University Hospitals Coventry and Warwickshire NHS Trust

Evaluating the reliability and clinical impact of the direct rapid antimicrobial susceptibility test (dRAST) for blood culture in a UK based hospital population

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Third party affiliations / Disclosures

- dRAST platform, equipment and kits supplied at no cost by Serosep UK, Crawley, United Kingdom and QuantaMatrix Europe, Villejuif, France
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Background

- Patients with bacteraemia are frequently septic and if not managed appropriately, can deteriorate to septic shock, multiorgan failure and death.
- Healthcare-associated infections (HCAI) are a risk to patients undergoing in-hospital care, and these HCAI are often resistant to antibiotics.
- Antimicrobial resistance (AMR) is a major factor leading to treatment ineffectiveness, clinical unresponsiveness, and a higher risk of mortality [WHO, 2020].

Antimicrobial susceptibility testing (AST)

- Determining antimicrobial susceptibility profiles rapidly is important in preventing delays in **effective treatment** of patients with bloodstream infections.
- Enables targeted therapy and de-escalation of broad-spectrum antibiotics encouraging **antimicrobial stewardship**.
- Identifying drug resistant organisms is also important for **managing infection prevention and control risks** and essential for **controlling antimicrobial resistance**.
- Traditional methods of determining AST usually take 24-72 hours so using a more rapid and accurate alternative method could enable optimal treatments and care sooner, improving clinical management and patient outcomes and could reduce healthcare costs.

direct & Rapid Antimicrobial Susceptibility Test (dRAST)

- Provides rapid AST direct from positive blood culture samples
- Phenotypic MIC by broth micro dilution
- 2 panels: 1 Gram Neg. + 1 Gram Pos.
- Results in as low as 4 hours; reducing time to results by up to 2 days compared to conventional method

CE-IVD, MFDS KOREA

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This study

- **Aim:** This study assesses the reliability of dRAST and the potential impact of its use on the clinical management of patients with bacteraemia in a UK hospital network.
- **Method:** AST on positive blood cultures from hospital patients were performed using standard disc diffusion method and by dRAST.

Methods

- 4 hospitals of three NHS Trusts in Coventry and Warwickshire, England, UK, including a large specialist tertiary level teaching hospital; between February and June 2020
- Blood cultures with single organisms only on Gram stain
- Standard laboratory method
  - Direct disc diffusion (and e-tests), interpretation using EUCAST clinical breakpoints
  - Identification of isolate species from colony growth using MALDI-TOF
- Clinical reports and patient records were assessed retrospectively for changes in clinical management due to AST including
  - antimicrobial changes due to resistance
  - de-escalation to more targeted therapy
  - switching intravenous to oral route

