A multicenter evaluation of a novel microfluidic rapid AST assay for Gram-negative bloodstream infections

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Ultra-rapid testing of antibiotic resistance

To successfully treat **sepsis**, quick administration of relevant antibiotics is required. Commonly used phenotypic methods for antibiotic susceptibility testing (AST) of bacteria are slow and with considerable technical variability. QuickMIC® is an ultra-rapid AST system, which utilises microfluidics and live imaging to monitor bacterial growth across a linear antibiotic concentration gradient. In this study we evaluate the performance of QuickMIC at four different laboratories with regard to speed, precision, accuracy and reproducibility in comparison to traditional diagnostic methods.

A total of 560 bacterial strains, including clinical blood cultures (n=148) and spiked Gram-negative isolates derived from blood cultures (n=412) were tested with the **QuickMIC system Gram-negative panel and compared with broth microdilution (BMD)** using at least two biological replicates for the 12 on-panel antibiotics (Figure 1). Logistic regression analysis was applied to explore factors affecting assay performance. To investigate reproducibility, a defined set of 10 clinically derived isolates were run in triplicate at each site.

The QuickMIC® system gives precise MIC values in 2-4 hours directly from positive blood cultures.

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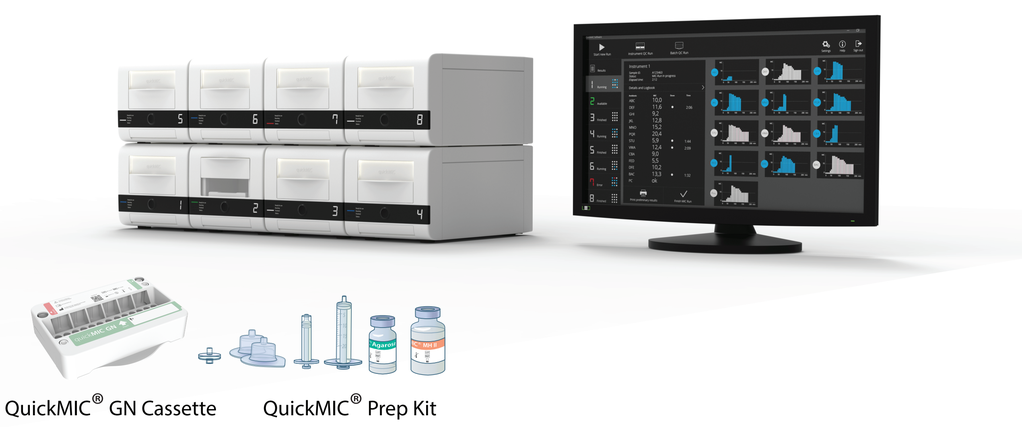

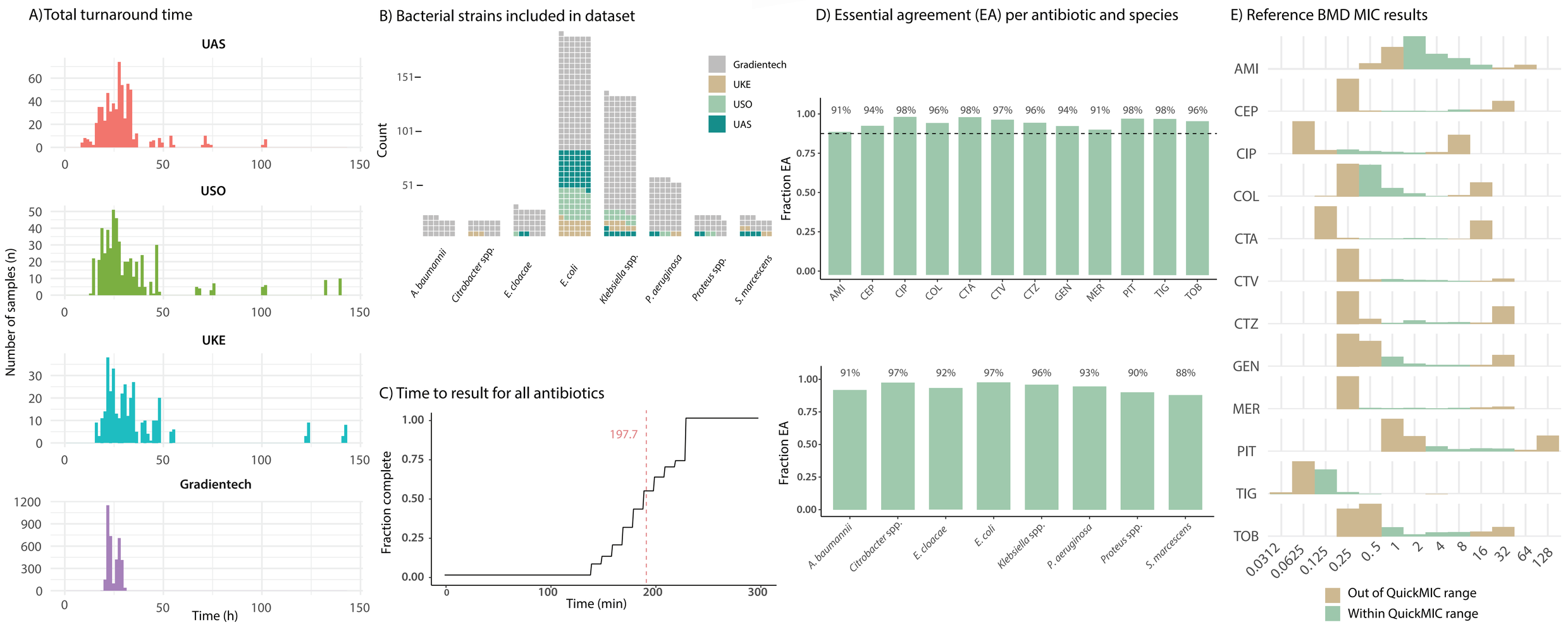

Figure 1: A) Total turnaround time from blood culture start to QuickMIC results, for the four laboratories in the study. B) Number of strains and bacterial species included in the study from the sites: Uppsala University Hospital (UAS), Örebro University Hospital (USO), University Medical Center Hamburg-Eppendorf (UKE) and Gradientech. C) Total in-instrument analysis time to result for all included antibiotics in the study. D) Overview of essential agreement split over all antibiotics and species in the study. E) Distribution of reference MIC results from BMD, and coverage on the QuickMIC linear concentration gradient.

Results

Of the collected 560 strains, 47.5% were wildtype to all, 52.5% resistant to at least one and 31.1% resistant to at least 3 antibiotic classes (MDR). The mean QuickMIC turn-around time (blood culture start to actionable result, excluding contrived samples) was 33.1h and the mean in-instrument analysis time overall was **3 h 18 min**. The overall essential agreement and categorical agreement between QuickMIC and BMD were 95.4% and 95.6% respectively, where 31.5% of all QuickMIC results were on-scale (59.0% for BMD). VMD, MD and mD rates were 1.1%, 0.9% and 2.4% respectively.

Inter-laboratory reproducibility between the sites was high at 98.7% using the acceptable standard of ±1 log2 unit. Regression analysis indicated that the QuickMIC method is robust with regard to initial bacterial concentration and delay time after blood culture positivity.

Conclusions

- QuickMIC can provide MIC results in **2-4 hours** directly from positive cultures in a clinical setting.
- QuickMIC has **high reproducibility and accuracy** between study sites.
- The linear gradient gives MIC values with a **low technical variation and high precision**.

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