



RESEARCH ARTICLE

Assessment of performance and implementation characteristics of rapid point of care SARS-CoV-2 antigen testing [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: The COVID-19 pandemic has resulted in a need for rapid identification of infectious cases. Testing barriers have prohibited adequate screening for SARS-CoV-2, resulting in significant delays in commencement of treatment and outbreak control measures. This study aimed to generate evidence on the performance and implementation characteristics of the BD Veritor™ Plus System rapid antigen test as compared to reverse transcription polymerase chain reaction (RT-PCR) for diagnosis of SARS-CoV-2 in Kenya.

Methods: This was a field test performance evaluation in adults undergoing testing for SARS-CoV-2. Recruited participants were classified as SARS-CoV-2-positive based on RT-PCR carried out on nasopharyngeal swabs. Antigen tests were performed with

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Any reports and responses or comments on the

simultaneous RT-PCR on 272 participants, allowing estimation of sensitivity, specificity, positive and negative predictive values for the rapid antigen test. Implementation characteristics were assessed.

Results: We enrolled 97 PCR negative symptomatic and 128 PCR negative asymptomatic, and 28 PCR positive symptomatic and 19 PCR positive asymptomatic participants. Compared to RT-PCR, the sensitivity of the rapid antigen test was 94% (95% confidence interval [CI] 86.6 to 100.0) while the specificity was 98% (95% CI 96 to 100). There was no association between sensitivity and symptom status, or between the cycle threshold value and sensitivity of the BD Veritor. The rapid test had a quick turnaround time, required minimal resources, and laboratory personnel conducting testing found it easier to use than RT-PCR.

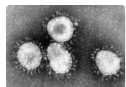
The relatively high sensitivity of BD Veritor may be partially attributed to shortages of RT-PCR testing materials, resulting in specimen analysis delays and potential degradation of viral genetic material. Therefore, in resource-constrained settings, rapid antigen tests may perform better than the reference RT-PCR, resulting in prompt institution of isolation and treatment measures.

Conclusion: The BD Veritor rapid antigen test's high sensitivity should be interpreted with consideration to the challenges occasioned by RT-PCR testing in resource-constrained settings.

Keywords

SARS-CoV-2, rapid antigen test, polymerase chain reaction, sensitivity, specificity, implementation

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article can be found at the end of the article.



This article is included in the [Coronavirus \(COVID-19\)](#) collection.

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Introduction

The coronavirus disease of 2019 (COVID-19) has placed enormous burden on individuals and society at large. Low- and middle-income countries in particular are disadvantaged as resources are already significantly stretched. Huge surges in infection carry the risk of quickly overwhelming health care systems, leading to excess mortality. Therefore, rapid identification and isolation of infectious cases is key to containing the pandemic.

Real-time reverse transcription polymerase chain reaction (RT-PCR) has been the reference standard method for detection of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection. Despite its excellent sensitivity and specificity, the method is limited by high initial set up costs, expensive consumables, the need for highly trained staff, prolonged turn-around-time, requirement for sample transport and an uninterrupted power supply¹. Recent evidence indicates test reporting delays as having a negative impact on isolation as a control measure of infection spread². There is therefore a need to optimize testing modalities that can be applied to large populations quickly enough to inform strategies that limit transmission^{3,4}.

The exigency for decentralized testing options and the rapid development of novel biomarkers has resulted in development and approval of rapid antigen tests as a complementary modality to RT-PCR. They are less costly, can easily be offered at the point of care, have fewer associated health worker training needs and likely identify the most infectious individuals early in the disease course. The use of rapid antigen tests can improve accessibility to testing, facilitate timely confirmation of suspected cases and expedite clinical and public health decision making. However, rapid antigen test performance varies depending on inherent test characteristics, quality of sample, timing of sample collection in disease course, SARS-CoV-2 viral load and presence of symptoms⁵.

While viral RNA can be detected by RT-PCR weeks after infection, culture-positive specimens are generally not found after nine days post-infection. Culture-positive samples contain more viral RNA than culture negative specimens^{6,7}. Peak RNA concentrations are reached before day five of symptom onset, and the potential for transmission declines after one week of symptom onset^{8,9}. RT-PCR amplifies and detects nucleic acids, including sub-genomic RNA that represent non-intact virus⁹. As cycle threshold (Ct) value and viral load levels are inversely correlated, samples with high Ct values on RT-PCR are from individuals who are less likely to be contagious⁸.

The World Health Organization (WHO) recommends that rapid antigen tests should have a sensitivity of $\geq 80\%$ and a specificity of $\geq 97\%$ (WHO - rapid immunoassays). Sensitivity of rapid antigen tests appears to be higher in symptomatic patients and in those with high viral loads^{5,10,11}. These are patients who are more likely to be infectious. Rapid antigen test sensitivity is also higher when carried out less than five days from symptom onset. The overall low sensitivity of rapid antigen tests has been attributed to false negative results seen in samples with high RT-PCR Ct values¹². There is a low probability of

transmission from patients whose samples test positive on RT-PCR but negative on rapid antigen tests¹³. At a population level, the lower sensitivity of rapid tests may be improved by high frequency testing^{14,15}.

It is necessary to evaluate rapid antigen tests at the end-user level, taking the local population into consideration before large-scale implementation¹⁶. Alignment with existing health systems is a determinant for the successful adoption of novel diagnostic methods. Besides technical performance, evaluation of rapid antigen tests should include aspects related to clinical utility, cost and patient satisfaction¹⁷. This information is useful to key stakeholders such as researchers, product developers, funding bodies and policy makers in understanding real-world context so as to meet the needs of SARS-CoV-2 testing.

The BD Veritor™ Plus System (BD Veritor; Becton, Dickinson and Company) for rapid detection of SARS-CoV-2 is a rapid chromatographic immunoassay for the detection of SARS-CoV-2 antigens in respiratory specimens. The viral nucleocapsid protein is targeted for detection. This study aims to evaluate the performance and implementation characteristics of the BD Veritor rapid antigen test compared to the gold-standard RT-PCR in asymptomatic and symptomatic adults undergoing testing for SARS-CoV-2 in Kenya. Findings from this study will inform the design of SARS-CoV-2 testing protocols and guide large scale use of rapid antigen tests.