AST panels

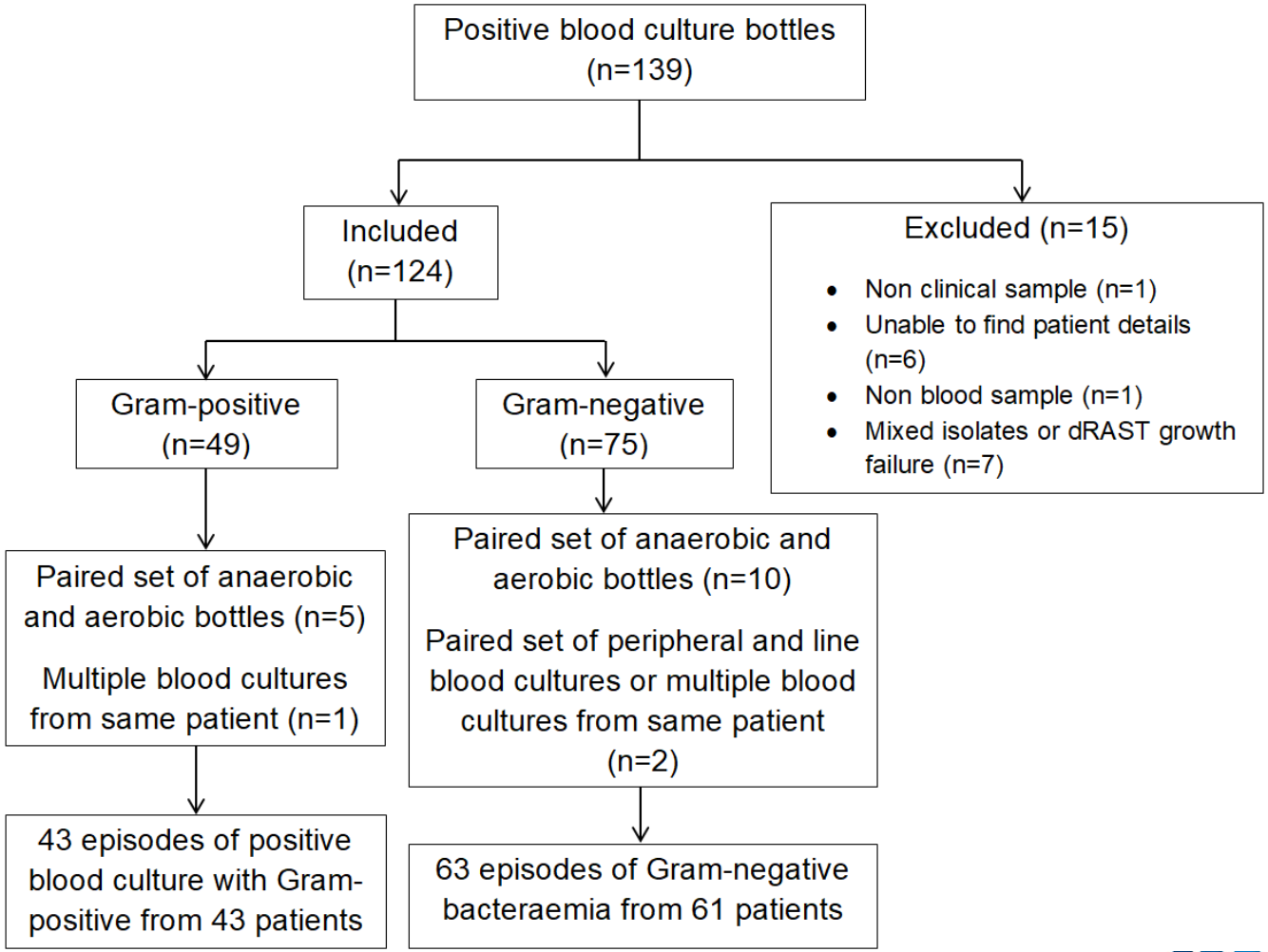
Gram positive

dRAST	Standard
Ampicillin Clindamycin Daptomycin Erythromycin Fusidic acid Gentamicin Levofloxacin Linezolid Oxacillin Penicillin Rifampin Teicoplanin Tetracycline Vancomycin Cefoxitin screen Inducible clindamycin resistance Gentamicin high-level Streptomycin high-level	Ampicillin* Ciprofloxacin Clindamycin Dalbavancin MIC** Daptomycin MIC** Erythromycin Flucloxacillin Fusidic Acid Gentamicin Linezolid Mupirocin Rifampicin Teicoplanin MIC Tetracycline Tigecycline* Trimethoprim/Sulfamethoxazole Vancomycin MIC Cefoxitin screen Inducible clindamycin resistance Gentamicin high-level**
	*for enterococci **when requested

