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Performance and operational feasibility of antigen and antibody rapid diagnostic tests for COVID-19 in symptomatic and asymptomatic patients in Cameroon: a clinical, prospective, diagnostic accuracy study

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Summary

Background Real-time PCR is recommended to detect SARS-CoV-2 infection. However, PCR availability is restricted in most countries. Rapid diagnostic tests are considered acceptable alternatives, but data are lacking on their performance. We assessed the performance of four antibody-based rapid diagnostic tests and one antigen-based rapid diagnostic test for detecting SARS-CoV-2 infection in the community in Cameroon.

Methods In this clinical, prospective, diagnostic accuracy study, we enrolled individuals aged at least 21 years who were either symptomatic and suspected of having COVID-19 or asymptomatic and presented for screening. We tested peripheral blood for SARS-CoV-2 antibodies using the Innovita (Biological Technology; Beijing, China), Wondfo (Guangzhou Wondfo Biotech; Guangzhou, China), SD Biosensor (SD Biosensor; Gyeonggi-do, South Korea), and Runkun tests (Runkun Pharmaceutical; Hunan, China), and nasopharyngeal swabs for SARS-CoV-2 antigen using the SD Biosensor test. Antigen rapid diagnostic tests were compared with Abbott PCR testing (Abbott; Abbott Park, IL, USA), and antibody rapid diagnostic tests were compared with Biomerieux immunoassays (Biomerieux; Marcy l'Etoile, France). We retrospectively tested two diagnostic algorithms that incorporated rapid diagnostic tests for symptomatic and asymptomatic patients using simulation modelling.

Findings 1195 participants were enrolled in the study. 347 (29%) tested SARS-CoV-2 PCR-positive, 223 (19%) rapid diagnostic test antigen-positive, and 478 (40%) rapid diagnostic test antibody-positive. Antigen-based rapid diagnostic test sensitivity was 80·0% (95% CI 71·0–88·0) in the first 7 days after symptom onset, but antibody-based rapid diagnostic tests had only 26·8% sensitivity (18·3–36·8). Antibody rapid diagnostic test sensitivity increased to 76·4% (70·1–82·0) 14 days after symptom onset. Among asymptomatic participants, the sensitivity of antigen-based and antibody-based rapid diagnostic tests were 37·0% (27·0–48·0) and 50·7% (42·2–59·1), respectively. Cohen's κ showed substantial agreement between Wondfo antibody rapid diagnostic test and gold-standard ELISA (κ=0·76; sensitivity 0·98) and between Biosensor and ELISA (κ=0·60; sensitivity 0·94). Innovita (κ=0·47; sensitivity 0·93) and Runkun (κ=0·43; sensitivity 0·76) showed moderate agreement. An antigen-based retrospective algorithm applied to symptomatic patients showed 94·0% sensitivity and 91·0% specificity in the first 7 days after symptom onset. For asymptomatic participants, the algorithm showed a sensitivity of 34% (95% CI 23·0–44·0) and a specificity of 92·0% (88·0–96·0).

Interpretation Rapid diagnostic tests had good overall sensitivity for diagnosing SARS-CoV-2 infection. Rapid diagnostic tests could be incorporated into efficient testing algorithms as an alternative to PCR to decrease diagnostic delays and onward viral transmission.

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Introduction

The global COVID-19 pandemic caused by SARS-CoV-2 has devastated communities worldwide since December, 2019,[1] causing more than 116 million infections and more than 2·5 million deaths as of March 7, 2021.[2] Africa represents 17% of the world's population, and yet has reported only around 2% of global COVID-19 infections, just over 2·8 million to date. Like many African countries, Cameroon has reported relatively few infections, only 35 714 cases in a country of 25 million people.[3] The low number of reported cases in sub-Saharan Africa has been attributed to low testing

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For the French translation of the abstract see **Online** for appendix 1

For the Spanish translation of the abstract see **Online** for appendix 2

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Research in context

Evidence before this study

Throughout 2020, a growing body of literature has described the clinical and epidemiological characteristics of COVID-19 globally. However, fewer publications have reported studies of SARS-CoV-2 testing or screening modalities, and most publications to date have been from high-income countries. We searched PubMed, MEDLINE, and Google Scholar on June 6, 2020, using the search terms "novel coronavirus" or "2019nCOV" or "SARS-CoV-2" and "evaluation of diagnostics" or "screening test" or "diagnostics" for studies done in Africa with no restrictions on date or language. At the time this study began, to our knowledge, there were no studies of SARS-CoV-2 rapid diagnostic tests published from Africa, and this remains the case.

Added value of this study

We evaluated the performance characteristics of antigen-based and antibody-based rapid diagnostic tests for SARS-CoV-2 in real-life conditions. We also report the potential utility of testing algorithms that incorporate SARS-CoV-2 rapid diagnostic tests into routine widespread testing. To our knowledge, this is the first study to provide evidence on rapid diagnostic test characteristics and performance compared with gold-standard diagnostics in symptomatic and asymptomatic patients with COVID-19.

