How can fast identification & antimicrobial susceptibility testing improve patient care and antibiotics stewardship in critically ill patients?

Houdini Wu[1], Steven Wilson[1], Li Xu-McCrae[1], Paul Connor[1], Ahmed Hussain[1], Karen Reynolds[1], Abid Hussain[1]

[1] PHE Public Health Birmingham Laboratory, Heartlands Hospital, Birmingham, United Kingdom B5 9SS

1. Background

• Current standard of care (SOC) methodology prior to routine microbial identification (ID) via matrix-assisted laser desorption ionisation time of flight (MALDI-TOF) and antimicrobial susceptibility testing (AST) via bioMérieux VITEK-2.

• Accelerate Pheno™ system is a new fully automated compact platform that can perform both ID and AST directly from positive blood cultures in ~ 7 hours (Fig. 1 – blue boxes for SOC; red numbers & arrows for Pheno™; Table 1 for the list of organisms detectable by Pheno™).

• NICE guideline – NG15 describes antimicrobial stewardship (AMS) and the prescription of antimicrobials may be empirical, and then focused when laboratory data becomes available. This is the national AMR strategy – start smart then focus.

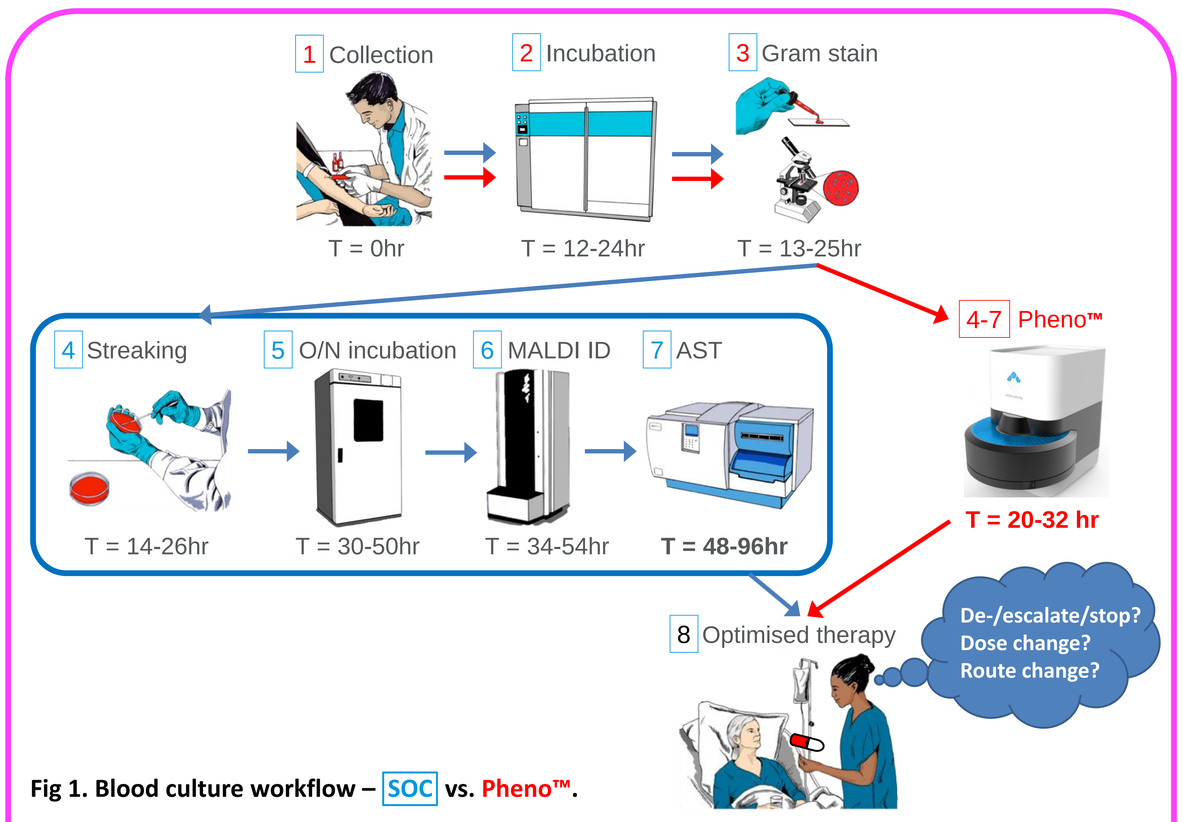

Fig 1. Blood culture workflow – SOC vs. Pheno™.