Methods

Study design and participants

Individuals aged 18 and over who were being tested for SARS-CoV-2 in Kenya and who gave written informed consent for participating in this study were enrolled consecutively between 31st January and 24th March 2021. The participants included travelers, university students, healthcare workers (HCWs), patients seeking services in hospital outpatient departments (OPD) and members of the general population. Healthcare workers and OPD patients were enrolled at Mary Help Hospital in Thika, Kenya, while students and the general population were enrolled at Mount Kenya University in Thika, Kenya. Our enrollment targets were 100 PCR negative symptomatic and asymptomatic participants each, and 30 PCR positive symptomatic and asymptomatic participants each. Known SARS-CoV-2 RT-PCR positive participants were retrospectively identified from laboratory records and invited to consent for re-testing within 24 hours of collection of the initial RT-PCR positive sample. These were mainly individuals that required SARS-CoV-2 testing before travel. At re-test, samples for RT-PCR and rapid antigen test were collected. Both symptomatic and asymptomatic PCR positive and negative participants were enrolled, and recruitment was carried out irrespective of duration of symptoms. Demographic and clinical information was obtained using clinical evaluation and an interviewer-administered questionnaire¹⁸.

All subjects gave their written informed consent for inclusion before they participated in the study. Ethical approval was granted by the Mount Kenya University Ethics Review Committee (MKU/ERC/1780).

Sample collection

Paired oropharyngeal and anterior nasal swabs were obtained in the same encounter for RT-PCR and rapid antigen testing respectively. For the rapid antigen test, anterior nasal specimens were obtained using regular-tipped flocked swabs inserted approximately 2–3cm into the anterior nares. The swab was rolled along the mucosa of each nostril. The specimen obtained was then processed according to the manufacturer's recommendations.

Samples for RT-PCR were obtained via oropharyngeal swabs. They were placed in viral transport medium and delivered in cooler boxes at two to eight degrees Celsius to the Kenya Medical Research Institute (KEMRI) laboratory, Nairobi, Kenya. Prior to testing, samples were removed from the cooler boxes and allowed to reach room temperature. Samples from asymptomatic participants were analyzed in pooled samples of 10, while those from symptomatic participants were run singly. This was in accordance with standard operating procedures at the laboratory. The RT-PCR assay used was Abbott RealTime SARS-CoV-2 and assays were conducted according to the manufacturer's protocols. The target sequences were the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) and N-genes. A positive result was confirmed when either a single-gene or a two-gene amplification occurred. Positive and negative internal controls were included in each run. Test results were interpreted as positive or negative at a Ct of 37 according to the manufacturer's recommendation¹⁹.

Qualitative data collection

Trained research assistants collected qualitative data using face-to-face key informant interviews. Semi-structured interview guides were used^{20,21}. Key informant interviews were conducted in three population subsets: travelers, individuals seeking care in hospital out-patient departments and health care workers offering testing services. Seven Key Informant Interviews (KIIs) with health care workers, seven KIIs with hospital clients and three KIIs with travelers were conducted. All three population subsets were interviewed on their perceptions of barriers and facilitators, satisfaction, ease of use and acceptability of the BD Veritor antigen test.

Statistical analysis

The primary pre-specified outcome measures for this study were sensitivity and specificity point estimates and 95% confidence intervals for the BD Veritor antigen test compared to results from the reference standard oropharyngeal swab RT-PCR. Statistical analysis was performed using SPSS version 23.0 software (IBM SPSS Statistics, RRID:SCR_019096). Overall sensitivity and specificity of the BD Veritor antigen test were calculated and then stratified between asymptomatic and symptomatic individuals. The diagnostic measures efficiency of the BD Veritor antigen test was further correlated with the Ct threshold values of RT-PCR and sensitivity stratified by persons with low and high Ct values. We calculated 95% confidence intervals (CI) for all the sensitivity and specificity proportions. Participants' characteristics were summarized and presented as percentages. The differences in participants' characteristics based on PCR positivity status and presence of symptoms were

explored and tested using chi square test of associations. The age of the participants was presented as mean and compared between groups using Student's t test. A p value less or equal to 0.05 was statistically significant.

Qualitative data was captured using audio tapes and field notes, transcribed and managed using QSR NVivo 12 software (RRID: SCR_014802), (an open-access alternative is RQDA: R-based Qualitative Data Analysis. R package version 0.2-8). The KII transcripts were coded and checked for coding consistency using a framework to classify and organize data into four themes. These included knowledge on COVID-19 testing, sample collection experience, applicability of the rapid antigen test and improvement suggestions for the test. We applied a grounded theory approach²². We used an iterative process to develop the thematic framework, and this was updated in two rounds of analysis. Analysis charts for each emergent theme were developed and categorized across all participants.

Results

A total of 287 participants were enrolled into the study but 15 did not meet the eligibility criteria for age and were not included in the analysis. We obtained 272 paired samples. The participants had a median age of 30 years (range 18 to 68), 135 (50%) were female and 125 (46%) participants were symptomatic (by design). RT-PCR found 47 (17%) positive samples while 49 (18%) were positive on the BD Veritor antigen test. Health care workers (HCWs) and out-patient department (OPD) patients comprised the majority of symptomatic participants (33% each), while students comprised the majority of asymptomatic participants (54%). The median duration of symptoms was five days (Table 1)²³.

Compared to RT-PCR, the sensitivity of the BD Veritor antigen test was 94% (95% confidence interval [CI] 87 to 100) while the specificity was 98% (95% confidence interval [CI] 96 to 100). Overall concordance was 97% (95% confidence interval [CI] 95 to 99) from 264/272 specimens (Table 2). The sensitivity of the BD Veritor antigen test was higher among symptomatic compared to asymptomatic participants (100% vs. 84%), although this did not reach statistical significance. Likewise, no significant difference in specificity was observed between symptomatic (96%) and asymptomatic (99%) participants (Table 3). There was no statistical difference in qualitative PCR results ($p = 0.581$), or quantitative Ct values ($p = 0.840$) and sensitivity of the rapid antigen test between those who had symptoms for less than five days (inclusive) and those who had symptoms for more than five days.