Implications of all the available evidence

Our results suggest that rapid diagnostic tests for SARS-CoV-2 are important tools in the fight against COVID-19. Our study suggests that testing algorithms that incorporate rapid diagnostic tests could be an efficient means to rapidly diagnose SARS-CoV-2 infection and reduce transmission of the virus, especially in settings where PCR testing has restricted availability.

rates, although other factors, including demographics and successful implementation of control measures might also contribute.[4,5]

Cameroon has done over 100 000 real-time PCR tests for SARS-CoV-2 since the first case was detected in the country on March 6, 2020, more tests than most other countries in Africa.[6] Initially, the only SARS-CoV-2 testing modality available in Cameroon was PCR at the Centre Pasteur du Cameroun (Yaounde, Cameroon).[5] Now, 15 laboratories countrywide are doing SARS-CoV-2 PCR testing. Unfortunately, in most other African countries, the paucity of molecular laboratories is restricting testing capacity and outbreak management. Furthermore, PCR testing is costly, and widespread testing is beyond the financial means of most low-income and middle-income countries (LMICs).[7] Thus, there is a clear need to develop new strategies for SARS-CoV-2 testing and outbreak detection that do not rely entirely on PCR.

One June 7, 2020, the Cameroon Ministry of Health adopted the Trace, Test, and Track approach proposed by the African Union and the Africa Centres for Disease Control and Prevention.[8] This approach includes using alternative diagnostic tests for SARS-CoV-2, such as rapid point-of-care antigen and antibody diagnostic tests. These tests can be done outside centralised laboratory facilities and return results in minutes to hours. Antigen tests detect SARS-CoV-2 antigens in nasopharyngeal swabs[7] and are intended to diagnose active infection. Antibody tests detect anti-SARS-CoV-2 IgM and IgG antibodies in the serum of actively-infected and recently-infected people.[9] However, there is a paucity of information on the performance of rapid diagnostic tests, especially in LMICs. We conducted a diagnostic accuracy study to evaluate the performance characteristics of rapid antigen and antibody tests compared with gold-standard SARS-CoV-2 PCR and ELISA. We also evaluated algorithms that incorporated rapid diagnostic tests to identify symptomatic and asymptomatic SARS-CoV-2 infection, which could be used in LMICs and other resource-limited settings.

Methods

Study design and participants

In this clinical, prospective, diagnostic accuracy study, we evaluated the performance characteristics of five SARS-CoV-2 rapid diagnostic tests in two groups of Cameroonian adult participants: 570 (48%) symptomatic individuals suspected of having SARS-CoV-2 or already on treatment and 625 (52%) asymptomatic individuals presenting for voluntary SARS-CoV-2 screening or referred for testing through contact tracing. 193 (34%) of 570 symptomatic participants were admitted to hospital. Two of the eight included sites (Palais de Sports, Yaoundé, Cameroon and Ecole de Police, Yaoundé, Cameroon) were dedicated exclusively to screening asymptomatic individuals, whereas the remaining six (EPC Djoungolo, Jamot Hospital, Yaoundé General Hospital, Clinique Jourdain, ORCA, and Yaoundé Central Hospital; all Yaoundé, Cameroon) sites provided asymptomatic screening and testing and treatment of symptomatic individuals.

Consecutive individuals aged 21 years and older who presented to any of the eight testing sites between June 2 and Aug 30, 2020, were eligible for the study. Following consent, demographic and clinical data were collected from participants, including self-reported age, race, ethnicity, and sex. A brief clinical history and case management of the suspected SARS-CoV-2 infection was recorded, including symptom duration, date of

symptom onset, date of exposure or infection (if known), symptoms on admission or presentation, disease stage (mild, severe, or critical per WHO classification),[10] admission and discharge dates (for hospitalised patients), and outcome. At the initial visit (visit 1), participants were invited to return for up to two follow-up visits. Visit 2 was scheduled 7 days after visit 1 and visit 3 was scheduled 14 days after visit 1. Individuals were included in the study regardless of clinical status and illness severity.

Written informed consent was obtained from all participants. The study protocol was approved by the Cameroon National Ethics Committee (2020/05/1220CE/CNERSH/SP).

Sample collection

At all visits, we collected whole blood by peripheral venepuncture into EDTA (edetic acid)-coated and clot-activator-containing tubes. Nasopharyngeal swabs were collected using sterile technique compliant with rigorous infection control guidelines. First, a sterile swab for PCR testing was inserted into the right nostril, and then a second sterile swab (Suzhou Cellpro Biotechnology; Suzhou, China) for antigen testing was inserted into the left nostril. Swab samples for PCR testing were immediately placed in virological transport medium in cold boxes and transferred to the National Laboratory of Public Health (Yaoundé, Cameroon) for storage at –20°C.