Gram Positive	Gram Negative	Yeast
Staphylococcus aureus	*Escherichia coli*	*Candida albicans*
Staphylococcus lugdunensis	*Klebsiella spp.*	*Candida glabrata*
Coagulase –ve Staphylococcus spp.	*Enterobacter spp.*	
Enterococcus faecalis	*Proteus spp.*	
Enterococcus faecium	*Citrobacter spp.*	
Streptococcus spp.	*Serratia marcescens*	
	Pseudomonas aeruginosa	
	Acinetobacter baumannii	

Table 1. Current list of blood culture positive organisms detectable by Pheno™ system.

2. Aim

• To compare the performances by both SOC & Pheno™ methods.
• Evaluate the potential clinical benefits from a quick ID & AST in hospital settings that commonly require heavy use of broad-spectrum antimicrobial agents (i.e. the critically ill setting).

3. Methods

• 84 episodes of bacteraemias were selected in real-time from four critically ill hospital settings, including the intensive care units (ITUs), neonatal units (NNUs), acute medical units (AMUs) and a haematology ward (Haem).
• A 25-weeks study (March to October 2018) was conducted to compare the performances of SOC and Pheno™ methods.
• The potential impact of these early Pheno™ results was investigated:-
- patient care and clinical outcome:– potential changes to antibiotic therapy and mortality.
- patient safety:– hospital re-admission, healthcare-associated infections (HCAIs) and serious adverse event (SAEs).
- antibiotic stewardship:– associated costs (Antibiotics, HCAIs, SAEs, ecological microbiota via CQUIN data).

5. Discussion

• 16% (3/19) of bacteraemias could have been escalated with antibiotics treatment, with the potential to life saving from serious infections.
• ~70% (16/23) of bacteraemias could have been de-escalated based on the Pheno™ results, potentially reducing the risks of HCAIs, SAEs in congruence with the national strategy.
• The clinical utility of Pheno™ could be targeted towards Gram negative bacteraemia – not just for de-escalation, but also for appropriate escalation.
• The Pheno™ could improved patient care and outcome by optimising the use of antibiotics in a timely fmanner (Fig 5).

