n/N** is the ratio of the cumulative number of *Klebsiella* spp. isolates that were non-susceptible to Cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. **CFDC-NS**, cefiderocol non-susceptible; **CL**, 95% confidence limit; **PL**, 95% prediction limit; **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**, ceftolozane/tazobactam

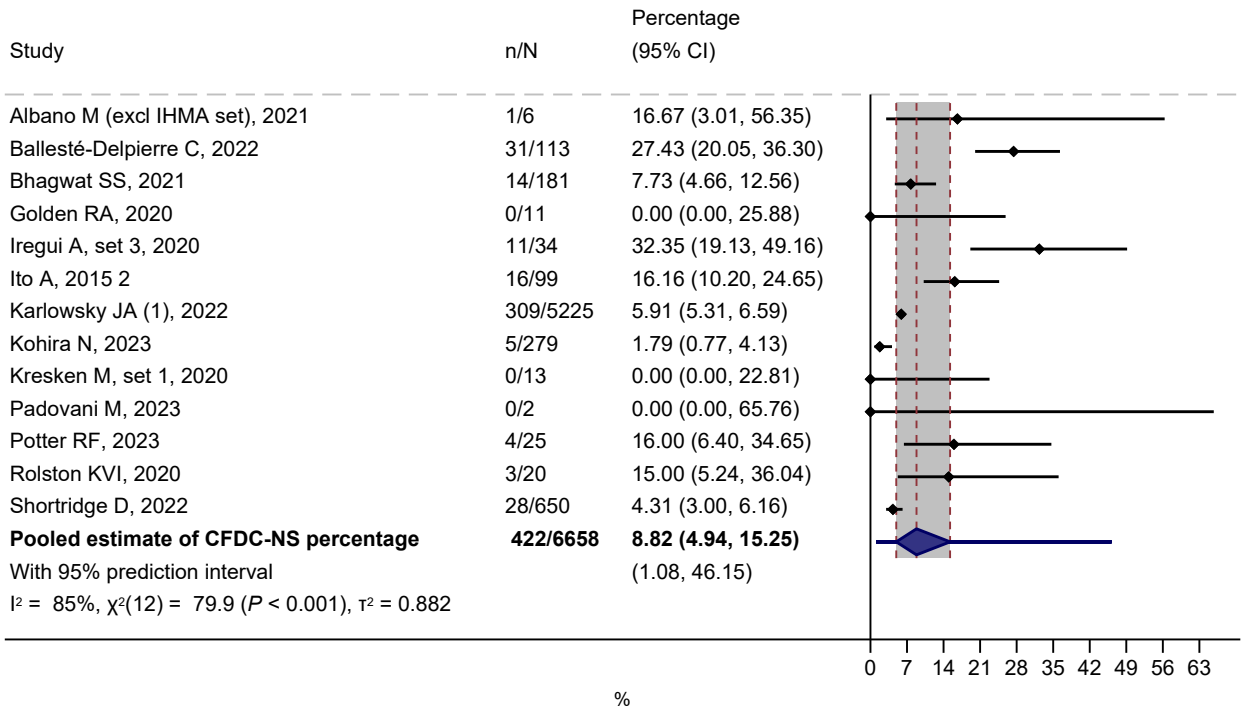
11.2 Forest plots

11.2.1 *A. baumannii*, any phenotype; CLSI



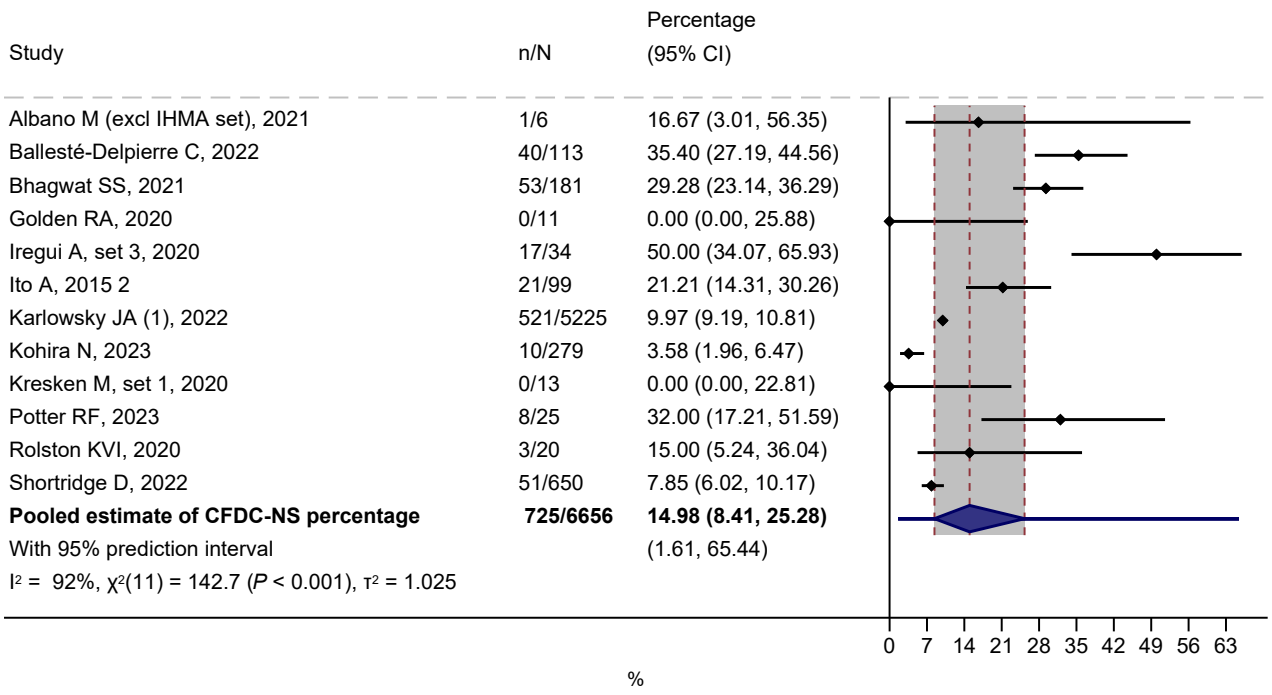
Note. n is the number of *A. baumannii* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of *A. baumannii* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.2 *A. baumannii*, any phenotype; EUCAST



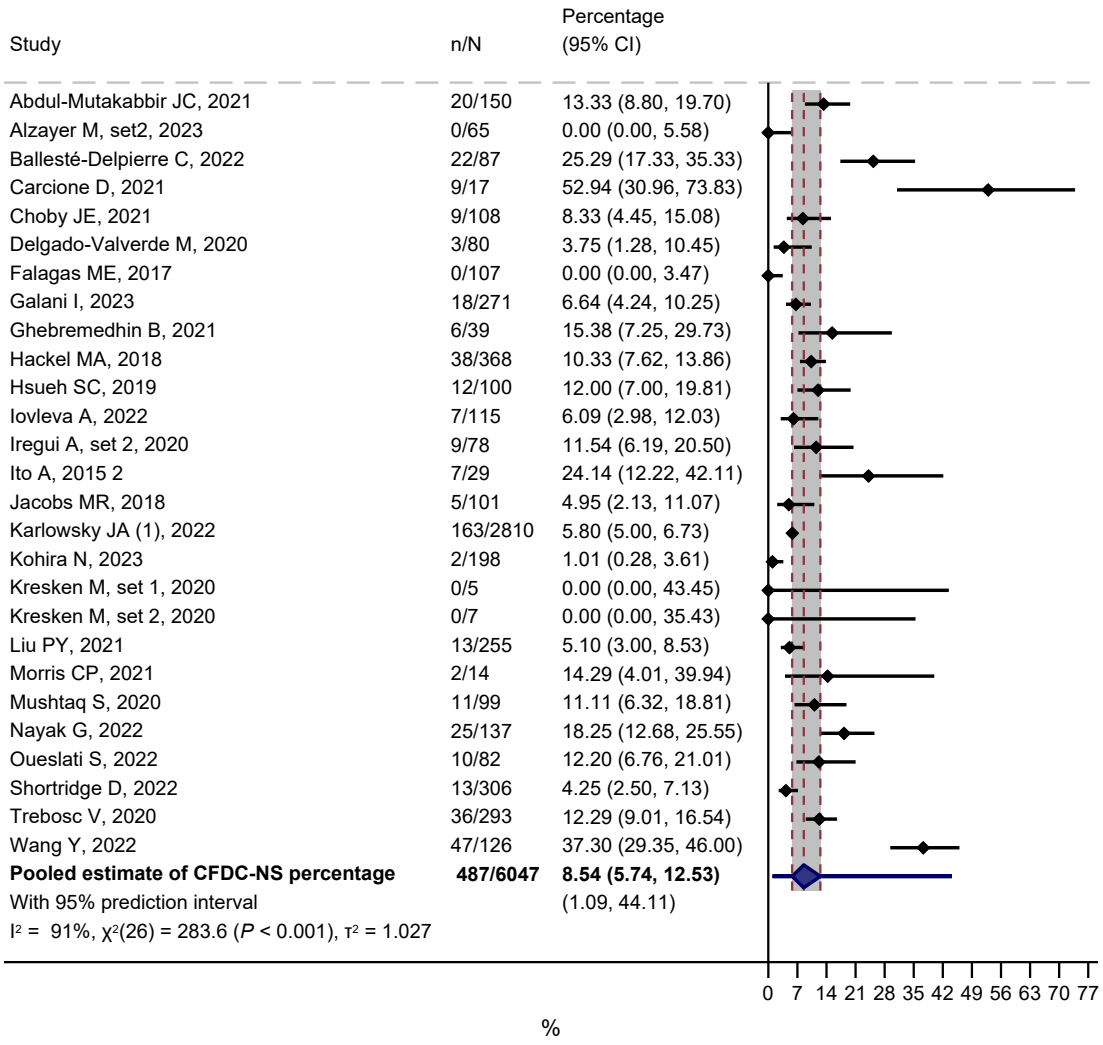
Note. n is the number of *A. baumannii* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of *A. baumannii* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.3 *A. baumannii*, any phenotype; FDA