Rapid diagnostic testing and ELISA testing

Four types of antibody rapid diagnostic tests were done at visit 1 at the point of sample collection on participant serum, according to the manufacturers' instructions. The Innovita test (Biological Technology; Beijing, China; colloidal gold; IgM and IgG; sensitivity 100·0%; specificity 97·5%) provided by the Cameroon Ministry of Health was the only antibody-based rapid diagnostic test done on all 1210 samples because of resource constraints. The Wondfo test (Guangzhou Wondfo Biotech; Guangzhou, China; lateral flow; combined IgM and IgG test; sensitivity 86·43%; specificity 99·57%) was simultaneously done on a subset of 400 samples tested with the Innovita test, and the SD Biosensor test (SD Biosensor; Gyeonggi-do, South Korea; lateral flow; IgM and IgG; sensitivity 94·3%; specificity 68·9%) and Runkun test (Runkun Pharmaceutical; Hunan, China; colloidal gold; IgM and IgG; sensitivity 98·8%; specificity 98·0%) were also done on a subset of 78 samples tested with the Innovita and Wondfo tests. Three antibody-based rapid diagnostic tests (Innovita, SD Biosensor, and Wondfo) were additionally done on a subset of 100 historical samples collected and stored 2 years before the pandemic, as negative controls. The VIDAS anti-SARS-CoV-2 IgM and IgG anti-SARS-CoV-2 ELISA (Biomerieux; Marcy l'Etoile, France; IgM and IgG; sensitivity 99·9%; specificity 96·6% >15 days after positive PCR) was done using a MINI VIDAS analyser on a subset of 200 whole blood samples also tested using the Innovita and Wondfo assays. Serum collected at visits 2 and 3 was tested for antibodies using the Innovita assay and repeat antigen rapid diagnostic testing was done on nasopharyngeal swabs collected from visit 3. The SD Biosensor antigen rapid diagnostic test (sensitivity 84·4%; specificity 100·0%) was done on visit 1 nasopharyngeal swabs for the entire cohort (appendix 3 p 3).

See Online for appendix 3

PCR

We used two different PCR protocols to amplify SARS-CoV-2 RNA: a manual extraction protocol and an automated extraction protocol. Protocols were interchangeable and selected based on reagent availability. Both completed amplification in real-time thermocyclers.

SARS-CoV-2 nucleic acid isolation and purification from nasopharyngeal swabs was done using 450 µL of sample and a reagent extraction kit (DAAN Gene; Sun Yat-sen University; Guangzhou, China). After lysis and precipitation, RNA immobilised on the anion exchange resin was washed serially to eliminate waste and purify RNA. After purification, eluted RNA was collected in a sterile microtube for amplification.

The Abbott Real-Time SARS-CoV-2 assay (Abbott; Abbott Park, IL, USA) amplifies and detects two SARS-CoV-2 genes (*RdRp* and *N*).[11] An internal control target sequence and hydroxypyruvate reductase gene control reaction was included with every sample at each analytic stage. Target sequence quantity was measured after each cycle using fluorescent-labelled oligonucleotides linked to the amplified products. The amplification cycle during which the fluorescent signal was detected (threshold cycle [Ct]) is inversely proportional to the logarithm of the concentration of SARS-CoV-2 RNA present in the original sample. Results were automatically interpreted by installed software as positive or negative, signifying virus presence or absence in the sample, respectively.

Following extraction, purified RNA underwent real-time amplification using Taqman probes in an ABI 7500 thermocycler (Applied Biosystems; Beverly, MA, USA). This triplex PCR targets the SARS-CoV-2 *OFR1ab* and *N* gene fragments. The fragments were linked with target-specific probes: FAM (maximum emission at 518 nm) for the *N* gene, VIC (maximum emission at 552 nm) for the gene *OFR1ab*, and Cy5 (maximum emission at 667 nm) for the endogenous internal control. Amplification curve interpretation was done by setting Ct values for *ORF1ab* and *N* genes. A sample was determined to be positive for SARS-CoV-2 when both genes were detected, and negative when both genes were not detected. Detection of one gene was considered indeterminate and the sample was retested. Two indeterminate results for the same sample were considered an overall positive.