Among the 47 specimens with positive PCR results, the mean Ct value was 16.3 (Figure 1). At Ct values of between 1 and 20 ($n = 37$), the sensitivity of the BD Veritor was 95%, while at Ct values of between 21 to 25 ($n = 11$), sensitivity was 91%. We could not detect an association between Ct values and sensitivity of the BD Veritor test at this sample size (Table 4). There was no association between Ct value and presence of symptoms ($p = 0.544$). There was also no difference in average Ct values between BD Veritor true positive and BD Veritor false negative samples ($p = 0.303$).

Table 1. Participants' characteristics.

Variable	Frequency (%)	PCR negative	PCR positive	P value
Sex				
Female	135 (50)	114 (51)	21 (45)	0.455
Male	137 (50)	111 (49)	26 (55)	
Mean age in years (SD)	30 (10)	29 (9)	37 (12)	<0.001
Min–Max	18–68			
Population				
General	30 (11)	16 (7)	14 (30)	
HCW	75 (28)	60 (27)	15 (32)	
OPD patient	41 (15)	41 (18)	0	
Student	90 (33)	89 (40)	1 (2)	
Traveler	36 (13)	19 (8)	17 (36)	
Clinical status				
Asymptomatic	147 (54)	128 (57)	19 (40)	0.039
Symptomatic	125 (46)	97 (43)	28 (60)	
Number of symptoms				
0	147 (54)	128 (57)	19 (40)	0.021
2	2 (1)	1 (0)	1 (2)	
3	1 (0)	0	1 (2)	
More	122 (50)	96 (43)	26 (55)	
Duration of symptoms in days (n=76)				
Median (IQR)	5 (2–7)	4 (1.5–6.5)	5 (2.5–7.5)	0.399
Category, n (%)				
5 days or less	42 (55)	32 (57)	10 (50)	0.581
More than 5 days	34 (45)	24 (43)	10 (50)	
Type of symptoms				
Sore throat	53 (60)			
Headache	48 (55)			
Cough	46 (52)			
Runny nose	39 (44)			
General weakness	33 (38)			
Fever/chills	32 (36)			
Shortness of breath	18 (21)			
Muscular pain	17 (20)			
Nausea/vomiting	14 (16)			
Joint pain	13 (15)			
Abdominal pain	12 (14)			
Chest pain	11 (13)			
Diarrhoea	9 (10)			
Irritability/confusion	7 (8)			

Abbreviations: PCR, Polymerase chain reaction; HCW, Health care worker; OPD, Out-patient Department; SD, Standard deviation; IQR, Inter quartile range

Table 2. Performance of BD Veritor antigen test against RT-PCR.

Results		BD performance	95% CI
Positive	PCR	47	-
	BD	44	-
	Sensitivity (PPA)	94%	87%, 100.0%
	False negatives	3 (6%)	-
Negative	PCR	225	-
	BD	220	-
	Specificity (NPA)	98%	96%, 100%
	False positives	5 (2%)	-
Concordance	Cumulative	272	-
	Agreement	264	-
	OPA	97%	95%, 99%
Accuracy	AUC	96%	91%, 100%

Abbreviations: PCR, Polymerase chain reaction; PPA, Positive percent agreement; NPA, Negative percent agreement; OPA, Overall percent agreement; AUC, Area under the curve; CI, Confidence interval

Statistical test for categorical variables: Chi-square test

Table 3. Performance of BD Veritor antigen test by symptom status.

Symptoms	Sensitivity			Specificity		
	PCR positive	BD positive (%)	95% CI	PCR negative	BD negative (%)	95% CI
Asymptomatic	19	16 (84%)	68, 100.0	128	127 (99%)	98, 100.0
Symptomatic	28	28 (100%)	-	97	93 (96%)	92, 100

Abbreviations: PCR, Polymerase chain reaction; CI, Confidence interval

Statistical test for categorical variables: Chi-square test

There was an association observed between Ct value and length of time from specimen collection to analysis. High Ct values were associated with longer time to analysis, with samples having a Ct value > 37 (PCR negative) having a median time to analysis of 18 days, and those with Ct value of between 1 and 20 having a median time to analysis of seven days ($p < 0.001$).

Implementation characteristics

Knowledge of testing strategies available. Participants demonstrated some level of understanding of the COVID-19 testing strategies available. The key source of this information was an electronic/digital media platform:

“I have only heard and seen on TV, but I have no experience or encountered other methods.” (KII, HCW)

“Not much, especially because Covid is a new disease and besides the normal information being shared on the media all I know is that for travelers like me, we have to take a test every time we want to travel.” (KII, Traveler)

Among the health care workers interviewed, there was a general indication of knowledge on current strategies in testing:

“Yes, I am aware of the PCR gold standard testing and antibody testing.” (KII, HCW).

Perceptions on sample collection and applicability of BD Veritor antigen test. Even though the clients reported the anterior nares method of sample collection as causing irritation and discomfort, it was the preferred method compared to oropharyngeal swabbing for RT-PCR:

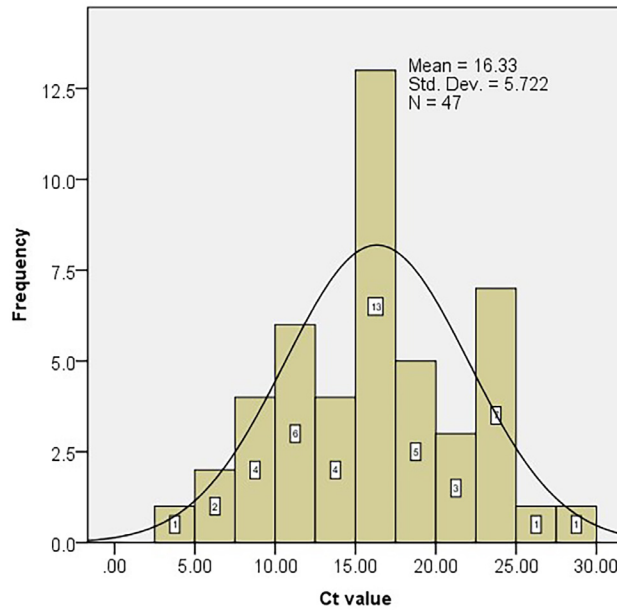


Figure 1. Frequency distribution of Ct values. Abbreviations: Ct, Cycle threshold.