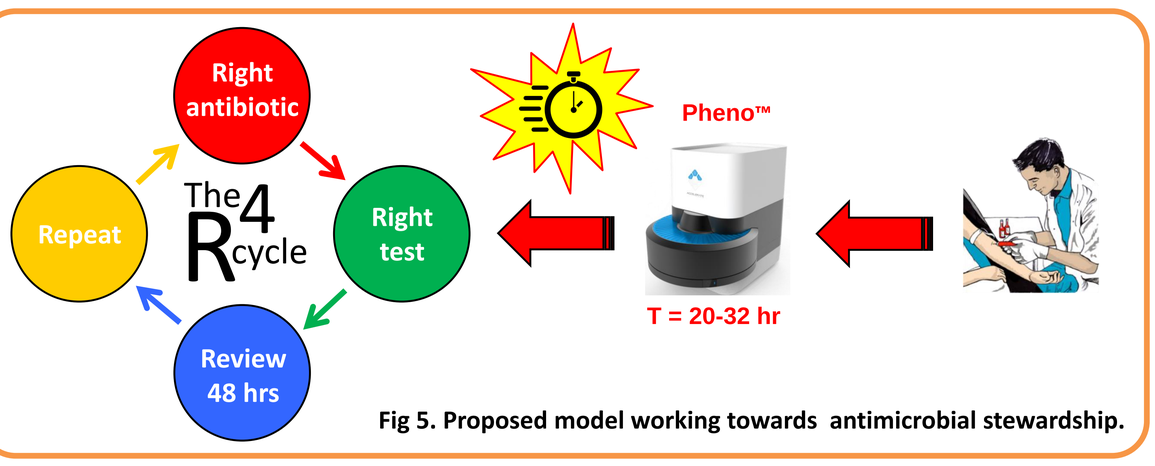

Fig 5. Proposed model working towards antimicrobial stewardship.

4a. Results – SOC vs. Pheno™ performances

• 73 blood cultures were eligible for this study:-
- Breakdown of patient groups (Fig 2A).
- Breakdown of tested microbials (Fig 2B).
- Microbiological contamination rate is 1.4%.

• Pheno™ system provided:
- definitive and correct result for 66/72 runs, along with an overall sensitivity of 91.7% and specificity of 99.4%.
- 3 off panel samples were also correctly identified (i.e. organisms outside Table 1).
- AST results for analysis in 57 instances (98.3%). The overall categorical agreement between the Pheno™ system and SOC was 95.4%, with 9 minor errors (2.4%), 5 major errors (1.7%) and 3 very major error (4%). See Table 2 for breakdown for gram +ve and –ve organisms.
- on average, an ID result in 1.5 hours and AST in 6.9 hours, reducing the time-to-result for ID by 18.3 hours (Fig 3A) and AST by 36.7 hours (Fig 3B), when compared to the SOC method in our clinical microbiology laboratory setting.

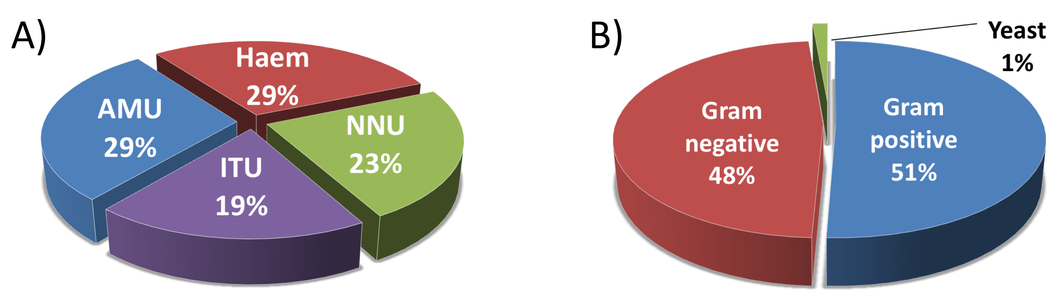

Fig 2. A) Sources of blood culture positive samples and B) microbial distribution of the study.

Pheno™ AST Data	Gram Positive	Gram Negative
Overall Essential Agreement	93.3%	94.4%
Overall Categorical Agreement	97.8%	95.1%
Gram specific Minor Errors	-	2.8% (9)
Gram specific Major Errors	-	2.0% (5)
Gram specific Very Major Errors	11.1% (1)	3.0% (2)

Table 2. Overall AST performance summary by Pheno™ system.

