# A rapid workflow for bacterial isolation and phenotypic AST directly from blood

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## 1 Saving lives with rapid AST

Rapid diagnostic methods can improve quality of care in patients with bloodstream infection. Low bacterial titers in blood necessitate blood culturing for bacterial growth prior to species determination and phenotypic antibiotic susceptibility testing (AST). However, blood culturing is slow and has low sensitivity. **SepsiPURE®** (Momentum Bioscience Ltd)[2] is a new method for extracting and enriching bacteria directly from blood. In this study, we combine the SepsiPURE technology with **QuickMIC®** (Gradientech AB)[3], a novel rapid AST system using low bacterial initial concentrations, and compare with QuickMIC after conventional blood culture.

## 2 Methods

A selection of 14 Gram-negative isolates (including *A. baumannii*, *E. coli*, *K. pneumoniae* and *P. aeruginosa*) were spiked into human blood to a target concentration mimicking drawn human blood (~20 CFU/mL). Bacterial inputs were prepared using SepsiPURE, then tested with the QuickMIC Gram-negative (GN) panel. Minimal inhibitory concentration (MIC), time-to-result and total workflow turnaround time were compared with QuickMIC after bloodculture (BD BACTEC Plus Aerobic) spiked with the same isolates at equivalent inocula in replicate (n=78). Regression analysis was applied to identify any significant differences in MIC value between the workflows.

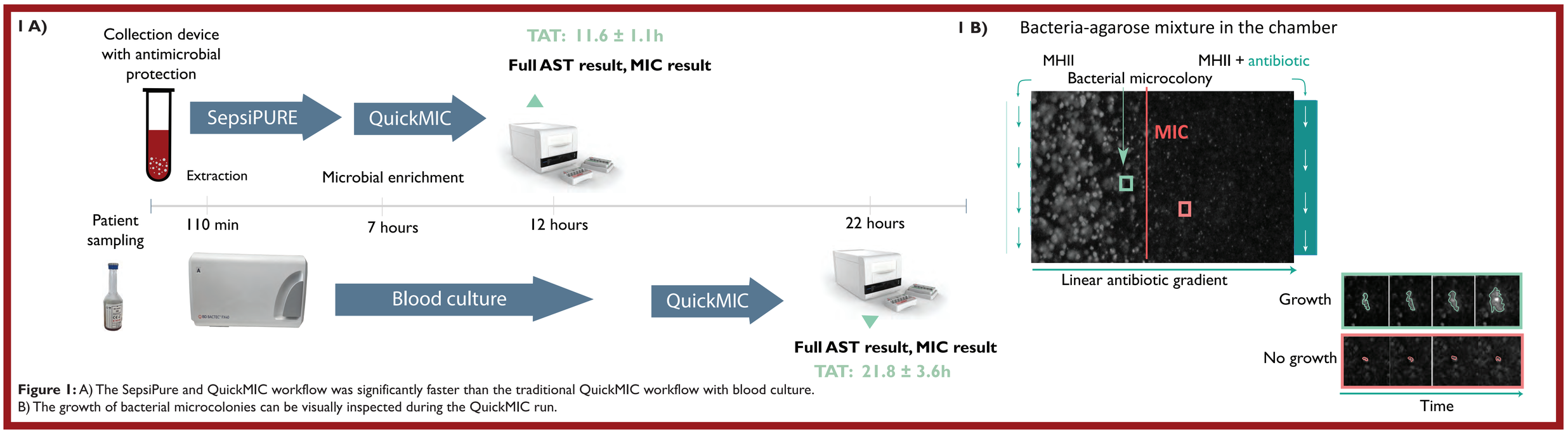


**Figure 1:** A) The SepsiPure and QuickMIC workflow was significantly faster than the traditional QuickMIC workflow with blood culture. B) The growth of bacterial microcolonies can be visually inspected during the QuickMIC run.

