A commercial assay versus traditional blood culture: correlation with clinical metadata and sepsis criteria

David Farlow[1], Lisa Simms[2], Corey Davies[2], Nadeesha Jayasundara[2], Sumeet Sandhu[2], Alex Pintara[2], Raffaella Giardino[2], Anton Lord[3], Flavia Huygens[2]

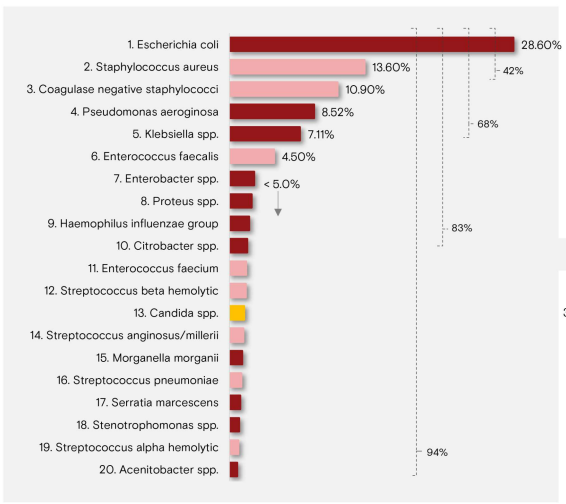
[1]Mackay Hospital and Health Service, Mackay, Australia [2]Microbio Pty Ltd., Brisbane, Australia [3]Specdata Consultants, Brisbane, Australia

InfectID-Bloodstream Infection: designed to improve the treatment of bloodstream infections (BSIs) and sepsis.

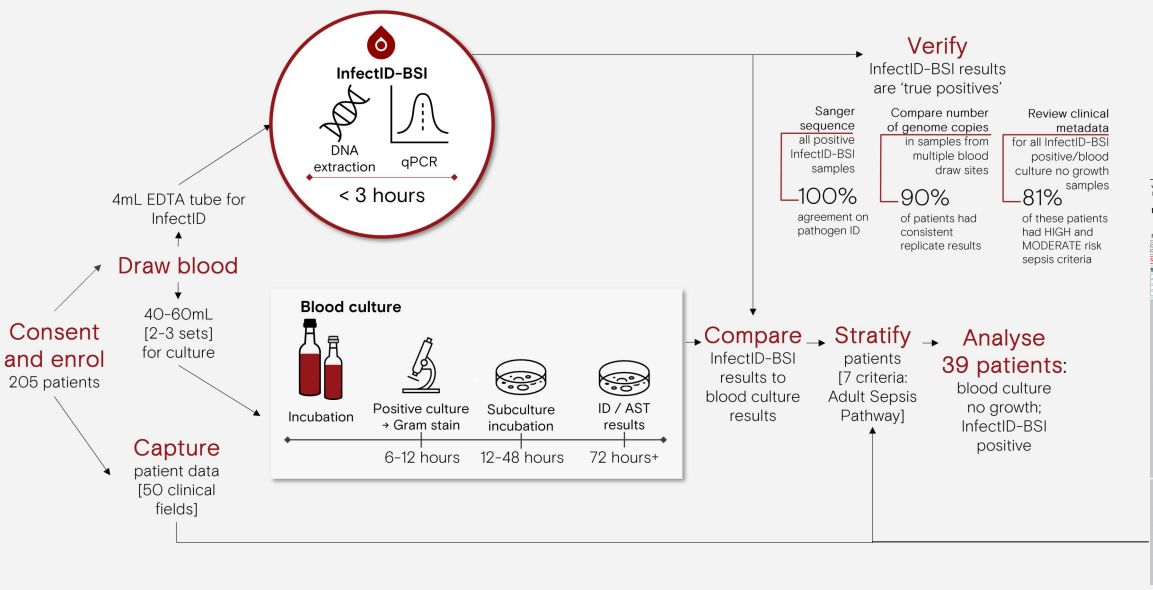
Sepsis is a leading killer worldwide, accounting for 11 million deaths each year[1]. The burden on health systems is immense, motivating Australian start-up Microbio to develop an effective method to detect and identify blood-borne pathogens for better patient management. Sixteen years of research have culminated in this commercial In Vitro Diagnostic assay: **InfectID-BSI**.

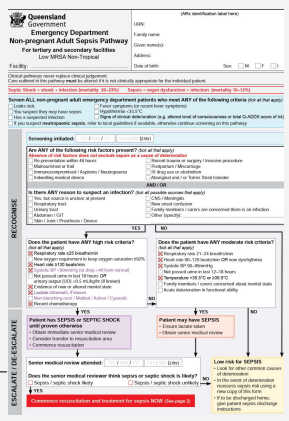
A bioinformatics approach underpins this highly discriminatory SNP fingerprint assay to detect and identify 26 of the most prevalent sepsis-causing bacteria and yeast directly from blood *in less than 3 hours*. The target pathogens for InfectID-BSI were selected based on research published by Opota and others in 2015, which identified these 20 pathogens responsible for causing 94% of sepsis cases in their multi-centre study cohort[2].

THE COMMERCIAL ASSAY



THE STUDY





Is there a correlation between pathogen DNA identified by InfectID-BSI and clinical indicators of sepsis?

The objective of the study was to determine if the DNA identified in patient samples correlated with patients displaying the clinical indicators of sepsis.

To achieve this, the clinical metadata of 39 patients was reviewed. These patients were selected because they returned positive InfectID-BSI results and no result from blood culture.