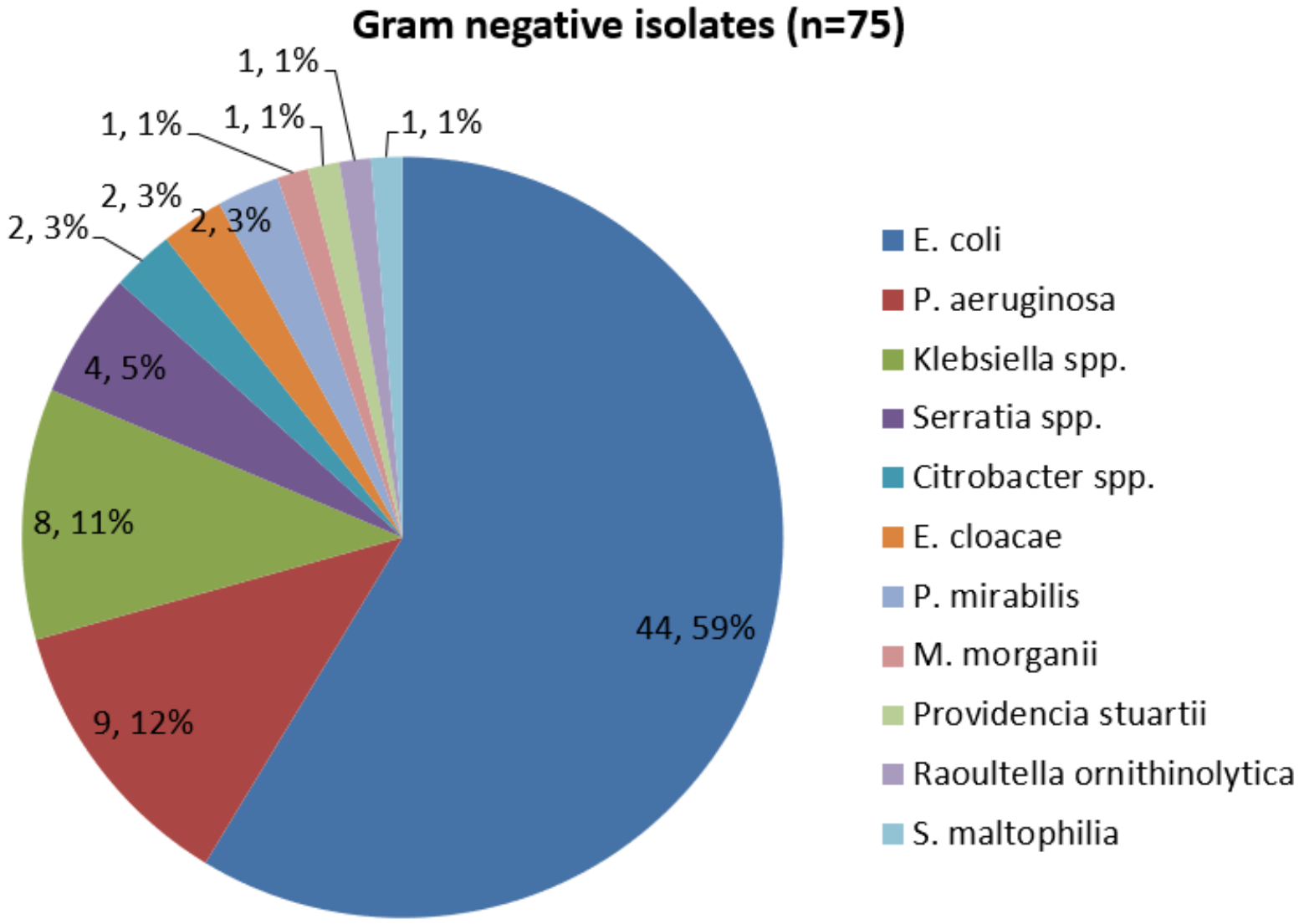
Gram negative

dRAST	Standard
Amikacin Amoxillin/clavulanate Ampicillin Cefepime Cefotaxime Ceftazidime Ceftazidime/Avibactam Ciprofloxacin Gentamicin Imipenem Levofloxacin Meropenem Piperacillin Piperacillin/Tazobactam Trimethoprim/Sulfamethoxazole ESBL	Amikacin Amoxicillin/Clavulanic acid Ampicillin Cefotaxime Cefpodoxime Ceftazidime Ciprofloxacin Ertapenem Gentamicin Meropenem Piperacillin/Tazobactam Trimethoprim/Sulfamethoxazole ESBL detection (Cefpodoxime, Cefpodoxime/Clavulanic acid, Cefepime, Cefepime/Clavulanic acid)