Table 4. Performance of the BD Veritor test compared to Ct values.

Ct value	Sensitivity			Specificity		
	PCR positive	BD positive (%)	95% CI	PCR negative	BD negative (%)	95% CI
0 to 20	37	35 (94.6%)	87.3, 100.0	234	229 (98%)	96.0, 99.7
21 to 25	11	10 (90.9%)	73.9, 100.0	0	-	-
>25	5	5 (100%)	-	0	-	-

Abbreviations: PCR, Polymerase chain reaction; Ct, Cycle threshold; CI, Confidence interval
 Statistical test for categorical variables: Chi-square test

“The anterior nares testing was a bit uncomfortable, but it was not painful. Comparing to the previous tests which were very invasive, this one was very friendly.” (KII, HCW)

“Comparing to the one I had before, this test was so comfortable. Although the anterior nares sample collection was a bit uncomfortable, irritation was mild and faded away after a few minutes. This cannot be compared to the nasopharyngeal which persists for hours after sample collection” (KII, Client)

“I wouldn’t say it was very comfortable. There was mild irritation on the nose, but it was not very invasive. I was surprised that it was not painful as earlier depicted on the TV.” (KII, Client)

“Well, the test is easy and sample collection was fast and comfortable.” (KII, HCW)

The BD Veritor antigen test was preferred among travelers, with the main reason cited as the quick turn-around-time in availing of results:

“It was easy, and besides the sampling took roughly 15 minutes I would prefer BD for now if it means saving time. (KII, Traveler)

“..... I found this test quick and I think it should be approved to be used for people traveling occasionally.” (KII Traveler)

HCWs indicated that the BD veritor antigen test was easy to use, going further to recommend its use in the pediatric population:

“I would choose BD Veritor. This testing method applies to everyone especially children and patients in ICUs.” (KII, HCW)

.....The kit application in the field is logical and easy to use and requires less training. (KII, HCW)

“It was very easy, especially the nasal swab. I would prefer the BD Veritor. I believe when it will be rolled out it will be cheap.” (KII, HCW)

Health providers also expressed that the BD antigen test meant a reduction in the cost of care provision with cheaper COVID-19 diagnosis:

“It was very easy, especially the oral swab. I would prefer the BD Veritor. I believe when it will be rolled out it will be cheap.” (KII, HCW)

The short duration for COVID-19 diagnosis made it largely acceptable among travelers, health providers and the public:

“It was easy, and besides the sampling it took roughly 15 minutes. I would prefer BD for now if it means saving time. (KII, Traveler)

“...As for retaking a test, I would prefer the BD Veritor as it gives the results much faster. I would also recommend this test to anyone willing to take a covid test based on my experience.” (KII, Client)

Participant-driven improvement suggestions. Some participants felt that there is a need for consideration of alternative methods of sample collection that minimized client discomfort. One HCW also mentioned the need for internal validation mechanisms:

“Sample collection. I almost vomited. I wish there was another way rather than swabbing the nose.” (KII, Traveler)

“Internal validation. The device should have the capability to print test results and have a sample counting ability. Also, I would wish if the device could display the viral load in terms of cycle number.” (KII, HCW)

“Maybe the swab being used for the nasal sample could be made more friendly to avoid irritation.” (KII, Client)

Discussion

The sensitivity and specificity of the BD Veritor™ System as reported by the manufacturer is 94% and 99% respectively. This study, nested in real-world-use case scenarios in Kenya, demonstrated a sensitivity and specificity of 94% and 98%, respectively, which was relatively high compared to that observed in similar studies²⁴.

The sensitivity of rapid antigen tests has been shown to be higher in symptomatic patients and in those with high viral loads. However, we did not detect an association between the presence of symptoms and sensitivity, or between the presence of symptoms and Ct value. This is potentially due to

our sample size (as demonstrated by the wide confidence intervals). There was also a lack of association between Ct value and sensitivity of the BD Veritor test, although we did not enroll many patients with high Ct value and were unable to adequately assess their potential effect on performance of the test.

The analysis of association between duration of symptoms and PCR results, Ct value and rapid antigen test sensitivity was carried out on a sample size of 76 participants for whom we had complete data. To assess for selection bias, we analyzed the sample characteristics of this group and compared it to that of individuals whose duration of symptoms was not recorded. There was no statistically significant difference in sex and mean age between the two groups.

When evaluating the accuracy of rapid antigen tests, factors affecting the performance of the reference standard RT-PCR must be considered. Important in this study is the source of and volume of samples taken, transport and storage conditions and the technical performance of the assay. Careful specimen collection and processing by qualified and experienced staff was carried out in order to ensure that adequate genetic material was obtained and that sample contamination was minimized. However, there were delays in analyzing test results caused by shortages of RT-PCR reagents and materials. The effect of these delays was assessed by comparing PCR results and Ct values by time from sample collection to analysis. A greater Ct value was observed in specimens for which there was an extended interval between sampling and analysis. This suggests that degradation of viral genetic material may have occurred, which may have had the effect of reducing the RT-PCR test positivity, and thus artificially increasing the sensitivity of the rapid antigen test. Contributing to the increased sensitivity of the rapid antigen test may also have been high viral loads (mean Ct value 16.10) in sampled participants during the peak second wave of SARS-CoV-2 infection in the country in March 2021. The stringent requirements related to sample processing and analysis are a recognized drawback to RT-PCR as a testing modality in field conditions. Sample degradation is a common outcome where transport networks to central laboratories are inefficient, and where reagent stock-outs occasioned by high demand for testing are typical. This may lead to inaccuracies in reported results and missed opportunities for effective isolation and treatment to prevent forward transmission. In these conditions, point of care testing with rapid antigen tests will likely perform better than the reference RT-PCR standard.