The sepsis criteria were adopted from the Queensland Government Emergency Department Non-pregnant Adult Sepsis Pathway. Data that matched 7 of the sepsis criteria were available to researchers: respiratory rate, heart rate, systolic BP, mental state (Glasgow coma score), lactate, recent chemotherapy, and temperature.

The clinical parameters stratify patients into three categories: the patient has sepsis, the patient may have sepsis or the patient is at low risk of sepsis.

Case study: 8 days; 100 tests; a life lost

The tortuous course of this patient's case highlights the frustration felt by the clinician, the patient and the family—'flying blind' with a septic patient and no aetiology identified.

A 74-year-old male presented with shortness of breath, fatigue and fevers. His past history included hypertension, osteoporosis, osteoarthritis, asthma, pulmonary embolism chronic hyponatraemia and T2 diabetes.

CXR showed multi-lobar pneumoniae (community acquired pneumonia). He was admitted to a medical ward and commenced on IV Benzyl Penicillin and oral Doxycycline. The following day IV Piptaz was added as his condition was deteriorating. He developed respiratory failure requiring ventilation support in Intensive Care (ICU). Antibiotics were escalated to Meropenem, Vancomycin and Azithromycin – the last line of defence in treating resistant bacteria. He failed to improve and, as a last attempt to find a treatment against the unknown pathogen, he was commenced on Fluconazole—an antifungal agent.

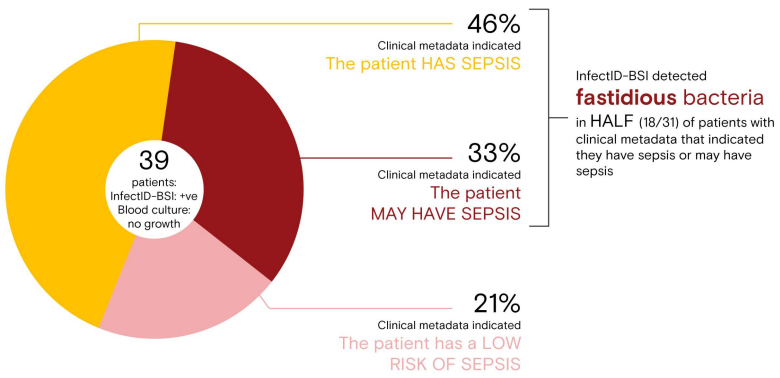
More than 100 tests ordered. Of those, 6 blood culture sets were taken—all with no growth. Respiratory PCR, *M. pnuemoniae* DNA, *S. pneumoniae* antigen, bronchoscopy sputum culture, viral faeces PCR, bacterial faeces PCR were done with no bacterium identified.

Despite 8 days of investigations and continually escalating treatment (accruing significant healthcare costs) the patient passed away.

InfectID-BSI was positive for *C. dublinensis* with 47 genome copies per 0.35 mL blood. The sample used for the InfectID test was taken on the day of the patient's admission.

If the clinicians had access to InfectID-BSI results, would the patient have had a different outcome?

THE RESULTS



CONCLUSION

There is a correlation between the presence of pathogen DNA and clinical indicators of sepsis. Molecular diagnostic techniques offer an advantage over blood culture because of the ability to detect and identify difficult-to-culture bacteria.

InfectID-BSI can inform targeted treatment of sepsis.

Consistent replicate results confirm 'true positives'

Table 1: All samples that were InfectID-BSI positive for *E. coli* and had 2 samples available from each patient; samples taken from different body sites (e.g. L arm, R arm). Note the consistency between the number of genome copies per 0.35 mL of blood for 9 out of the 10 patients.

Patient ID	Sample ID	Blood culture result	InfectID-BSI result	# of genome copies 0.35 mL blood	Expert clinical opinion
RB18	13	*E. coli*	*E. coli*	**42**	BSI
	14	*E. coli*	*E. coli*	**40**	
RB130	217	*E. coli*	*E. coli*	**64**	BSI
	218	*E. coli*	*E. coli*	**94**	
RB20	31	*S. aureus*	*E. coli (and S. aureus)*	**106**	Sepsis
	32	*S. aureus*	*E. coli (and S. aureus)*	**111**	
RB54	91	*E. coli* (ESBL producer)	*E. coli*	**145**	Sepsis
	92	*E. coli* (ESBL producer)	*E. coli*	**141**	
RB85	136	*S. aureus* (MRSA)	*E. coli (and S. aureus)*	**254**	Septic shock
	137	*S. aureus* (MRSA)	*E. coli (and S. aureus)*	**174**	
MB5	9	*E. coli*	*E. coli*	**733**	BSI
	10	*E. coli*	*E. coli*	**619**	
RB153	266	*E. coli*	*E. coli*	**988**	Sepsis
	267	*E. coli*	*E. coli*	**1058**	
RB66	118	*E. coli*	*E. coli*	**881**	BSI
	119	*E. coli*	*E. coli*	**1237**	
RB10	19	*E. coli, E. gallinarum*	*E. coli*	**17499**	Septic shock
	20	*E. coli, E. gallinarum*	*E. coli*	**14453**	
MB39	76	No growth	*E. coli*	27478	Sepsis
	77	No growth	*E. coli*	7688	

1 Rudd, K. et al (2020). Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet, 395:200–11. doi:10.1016/S0140-6736(19)32989-7

2 Opota, O., Croxatto, A., Prod'hom, G., & Greub, G. (2015). Blood culture-based diagnosis of bacteraemia: state of the art. Clinical Microbiology and Infection, 311–322. doi:10.1016/j.cmi.2015.01.003

microbio.com.au