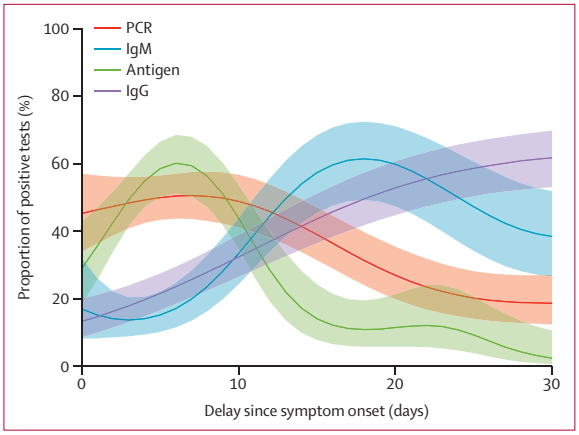

Figure 1: **Proportion of positive tests by diagnostic modality by days since symptom onset**
IgM and IgG testing reflect Innovita antibody rapid diagnostic test results. Antigen reflects antigen rapid diagnostic testing, and PCR reflects gold-standard SARS-CoV-2 PCR. Shading represents the 95% CI.

Statistical analysis

We estimated the proportion of positive samples by day since symptom onset using a generalised additive logistic regression model including a random effect for repeated measures. Test sensitivity and confidence intervals for the SD Biosensor antigen and Innovita antibody rapid diagnostic tests were calculated as the proportion of positive results among PCR-confirmed SARS-CoV-2 infections (positive PCR result at any time). The specificity of the SD Biosensor antigen rapid diagnostic test was estimated as the proportion of negative results among patients who tested negative by PCR. Innovita antibody rapid diagnostic test sensitivity and specificity was estimated using historical samples. Cohen's κ was used to measure agreement between antibody tests, and between each antibody test and gold-standard ELISA.

Analyses were done with R version 4.0.3.

Role of the funding source

Médecins Sans Frontières members had a role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

1195 participants were enrolled in the study. 570 (48%) were symptomatic and 193 (16%) were admitted to hospital. 347 (29%) tested SARS-CoV-2 PCR-positive, 223 (19%) rapid diagnostic test antigen-positive, and 478 (40%) rapid diagnostic test antibody-positive. 1123 (94%) of 1195 participants had nasopharyngeal swabs and 928 (78%) participants had blood collected at visit 1. 296 (25%) of 1195 participants returned for visit 2—277 (94%) participants had nasopharyngeal swabs and 233 (79%) had blood collected. 197 (16%) of 1195 participants returned for visit 3—164 (83%) had nasopharyngeal swabs and 181 (92%) had blood collected (appendix 3 pp 2–3). 300 (27%) of 1195 participants tested positive for SARS-CoV-2 by PCR at visit 1. The median age of participants who tested positive by PCR was 38·0 years (IQR 30·0–50·0). 549 (46%) of 1195 participants were women. Among those who tested positive by PCR at visit 1, 51 (17%) of 300 participants reported a medical comorbidity. Considering all samples, the probability of testing positive by PCR was highest within 7 days of symptom onset. PCR test positivity was not associated with being admitted to hospital (p=0·14) but was associated with being symptomatic at the time of testing (p=0·0010).

SARS-CoV-2 PCR and SD Biosensor antigen positivity were high (60·0% and 54·0%, respectively) during the first week of symptoms and then decreased (figure 1). Antigen positivity decreased earlier and more rapidly than did PCR positivity, and there was a large decrease in positivity by symptom day 20. Antigen rapid diagnostic test positivity exceeded PCR positivity on symptom days 4–8. The Innovita antibody rapid diagnostic test showed good sensitivity beginning around 10 days after symptom onset. IgM positivity peaked at around day 20 and plateaued through day 30. IgG positivity rose around symptom day 7 and plateaued between symptom days 20 and 30 (figure 1).

Among asymptomatic participants, 50·7% (95% CI 42·2–59·1) tested positive by antibody-based rapid diagnostic test and 37·0% (27·0–48·0) tested positive by antigen-based rapid diagnostic test (table 1). In symptomatic patients during the first 7 days after symptom onset, antigen-based rapid diagnostic tests had 80·0% sensitivity (71·0–88·0), but antibody-based rapid diagnostic tests had only 26·8% sensitivity (18·3–36·8). Antibody rapid diagnostic test sensitivity increased to 76·4% (70·1–82·0; table 1) 14 days after symptom onset.

295 PCR-positive participants had recorded Ct values. The mean Ct value was 26·8 (appendix 3 p 1). The mean Ct value among symptomatic antigen rapid diagnostic test-positive participants was 23·7, significantly lower than antigen rapid diagnostic test-negative participants (29·3; p=0·0011). The mean Ct value was 25·8 among asymptomatic antigen rapid diagnostic test-positive participants and 31·8 among antigen rapid diagnostic test-negative participants (p=0·0010). Participants who tested PCR-positive less than 14 days after the start of symptoms and antigen rapid diagnostic test-positive had a mean Ct value of 22·9, lower than those who tested negative (29·1; p=0·0010; appendix 3 pp 1, 4). Antigen-positive participants had lower Ct values than did antigen-negative participants, whereas IgM-positive or IgG-positive participants had higher Ct values than did antibody-negative participants. Samples from asymptomatic participants had higher mean Ct values (appendix 3 p 2).