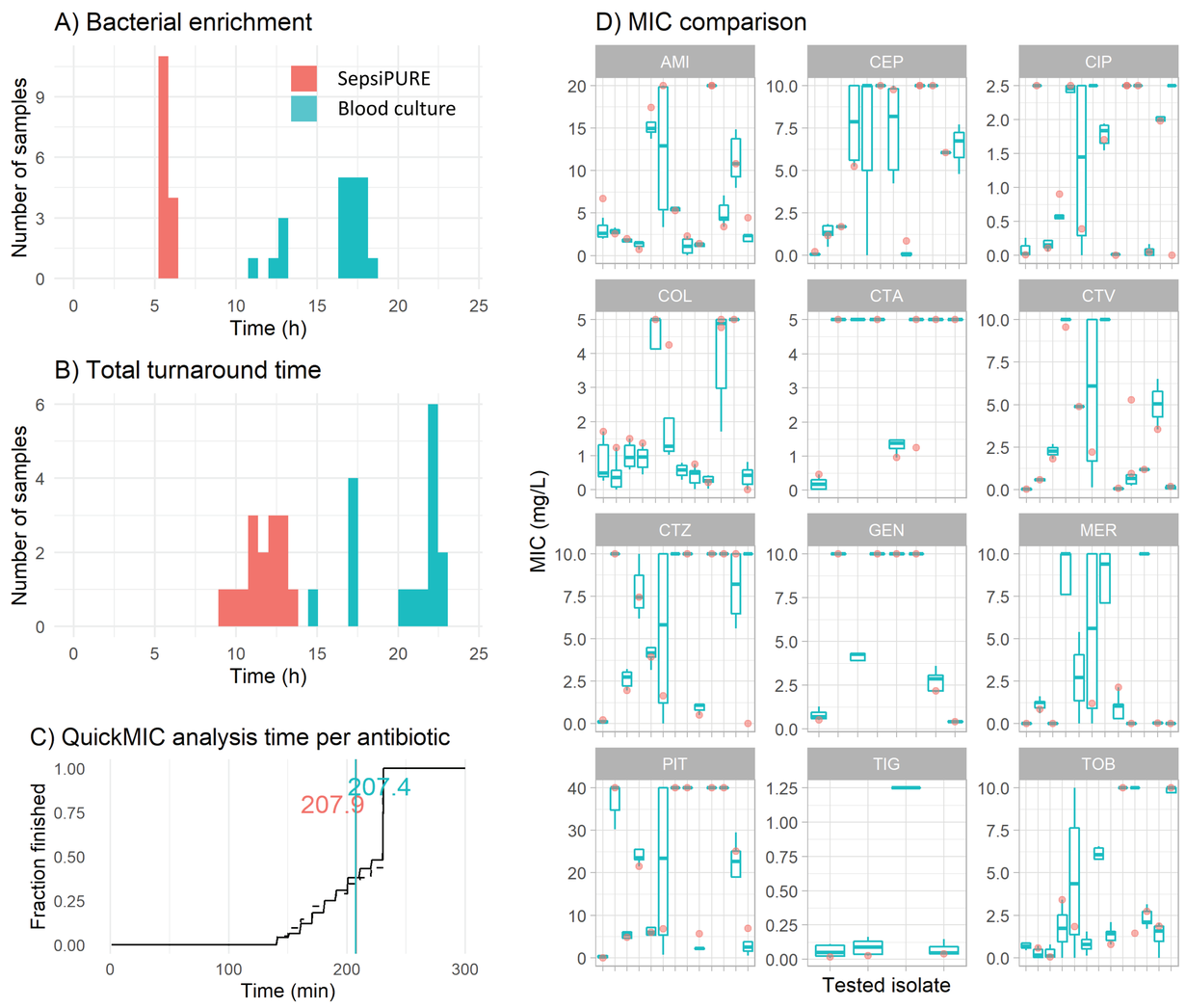


**Figure 2**: A) Time for bacterial isolation and enrichment using SepsiPURE (red) or blood culture (blue). B) Turnaround time from blood sample to QuickMIC result. C) Analysis time in QuickMIC per antibiotic using samples from SepsiPURE (red) and from blood culture (blue). D) Comparison of MIC results between the SepsiPURE and blood culture sample preparations. Red dots show MICs from SepsiPURE preparations, blue boxes show the mean and interquartile range of MICs from multiple blood culture preparations.

## 3 Precise MIC results in 2-4 hours

SepsiPURE took 110 min for bacterial extraction plus up to 5 h post-extraction enrichment (Figure 2). SepsiPURE workflow was significantly faster than standard QuickMIC workflow from blood culture (total turnaround time 11.6 ± 1.1h vs 21.8 ± 3.6h, $p<0.001$). 53% of SepsiPURE samples provided AST results before blood culture even flags positive. QuickMIC (GN panel) results took on average 208 ± 31 min from SepsiPURE-derived samples and 207 min± 29 min for blood culture samples, respectively. Linear regression analysis with Tukey's post-test did not identify significant differences in MIC value between the workflows. ($p>0.05$, $R2 = 0.99$).

## Conclusions

- SepsiPURE yields a bacterial inoculate compatible with QuickMIC.
- The combination of SepsiPURE and QuickMIC appears promising, as it:
  - provides phenotypic AST directly from blood substantially faster than traditional blood culture.
  - has the potential to reduce morbidity and mortality, lower healthcare costs and reduce the emergence of antimicrobial resistance.

In collaboration with:
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