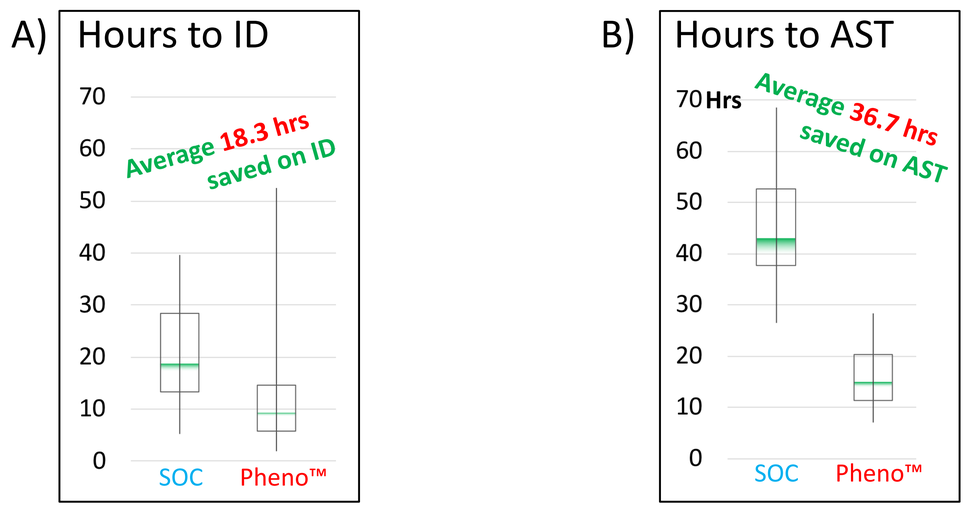

Fig 3. Comparison of Hours to A) ID and B) AST from positive blood culture

4b. Results – Clinical significance of Quick ID & AST by Pheno™

Potential impact of Pheno™ ID & AST results to:-
• Patient care and clinical outcome (Fig 4A):
- 19 cases (26%) Escalate antibiotics treatment ➔ Potential life saving
- 23 cases (32%) De-escalate / stop ➔ AMS (↓ HCAIs & SAEs)
- 31 cases (42%) with no changes in antibiotics treatment

• Within the antibiotics treatment escalation and de-escalation (n=42; Fig 4B for a further breakdown according to):
- 15 cases (36%) resulted in a 28-day hospital re-admission
- 4 cases (10%) with a 30-day mortality ➔ **3 casualties!**
- 18 cases (43%) could lead to HCAIs reduction
- 17 cases (40%) could lead to SAEs reduction

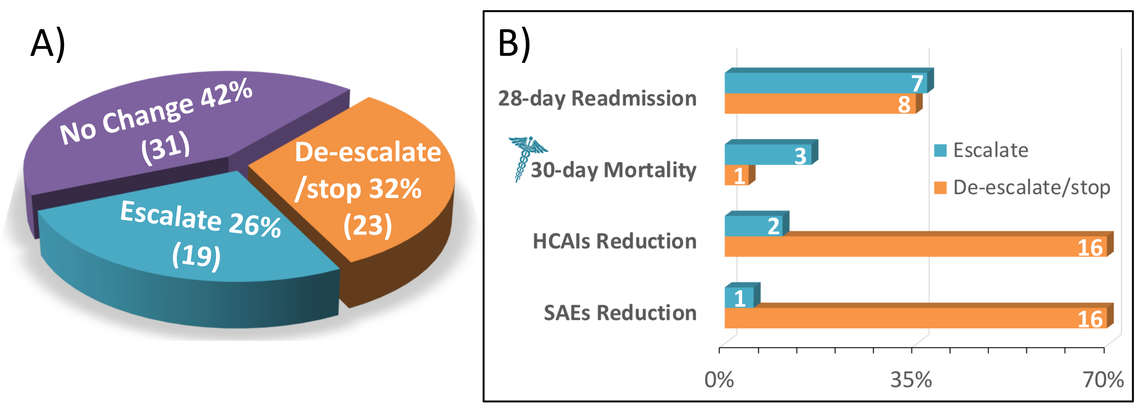

Fig 4. A) Potential changes in antibiotics treatment after Pheno™ results and B) a breakdown of patient safety according to potential antibiotics treatment escalation or de-escalation.

Conclusion

This study demonstrated the use of Pheno™ system is able to provide a fast organism ID & AST data, while significantly improve the turn-around time in blood culture diagnostics. In light of this advancement, this would likely to result in a better clinical outcome (potential life saving) for critically ill patients and reduce the pressure of AMR while implementing antibiotic stewardship.

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