	Antigen positive	Antigen sensitivity, %	Antibody positive	Antibody sensitivity, %	IgM positive	IgM sensitivity, %	IgG positive	IgG sensitivity, %
Positive rapid diagnostic test or reference test	224/288	59·0% (53·0–65·0)	313/566	56·3% (52·1–60·5)	195/566	35·1% (31·1–39·2)	256/566	46·0% (41·8–50·3)
Symptomatic	161/198	69·0% (62·0–75·0)	212/357	59·0% (54·0–65·0)	142/357	39·8% (34·7–45·1)	172/357	48·2% (42·9–53·2)
Asymptomatic*	33/89	37·0% (27·0–48·0)	73/144	50·7% (42·2–59·1)	38/144	26·4% (19·4–34·4)	58/144	40·3% (32·2–48·8)
0–7 days	88/95	80·0% (71·0–88·0)	26/97	26·8% (18·3–36·8)	19/97	19·6% (12·2–28·9)	14/97	14·4% (8·1–23·0)
8–14 days	33/37	76·0% (59·0–88·0)	27/52	51·9% (37·6–66·0)	23/52	44·2% (30·5–58·7)	24/52	46·2% (32·2–60·5)
>14 days	7/27	19·0% (6·0–38·0)	159/208	76·4% (70·1–82·0)	100/208	48·1% (41·1–55·1)	134/208	64·4% (57·5–70·9)

Data are n (number who tested positive)/N (number tested using a given test) or mean (95% CI). *Including those referred for testing through contact tracing.

Table 1: **SARS-CoV-2 antigen and antibody rapid diagnostic test positivity and sensitivity compared with gold-standard PCR testing**

All 100 pre-pandemic samples tested negative for SARS-CoV-2 antibodies using Wondfo, SD Biosensor, and Innovita assays. Cohen's κ showed substantial agreement between Wondfo antibody rapid diagnostic test and gold-standard ELISA (κ=0·76; sensitivity 0·98) and between Biosensor and ELISA (κ=0·60; sensitivity 0·94). Innovita (κ=0·47; sensitivity 0·93) and Runkun (κ=0·43; sensitivity 0·76) showed moderate agreement (appendix 3 p 1).

We designed separate antigen-based SARS-CoV-2 diagnostic testing algorithms for symptomatic and asymptomatic individuals (figure 2). The algorithm approach was decided upon in a meeting of 50 Cameroonian and international public health experts organised by the Cameroon Ministry of Health.[11] The study statistical team then ran 1000 simulations to estimate the sensitivity and specificity of each algorithm. We retrospectively tested our data to compute the sensitivity and specificity of each algorithm. The symptomatic algorithm showed 94·0% sensitivity at symptom days 0–7, superior to that of PCR alone (75·0%; figure 2A). At symptom days 8–14, sensitivity decreased to 84·0% but was still superior to PCR alone (65·0%). The specificity of the algorithm 14 days after start of symptoms was 91·0%, lower than PCR testing alone (99·0%; tables 2, 3). Applying these projections to our data, where 118 (11%) of 1082 samples tested using antigen rapid diagnostic tests had false-positive results, 862 individuals would require PCR testing to confirm their infection status (table 4). The number of samples that require retesting would decrease with increased infection prevalence.

For asymptomatic individuals who tested negative for SARS-CoV-2 antigen, the Innovita antibody rapid diagnostic would be done, and if the IgM or IgG antibody rapid diagnostic test was positive, confirmatory PCR testing would then be done (figure 2B). A positive antigen rapid diagnostic test or PCR test result would confirm the diagnosis of SARS-CoV-2 infection. We retrospectively tested our data to compute the sensitivity and specificity of this algorithm. Although the algorithm showed slightly higher sensitivity than that of PCR alone, specificity was 92·0%, lower than that of PCR alone (99·0%; tables 5, 6).

