

Development of a rapid susceptibility testing system for cefiderocol, aztreonam-avibactam, ceftolozane-tazobactam and meropenem-vaborbactam directly from positive blood cultures

F. Carrozzo², C. Chilleri^{1,2}, F. Del Conte^{1,2}, M. Rosati^{1,2}, A. Olsson³, T.E.P. Kimkes³, A. Antonelli^{1,2}, T. Gianì^{1,2}, G.M. Rossolini^{1,2}, C. Malmberg^{3,4}

¹Department of Experimental and Clinical Medicine, University of Florence - Florence (Italy), ²Microbiology and Virology Unit, Careggi University Hospital - Florence (Italy),

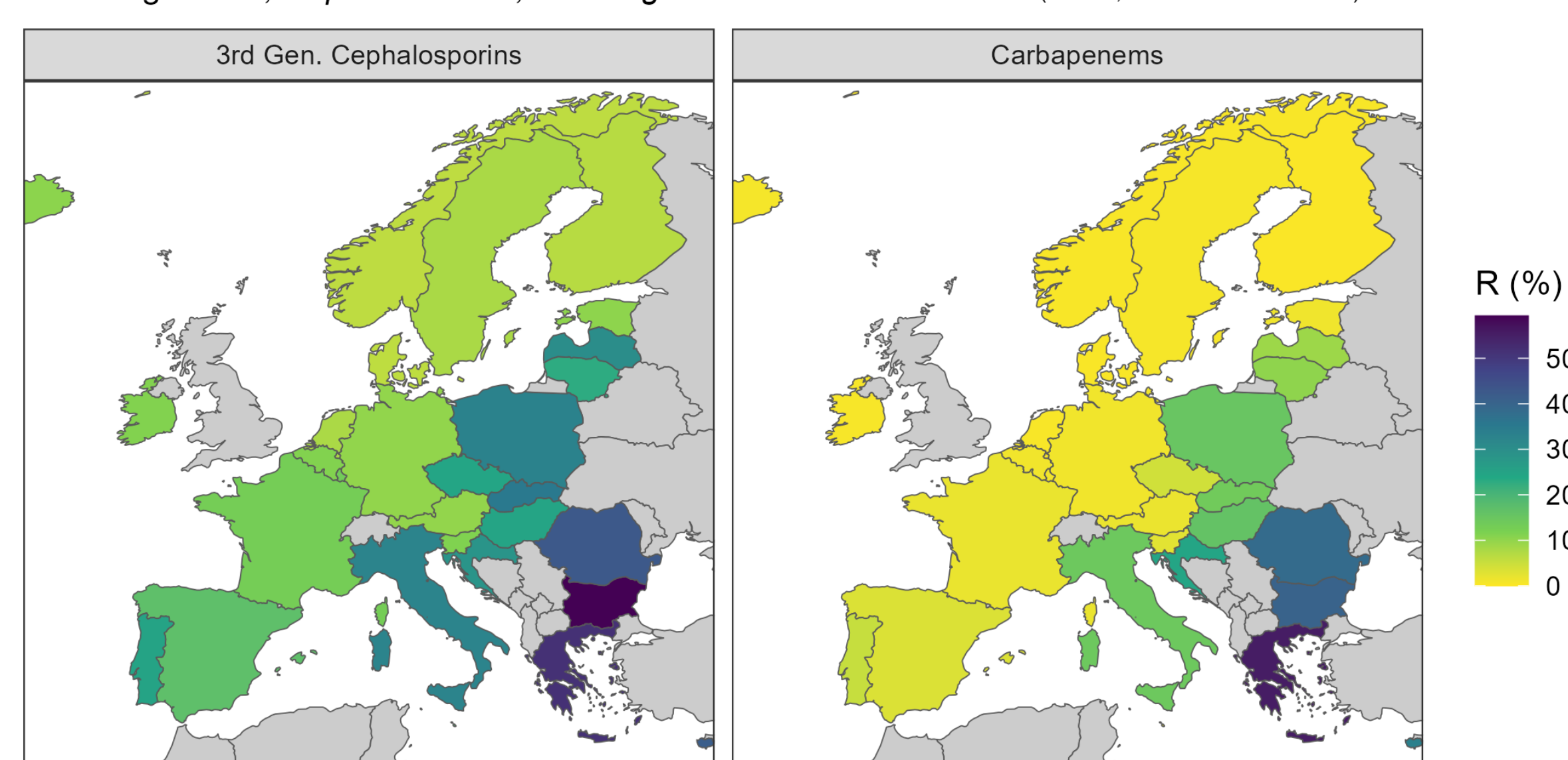
³Gradientech AB - Uppsala (Sweden), ⁴Department of Medical Sciences, Uppsala University - Uppsala (Sweden)