Pooled testing is a strategy that is used when conducting RT-PCR assays. It is accepted as an approach that effectively identifies SARS-CoV-2 infection while conserving laboratory resources^{25,26}. In addition, pooling has been shown to increase test specificity as positive samples are tested twice²⁷. Evidence suggests that testing accuracy is retained in pool sizes of up to 32 samples²⁵. In our study, samples from asymptomatic patients were included in pool sizes of 10, in line with local laboratory protocols. Deconvolution was carried out for all positive pools.

The feasibility assessment in this study shed some light on the facilitators and barriers to use of rapid antigen tests. There were different levels of understanding among participants on the COVID-19 testing strategies available. Electronic platforms were the main source of information on testing methods and the need for testing particularly before travel. There was discomfort reported on both the anterior nares and oropharyngeal swabbing methods, but a general preference for the former. Both methods were reported to be more comfortable compared to nasopharyngeal swabbing that was commonly depicted in the media. Most users, and especially travelers, appreciated the rapid nature of receiving results. Health care workers highlighted challenges posed by RT-PCR testing including prolonged turn-around-time, high cost, equipment breakdown and rigorous sample handling requirements. They showed appreciation for the ease of use of the rapid test and postulated that they would be applicable in a wide array of health settings. However, there was concern about inconclusive results and the lack of a physical report accompanying the test.

Central laboratories have as their focus the quality and reliability of a test. Clinicians and patients may in addition value methods that expedite decision making at the first point of contact¹⁷. These include decisions to rule out life-threatening conditions, or as with COVID-19, whether or not to isolate an individual. This study demonstrated the potential for rapid antigen tests to facilitate timely clinical decision making.

Our study relied on field laboratory personnel to carry out the rapid antigen test. However, the ideal point-of-care test is one that can be used during the clinician-patient interaction. This would require additional training and mentorship for health workers in areas that are traditionally laboratory-centered, thus increasing their workload and potentially affecting their acceptance of the method. Concerns about quality assurance and availability of technical support when required should be considered and factored into any future cost analysis. Also important to consider is the impact of a wrong clinical decision resulting from inaccurate test results when employing a new method or strategy, and the effect that this may have on acceptability by health care workers¹⁷. Further studies would shed more light on these crucial aspects.

Overall, we observed an exponential increase in demand for COVID-19 testing in participating health facilities over the course of the study, indicative of a general acceptability and positive user experience with the rapid antigen test in this population.

Conclusions

The BD Veritor rapid antigen test exhibited relatively high sensitivity and specificity when used to detect SARS-CoV-2

infection among symptomatic and asymptomatic individuals in varied populations. These results should be interpreted with consideration of the challenges occasioned by RT-PCR testing in resource-constrained settings. Its implementation feasibility, acceptability and ease-of-use would potentially result in bridging the testing gap and contribute towards a reduction in community transmission. Special protocols should be designed that distinguish workflows related to SARS-CoV-2 testing for identification and isolation of infectious individuals. Further areas of study to describe the most appropriate cadre of staff and skill set required in busy clinical settings, as well as strategies to ensure acceptable quality of rapid antigen testing are recommended.

Data availability

Underlying data

Figshare: Underlying data for 'Assessment of performance and implementation characteristics of rapid point of care SARS-CoV-2 antigen testing'.

This project contains the following underlying data:

- BD study data set.xlsx <https://doi.org/10.6084/m9.figshare.14958198.v3>¹⁹
- Covid symptoms among participants_Supplementary materials_table 1.docx <https://doi.org/10.6084/m9.figshare.17125634.v3>²³

Extended data

Figshare: Extended data for 'Assessment of performance and implementation characteristics of rapid point of care SARS-CoV-2 antigen testing'.

This project contains the following extended data:

- Key informant interview guide for SARS CoV2 Antigen Testing_travel, patient.docx <https://doi.org/10.6084/m9.figshare.17125619.v1>²⁰
- Key informant interview guide for SARS CoV2 Antigen Testing_HCWX.docx <https://doi.org/10.6084/m9.figshare.17125616.v1>²¹
- Kenya MoH_Case investigation form for 2019 Novel Coronavirus.docx <https://doi.org/10.6084/m9.figshare.17126252.v3>¹⁸

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Consent

Written informed consent for publication of the participants details was obtained from the participants.