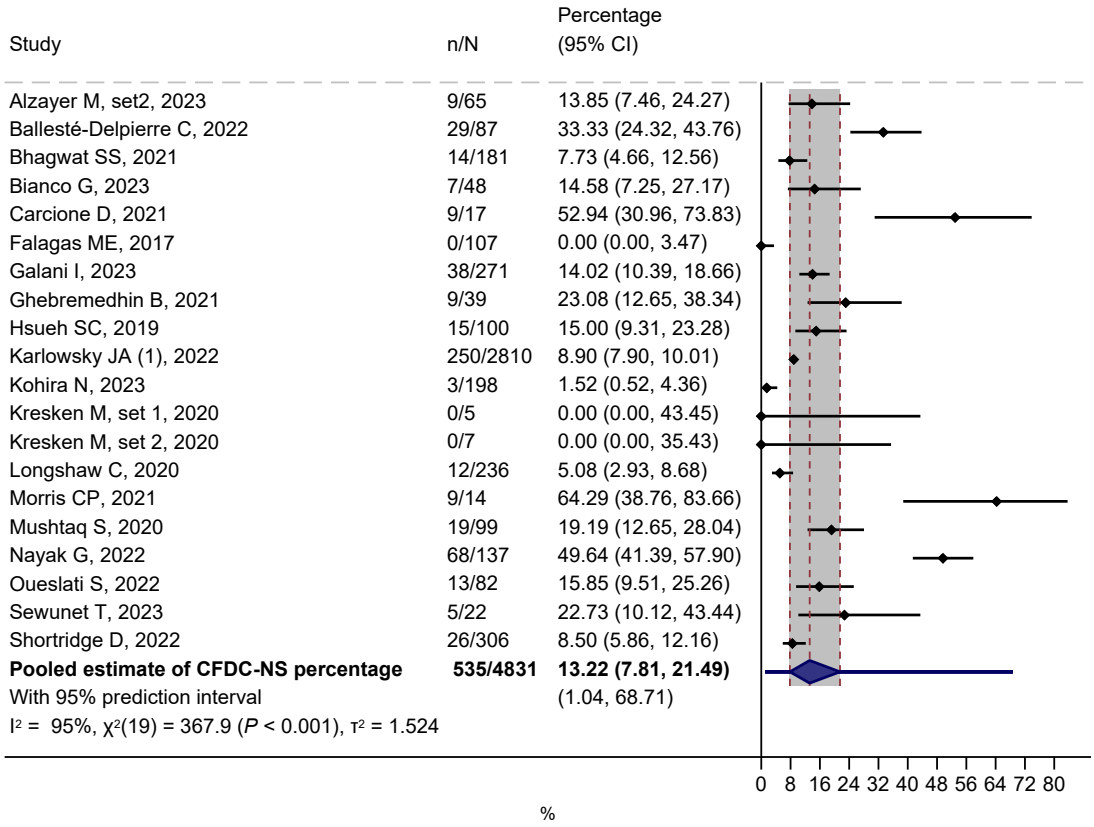
Note. n is the number of *A. baumannii* (any phenotype) isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of *A. baumannii* (any phenotype) clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.4 *A. baumann*ii, carbapenem-resistant; CLSI



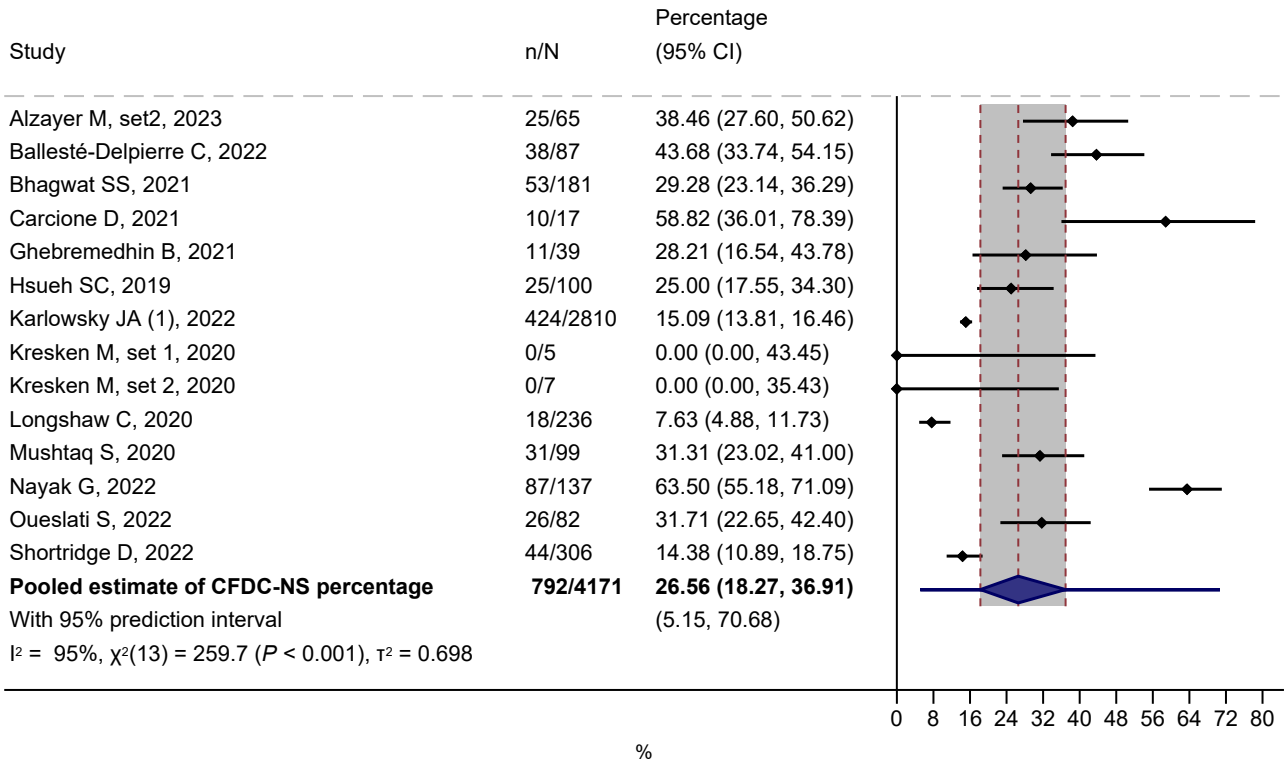
Note. n is the number of CR *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of CR *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.5 *A. baumann*ii, carbapenem-resistant; EUCAST



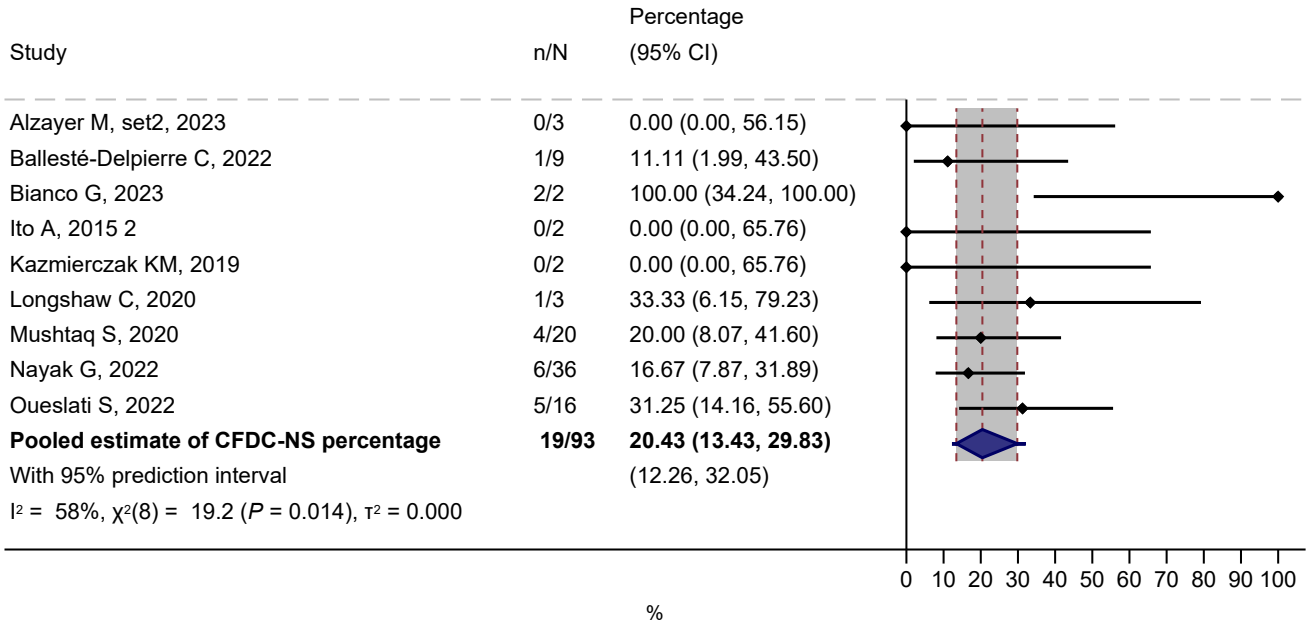
Note. n is the number of CR *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of CR *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.6 *A. baumann*ii, carbapenem-resistant; FDA



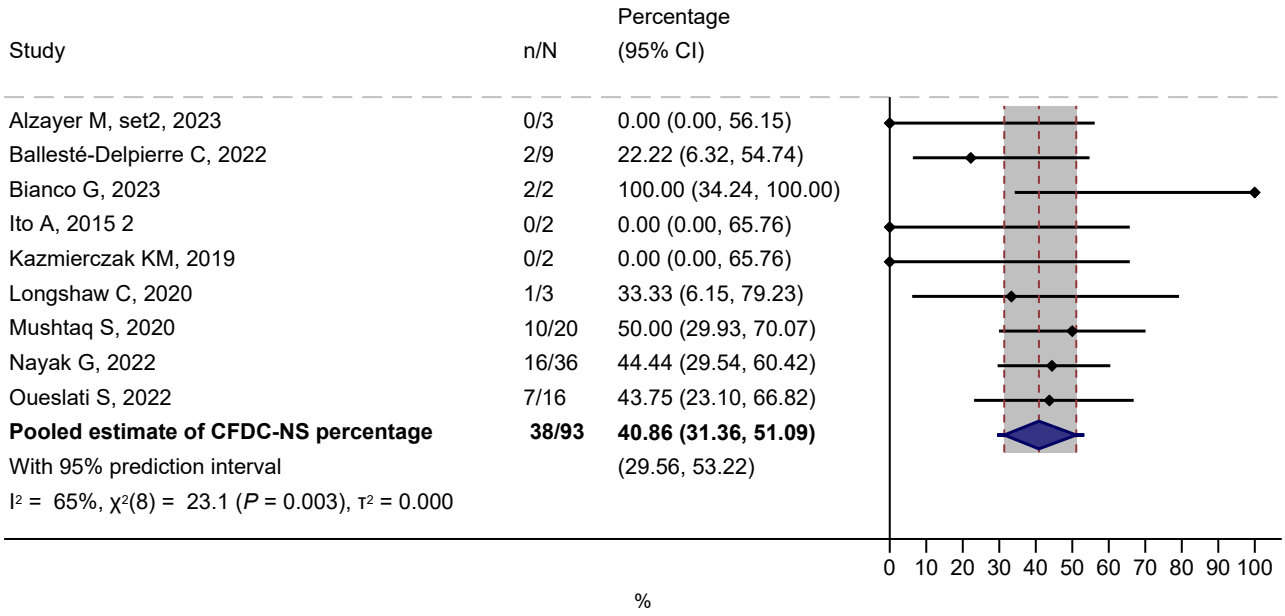
Note. n is the number of CR *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of CR *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.7 *A. baumann*ii, MBL-producing; CLSI