RESULTS – Patient episodes

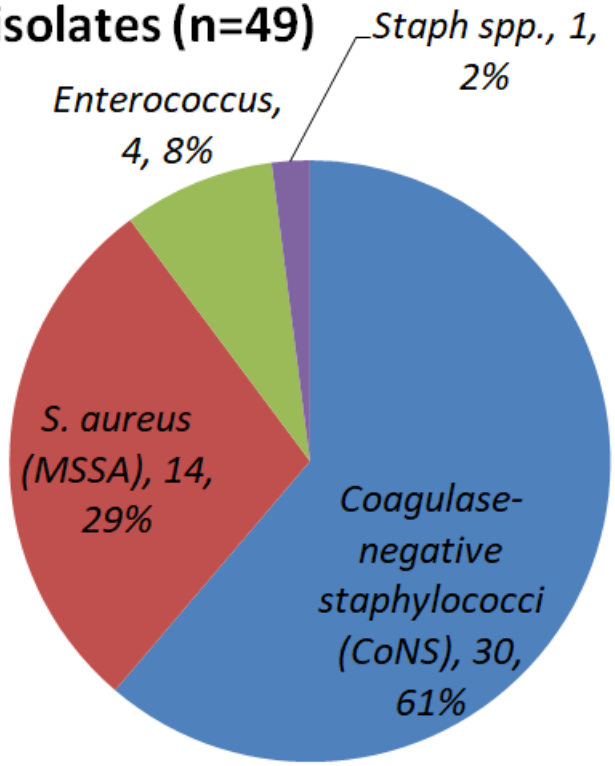


- 11.4% (n=12/104) patients were admitted to level 3 intensive care during their admission
- 24.6% (n=15/61) patients with Gram-negative bacteraemia died

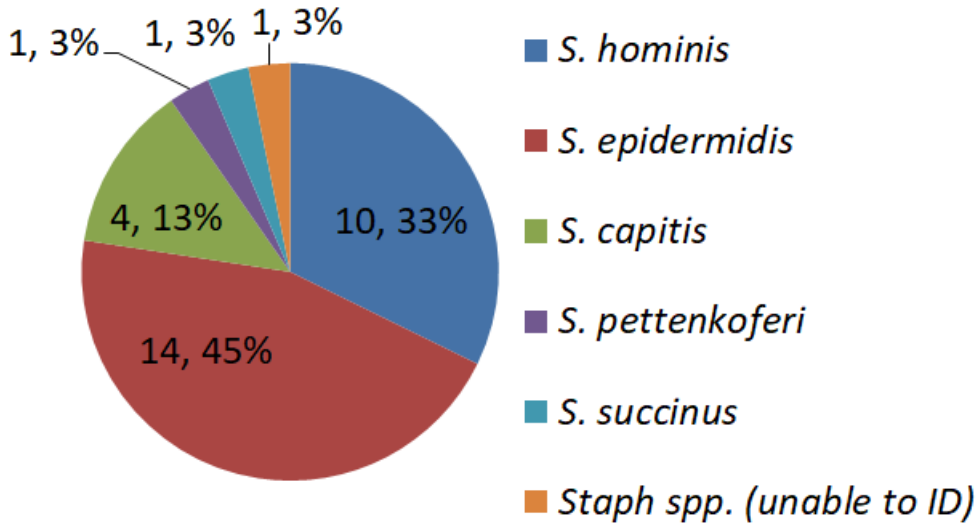


- 8 *Klebsiella* spp. = 6 *K. pneumoniae*, 2 *K. oxytoca*
- 4 *Serratia* spp. = 1 *S. marcescens*, 3 *S. liquefaciens*
- 2 *Citrobacter* spp. = 1 *C. freundii*, 1 *C. koseri*