Introduction

Multidrug-resistant Enterobacterales, *Pseudomonas aeruginosa* and carbapenem-resistant *Acinetobacter baumannii* represent a growing public health-threat across Europe, especially in Southern and Eastern Europe [1]. These pathogens are associated with high mortality, due to limited treatment options and delays in effective therapy [2]. Recent therapeutic advances include the cephalosporin cefiderocol (FDC), and novel β -lactam/ β -lactamase inhibitor combinations, such as aztreonam-avibactam (AZA), ceftolozane-tazobactam (CTT) and meropenem-vaborbactam (MEV) [3-4]. Despite their potent activity, susceptibility varies by resistance mechanism, underscoring the need for rapid and precise diagnostic tools. However, few rapid systems are currently available to test these antimicrobials. This feasibility study evaluates the performance of these new antimicrobials on the QuickMIC direct-from-blood-culture rapid AST system.

Percentage resistant isolates

Including *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii*. (ECDC, data from 2020-2024)

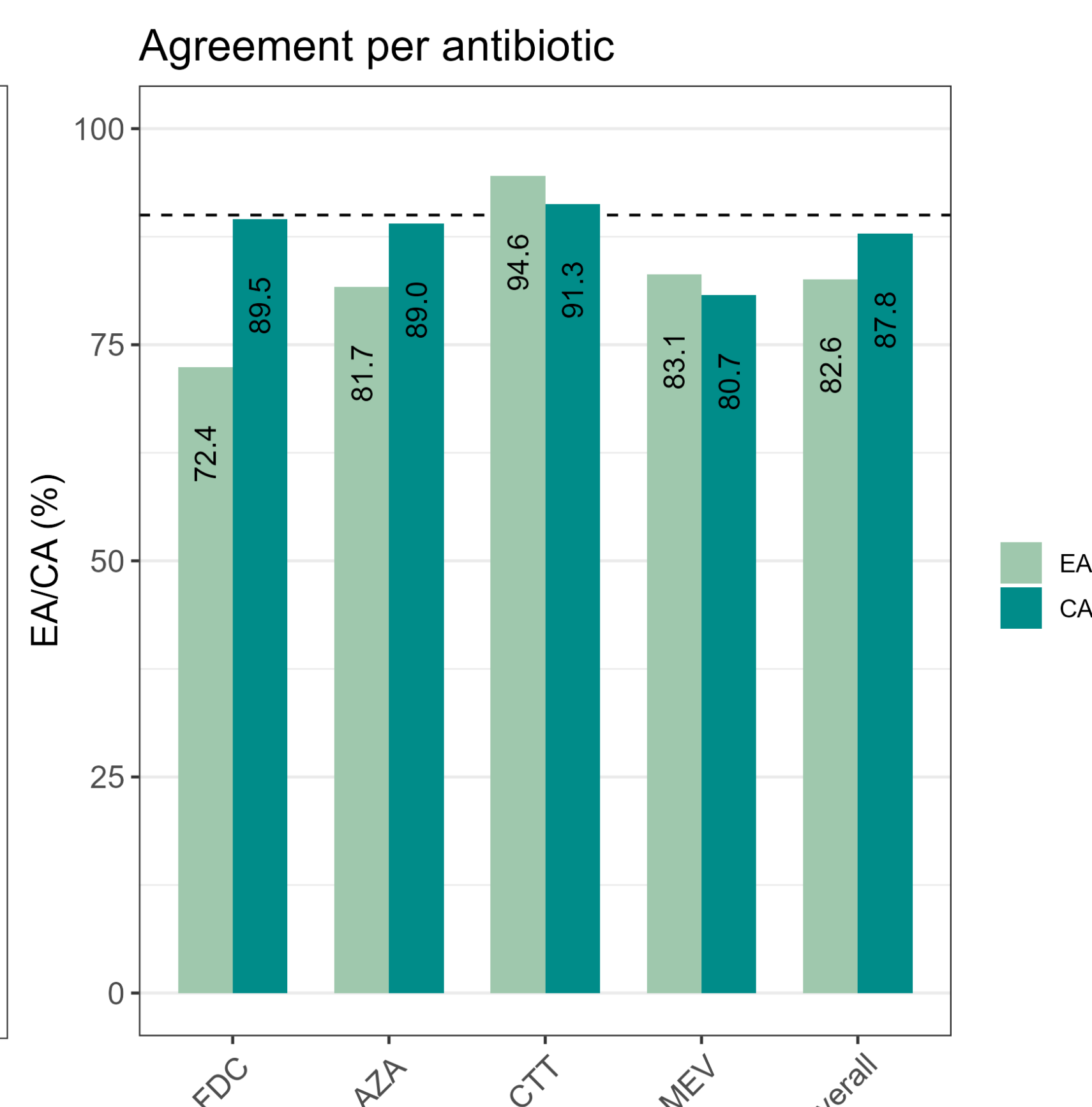
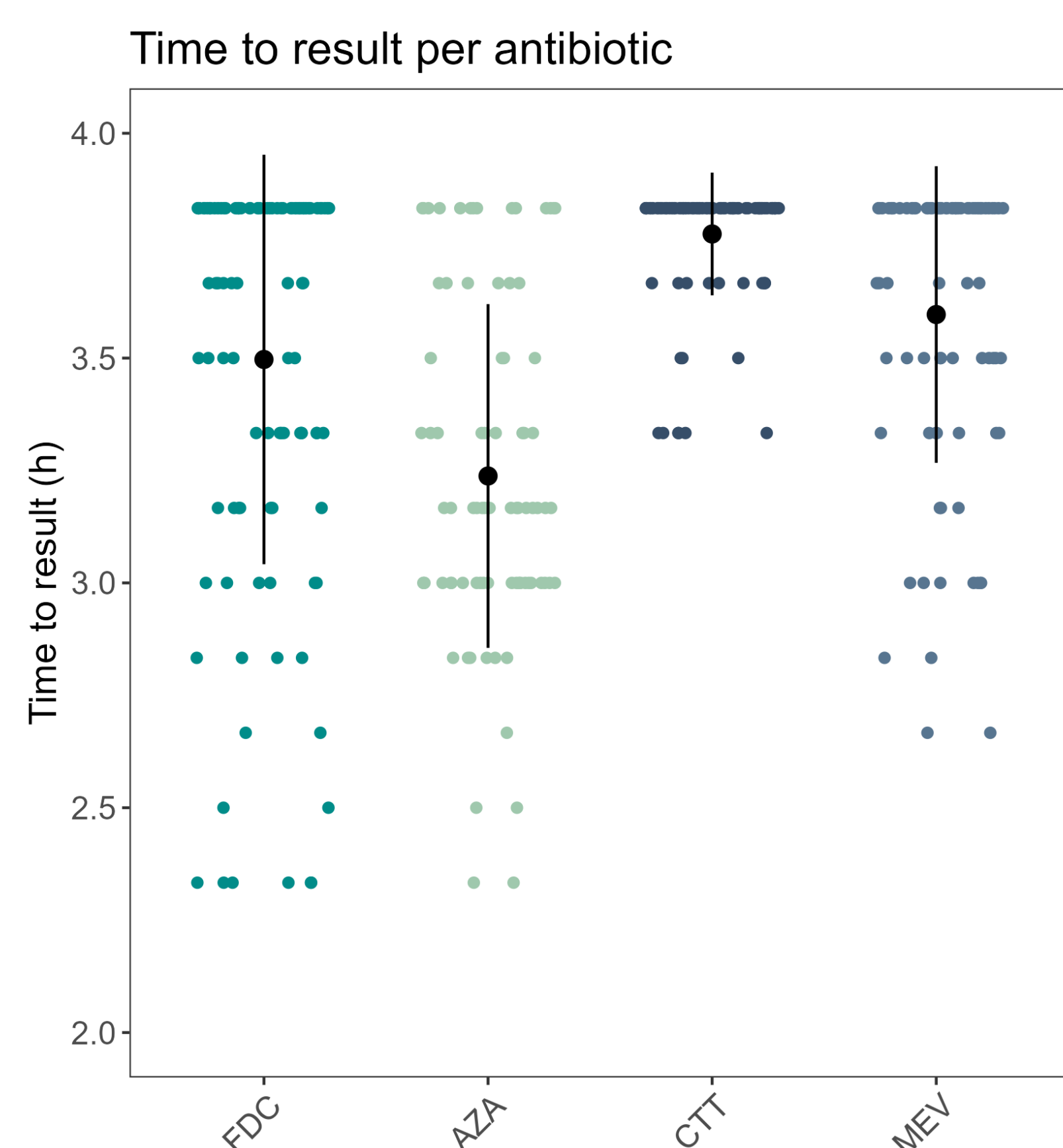