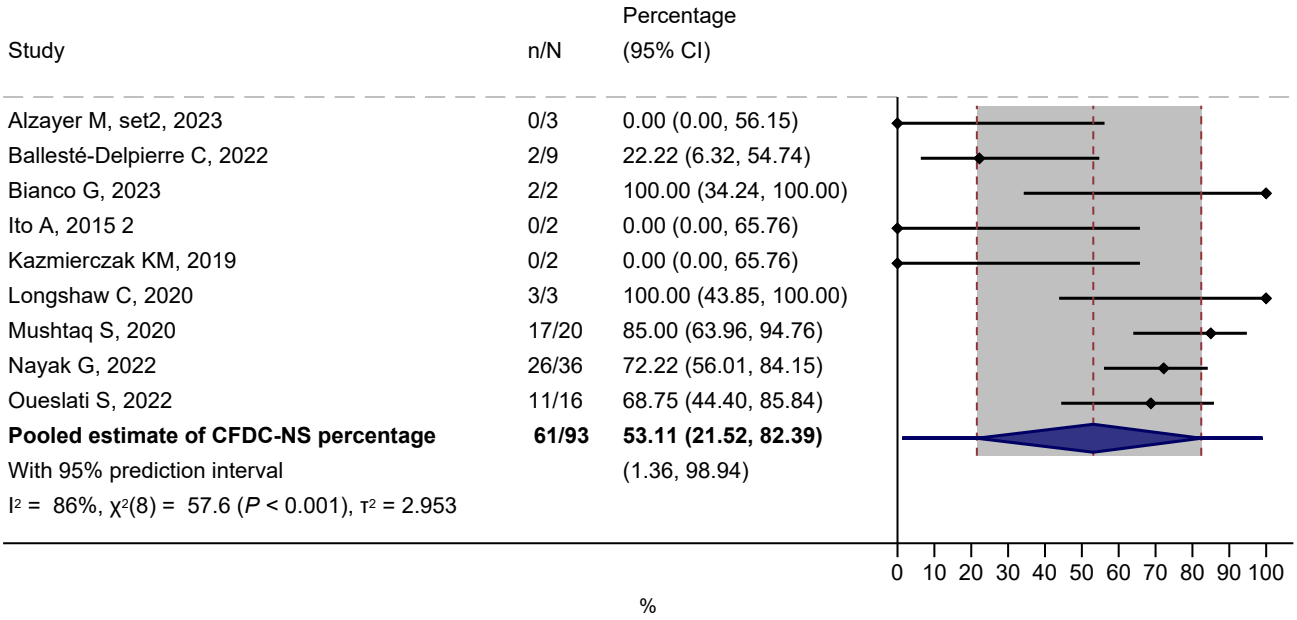
Note. n is the number of MBL-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of MBL-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.8 *A. baumann*ii,MBL-producing; EUCAST



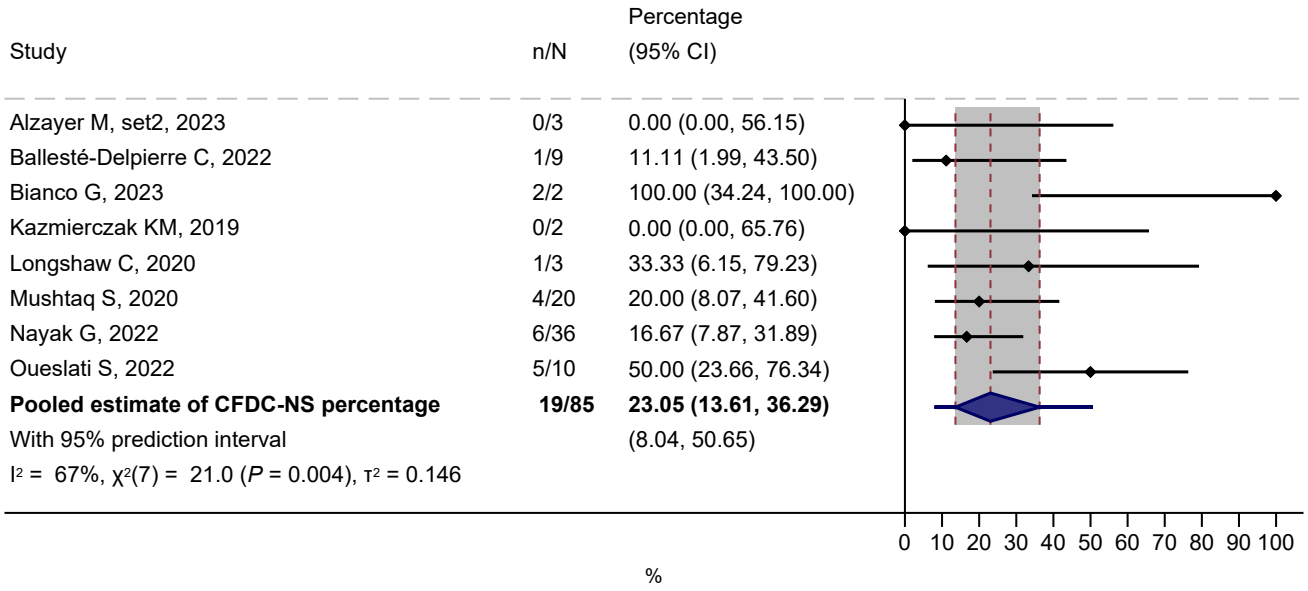
Note. n is the number of MBL-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of MBL-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.9 *A. baumann*ii,MBL-producing; FDA



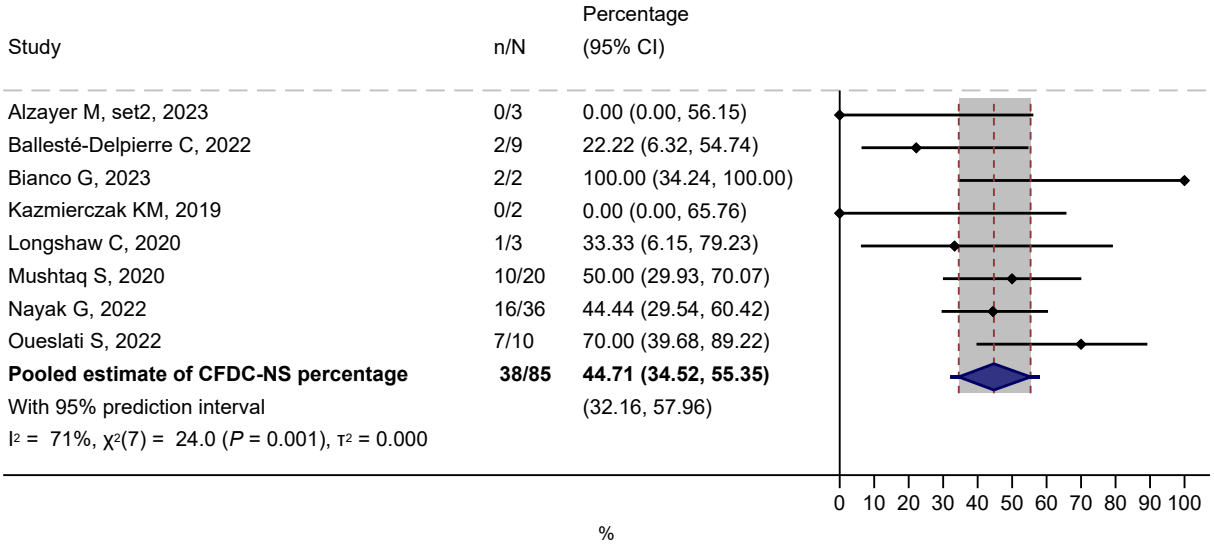
Note. n is the number of MBL-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of MBL-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.10 *A. baumannii*, NDM-producing; CLSI



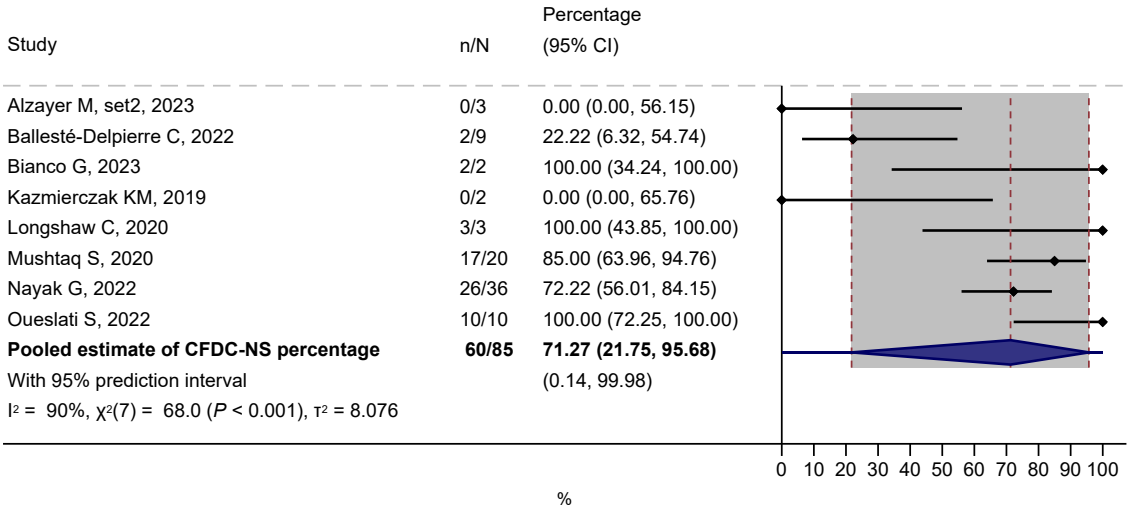
Note. n is the number of NDM-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI breakpoints. N is the overall number of NDM-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.11 *A. baumannii*, NDM-producing; EUCAST



Note. n is the number of NDM-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of NDM-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

11.2.12 *A. baumannii*, NDM-producing; FDA



Note. n is the number of NDM-producing *A. baumannii* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to FDA breakpoints. N is the overall number of NDM-producing *A. baumannii* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

