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An antibiotic stewardship programme (ASP) blueprint for optimizing Verigene BC-GN within an institution: a tale of two cities

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Background: Time to appropriate antimicrobial therapy (TTAT) is the most important modifiable risk for poor patient outcomes in bloodstream infections (BSIs). Rapid diagnostic tests (RDTs) have revolutionized the ability of ASPs to optimize TTAT. Unlike Gram-positive BSIs, implementation of RDT-guided treatment algorithms in Gram-negative (GN) BSIs remains challenging due to the multitude and complexities of resistance mechanisms in GN bacilli and concerns that absence of common beta-lactamase genes detected by RDTs might not predict susceptibility to target antimicrobials. Therefore, we assessed the performance of a GN RDT organism ID and beta-lactamase gene positivity/negativity on the ability to predict antibiotic susceptibility.

Material/methods: This was a retrospecitve microbiogical analysis at two urban health systems in the United States; The Detroit Medical Center (DMC) and University of Maryland Medical Center (UMMC).

All positive GN blood cultures were reviewed from June 2015 through July 2016. The results from Verigene® BC-GN were compared with conventional antimicrobial susceptibility testing. Data were aggregated separately at each site. Negative predictive values (NPVs) were calculated to determine likelihood of susceptibility to target antimicrobials based on the absence of beta-lactamase genes detected by Verigene® BC-GN and stratified by organism species.

Results: The absence of the target beta-lactamase genes largely ruled out resistance to target antimicrobials, with the notable exception of *P. aeruginosa*. NPVs were > 90% at both sites for all other organism/antimicrobial combinations.

		DMC				UMMC			
Organism	Target antimicrobial	Total Isolates	N,% resistant	N resistance marker detected	NPV	Total Isolates	N,% resistant	N resistance marker detected	NPV
E. coli	Ceftriaxone	384	63 (16)	56	98	106	16 (15)	14	98
K. pneumoniae	Ceftriaxone	140	39 (28)	33	94	58	16 (28)	12	91
	Ertapenem		7 (5)	6	99		5 (9)	5	100
P. aeruginosa	Cefepime	51	6 (12)	0	88	43	15 (35)	0	65
Enterobacter spp.	Cefepime	61	3 (5)	1	97	31	3 (9)	3	100
Proteus spp.	Ceftriaxone	57	7 (12)	4	94	12	0	0	100
Acinetobacter spp.	Meropenem	39	10 (26)	8	93	14	5 (36)	5	100
K. oxytoca	Ceftriaxone	23	2 (9)	1	95	9	0	0	100
Citrobacter spp.	Cefepime	10	0	0	100	6	0	0	100

cephalosporin-resistance marker = any CTX-M, KPC, VIM, NDM, OXA; carbapenem-resistance marker = KPC, VIM, NDM, OXA

Conclusions: Susceptibility to the target antibmicrobials was largely predicted by the absence of beta-lactamase genes, with the exception of *P. aeruginosa*. Clinicians at both sites should feel confident selecting definitive therapy based on the results of Verigene® GN-BC. As local antimicrobial resistance patterns vary, these data should not be applied to other sites. This analysis does however provide a blueprint for similar investigations in order to develop institution-specific GN RDT BSI pathways.