Methods

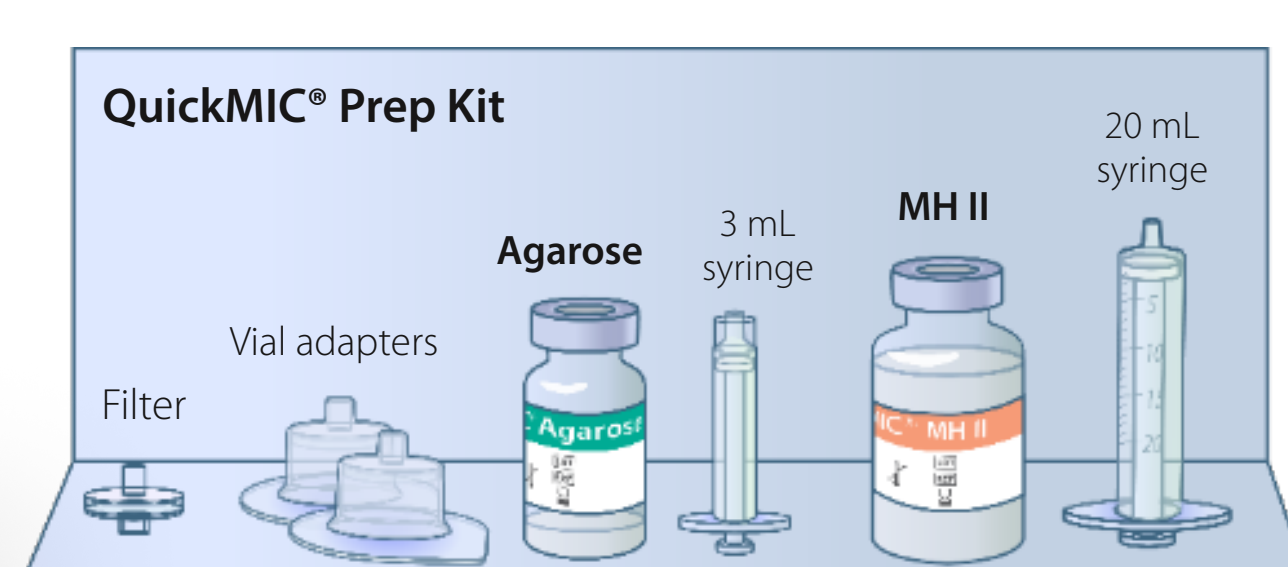
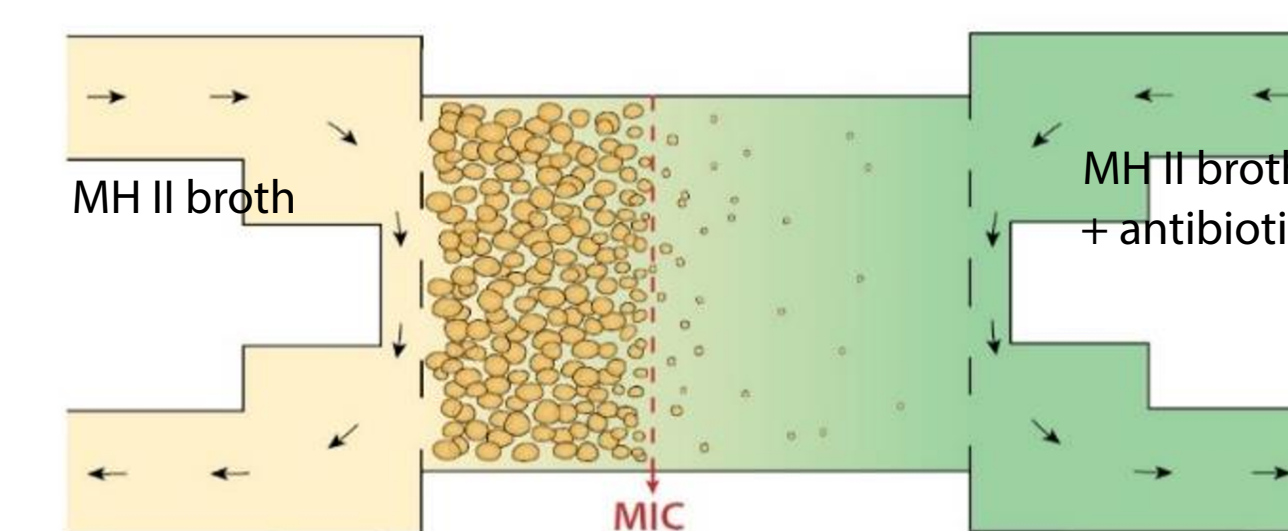
A total of 136 Gram-negative isolates (91 Enterobacterales, 22 *A. baumannii*, 23 *P. aeruginosa*) were spiked in horse blood, cultured until positivity, and analysed with the QuickMIC system using a prototype development panel. The tested collection included 37 serine-carbapenemase producers, 38 metallo beta-lactamase producers and 8 ESBL producers. Minimum inhibitory concentration (MIC) and SIR category results were interpreted according to EUCAST clinical breakpoints (when available, except cefiderocol for *Acinetobacter* with a tentative breakpoint of 2 mg/L) and compared to reference broth microdilution method (BMD). Iron-depleted Mueller-Hinton broth was used for reference cefiderocol susceptibility testing [5].