12 Meta-analysis of cefiderocol non-susceptibility in *S. maltophilia*

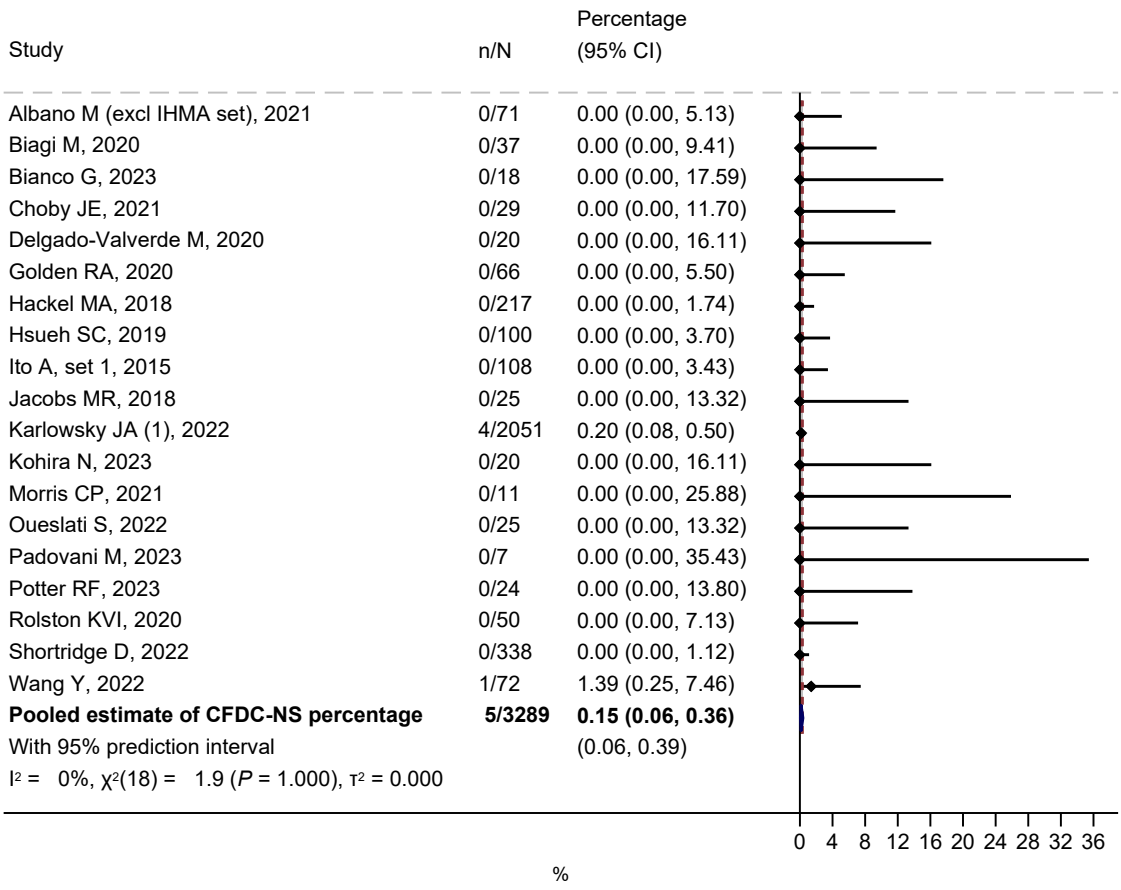
12.1 Summary table

S. maltophilia	**Breakpoints**	**S**	**n/N**	**CFDC-NS %**	**Lower CL, %**	**Upper CL, %**	**I^2, %**	**τ^2**	**Lower PL, %**	**Upper PL, %**
	CLSI old	19	5/3289	0.2	0.1	0.4	0	0.000	0.1	0.4
	CLSI new	13	81/3003	0.1	0.0	3.7	96	21.388	0.0	98.2
	EUCAST	15	11/3030	0.4	0.2	0.7	0	0.000	0.2	0.7

S is the number of independent datasets in the analysis (a single study may have contributed more than one sets of data). **n/N** is the ratio of the cumulative number of *Klebsiella* spp. isolates that were non-susceptible to Cefiderocol (**CFDC-NS**) over the total number of isolates, according to the respective definition of breakpoints and resistance phenotype. **CFDC-NS**, cefiderocol non-susceptible; **CL**, 95% confidence limit; **PL**, 95% prediction limit; **CAR**, carbapenem; **MBL**, metallo-β-lactamase; **NDM**, New Delhi metallo-β-lactamase; **CZA**, ceftazidime/avibactam; **CTA**, ceftolozane/tazobactam

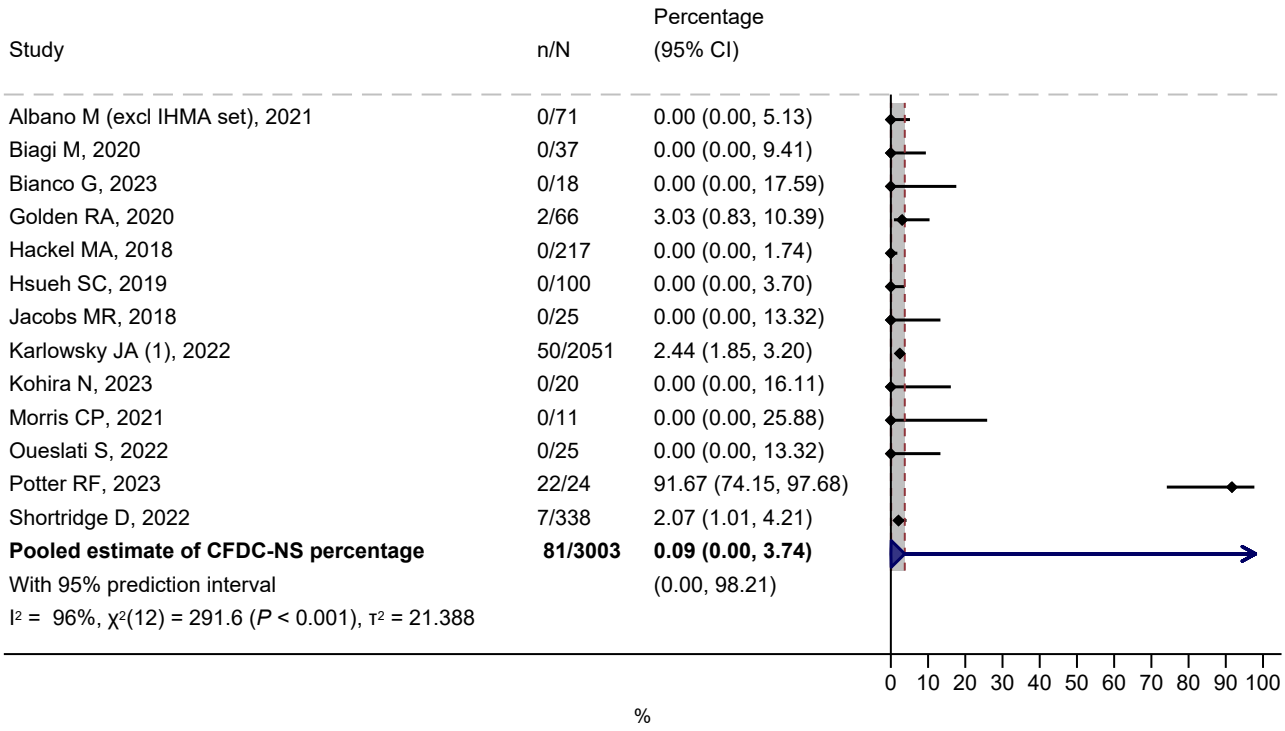
12.2 Forest plots

12.2.1 Previous CLSI breakpoints



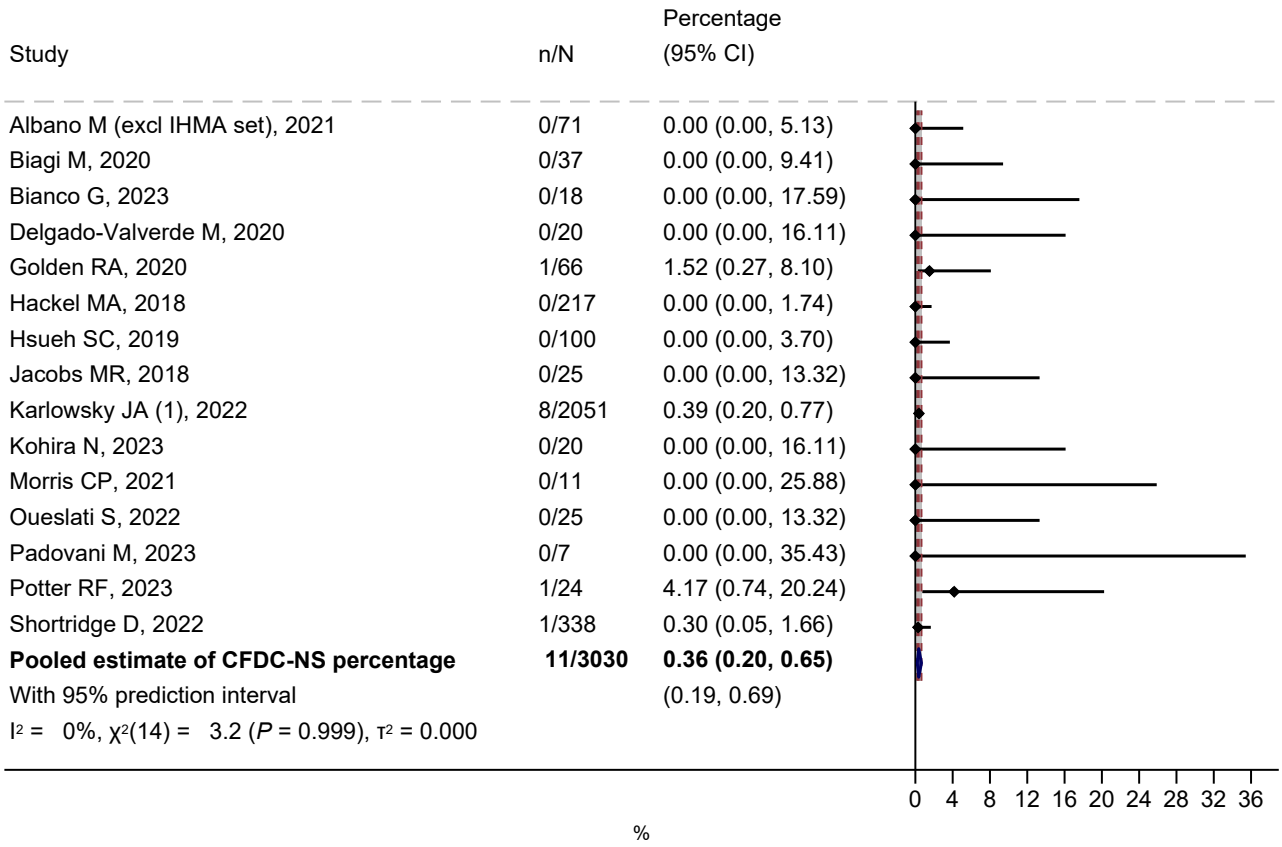
Note. n is the number of *S. maltophilia* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI old breakpoints. N is the overall number of *S. maltophilia* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

12.2.2 New CLSI breakpoints



Note. n is the number of *S. maltophilia* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to CLSI new breakpoints. N is the overall number of *S. maltophilia* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

12.2.3 EUCAST breakpoints



Note. n is the number of *S. maltophilia* isolates that were non-susceptible to Cefiderocol (CFDC-NS) according to EUCAST breakpoints. N is the overall number of *S. maltophilia* clinical isolates in the study. The diamond's center is the population-averaged percentage (pooled estimate) of CFDC-NS isolates. The diamond's length and the respective grey vertical area indicate the 95% confidence interval of the pooled estimate. The extended line continuing through the confidence interval represents the 95% prediction interval of the percentage of CFDC-NS isolates expected in new studies.