References

1. Esbin MN, Whitney ON, Chong S, *et al.*: **Overcoming the bottleneck to widespread testing: A rapid review of nucleic acid testing approaches for COVID-19 detection.** *RNA*. Cold Spring Harbor Laboratory Press; 2020; **26**(7): 771–83.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
2. Larremore DB, Wilder B, Lester E, *et al.*: **Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening.** *Sci Adv*. 2021; **7**(1): eabd5393.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
3. Kobia F, Gitaka J: **COVID-19: Are Africa's diagnostic challenges blunting response effectiveness?** [version 1; peer review: 2 approved]. *AAS Open Res*. 2020; **3**: 4.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. Badu K, Thorn JPR, Goonoo N, *et al.*: **Africa's response to the COVID-19 pandemic: A review of the nature of the virus, impacts and implications for preparedness** [version 1; peer review: 2 approved with reservations]. *AAS Open Res*. 2020; **3**: 19.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
5. Landaas ET, Storm ML, Tollånes MC, *et al.*: **Diagnostic performance of a SARS-CoV-2 rapid antigen test in a large, Norwegian cohort.** *J Clin Virol*. 2021; **137**: 104789.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Huang CG, Lee KM, Hsiao MJ, *et al.*: **Culture-based virus isolation to evaluate potential infectivity of clinical specimens tested for COVID-19.** *J Clin Microbiol*. 2020; **58**(8): e01068–20.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
7. Mina MJ, Peto TE, García-Fiñana M, *et al.*: **Clarifying the evidence on SARS-CoV-2 antigen rapid tests in public health responses to COVID-19.** *Lancet*. 2021; **397**(10283): 1425–1427.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
8. Walsh KA, Jordan K, Clyne B, *et al.*: **SARS-CoV-2 detection, viral load and infectivity over the course of an infection.** *J Infect*. W.B. Saunders Ltd; 2020; **81**(3): 357–71.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
9. Jefferson T, Spencer EA, Brasseur J, *et al.*: **Viral Cultures for Coronavirus Disease 2019 Infectivity Assessment: A Systematic Review.** *Clin Infect Dis*. 2020; **73**(11): e3884–e3899.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
10. Prince-Guerra JL, Almendares O, Nolen LD, *et al.*: **Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites - Pima County, Arizona, November 3-17, 2020.** *MMWR Morb Mortal Wkly Rep*. 2021; **70**(3): 100–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. Salvagno GL, Gianfilippi G, Bragantini D, *et al.*: **Clinical assessment of the Roche SARS-CoV-2 rapid antigen test.** *Diagnosis (Berl)*. 2021; **8**(3): 322–326.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. Strömer A, Rose R, Schäfer M, *et al.*: **Performance of a Point-of-Care Test for the Rapid Detection of SARS-CoV-2 Antigen.** *Microorganisms*. 2020; **9**(1): 58.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
13. Albert E, Torres I, Bueno F, *et al.*: **Fiel (Panbio™ COVID-19 Ag Rapid Test Device) for COVID-19 diagnosis in primary healthcare centres.** *Clin Microbiol Infect*. 2021; **27**(3): 472.e7–472.e10.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
14. Mina MJ, Parker R, Larremore DB: **Rethinking Covid-19 Test Sensitivity — A Strategy for Containment.** *N Engl J Med*. 2020; **383**(22): e120.
[PubMed Abstract](#) | [Publisher Full Text](#)
15. Nash B, Badea A, Reddy A, *et al.*: **The impact of high frequency rapid viral antigen screening on COVID-19 spread and outcomes: a validation and modeling study 2 3.** *medRxiv*. 2020 Nov 4.
[Publisher Full Text](#)
16. Kosack CS, Page AL, Klatser PR: **A guide to aid the selection of diagnostic tests.** *Bull World Health Organ*. 2017; **95**(9): 639–45.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
17. Lingervelder D, Koffijberg H, Kusters R, *et al.*: **Point-of-care testing in primary care: A systematic review on implementation aspects addressed in test evaluations.** *Int J Clin Pract*. Blackwell Publishing Ltd; 2019; **73**(10): e13392.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
18. Muthamia E, Mungai S, Gitaka J: **Kenya MoH_Case investigation form for 2019 Novel Coronavirus.docx.** *Figshare*. Dataset. 2021.
<http://www.doi.org/10.6084/m9.figshare.17126252.v3>
19. Muthamia E, Mungai S, Gitaka J, *et al.*: **BD study dataset_final.xlsx.** *Figshare*. Dataset. 2021.
<http://www.doi.org/10.6084/m9.figshare.14958198.v3>
20. Muthamia E, Mungai S, Gitaka J: **Key informant interview guide for SARS CoV2 Antigen Testing_travel, patient.docx.** *Figshare*. Dataset. 2021.
<http://www.doi.org/10.6084/m9.figshare.17125619.v1>
21. Muthamia E, Mungai S, Gitaka J: **Key informant interview guide for SARS CoV2 Antigen Testing_HCW.docx.** *Figshare*. Dataset. 2021.
<http://www.doi.org/10.6084/m9.figshare.17125616.v1>
22. Chun Tie Y, Birks M, Francis K: **Grounded theory research: A design framework for novice researchers.** *SAGE Open Med*. 2019; **7**: 050312118822927.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Muthamia E, Mungai S, Gitaka J: **Covid symptoms among participants_Supplementary materials_table 1.docx.** *Figshare*. Dataset. 2021.
<http://www.doi.org/10.6084/m9.figshare.17125634.v3>
24. van der Moeren N, Zwart VF, Lodder EB, *et al.*: **Performance evaluation of a SARS-CoV-2 rapid antigen test: Test performance in the community in the netherlands.** *medRxiv*. 2020.
[Publisher Full Text](#)
25. Deckert A, Bärnighausen T, Kyei NN: **Simulation of pooled-sample analysis strategies for covid-19 mass testing.** *Bull World Health Organ*. 2020; **98**(9): 590–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
26. Agoti CN, Mutunga M, Lambisia AW, *et al.*: **Pooled testing conserves SARS-CoV-2 laboratory resources and improves test turn-around time: experience on the Kenyan Coast** [version 2; peer review: 3 approved]. *Wellcome Open Res*. 2021; **5**: 186.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
27. Pikovski A, Bentele K: **Pooling of Coronavirus Tests under Unknown Prevalence.** *Epidemiol Infect*. 2020; **148**: e183.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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Alexander Viloría Winnett

UCLA-Caltech Medical Scientist Training Program, California Institute of Technology, California, USA

Overall comment:

The authors present valuable data about the performance and perception of the BD Veritor Plus System rapid antigen diagnostic test in the context of Kenya. Results of the antigen rapid diagnostic test, which uses anterior nares swabs, were compared to results of the Abbott Real Time SARS-CoV-2 RT-PCR assay performed on a paired oropharyngeal swab specimen.