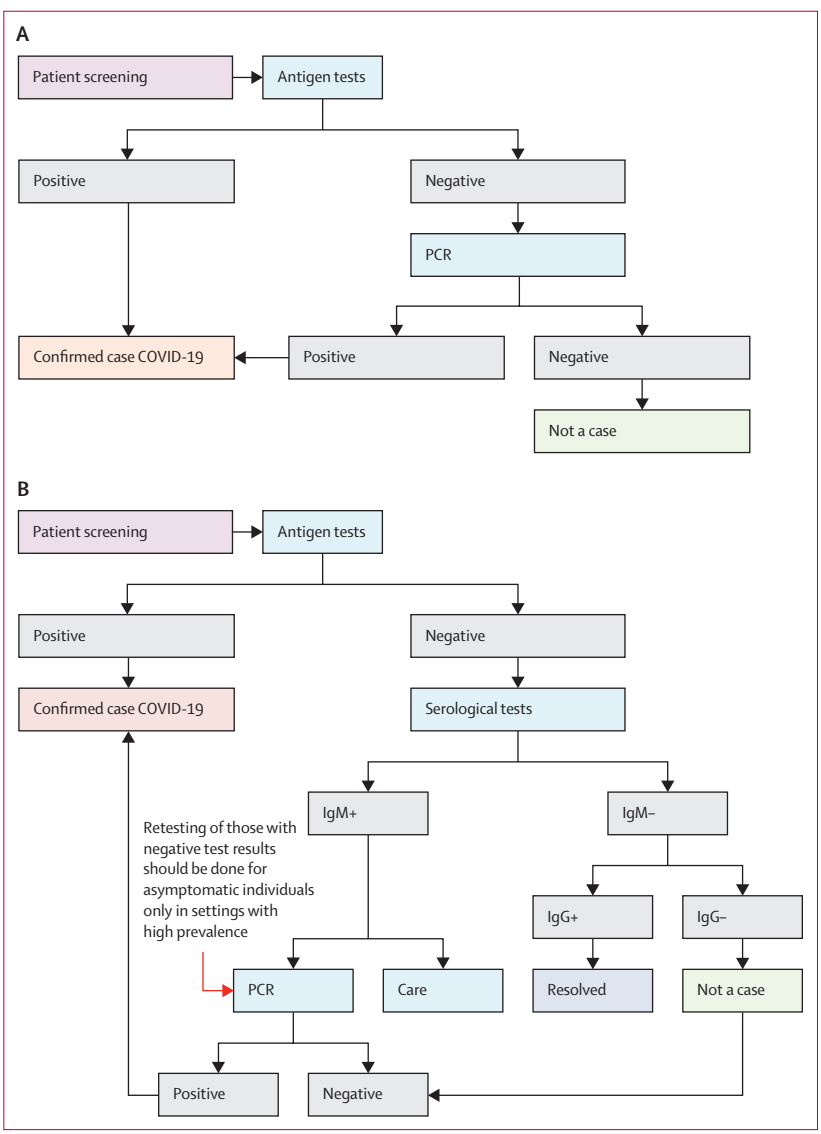

Figure 2: **Diagnostic algorithm for SARS-CoV-2 screening and diagnosis**
(A) In symptomatic individuals. (B) In asymptomatic individuals.

Discussion

In this study, we present, to our knowledge, the first field evaluation of COVID-19 rapid diagnostic tests to address the gap in knowledge about rapid diagnostic test performance for SARS-CoV-2 infection in LMICs and other settings where gold-standard PCR testing is not readily available. We evaluated five commercial rapid diagnostic tests for SARS-CoV-2, including one antigen-based (SD Biosensor) and four antibody-based (Innovita, SD Biosensor, Wondfo, and Runkun) rapid diagnostic tests over three visits among hospitalised and non-hospitalised individuals seeking COVID-19 testing in Cameroon. We compared antigen test positivity with gold-standard PCR and compared all antibody rapid diagnostic tests with ELISA.

We found good overall rapid diagnostic test sensitivity and specificity. Early in the course of symptoms (days 0–7 after symptom onset) the SARS-CoV-2 antigen test performed well, with similar sensitivity to PCR testing. We expected this result on the basis of previous SARS-CoV-2 studies showing viral persistence with high amounts of viral shedding during the early phase of disease, decreasing 8–9 days after symptom onset. Because antigen rapid diagnostic tests do not amplify the virus present in clinical samples, antigen rapid diagnostic test positivity closely mirrors the phase of high viral shedding and antigen test positivity decreases as viral shedding decreases. Studies have shown live SARS-CoV-2 viral shedding up to 9 days after symptom onset. SARS-CoV-2 virus was difficult to grow from sputum and throat swabs after symptom day 8.[13,14] We observed that antigen-based rapid diagnostic test positivity declined earlier than PCR test positivity, which we expected since the threshold for viral detection is higher in antigen tests because of the

	Sensitivity on symptom days 0–7	Sensitivity on symptom days 8–14	Specificity
Antigen rapid diagnostic test alone	76·0%	55·0%	92·0%
PCR alone	75·0%	65·0%	99·0%
Algorithm	94·0%	84·0%	91·0%

Table 2: **Sensitivity and specificity of algorithm for SARS-CoV-2 testing in symptomatic individuals**