13 Univariate meta-regression analyses

13.1 CR Enterobacterales

Study characteristic	Level	S	Predicted CFDC-NS % (CI)	Odds ratio (CI)	P-value	R^2
Year	2015-2019	5	5.4 (0.0 - 16.3)	Ref.	0.718	0.9%
	2020-2023	31	3.6 (0.5 - 6.7)	0.66 (0.07 - 6.46)		
Region [1]	EUR	12	3.1 (0.0 - 7.2)	0.72 (0.13 - 3.88)	0.700	6.8%
	AMR	8	1.1 (0.0 - 3.3)	0.21 (0.03 - 1.63)	0.136	
	WPR	6	9.6 (0.0 - 26.2)	3.27 (0.40 - 27.02)	0.272	
	Multi-regional	10	6.1 (0.0 - 15.1)	2.05 (0.33 - 12.64)	0.440	
Multinational	No	30	4.1 (0.5 - 7.7)	Ref.	0.662	1.5%
	Yes	6	2.6 (0.0 - 7.7)	0.61 (0.07 - 5.59)		
Multicenter	No	8	27.9 (0.0 - 57.9)	Ref.	0.001	28.1%
	Yes	28	2.2 (0.3 - 4.1)	0.06 (0.01 - 0.33)		
RoB, population and setting	Moderate/High risk	33	4.3 (0.7 - 7.8)	Ref.	0.337	3.1%
	Low risk	3	1.1 (0.0 - 4.1)	0.25 (0.01 - 4.23)		
RoB, condition measurement	Moderate/High risk	19	3.8 (0.0 - 7.9)	Ref.	0.992	0.0%
	Low risk	17	3.8 (0.0 - 8.2)	1.01 (0.20 - 5.06)		

Univariate meta-regression analysis of the associations between study-level characteristics and prevalence of Cefiderocol non-susceptible CR Enterobacterales based on CLSI-FDA breakpoints.

S, the number of independent data sets in the analysis; **CFDC-NS**, Cefiderocol non-susceptible; **CI**, 95% confidence interval; **EUR**, European region; **AMR**, Region of the Americas; **WPR**, Western Pacific Region; **RoB**, risk of bias.

[1] Region defined by the WHO grouping. The odds ratio for each region compares that region to all other regions combined (e.g. EUR vs. elsewhere).

13.2 CR *K. pneumoniae*

Study characteristic	Level	S	Predicted CFDC-NS % (CI)	Odds ratio (CI)	P-value	R^2
Year	2015-2019	4	0.2 (0.0 - 0.8)	Ref.	0.101	13.2%
	2020-2023	19	2.4 (0.1 - 4.8)	11.42 (0.62 - 209.44)		
Region [1]	EUR	8	0.9 (0.0 - 2.3)	0.36 (0.05 - 2.38)	0.287	23.9%
	AMR	5	2.8 (0.0 - 8.3)	1.92 (0.21 - 17.35)	0.560	
	WPR	3	0.5 (0.0 - 1.7)	0.23 (0.02 - 2.93)	0.258	
	Multi-regional	7	4.3 (0.0 - 10.8)	3.77 (0.58 - 24.67)	0.165	
Multinational	No	20	2.0 (0.0 - 3.9)	Ref.	0.384	3.5%
	Yes	3	0.5 (0.0 - 1.9)	0.23 (0.01 - 6.26)		
Multicenter	No	5	4.7 (0.0 - 12.8)	Ref.	0.204	7.5%
	Yes	18	1.3 (0.0 - 2.6)	0.26 (0.03 - 2.08)		
RoB, population and setting	Moderate/High risk	20	1.8 (0.0 - 3.6)	Ref.	0.840	0.6%
	Low risk	3	1.3 (0.0 - 4.6)	0.77 (0.06 - 10.27)		
RoB, condition measurement	Moderate/High risk	13	2.3 (0.0 - 5.1)	Ref.	0.462	4.6%
	Low risk	10	1.2 (0.0 - 2.8)	0.51 (0.08 - 3.09)		

Univariate meta-regression analysis of the associations between study-level characteristics and prevalence of Cefiderocol non-susceptible CR *K. pneumoniae* based on CLSI breakpoints.

S, the number of independent data sets in the analysis; **CFDC-NS**, Cefiderocol non-susceptible; **CI**, 95% confidence interval; **EUR**, European region; **AMR**, Region of the Americas; **WPR**, Western Pacific Region; **RoB**, risk of bias.

[1] Region defined by the WHO grouping. The odds ratio for each region compares that region to all other regions combined (e.g. EUR vs. elsewhere).

13.3 CR *P. aeruginosa*

Study characteristic	Level	S	Predicted CFDC-NS % (CI)	Odds ratio (CI)	P-value	R^2
Year	2015-2019	5	0.6 (0.0 - 1.8)	Ref.	0.739	2.0%
	2020-2023	18	0.9 (0.0 - 1.9)	1.43 (0.17 - 12.01)		
Region [1]	EUR	9	1.1 (0.0 - 2.9)	1.59 (0.26 - 9.60)	0.613	18.8%
	AMR	5	0.5 (0.0 - 1.7)	0.60 (0.06 - 5.99)	0.661	
	WPR	4	0.1 (0.0 - 0.4)	0.07 (0.00 - 1.48)	0.089	
	Multi-regional	5	2.0 (0.0 - 5.2)	3.61 (0.46 - 28.51)	0.223	
Multinational	No	19	1.0 (0.0 - 2.1)	Ref.	0.552	8.4%
	Yes	4	0.5 (0.0 - 1.5)	0.52 (0.06 - 4.41)		
Multicenter	No	5	1.2 (0.0 - 3.4)	Ref.	0.618	0.0%
	Yes	18	0.7 (0.0 - 1.6)	0.59 (0.08 - 4.66)		
RoB, population and setting	Moderate/High risk	22	0.9 (0.0 - 1.8)	Ref.	.	4.5%
	Low risk	1	Insufficient data	Non-estimable		
RoB, condition measurement	Moderate/High risk	8	1.0 (0.0 - 2.5)	Ref.	0.784	1.6%
	Low risk	15	0.8 (0.0 - 1.7)	0.77 (0.12 - 4.87)		

Univariate meta-regression analysis of the associations between study-level characteristics and prevalence of Cefiderocol non-susceptible CR *P. aeruginosa* based on CLSI breakpoints).

S, the number of independent data sets in the analysis; **CFDC-NS**, Cefiderocol non-susceptible; **CI**, 95% confidence interval; **EUR**, European region; **AMR**, Region of the Americas; **WPR**, Western Pacific Region; **RoB**, risk of bias.

[1] Region defined by the WHO grouping. The odds ratio for each region compares that region to all other regions combined (e.g. EUR vs. elsewhere).

13.4 CR *A. baumannii*

Study characteristic	Level	S	Predicted CFDC-NS % (CI)	Odds ratio (CI)	P-value	R^2
Year	2015-2019	4	5.0 (0.0 - 10.2)	Ref.	0.298	4.1%
	2020-2023	22	9.0 (5.2 - 12.8)	1.86 (0.58 - 6.01)		
Region [1]	EUR	9	7.7 (2.0 - 13.4)	0.90 (0.35 - 2.34)	0.836	0.0%
	AMR	6	8.5 (1.6 - 15.5)	1.06 (0.38 - 2.94)	0.907	
	WPR	4	8.2 (0.3 - 16.2)	1.01 (0.32 - 3.18)	0.991	
	Multi-regional	7	8.4 (2.3 - 14.5)	1.04 (0.41 - 2.68)	0.929	
Multinational	No	20	7.6 (4.0 - 11.2)	Ref.	0.556	0.0%
	Yes	6	9.9 (2.5 - 17.4)	1.34 (0.50 - 3.56)		
Multicenter	No	5	18.8 (5.5 - 32.1)	Ref.	0.020	20.6%
	Yes	21	6.7 (3.9 - 9.5)	0.31 (0.12 - 0.83)		
RoB, population and setting	Moderate/High risk	23	7.8 (4.6 - 11.0)	Ref.	0.401	6.3%
	Low risk	3	13.3 (0.0 - 28.6)	1.82 (0.45 - 7.31)		
RoB, condition measurement	Moderate/High risk	10	8.7 (3.2 - 14.2)	Ref.	0.798	0.4%
	Low risk	16	7.9 (3.8 - 11.9)	0.89 (0.37 - 2.15)		

Univariate meta-regression analysis of the associations between study-level characteristics and prevalence of Cefiderocol non-susceptible CR *A. baumannii* based on CLSI breakpoints.

S, the number of independent data sets in the analysis; **CFDC-NS**, Cefiderocol non-susceptible; **CI**, 95% confidence interval; **EUR**, European region; **AMR**, Region of the Americas; **WPR**, Western Pacific Region; **RoB**, risk of bias.

[1] Region defined by the WHO grouping. The odds ratio for each region compares that region to all other regions combined (e.g. EUR vs. elsewhere).

14 References

[1] FDA, Cefiderocol Injection. FDA Identified Breakpoints. <https://www.fda.gov/drugs/development-resources/cefiderocol-injection>, 2020 (accessed 22/12/2022.2022).

[2] CLSI, Performance Standards for Antimicrobial Susceptibility Testing. 32st ed. CLSI supplement M100., Clinical Laboratory Standards Institute, Wayne, 2022.

[3] The European Committee on Antimicrobial Susceptibility Testing, Breakpoint tables for interpretation of MICs and zone diameters. Version 12.0. <http://www.eucast.org/>, 2023 (accessed 2023-03-24.2023).

[4] C.P. Morris, Y. Bergman, T. Tekle, J.A. Fissel, P.D. Tamma, P.J. Simner, Cefiderocol Antimicrobial Susceptibility Testing against Multidrug-Resistant Gram-Negative Bacilli: a Comparison of Disk Diffusion to Broth Microdilution, Journal of clinical microbiology 59(1) (2020).

[5] R.A. Bonnin, C. Emeraud, A.B. Jousset, T. Naas, L. Dortet, Comparison of disk diffusion, MIC test strip and broth microdilution methods for cefiderocol susceptibility testing on carbapenem-resistant enterobacterales, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 28(8) (2022) 1156.e1-1156.e5.

[6] C.B. Migliavaca, C. Stein, V. Colpani, Z. Munn, M. Falavigna, Quality assessment of prevalence studies: a systematic review, Journal of clinical epidemiology 127 (2020) 59-68.

[7] Z. Munn, S. Moola, K. Lisy, D. Riitano, C. Tufanaru, Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data, International journal of evidence-based healthcare 13(3) (2015) 147-53.

[8] European Society for Clinical Microbiology and Infectious Diseases, Guidance document on broth microdilution testing of cefiderocol. <https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Guidance_documents/Cefiderocol_MIC_testing_EUCAST_guidance_document_201217.pdf>, 2020 (accessed February 2022.).

[9] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth, Diagnostic microbiology and infectious disease 94(4) (2019) 321-325.

[10] J.A. Karlowsky, M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, D.F. Sahm, In Vitro Activity of Cefiderocol, a Siderophore Cephalosporin, Against Gram-Negative Bacilli Isolated by Clinical Laboratories in North America and Europe in 2015-2016: SIDERO-WT-2015, International journal of antimicrobial agents (2018).

[11] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, In Vitro Activity of the Siderophore Cephalosporin, Cefiderocol, against a Recent Collection of Clinically Relevant Gram-Negative Bacilli from North America and Europe, Including Carbapenem-Nonsusceptible Isolates (SIDERO-WT-2014 Study), Antimicrobial agents and chemotherapy 61(9) (2017).