The study is well-designed, and the results are thoroughly and clearly described. I particularly appreciate that the authors interviewed community stakeholders about their experience with the antigen rapid diagnostic test, and that the authors investigated the potential for degradation of viral material in specimens that experienced a delay between collection and RT-PCR testing. Given that each test (the rapid antigen diagnostic test, and the reference RT-PCR test) were performed on different specimen types, I believe the manuscript would benefit from additional discussion/consideration of how differences due to specimen type might impact the observed performance, and potentially explain some findings that are not consistent with other studies: for example, that viral load (of oropharyngeal swabs) was not associated with the rapid antigen test result (of anterior nares swab). This may be of particular relevance, given that four of five participants with false positive antigen test results were symptomatic at the time of testing, and that we have previously found that there can be quite extreme differences in viral load between an oropharyngeal swab and an anterior nares swab collected at the same time from a person (Viloría Winnett *et al.*, 2023¹).

I hope the authors find my specific comments provided below useful for further strengthening their manuscript.

Major Comments:

1. Figure 1: It was surprising to see specimens with Ct values of 5 or less. Background fluorescence signal can sometimes trigger very low Ct values despite the sample clearly

lacking exponential amplification of a target, due to auto-thresholding and/or fluorescence drift. In these cases, plate controls can still appear normal. Could the authors please confirm the seven samples with very low Ct values (<10) indeed had exponential rises in fluorescent signal that would be consistent with true amplification of a target? Alternatively, some assays perform a number of amplification cycles at the beginning of a protocol that are not 'counted' in the resulting Ct value, which can result in such low Ct's being output. If this was the case, could this note be added to the figure caption to aid in interpretation of the Ct values?

2. "Even though the clients reported the anterior nares method of sample collection as causing irritation and discomfort, it was the preferred method compared to oropharyngeal swabbing for RT-PCR": this statement does not appear supported by the participant remarks provided in the manuscript. For example, in the second quotation in this section ("Comparing to the one I had before, this test was so comfortable. Although the anterior nares sample collection was a bit uncomfortable, irritation was mild and faded away after a few minutes. This cannot be compared to the nasopharyngeal which persists for hours after sample collection"), the participant seems to be saying that the anterior nares specimen is preferred to nasopharyngeal swab specimen, not oropharyngeal swab specimen collection. And in quotations 1 and 3 in this section, it is not clear whether the participants are comparing the anterior nares swab to oropharyngeal swab, or anterior nares swab to nasopharyngeal swab. Further, three quotes presented in a later section ("It was very easy, especially the oral swab", and "Sample collection. I almost vomited. I wish there was another way rather than swabbing the nose.", and "Maybe the swab being used for the nasal sample could be made more friendly to avoid irritation.") appear to contradict the statement that anterior nares swab was preferred over oropharyngeal swab by participants.
3. "However, we did not detect an association between the presence of symptoms and sensitivity, or between the presence of symptoms and Ct value. This is potentially due to our sample size (as demonstrated by the wide confidence intervals). There was also a lack of association between Ct value and sensitivity of the BD Veritor test, although we did not enroll many patients with high Ct value and were unable to adequately assess their potential effect on performance of the test.": Both these points might be due to each test using distinct specimen types (oropharyngeal swab vs. anterior nares swab). Could the authors consider and comment on this point?
4. "Contributing to the increased sensitivity of the rapid antigen test may also have been high viral loads (mean Ct value 16.10) in sampled participants during the peak second wave of SARS-CoV-2 infection in the country in March 2021.": could the authors consider adding a sentence to the Results a sentence that compares the distributions of Ct values from what they consider distinct waves, to help substantiate this statement? Further, an analysis of whether antigen test result was associated with Ct value for each stage should be performed, otherwise this point (that high viral load samples may have driven antigen test performance) would be inconsistent with the previously stated finding that antigen test result was not associated with Ct value.

Minor Comments:

1. Please add the name of the RT-PCR assay used as a reference test to the text of the abstract. This would be useful because even RT-PCR assays can exhibit a large range in analytical

sensitivity, and the analytical sensitivity of the reference test can impact the observed antigen test performance.

2. "Recent evidence indicates test reporting delays as having a negative impact on isolation as a control measure of infection spread[2]": this point is supported, but perhaps better evidenced at this stage of the pandemic by an observational study rather than [2] modeling study. For example, consider Nunez *et al.* (2022²) and Cobre *et al.* (2020³).
3. "However, rapid antigen test performance varies depending on inherent test characteristics, quality of sample, timing of sample collection in disease course, SARS-CoV-2 viral load and presence of symptoms[5]": consider including specimen type used for testing as a factor that substantially affects performance, as well. The effect of timing of sample collection in disease course on test performance may be better evidenced by a longitudinal rather than [5] cross-sectional study design. For example, consider our work (Viloria Winnett *et al.*, 2023⁴), where daily rapid antigen diagnostic tests were taken by cohort of participants at heightened risk of infection.
4. "Rapid antigen test sensitivity is also higher when carried out less than five days from symptom onset.": I believe this statement is based on evidence in [5]; please add reference to [5] here.
5. "The overall low sensitivity of rapid antigen tests has been attributed to false negative results seen in samples with high RT-PCR Ct values[12]": while you state the relationship before this statement, consider adding '(lower viral loads)' to assist readers who are less familiar with the inverse relationship between RT-PCR Ct values and viral load.
6. "There is a low probability of transmission from patients whose samples test positive on RT-PCR but negative on rapid antigen tests [13]": I don't believe the study cited provides sufficient evidence for this statement for three reasons. First, the cited study only recruited symptomatic participants for evaluation, who were likely later in the course of the infection. when replication-competent virus is less likely to be observed. Second, only 11 specimens with positive PCR and negative RAD were assessed for the presence of replication competent virus in the cited study. Third, the study only considered nasopharyngeal swab RT-PCR versus nasopharyngeal swab viral culture, while additional studies have demonstrated that different specimen types can contain infectious virus, and that infectious virus may be present in each specimen type at different points of the infection. For these reasons I would encourage the authors to add precision by revising this sentence to include additional nuance points – e.g. 'that there is low probability of transmission from patients after symptom onset whose samples test positive on RT-PCR but negative on a rapid antigen test of the same specimen type (e.g. nasopharyngeal swab)[13]'.