Results

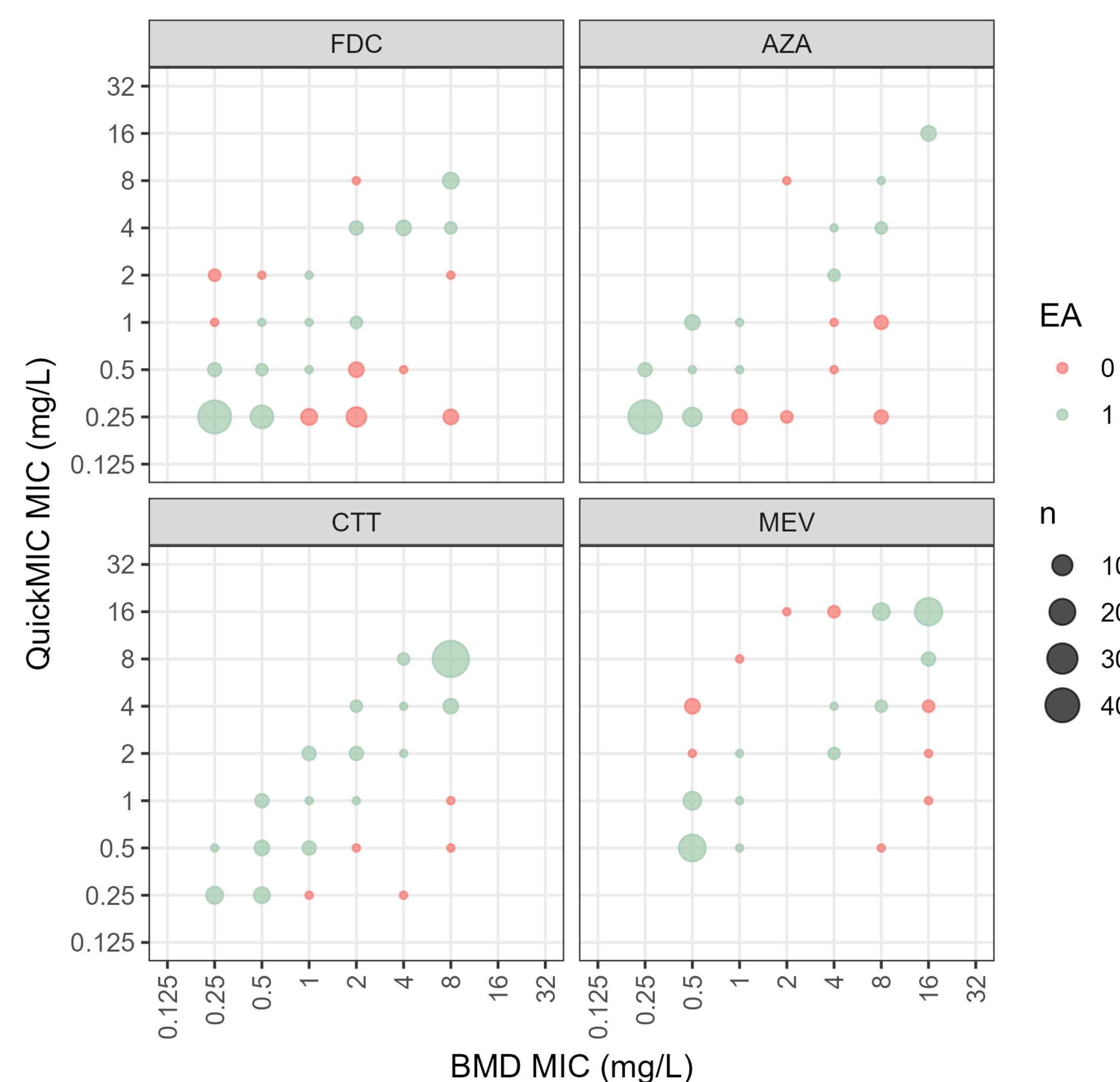
A total of 121 tests were evaluable for performance analysis. As determined by BMD, 20.5% (24/117), 16.9% (14/83), 59.4% (57/96) and 33.7% (31/92) of the included isolates were resistant to FDC, AZA, CTT, and MEV, respectively. The QuickMIC prototype cassette yielded reportable MIC-values for 93.2% of tests, with MIC results available in 3h 32 min \pm 24 min after starting the run. Overall essential and categorical agreement were 82.6% and 87.8%, respectively, with 83.2% and 88.4% for Enterobacterales and 78.8% and 84.6% for non-fermenters, respectively.



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QuickMIC vs. BMD



Overview per antibiotic

	Species	# isolates	# resistant	# results	EA (%)	CA (%)
Cefiderocol (FDC)	<i>A. baumannii</i>	20	10	17	70.6	70.6
	Enterobacterales	84	14	75	72.0	92.0
	<i>P. aeruginosa</i>	17	0	17	76.9	100.0
Aztreonam-Avibactam (AZA)	Enterobacterales	83	14	82	81.7	89.0
Ceftolozane-Tazobactam (CTT)	Enterobacterales	83	52	81	93.8	92.6
	<i>P. aeruginosa</i>	17	5	15	100.0	81.8
Meropenem-Vaborbactam (MEV)	Enterobacterales	80	24	72	84.7	79.2
	<i>P. aeruginosa</i>	16	7	14	72.7	90.9

Conclusion

This feasibility study showed promising results for the ultra-rapid AST of cefiderocol, aztreonam-avibactam, ceftolozane-tazobactam and meropenem-vaborbactam using the QuickMIC microfluidic AST platform with an approximate time-to-result of ~3.5h, although further development is necessary to improve performance.

References

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