[12] M. Alzayer, M.F. Alghoribi, B. Alalwan, A. Alreheli, S. Aljohani, M. Bosaeed, M. Doumith, In vitro activity of cefiderocol against clinically important carbapenem non-susceptible Gram-negative bacteria from Saudi Arabia, Journal of global antimicrobial resistance 32 (2023) 176-180.

[13] Y.D. Bakthavatchalam, A. Shankar, Y. Manokaran, K. Walia, B. Veeraraghavan, Can fosfomycin be an alternative therapy for infections caused by E. coli harbouring dual resistance: NDM and four-amino acid insertion in PBP3?, JAC-antimicrobial resistance 5(2) (2023) dlad016.

[14] G. Bianco, M. Boattini, S. Comini, G. Banche, R. Cavallo, C. Costa, Disc Diffusion and ComASP(®) Cefiderocol Microdilution Panel to Overcome the Challenge of Cefiderocol Susceptibility Testing in Clinical Laboratory Routine, Antibiotics (Basel, Switzerland) 12(3) (2023).

[15] J.E. Cañada-García, E. Ramírez de Arellano, M. Jiménez-Orellana, E. Viedma, A. Sánchez, A. Alhambra, J. Villa, A. Delgado-Iribarren, V. Bautista, N. Lara, S. García-Cobos, B. Aracil, E. Cercenado, M. Pérez-Vázquez, J. Oteo-Iglesias, Carbapenemase-Producing Klebsiella pneumoniae in COVID-19 Intensive Care Patients: Identification of IncL-VIM-1 Plasmid in Previously Non-Predominant Sequence Types, Antibiotics (Basel, Switzerland) 12(1) (2023).

[16] I. Galani, V. Papoutsaki, I. Karaiskos, N. Moustakas, L. Galani, S. Maraki, V.E. Mavromanolaki, O. Legga, K. Fountoulis, E.D. Platsouka, P. Giannopoulou, H. Papadogeorgaki, M. Damala, E. Chinou, A. Pasxali, I.

Deliolanis, H. Vagiakou, E. Petinaki, A. Chli, E. Vagdatli, P. Kazila, V. Papaioannou, K. Kontopoulou, A.N. Ferke, E. Moraitou, A. Antoniadou, H. Giamarellou, In vitro activities of omadacycline, eravacycline, cefiderocol, apramycin, and comparator antibiotics against Acinetobacter baumannii causing bloodstream infections in Greece, 2020-2021: a multicenter study, European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology 42(7) (2023) 843-852.

[17] L. Devoos, A. Biguenet, J. Rousselot, M. Bour, P. Plésiat, D. Fournier, K. Jeannot, Performance of discs, sensititre EUMDROXF microplates and MTS gradient strips for the determination of the susceptibility of multidrug-resistant Pseudomonas aeruginosa to cefiderocol, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 29(5) (2023) 652.e1-652.e8.

[18] Y.S. Huang, P.Y. Chen, P.C. Chou, J.T. Wang, In Vitro Activities and Inoculum Effects of Cefiderocol and Aztreonam-Avibactam against Metallo-β-Lactamase-Producing Enterobacteriaceae, Microbiology spectrum 11(3) (2023) e0056923.

[19] B. Ihssane, E.O. Fatima, K. Aboubakr, B. Fatna, T. Mohammed, B. Pierre, H. Te-Din, N. Kaotar, First report of Pseudomonas aeruginosa strains co-harboring bla(NDM)-bla(VIM) and bla(VIM)-bla(IMP) metallo-β-lactamase genes in Morocco, Journal of global antimicrobial resistance 33 (2023) 42-43.

[20] N. Kohira, M.A. Hackel, M. Oota, M. Takemura, F. Hu, H. Mizuno, D.F. Sahm, Y. Yamano, In vitro antibacterial activities of cefiderocol against Gram-negative clinical strains isolated from China in 2020, Journal of global antimicrobial resistance 32 (2023) 181-186.

[21] C. Lasarte-Monterrubio, P. Guijarro-Sánchez, J.C. Vázquez-Ucha, I. Alonso-Garcia, L. Alvarez-Fraga, M. Outeda, M. Martinez-Guitian, A. Peña-Escolano, R. Maceiras, E. Lence, C. González-Bello, J. Arca-Suárez, G. Bou, A. Beceiro, Antimicrobial Activity of Cefiderocol against the Carbapenemase-Producing Enterobacter cloacae Complex and Characterization of Reduced Susceptibility Associated with Metallo-β-Lactamase VIM-1, Antimicrobial agents and chemotherapy 67(5) (2023) e0150522.

[22] C. Le Terrier, P. Nordmann, L. Poirel, In vitro activity of aztreonam in combination with newly developed β-lactamase inhibitors against MDR Enterobacterales and Pseudomonas aeruginosa producing metallo-β-lactamases, Journal of Antimicrobial Chemotherapy 78(1) (2022) 101-107.

[23] S. Maraki, V.E. Mavromanolaki, D. Stafylaki, E. Scoulica, In vitro activity of newer β-lactam/β-lactamase inhibitor combinations, cefiderocol, plazomicin and comparators against carbapenemase-producing Klebsiella pneumoniae isolates, Journal of chemotherapy (Florence, Italy) (2023) 1-5.

[24] M. Marner, L. Kolberg, J. Horst, N. Böhringer, J. Hübner, I.D.M. Kresna, Y. Liu, U. Mettal, L. Wang, M. Meyer-Bühn, S. Mihajlovic, M. Kappler, T.F. Schäberle, U. von Both, Antimicrobial Activity of Ceftazidime-Avibactam, Ceftolozane-Tazobactam, Cefiderocol, and Novel Darobactin Analogs against Multidrug-Resistant Pseudomonas aeruginosa Isolates from Pediatric and Adolescent Cystic Fibrosis Patients, Microbiology spectrum 11(1) (2023) e0443722.

[25] M. Padovani, A. Bertelli, S. Corbellini, G. Piccinelli, F. Gurrieri, M.A. De Francesco, In Vitro Activity of Cefiderocol on Multiresistant Bacterial Strains and Genomic Analysis of Two Cefiderocol Resistant Strains, Antibiotics (Basel, Switzerland) 12(4) (2023).

[26] P. Perez-Palacios, D. Girlich, N. Soraa, A. Lamrani, F.M.R. Maoulainine, F. Bennaoui, H. Amri, N.S. El Idrissi, M. Bouskraoui, A. Birer, A.B. Jousset, S. Oueslati, J. Raymond, T. Naas, Multidrug-resistant Enterobacterales responsible for septicaemia in a neonatal intensive care unit in Morocco, Journal of global antimicrobial resistance 33 (2023) 208-217.

[27] R.F. Potter, M.A. Wallace, C.E. Muenks, K. Alvarado, M.L. Yarbrough, C.D. Burnham, Evaluation of Variability in Interpretation of Disk Diffusion Testing for Cefiderocol Using Different Brands of Mueller-Hinton Agar, The journal of applied laboratory medicine 8(3) (2023) 523-534.

[28] A. Ruedas-López, I. Alonso-García, C. Lasarte-Monterrubio, P. Guijarro-Sánchez, E. Gato, J.C. Vázquez-Ucha, J.A. Vallejo, P.A. Fraile-Ribot, B. Fernández-Pérez, D. Velasco, J.M. Gutiérrez-Urbón, M. Oviaño, A. Beceiro, C. González-Bello, A. Oliver, J. Arca-Suárez, G. Bou, Selection of AmpC β-Lactamase Variants and Metallo-β-Lactamases Leading to Ceftolozane/Tazobactam and Ceftazidime/Avibactam Resistance during Treatment of MDR/XDR Pseudomonas aeruginosa Infections, Antimicrob Agents Chemother 66(2) (2022) e0206721.

[29] T. Sewunet, D. Asrat, Y. Woldeamanuel, A. Aseffa, C.G. Giske, Molecular epidemiology and antimicrobial susceptibility of Pseudomonas spp. and Acinetobacter spp. from clinical samples at Jimma medical center, Ethiopia, Frontiers in microbiology 13 (2022) 951857.