7. "It is necessary to evaluate rapid antigen tests at the end-user level, taking the local population into consideration before large-scale implementation[16]": excellent point.
8. "The specimen obtained was then processed according to the manufacturer's recommendations.": please add citation.
9. "Samples from asymptomatic participants were analyzed in pooled samples of 10,": It is not

clear whether Ct values presented are from individual specimens or the pool. Could the authors please add clarification whether individual specimens from positive pools were rerun? This appears to be the case from the Discussion, but it is not clear from the Methods as currently written.

10. "The RT-PCR assay used was Abbott RealTime SARS-CoV-2 and assays were conducted according to the manufacturer's protocols.": please add citation to the protocol used.
11. "We calculated 95% confidence intervals (CI) for all the sensitivity and specificity proportions.": please add what method was used for calculation of 95% CI of binomially distributed data.
12. "Test results were interpreted as positive or negative at a Ct of 37 according to the manufacturer's recommendation[19]": it appears that reference [19] is a dataset, and not the manufacturer's recommendation as the sentence would suggest. Please add reference to the manufacturer protocol for the test here or after the sentence "The RT-PCR assay used was Abbott RealTime SARS-CoV-2 and assays were conducted according to the manufacturer's protocols."
13. Figure 1: An interesting point raised later in the manuscript is that Ct value was not associated with antigen test result. The authors might consider modifying this figure such that each bin of the histogram contains stacked bars colored by antigen test result. This modification would further visualize the point.
14. ".....The kit application in the field is logical and easy to use and requires less training. (KII, HCW)": missing quotation marks around the participant's statement
15. "Contributing to the increased sensitivity of the rapid antigen test may also have been high viral loads (mean Ct value 16.10) in sampled participants during the peak second wave of SARS-CoV-2 infection in the country in March 2021.": To aid in logical flow, the authors might consider moving this sentence (and associated points) to the first paragraph of the Discussion section, after "was relatively high compared to that observed in similar studies [24]". Otherwise, this sentence, which discusses why the observed performance of the antigen test was higher than other studies, comes in the middle of a paragraph that discusses potential degradation of viral material.
16. "This suggests that degradation of viral genetic material may have occurred, which may have had the effect of reducing the RT-PCR test positivity, and thus artificially increasing the sensitivity of the rapid antigen test.": excellent consideration and analysis. I commend the authors for investigating and reporting this.
17. Could the authors please clarify in the underlying data sheet 'BD study dataset_final.xlsx' the difference between columns labeled 'BDVeritor' vs. 'BDcat', and 'PCR' vs. 'PCRcat'?

References

1. Vilorio Winnett A, Akana R, Shelby N, Davich H, et al.: Extreme differences in SARS-CoV-2 viral loads among respiratory specimen types during presumed pre-infectious and infectious periods.

PNAS Nexus. 2023; **2** (3): pgad033 [PubMed Abstract](#) | [Publisher Full Text](#)

2. Núñez I, Belaunzarán-Zamudio PF, Caro-Vega Y: Result Turnaround Time of RT-PCR for SARS-CoV-2 is the Main Cause of COVID-19 Diagnostic Delay: A Country-Wide Observational Study of Mexico and Colombia. *Rev Invest Clin*. 2022; **74** (2): 071-080 [PubMed Abstract](#) | [Publisher Full Text](#)

3. Cobre AF, Böger B, Fachi MM, Vilhena RO, et al.: Risk factors associated with delay in diagnosis and mortality in patients with COVID-19 in the city of Rio de Janeiro, Brazil. *Cien Saude Colet*. 2020; **25** (suppl 2): 4131-4140 [PubMed Abstract](#) | [Publisher Full Text](#)

4. Vilorio Winnett A, Akana R, Shelby N, Davich H, et al.: Daily SARS-CoV-2 Nasal Antigen Tests Miss Infected and Presumably Infectious People Due to Viral Load Differences among Specimen Types. *Microbiol Spectr*. 2023. e0129523 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious disease diagnostics, COVID-19 testing strategies, clinical microbiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 06 July 2022

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**Angela Amayo**

Clinical Chemistry Thematic Unit, Department of Human Pathology, School of Medicine, University of Nairobi, Nairobi, Kenya

Abstract: A good summary of the study.

Introduction: The introduction provides sufficient background and rationale for the study.

Methods: The researchers have provided an in-depth description of the study participants, sample collection and analysis. They planned to enroll 200 PCR-negative and 60 PCR-positive subjects. They should explain the rationale that informed this distribution of participants. The researchers should describe where and how the rapid test was done the way they have described the PCR test analysis. They should also describe how long the samples were stored before analysis by both rapid test and PCR, because correlation between time of analysis and PCR has been presented in results.

Qualitative data collection: Key Informant Interviews refer to individuals with sufficient knowledge of the subject matter under evaluation. The researchers need to describe how these were selected from the three populations to support validity of their responses as indicative of the general populations they were representing.

Results: The 15 participants excluded, did not meet inclusion criteria so should not have been enrolled into the study. The researchers should not mention them at all. The distribution of enrolled participants was not as planned. The researchers should mention whether the unequal distribution would affect the performance characteristics.

Some of the KII responses on perception of sample collection are contradicted under the participant driven improvement suggestions.

Discussion: In paragraph 3, analysis of Ct value and antigen test sensitivity could not have been carried out on 76 participants because only 47 were PCR-positive. In this study, the PCR-positive participants were enrolled retrospectively having tested positive. The researchers should have compared the Ct values of the initial positive results with those obtained when PCR was delayed, to assess the effects of the delay. They should mention whether any of the re-tested samples were negative. They did not find any correlation between high CT values and rapid tests positivity to support the suggestion on high test sensitivity being due to second wave. The discussion in paragraph 4 is not adequately supported by the results from this study.

The last paragraph in the discussion does not appear to be arising from the results of the study as no data was collected or reported on the same. It may therefore not be appropriate to include it.

Conclusion: Adequate.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical utility of laboratory tests. Point of Care tests.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