	Positive predictive value	Negative predictive value	Number of false positives of 1000 people tested (95% CI)	Number of false negatives of 1000 people tested (95% CI)
0–7 days after symptom onset				
1·0%	9·6	99·9	88·0 (70·0–105·0)	0·0 (0·0–2·0)
5·0%	35·6	99·6	85·0 (68·0–101·0)	3·0 (0·0–7·0)
10·0%	53·9	99·2	80·0 (65·0–98·0)	6·0 (2·0–12·0)
20·0%	72·4	98·3	71·0 (57·0–88·0)	12·0 (6·0–19·0)
8–14 days after symptom onset				
1·0%	8·7	99·8	88·0 (71·0–107·0)	1·0 (0·0–4·0)
5·0%	33·2	99·1	85·0 (68·0–102·0)	8·0 (3·0–14·0)
10·0%	51·2	98·1	80·0 (65·0–97·0)	16·0 (9·0–24·0)
20·0%	70·2	95·9	71·0 (57·0–88·0)	32·0 (21·0–42·0)

Table 3: **Diagnostic accuracy of algorithm for SARS-CoV-2 testing in symptomatic individuals at various levels of prevalence**

	Antibody rapid tests *vs* Mini Vidas Biomereux ELISA					Antigen rapid test *vs* Abbott RT-PCR				
	Negative	Positive	Total	Sensitivity	Specificity	Negative	Positive	Total	Sensitivity	Specificity
Runkun										
Negative	31	8	39	..	..	..	..	..	..	..
Positive	14	25	39	..	..	..	..	..	..	..
Total	45	33	78	..	..	..	..	..	..	..
Diagnostic accuracy	..	..	..	0·76 (0·58–0·89)	0·69 (0·53–0·82)	..	..	..	..	..
Wondfo										
Negative	36	2	38	..	..	..	..	..	..	..
Positive	12	82	94	..	..	..	..	..	..	..
Total	48	84	132	..	..	..	..	..	..	..
Diagnostic accuracy	..	..	..	0·98 (0·92–1·00)	0·75 (0·60–0·86)	..	..	..	..	..
SD Biosensor										
Negative	31	2	33	..	..	745	121	866	..	..
Positive	14	32	46	..	..	54	170	224	..	..
Total	45	34	79	..	..	799	291	1090	..	..
Diagnostic accuracy	..	..	..	0·94 (0·80–0·96)	0·69 (0·53–0·82)	..	..	..	0·58 (0·53–0·64)	0·94 (0·88–0·97)
Innovita										
Negative	42	13	55	..	..	..	..	..	..	..
Positive	43	173	216	..	..	..	..	..	..	..
Total	85	186	271	..	..	..	..	..	..	..
Diagnostic accuracy	..	..	..	0·93 (0·88–0·96)	0·49 (0·38–0·60)	..	..	..	..	..

Table 4: **Two-by-two table comparing rapid diagnostic tests with reference tests**

absence of viral amplification. Most participants with low PCR Ct values (corresponding to high SARS-CoV-2 viral load) tested positive using antigen-based rapid diagnostic tests, particularly symptomatic participants within 14 days of symptom onset. This result reflects the findings of Omi and colleagues,[15] who reported that antigen-based rapid diagnostic test performance was optimal at Ct values lower than 25. Low Ct values are associated with an increased probability of SARS-CoV-2 positive culture and onward viral transmission, probably reflecting higher amounts of live virus in samples with low Ct values.[16,17]

Antibody rapid diagnostic tests had low sensitivity (26·8%) during the first week of symptoms, which increased to 76·4% 14 days after symptom onset. Despite increasing sensitivity later in the course of disease, antibody rapid diagnostic test positivity in our study was lower than that published by Public Health England, who reported 93·9% sensitivity for the Abbott SARS-CoV-2 IgG test and 87·0% sensitivity for the Roche assay.[18] Low antibody rapid diagnostic test sensitivity during the early stages of disease and high sensitivity in later stages (>14 days) indicate a low diagnostic value for these tests in the first 7 days of symptoms. Seroconversion in SARS-CoV-2 infection is reported to peak at around days 17–20,[19,20] similar to the results of our study. We found that both IgM and IgG began to rise around symptom day 5. IgM positivity then decreased gradually around symptom day 20, and IgG levels persisted. The late persistence of IgG antibodies could explain the higher κ agreement between the Wondfo antibody test and ELISA, as Wondfo is a combined immunoglobulin test that does not distinguish whether a positive result reflects detection of IgM, IgG, or both. The high sensitivity of antibody rapid tests when compared with ELISA was encouraging. However, the lower specificity of antibody rapid tests raises the question of crossed reactivity of the rapid test from pre-existing antibodies or other possible causes, including other coronaviruses,[15] which could explain a higher immunity to COVID-19 in the African population.