[30] P.D. Tamma, Y. Bergman, E.B. Jacobs, J.H. Lee, S. Lewis, S.E. Cosgrove, P.J. Simner, Comparing the activity of novel antibiotic agents against carbapenem-resistant Enterobacterales clinical isolates, Infection control and hospital epidemiology 44(5) (2023) 762-767.
[31] J. Xu, H. Guo, L. Li, F. He, Molecular epidemiology and genomic insights into the transmission of carbapenem-resistant NDM-producing Escherichia coli, Computational and structural biotechnology journal 21 (2023) 847-855.
[32] S.G. Badran, M.M. Malek, R.M. Ateya, A.H. Afifi, M.M. Magdy, E.S. Elgharabawy, Susceptibility of carbapenem-resistant Enterobacterales isolates to new antibiotics from a tertiary care hospital, Egypt: A matter of hope, Journal of infection in developing countries 16(12) (2022) 1852-1859.
[33] C. Ballesté-Delpierre, Á. Ramírez, L. Muñoz, C. Longshaw, I. Roca, J. Vila, Assessment of In Vitro Cefiderocol Susceptibility and Comparators against an Epidemiologically Diverse Collection of Acinetobacter baumannii Clinical Isolates, Antibiotics (Basel, Switzerland) 11(2) (2022).
[34] J.E. Cañada-García, Z. Moure, P.J. Sola-Campoy, M. Delgado-Valverde, M.E. Cano, D. Gijón, M. González, I. Gracia-Ahufinger, N. Larrosa, X. Mulet, C. Pitart, A. Rivera, G. Bou, J. Calvo, R. Cantón, J.J. González-López, L. Martínez-Martínez, F. Navarro, A. Oliver, Z.R. Palacios-Baena, Á. Pascual, G. Ruiz-Carrascoso, J. Vila, B. Aracil, M. Pérez-Vázquez, J. Oteo-Iglesias, CARB-ES-19 Multicenter Study of Carbapenemase-Producing Klebsiella pneumoniae and Escherichia coli From All Spanish Provinces Reveals Interregional Spread of High-Risk Clones Such as ST307/OXA-48 and ST512/KPC-3, Front Microbiol 13 (2022) 918362.
[35] F.J. Candel, A. Santerre Henriksen, C. Longshaw, Y. Yamano, A. Oliver, In vitro activity of the novel siderophore cephalosporin, cefiderocol, in Gram-negative pathogens in Europe by site of infection, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 28(3) (2022) 447.e1-447.e6.
[36] V. Di Pilato, L. Henrici De Angelis, N. Aiezza, I. Baccani, C. Niccolai, E.M. Parisio, C. Giordano, G. Camarlinghi, S. Barnini, S. Forni, L. Righi, M.T. Mechi, T. Giani, A. Antonelli, G.M. Rossolini, Resistome and virulome accretion in an NDM-1-producing ST147 sublineage of Klebsiella pneumoniae associated with an outbreak in Tuscany, Italy: a genotypic and phenotypic characterisation, The Lancet. Microbe 3(3) (2022) e224-e234.
[37] L. Daoud, F. Al-Marzooq, C.A. Moubareck, A. Ghazawi, T. Collyns, Elucidating the effect of iron acquisition systems in Klebsiella pneumoniae on susceptibility to the novel siderophore-cephalosporin cefiderocol, PloS one 17(12) (2022) e0277946.
[38] A. Iovleva, M.M. Mustapha, M.P. Griffith, L. Komarow, C. Luterbach, D.R. Evans, E. Cober, S.S. Richter, K. Rydell, C.A. Arias, J.T. Jacob, R.A. Salata, M.J. Satlin, D. Wong, R.A. Bonomo, D. van Duin, V.S. Cooper, D. Van Tyne, Y. Doi, Carbapenem-Resistant Acinetobacter baumannii in U.S. Hospitals: Diversification of Circulating Lineages and Antimicrobial Resistance, mBio 13(2) (2022) e0275921.
[39] J.A. Karlowsky, M.A. Hackel, M. Takemura, Y. Yamano, R. Echols, D.F. Sahm, In Vitro Susceptibility of Gram-Negative Pathogens to Cefiderocol in Five Consecutive Annual Multinational SIDERO-WT Surveillance Studies, 2014 to 2019, Antimicrobial agents and chemotherapy 66(2) (2022) e0199021.
[40] J.A. Karlowsky, A.J. Walkty, M.R. Baxter, H.J. Adam, P.R.S. Lagacé-Wiens, F. Schweizer, D. Bay, J.P. Lynch, 3rd, M.R. Mulvey, G.G. Zhanel, In Vitro Activity of Cefiderocol against Extensively Drug-Resistant Pseudomonas aeruginosa: CANWARD, 2007 to 2019, Microbiology spectrum 10(4) (2022) e0172422.
[41] Karpova E.V., T. D.V., Activity of Cefiderocol and Other New Antibiotics Against Extensively Drug-Resistant Klebsiella pneumoniae Strains. , Antibiotics and Chemotherapy. 67(11) (2022) 16-21.
[42] P. Lan, Y. Lu, Z. Chen, X. Wu, X. Hua, Y. Jiang, J. Zhou, Y. Yu, Emergence of High-Level Cefiderocol Resistance in Carbapenem-Resistant Klebsiella pneumoniae from Bloodstream Infections in Patients with Hematologic Malignancies in China, Microbiology spectrum 10(2) (2022) e0008422.
[43] C. Lasarte-Monterrubio, P.A. Fraile-Ribot, J.C. Vázquez-Ucha, G. Cabot, P. Guijarro-Sánchez, I. Alonso-García, S. Rumbo-Feal, F. Galán-Sánchez, A. Beceiro, J. Arca-Suárez, A. Oliver, G. Bou, Activity of cefiderocol, imipenem/relebactam, cefepime/taniborbactam and cefepime/zidebactam against ceftolozane/tazobactam- and ceftazidime/avibactam-resistant Pseudomonas aeruginosa, J Antimicrob Chemother 77(10) (2022) 2809-2815.
[44] H.C. Mİrza, G. İnce Cevİz, Comparison of in vitro activities of cefiderocol, imipenem/relebactam and other antibiotics against carbapenem-resistant Pseudomonas aeruginosa isolates, Turk Hij Den Biyol Derg 79(3) (2022) 433-442.

[45] G. Morroni, L. Brescini, A. Antonelli, V. Di Pilato, S. Castelletti, A. Brenciani, G. D'Achille, M. Mingoia, E. Giovanetti, S. Fioriti, A. Masucci, T. Giani, A. Giacometti, G.M. Rossolini, O. Cirioni, Clinical and microbiological features of ceftolozane/tazobactam-resistant Pseudomonas aeruginosa isolates in a university hospital in central Italy, Journal of global antimicrobial resistance 30 (2022) 377-383.
[46] G. Nayak, B. Behera, S. Mohanty, P. Kar, J. Jena, Analysis of In Vitro Activity of Cefiderocol Against Carbapenem-Resistant Gram-Negative Bacilli by Broth Microdilution and Disk Diffusion Method: A Single-Center Study in Odisha, India, Infection and drug resistance 15 (2022) 5887-5897.
[47] R.A. Ramadan, A.M. Bedawy, E.M. Negm, T.H. Hassan, D.A. Ibrahim, S.M. ElSheikh, R.M. Amer, Carbapenem-Resistant Klebsiella pneumoniae Among Patients with Ventilator-Associated Pneumonia: Evaluation of Antibiotic Combinations and Susceptibility to New Antibiotics, Infection and drug resistance 15 (2022) 3537-3548.
[48] S. Oueslati, P. Bogaerts, L. Dortet, S. Bernabeu, H. Ben Lakhal, C. Longshaw, Y. Glupczynski, T. Naas, In vitro Activity of Cefiderocol and Comparators against Carbapenem-Resistant Gram-Negative Pathogens from France and Belgium, Antibiotics (Basel, Switzerland) 11(10) (2022).
[49] D. Shortridge, J.M. Streit, R. Mendes, M. Castanheira, In Vitro Activity of Cefiderocol against U.S. and European Gram-Negative Clinical Isolates Collected in 2020 as Part of the SENTRY Antimicrobial Surveillance Program, Microbiology spectrum 10(2) (2022) e0271221.
[50] Q. Wang, L. Jin, S. Sun, Y. Yin, R. Wang, F. Chen, X. Wang, Y. Zhang, J. Hou, Y. Zhang, Z. Zhang, L. Luo, Z. Guo, Z. Li, X. Lin, L. Bi, H. Wang, Occurrence of High Levels of Cefiderocol Resistance in Carbapenem-Resistant Escherichia coli before Its Approval in China: a Report from China CRE-Network, Microbiology spectrum (2022) e0267021.
[51] Q. Wang, L. Jin, S. Sun, Y. Yin, R. Wang, F. Chen, X. Wang, Y. Zhang, J. Hou, Y. Zhang, Z. Zhang, L. Luo, Z. Guo, Z. Li, X. Lin, L. Bi, H. Wang, Occurrence of High Levels of Cefiderocol Resistance in Carbapenem-Resistant Escherichia coli before Its Approval in China: a Report from China CRE-Network, Microbiology spectrum 10(3) (2022) e0267021.
[52] C. Weber, T. Schultze, S. Göttig, J. Kessel, A. Schröder, M. Tietgen, S. Besier, T. Burbach, S. Häussler, T.A. Wichelhaus, D. Hack, V.A.J. Kempf, M. Hogardt, Antimicrobial Activity of Ceftolozane-Tazobactam, Ceftazidime-Avibactam, and Cefiderocol against Multidrug-Resistant Pseudomonas aeruginosa Recovered at a German University Hospital, Microbiology spectrum 10(5) (2022) e0169722.
[53] P. Zalas-Więcek, K. Płachta, E. Gospodarek-Komkowska, Cefiderocol against Multi-Drug and Extensively Drug-Resistant Escherichia coli: An In Vitro Study in Poland, Pathogens 11(12) (2022).
[54] Q. Zhang, N. Neidig, T.Y. Chu, C. Divoky, J. Carpenter, C. Lee-Hsiao, H. Threatt, R. Sultana, K. Bush, In vitro antibacterial activity of cefiderocol against recent multidrug-resistant carbapenem-nonsusceptible Enterobacterales isolates, Diagnostic microbiology and infectious disease 103(1) (2022) 115651.
[55] J.C. Abdul-Mutakabbir, L. Nguyen, P.T. Maassen, K.C. Stamper, R. Kebriaei, K.S. Kaye, M. Castanheira, M.J. Rybak, In Vitro Antibacterial Activity of Cefiderocol against Multidrug-Resistant Acinetobacter baumannii, Antimicrobial agents and chemotherapy 65(9) (2021) e0264620.
[56] M. Albano, M.J. Karau, A.N. Schuetz, R. Patel, Comparison of Agar Dilution to Broth Microdilution for Testing In Vitro Activity of Cefiderocol against Gram-Negative Bacilli, Journal of clinical microbiology 59(1) (2020).
[57] S.S. Bhagwat, N.J. Legakis, T. Skalidis, A. Loannidis, C. Goumenopoulos, P.R. Joshi, R. Shrivastava, S.R. Palwe, H. Periasamy, M.V. Patel, S. Chatzipanagiotou, In vitro activity of cefepime/zidebactam (WCK 5222) against recent Gram-negative isolates collected from high resistance settings of Greek hospitals, Diagnostic microbiology and infectious disease 100(3) (2021) 115327.
[58] D. Carcione, C. Siracusa, A. Sulejmani, R. Migliavacca, A. Mercato, A. Piazza, L. Principe, N. Clementi, N. Mancini, V. Leoni, J. Intra, In Vitro Antimicrobial Activity of the Siderophore Cephalosporin Cefiderocol against Acinetobacter baumannii Strains Recovered from Clinical Samples, Antibiotics (Basel, Switzerland) 10(11) (2021).
[59] J.E. Choby, T. Ozturk, S.W. Satola, J.T. Jacob, D.S. Weiss, Widespread cefiderocol heteroresistance in carbapenem-resistant Gram-negative pathogens, The Lancet Infectious Diseases 21(5) (2021) 597-598.
[60] B. Ghebremedhin, P. Ahmad-Nejad, In-Vitro Efficacy of Cefiderocol in Carbapenem-Non-Susceptible Gram-Negative Bacilli of Different Genotypes in Sub-Region of North Rhine Westphalia, Germany, Pathogens 10(10) (2021).