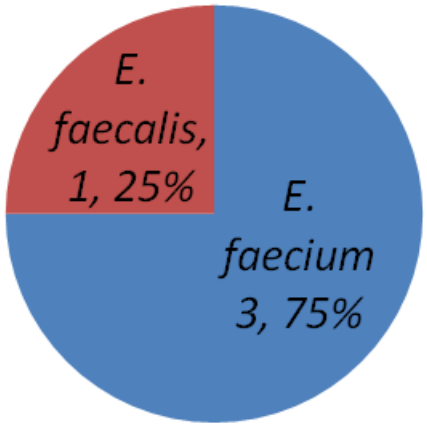
Gram positive isolates (n=49)



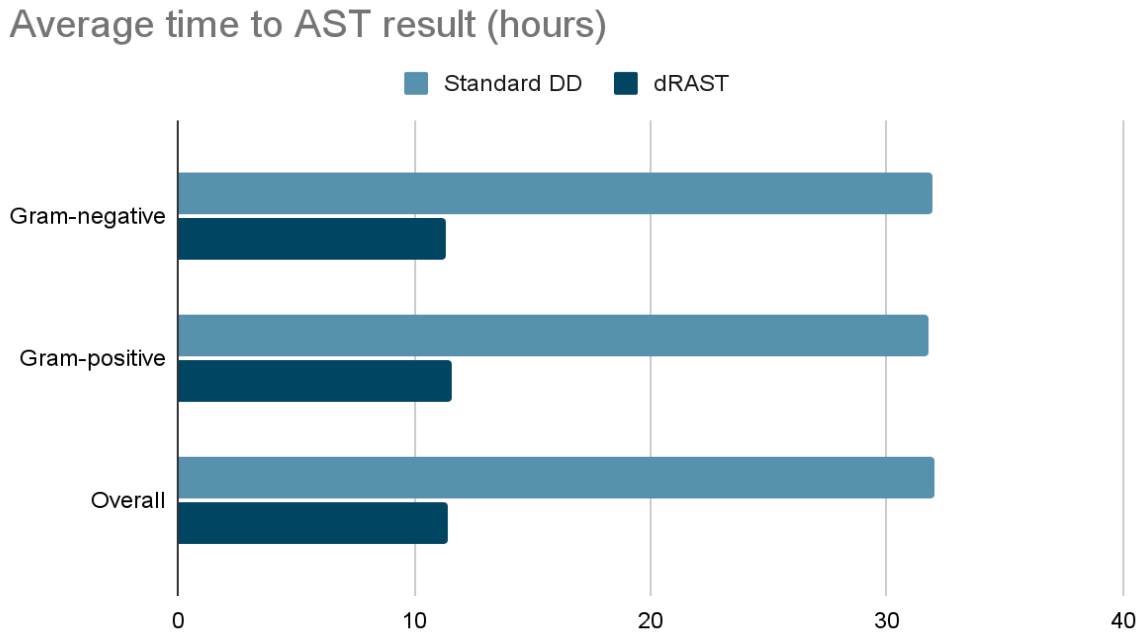
Coagulse-negative staphylococci



Enterococci



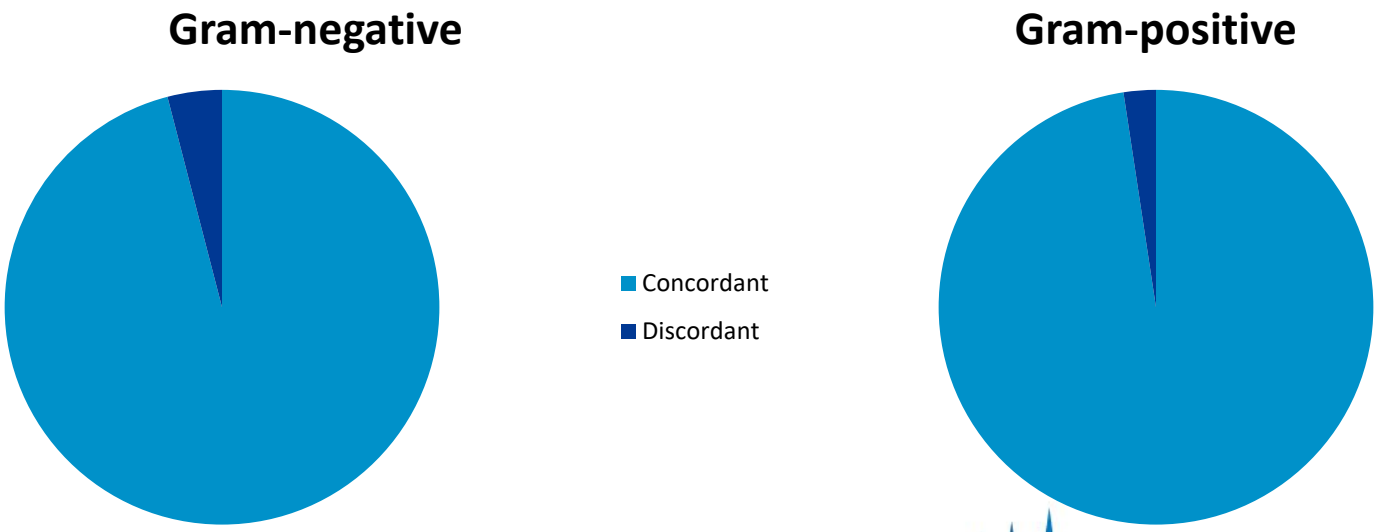
RESULTS – AST turnaround time



- The average time from blood culture positivity to AST result was **11.4 hours** by dRAST compared to 31.9 hours by standard method ($p<0.05$)

RESULTS – AST concordance

- Preliminary concordance for AST results, between standard method and dRAST:
- 96.0% (n=689/718) for Gram-negative isolates
- 97.6% (n=326/334) for Gram-positive isolates
- Overall 96.5% (n=1015/1052)



RESULTS – Clinical impact

- dRAST could have made an earlier difference to clinical management in **60.3%** (n=38/63) of cases of GN bacteraemia and 16.3% (n=7/43) of cases of GP bloodstream infections.

Antimicrobial change	Gram negative (n=63)	Gram positive (n=43)
Any antimicrobial change recommended	54.0% (n=34)	16.3% (n=7)
i.e.		
• Change due to detected resistance	31.7% (n=20)	2.3% (n=1)
• De-escalation to more targeted therapy	19.0% (n=12)	4.7% (n=2)
• Switching intravenous to oral route	15.9% (n=10)	0 (n=0)

Antimicrobial resistance (AMR)

- In our sample, e.g.;
  - >50% of our *E. coli* isolates were found to be resistant to co-amoxiclav (n=25/44)
  - >30% of patients with Gram-negative bacteraemia required an antibiotic change to an effective antibiotic due to resistance
  - Detected a few cases of ESBL and VRE
- With increasing AMR, earlier detection and rapid AST reporting is becoming increasingly important

Other impacts to clinical management

- There could have been **infection prevention and control implications** in 3/106 cases (2.83%) due to detection of ESBL-positive organisms or VRE
- Patients potentially could have been discharged sooner reducing hospital length of stay (n=5)

Conclusion

- dRAST provides AST reports for blood cultures on average over 20 hours sooner than by standard laboratory disc diffusion method
- Facilitating optimisation of the clinical management of patients with bloodstream infections much sooner

The positive impacts of dRAST include

- Guiding early effective and targeted antimicrobials; reducing the risk of clinical deterioration and the risk of poor patient outcomes
- Reducing unnecessary and inappropriate antibiotic use and promoting antimicrobial stewardship
- Informing early infection prevention and control management; reducing the chances of spreading HCAI and AMR
- Potentially supporting earlier hospital discharge, reducing hospital length of stay and reducing healthcare costs

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