Overall, our data show that even when used independently, antigen-based rapid tests have important diagnostic value early in the course of disease, as they are positive in those with the lowest Ct values, inversely proportional to viral load.[21] However, antigen-based rapid diagnostic tests have poor performance after 7 days of illness. We observed the opposite pattern in antibody-based rapid diagnostic tests, with many false positives soon after symptom onset. When incorporating these tests into a diagnostic algorithm for symptomatic patients, the algorithm performed well when retrospectively tested on our dataset. For every ten participants tested, an additional two patients with COVID-19 would be detected using this algorithm compared with a testing strategy using PCR testing alone. The symptomatic patient algorithm also performed better at 8–14 days compared with PCR testing alone. Supporting our findings, a previous study showed that 63·0% of antigen-negative rapid diagnostic tests subsequently tested PCR-positive for SARS-CoV-2,[22] implying that antigen-based rapid diagnostic tests have a higher diagnostic value when negative tests require PCR testing for confirmation. Using this testing algorithm for symptomatic patients would be expected to result in somewhat reduced PCR costs, since those who test antigen-positive would not need PCR confirmation, and fewer false-negatives, as those who test antigen-negative would require PCR confirmation before being declared true negatives. However, if confirmatory PCR testing is scarce or unavailable, this strategy could yield a substantial number of false negative test results.

The algorithm for asymptomatic patients performed less well than the algorithm for symptomatic patients but showed superior sensitivity than did PCR testing alone. The importance of accurately diagnosing asymptomatic participants was highlighted by Chen and colleagues,[23] who reported no difference in infectivity between symptomatic and asymptomatic individuals who tested positive for SARS-CoV-2. Using this algorithm among asymptomatic individuals could detect more infections than using any one of the three testing modalities in isolation. However, because of low sensitivity and specificity, this strategy might lead to many false negative results and added costs of additional confirmatory tests. Both algorithms performed well when retrospectively tested on our data, although their good performance might be overestimated because of training and testing the algorithm on the same dataset.

Our study has many strengths: reporting real-world performance data based on field testing, simultaneous comparison of multiple commercially available tests with different test characteristics, and describing rapid diagnostic performance in a low-income setting in

	Sensitivity	Specificity
Antigen rapid diagnostic test alone	28·0%	92·0%
IgM or IgG rapid diagnostic test alone	26·0%	90·0%
PCR alone	30·0%	99·0%
Algorithm	34·0%	92·0%

Table 5: **Sensitivity and specificity of algorithm for SARS-CoV-2 screening in asymptomatic individuals**

	Positive predictive value	Negative predictive value	Number of false positives per 1000 people tested (95% CI)	Number of missed infections per 1000 people tested (95% CI)	Number of antigen negative or IgM positive requiring PCR testing per 1000 people tested (95% CI)
1·0%	4·0	99·3	80·0 (64·0–97·0)	6·0 (2·0–12·0)	93·0 (76·0–110·0)
5·0%	17·9	96·3	77·0 (61·0–94·0)	33·0 (23·0–44·0)	97·0 (78·0–116·0)
10·0%	31·6	92·6	73·0 (58·0–89·0)	67·0 (51·0–82·0)	102·0 (83·0–123·0)
20·0%	50·9	84·7	64·0 (50·0–79·0)	132·0 (112·0–153·0)	111·0 (91·0–131·0)

Table 6: **Diagnostic accuracy of algorithm for SARS-CoV-2 screening in asymptomatic individuals at various levels of prevalence**

which alternate diagnostic tests are desperately needed. We were able to develop reasonably efficient and accurate diagnostic algorithms for both symptomatic and asymptomatic patients presenting for SARS-CoV-2 testing using antigen and antibody rapid diagnostic tests and PCR to optimise diagnosis. An antigen-based algorithm could perform well in settings in which PCR availability is scarce or PCR has a long turnaround time.

Based on the preliminary results of our study, Cameroon began using rapid diagnostic tests for SARS-CoV-2 in July 12, 2020, and has used more than 600 000 such tests yielding a total of 10 793 (40%) positive cases out of the 26 848 positive cases reported countrywide.[19] Rapid diagnostic tests have been a critical foundation of Cameroon's national testing strategy, allowing decentralised and mobile testing in public places well-suited to low-resource environments. Due in part to Cameroon's rapid diagnostic test deployment experience and results, these tests are rapidly being integrated as a key tool to fight COVID-19 globally.

Contributors

YB conceived the study. YB, FL, CL, and LE designed the study. BN, KNF, YB, and MN analysed the data. YB, BN, KNF, ABM, MN, AA, RE, LE, NFM, RGE, BDB, TMC, BTK, NM, MF, A-CZ-KB, SE, AH, JPO, MTK, RN, OMC, LE, EE, GAEM carried out the investigations and study methods. LMB, KNF, YB, CBN, and BN critically reviews and edited the manuscript. YB, KNF, BN, and MN accessed and verified the data. All authors had full access to all the data reported in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no conflicting interests.

Data sharing

The data collected in the study, including deidentified individual participant data and a data dictionary defining each field in the set, will be made available to researchers. These data will be made available after publication on a collaborative and protected platform after reasonable request and approval of proposal by the principal investigator. Request should be sent to the principal investigator (YB; yap.boum@epicentre.msf.org), accompanied by a signed data access agreement.

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