[61] A.S. Jacob, G.L. Chong, K. Lagrou, M. Depypere, S. Desmet, No in vitro activity of cefiderocol against OXA-427-producing Enterobacterales, J Antimicrob Chemother 76(12) (2021) 3317-3318.
[62] B.D. Johnston, P. Thuras, S.B. Porter, C. Clabots, J.R. Johnsona, Activity of cefiderocol, ceftazidime-avibactam, and eravacycline against extended-spectrum cephalosporin-resistant Escherichia coli clinical isolates (2012-20017) in relation to phylogenetic background, sequence type 131 subclones, bla(CTX-M) genotype, and coresistance, Diagnostic microbiology and infectious disease 100(1) (2021) 115314.
[63] Y.L. Lee, W.C. Ko, W.S. Lee, P.L. Lu, Y.H. Chen, S.H. Cheng, M.C. Lu, C.Y. Lin, T.S. Wu, M.Y. Yen, L.S. Wang, C.P. Liu, P.L. Shao, Z.Y. Shi, Y.S. Chen, F.D. Wang, S.H. Tseng, C.N. Lin, Y.H. Chen, W.H. Sheng, C.M. Lee, H.J. Tang, P.R. Hsueh, In-vitro activity of cefiderocol, cefepime/zidebactam, cefepime/enmetazobactam, omadacycline, eravacycline and other comparative agents against carbapenem-nonsusceptible Enterobacterales: results from the Surveillance of Multicenter Antimicrobial Resistance in Taiwan (SMART) in 2017-2020, International journal of antimicrobial agents 58(3) (2021) 106377.
[64] P.Y. Liu, W.C. Ko, W.S. Lee, P.L. Lu, Y.H. Chen, S.H. Cheng, M.C. Lu, C.Y. Lin, T.S. Wu, M.Y. Yen, L.S. Wang, C.P. Liu, P.L. Shao, Y.L. Lee, Z.Y. Shi, Y.S. Chen, F.D. Wang, S.H. Tseng, C.N. Lin, Y.H. Chen, W.H. Sheng, C.M. Lee, H.J. Tang, P.R. Hsueh, In vitro activity of cefiderocol, cefepime/enmetazobactam, cefepime/zidebactam, eravacycline, omadacycline, and other comparative agents against carbapenem-non-susceptible Pseudomonas aeruginosa and Acinetobacter baumannii isolates associated from bloodstream infection in Taiwan between 2018-2020, Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi (2021).
[65] M. Biagi, A. Vialichka, M. Jurkovic, T. Wu, A. Shajee, M. Lee, S. Patel, R.E. Mendes, E. Wenzler, Activity of Cefiderocol Alone and in Combination with Levofloxacin, Minocycline, Polymyxin B, or Trimethoprim-Sulfamethoxazole against Multidrug-Resistant Stenotrophomonas maltophilia, Antimicrob Agents Chemother 64(9) (2020).
[66] M. Delgado-Valverde, M.D.C. Conejo, L. Serrano, F. Fernández-Cuenca, Á. Pascual, Activity of cefiderocol against high-risk clones of multidrug-resistant Enterobacterales, Acinetobacter baumannii, Pseudomonas aeruginosa and Stenotrophomonas maltophilia, J Antimicrob Chemother 75(7) (2020) 1840-1849.
[67] A.R. Golden, H.J. Adam, M. Baxter, A. Walkty, P. Lagacé-Wiens, J.A. Karlowsky, G.G. Zhanel, In Vitro Activity of Cefiderocol, a Novel Siderophore Cephalosporin, against Gram-Negative Bacilli Isolated from Patients in Canadian Intensive Care Units, Diagnostic microbiology and infectious disease 97(1) (2020) 115012.
[68] A. Iregui, Z. Khan, D. Landman, J. Quale, Activity of Cefiderocol Against Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter baumannii Endemic to Medical Centers in New York City, Microbial drug resistance (Larchmont, N.Y.) 26(7) (2020) 722-726.
[69] B.D. Johnston, P. Thuras, S.B. Porter, M. Anacker, B. VonBank, P. Snippes Vagnone, M. Witwer, M. Castanheira, J.R. Johnson, Activity of Cefiderocol, Ceftazidime-Avibactam, and Eravacycline against Carbapenem-Resistant Escherichia coli Isolates from the United States and International Sites in Relation to Clonal Background, Resistance Genes, Coresistance, and Region, Antimicrobial agents and chemotherapy 64(10) (2020).
[70] M. Kresken, M. Korte-Berwanger, S.G. Gatermann, Y. Pfeifer, N. Pfennigwerth, H. Seifert, G. Werner, In vitro activity of cefiderocol against aerobic Gram-negative bacterial pathogens from Germany, International journal of antimicrobial agents 56(4) (2020) 106128.
[71] C. Longshaw, D. Manissero, M. Tsuji, R. Echols, Y. Yamano, In vitro activity of the siderophore cephalosporin, cefiderocol, against molecularly characterized, carbapenem-non-susceptible Gram-negative bacteria from Europe, JAC-antimicrobial resistance 2(3) (2020).
[72] M.A. Hackel, M. Tsuji, Y. Yamano, R. Echols, J.A. Karlowsky, D.F. Sahm, In Vitro Activity of the Siderophore Cephalosporin, Cefiderocol, against Carbapenem-Nonsusceptible and Multidrug-Resistant Isolates of Gram-Negative Bacilli Collected Worldwide in 2014 to 2016, Antimicrobial agents and chemotherapy 62(2) (2018).
[73] S. Mushtaq, Z. Sadouki, A. Vickers, D.M. Livermore, N. Woodford, In Vitro Activity of Cefiderocol, a Siderophore Cephalosporin, against Multidrug-Resistant Gram-Negative Bacteria, Antimicrobial agents and chemotherapy 64(12) (2020).
[74] K.V.I. Rolston, B. Gerges, S. Shelburne, S.L. Aitken, I. Raad, R.A. Prince, Activity of Cefiderocol and Comparators against Isolates from Cancer Patients, Antimicrobial agents and chemotherapy 64(5) (2020).
[75] D.A. Talan, S.S. Takhar, A. Krishnadasan, W.R. Mower, D.J. Pallin, M. Garg, J. Femling, R.E. Rothman, J.C. Moore, A.E. Jones, F. Lovecchio, J. Jui, M.T. Steele, A.M. Stubbs, W.K. Chiang, G.J. Moran, Emergence of

Extended-Spectrum β-Lactamase Urinary Tract Infections Among Hospitalized Emergency Department Patients in the United States, Annals of emergency medicine 77(1) (2021) 32-43.
[76] V. Trebosc, B. Schellhorn, J. Schill, V. Lucchini, J. Bühler, M. Bourotte, J.J. Butcher, M. Gitzinger, S. Lociuro, C. Kemmer, G.E. Dale, In vitro activity of rifabutin against 293 contemporary carbapenem-resistant Acinetobacter baumannii clinical isolates and characterization of rifabutin mode of action and resistance mechanisms, J Antimicrob Chemother (2020).
[77] O. Xie, K. Cisera, L. Taylor, C. Hughes, B. Rogers, Clinical syndromes and treatment location predict utility of carbapenem sparing therapies in ceftriaxone-non-susceptible Escherichia coli bloodstream infection, Annals of clinical microbiology and antimicrobials 19(1) (2020) 57.
[78] S.C. Hsueh, Y.J. Lee, Y.T. Huang, C.H. Liao, M. Tsuji, P.R. Hsueh, In vitro activities of cefiderocol, ceftolozane/tazobactam, ceftazidime/avibactam and other comparative drugs against imipenem-resistant Pseudomonas aeruginosa and Acinetobacter baumannii, and Stenotrophomonas maltophilia, all associated with bloodstream infections in Taiwan, The Journal of antimicrobial chemotherapy 74(2) (2019) 380-386.
[79] M.R. Jacobs, A.M. Abdelhamed, C.E. Good, D.D. Rhoads, K.M. Hujer, A.M. Hujer, T.N. Domitrovic, S.D. Rudin, S.S. Richter, D. van Duin, B.N. Kreiswirth, C. Greco, D.E. Fouts, R.A. Bonomo, ARGONAUT-I: Activity of Cefiderocol (S-649266), a Siderophore Cephalosporin, against Gram-Negative Bacteria, Including Carbapenem-Resistant Nonfermenters and Enterobacteriaceae with Defined Extended-Spectrum β-Lactamases and Carbapenemases, Antimicrobial agents and chemotherapy 63(1) (2019).
[80] K.M. Kazmierczak, M. Tsuji, M.G. Wise, M. Hackel, Y. Yamano, R. Echols, D.F. Sahm, In vitro activity of cefiderocol, a siderophore cephalosporin, against a recent collection of clinically relevant carbapenem-non-susceptible Gram-negative bacilli, including serine carbapenemase- and metallo-β-lactamase-producing isolates (SIDERO-WT-2014 Study), International journal of antimicrobial agents 53(2) (2019) 177-184.
[81] M.E. Falagas, T. Skalidis, K.Z. Vardakas, N.J. Legakis, Activity of cefiderocol (S-649266) against carbapenem-resistant Gram-negative bacteria collected from inpatients in Greek hospitals, The Journal of antimicrobial chemotherapy 72(6) (2017) 1704-1708.
[82] S. Kanazawa, T. Sato, N. Kohira, T. Ito-Horiyama, M. Tsuji, Y. Yamano, Susceptibility of Imipenem-Susceptible but Meropenem-Resistant bla(IMP-6)-Carrying Enterobacteriaceae to Various Antibacterials, Including the Siderophore Cephalosporin Cefiderocol, Antimicrobial agents and chemotherapy 61(7) (2017).
[83] A. Ito, N. Kohira, S.K. Bouchillon, J. West, S. Rittenhouse, H.S. Sader, P.R. Rhomberg, R.N. Jones, H. Yoshizawa, R. Nakamura, M. Tsuji, Y. Yamano, In vitro antimicrobial activity of S-649266, a catechol-substituted siderophore cephalosporin, when tested against non-fermenting Gram-negative bacteria, J Antimicrob Chemother 71(3) (2016) 670-7.
[84] N. Kohira, J. West, A. Ito, T. Ito-Horiyama, R. Nakamura, T. Sato, S. Rittenhouse, M. Tsuji, Y. Yamano, In Vitro Antimicrobial Activity of a Siderophore Cephalosporin, S-649266, against Enterobacteriaceae Clinical Isolates, Including Carbapenem-Resistant Strains, Antimicrobial agents and chemotherapy 60(2) (2016) 729-34.
[85] P. Thelen, A.S. Henriksen, C. Longshaw, Y. Yamano, B. Caldwell, A. Hamprecht, In vitro activity of cefiderocol against Gram-negative bacterial pathogens in Germany, Journal of global antimicrobial resistance 28 (2022) 12-17.
[86] S. Stracquadanio, E. Torti, C. Longshaw, A.S. Henriksen, S. Stefani, In vitro activity of cefiderocol and comparators against isolates of Gram-negative pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in Italy, Journal of global antimicrobial resistance 25 (2021) 390-398.
[87] E. Cercenado, L. Cardenoso, R. Penin, C. Longshaw, A.S. Henriksen, A. Pascual, In vitro activity of cefiderocol and comparators against isolates of Gram-negative bacterial pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in Spain, Journal of global antimicrobial resistance 26 (2021) 292-300.
[88] T. Naas, G. Lina, A. Santerre Henriksen, C. Longshaw, F. Jehl, In vitro activity of cefiderocol and comparators against isolates of Gram-negative pathogens from a range of infection sources: SIDERO-WT-2014-2018 studies in France, JAC-antimicrobial resistance 3(2) (2021) dlab081.
[89] V. Gant, A. Hussain, M. Bain, C. Longshaw, A.S. Henriksen, In vitro activity of cefiderocol and comparators against Gram-negative bacterial isolates from a series of surveillance studies in England: 2014-2018, Journal of global antimicrobial resistance 27 (2021) 1-11.
[90] T. Sato, A. Ito, Y. Ishioka, S. Matsumoto, M. Rokushima, K.M. Kazmierczak, M. Hackel, D.F. Sahm, Y. Yamano, Escherichia coli strains possessing a four amino acid YRIN insertion in PBP3 identified as part of the SIDERO-WT-2014 surveillance study, JAC-antimicrobial resistance 2(3) (2020) dlaa081.

[91] N. Kohira, M.A. Hackel, Y. Ishioka, M. Kuroiwa, D.F. Sahm, T. Sato, H. Maki, Y. Yamano, Reduced susceptibility mechanism to cefiderocol, a siderophore cephalosporin, among clinical isolates from a global surveillance programme (SIDERO-WT-2014), Journal of global antimicrobial resistance 22 (2020) 738-741.