Supplementary material

Comparison of *QUIK CHEK*, Xpert, BDM and two-step algorithm to composite reference standard (CRS).

Employing the CRS, 42/223 (18.8%) of samples were *C. difficile* positive. Of these, 37/42 (88.1%) were positive by TC. The remaining five were TC-negative samples: 4/5 were positive by both molecular assays and one was positive by both molecular assays and *QUIK CHEK* (Supplementary table 1).

The Xpert, BDM and two-step algorithm showed higher sensitivities, specificities and PPV in comparison with the CRS, but the NPV of all the assays were similar.

Supplementary Table 1. Performance characteristics of diagnostic assays in comparison withCRS/composite positive on stool samples submitted to the National Health Laboratory Service Microbiology Laboratory, at Tygerberg Hospital, Cape Town, South Africa, from October 2017 to October 2018..

n = 223		CRS_g		Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV_i (%) (95% CI)	NPV_h (%) (95% CI)
		Pos n=42	Neg n=181				
QUIK CHEK Tox A/B	Pos	21	1	50.0% (34%–66%)	99.4% (96%–100%)	95.5% (75%–100%)	89.6% (84%–93%)
	Neg	21	180				
Xpert	Pos	37	1	88.1% (74%–96%)	99.5% (97%–100%)	97.4% (85%–100%)	97.3% (94%–99%)
	Neg	5	180				
BDM	Pos	38	1	90.5% (76%–97%)	99.4% (96%–100%)	97.4% (85%–100%)	97.8% (94%–99%)
	Neg	4	180				
Algorithm (SOC)j	Pos	38	2	90.5% (76%–97%)	98.9% (96%–100%)	95.0% (82%–99%)	97.8% (94%–99%)
	Neg	4	179				

g CRS: Composite reference standard/composite positive toxigenic culture -positive or positive by two commercial assays in a

toxigenic culture-negative sample.

h: NPV: negative predicative value

i: PPV: positive predicative value

j: SOC: standard of care