Performance of six rapid diagnostic tests for SARS-CoV-2 antigen detection and implications for practical use

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ABSTRACT

Background: Direct detection of SARS-CoV-2 viral proteins in nasopharyngeal swabs using lateral flow immunoassays is a simple, fast and cheap approach to diagnose the infection.
Aims and Methods: The performance of 6 SARS-CoV-2 antigen rapid diagnostic tests has been assessed in 634 hospitalized patients or outpatients including 297 patients found to be positive for SARS-CoV-2 RNA by means of RT-PCR and 337 patients presumed to be SARS-CoV-2 RNA-negative.
Results: The specificity of SARS-CoV-2 RDTs was generally high (398.5%). One assay had a lower specificity of 93.2%. The overall sensitivity of the 6 RDTs was variable, from 32.3% to 61.7%. Sensitivity correlated with the delay of sampling after the onset of symptoms and the viral load estimated by the Ct value in RT-PCR. Four out of 6 RDTs tested achieved sensitivities 380% when clinical specimens were collected during the first 3 days following symptom onset or with a Ct value $\leq$25.
Conclusions: The present study shows that SARS-CoV-2 antigen can be easily and reliably detected by RDTs. These tests are easy and rapid to perform. However, the specificity and sensitivity of COVID-19 antigen RDTs may widely vary across different tests and must therefore be carefully evaluated before releasing these assays for realworld applications.

1. Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the viral agent responsible for Coronavirus Disease 2019 (COVID-19). Diagnosis and screening of SARS-CoV-2 infections raise important challenges. Several diagnostic tools are available to diagnose or rule out an ongoing infection, identify people in need of care, or test for past infection. In waiting for a large coverage of protective immunization or specific antiviral treatments, early accurate diagnosis of SARS-CoV-2 infection and isolation of infected individuals are crucial to prevent viral transmission.

The reference method to diagnose SARS-CoV-2 infection is viral RNA detection from patient nasopharyngeal swabs (NPS) using a target amplification method, *i.e.* either polymerase chain reaction (PCR), transcription-mediated amplification (TMA) or loop-mediated isothermal amplification (LAMP). Reverse transcriptase PCR (RT-PCR) is the most widely used technique. RT-PCR is both sensitive and specific, although falsely-negative results have been reported in small proportions of symptomatic cases, generally as a result of insufficient cellular materials in the NPS sample [1]. However, RT-PCR is costly and must be performed in certified biology laboratories, while requiring

technical skills and sophisticated equipment. Most SARS-CoV-2 RNA assays and platforms require batches of multiple specimens within a single run, while at least 4 to 6 hours are required to complete the analyses. Furthermore, because of the scale of the worldwide pandemic, intermittent reagent and materials shortages limit COVID-19 diagnostic capacities. For all these reasons, scaling-up RT-PCR for larger-scale screening will not be possible, especially in low-and middle-income settings, emphasizing the need for easier, shorter and cheaper virus detection methods.

Direct detection of SARS-CoV-2 viral proteins in NPS using lateral flow immunoassays (SARS-CoV-2 antigen assays) is a simple, fast and cheap approach to diagnose the infection. SARS-CoV-2 antigen assays generate individual results in less than 30 minutes and can be performed at the patient's sampling site, outside of the clinical laboratory. Therefore, SARS-CoV-2 antigen tests may be used for individual diagnosis as well as for large-scale testing by a variety of healthcare workers in decentralized settings, allowing for early detection and isolation of infected individuals, with the aim of reducing community transmission. Nevertheless, the sensitivity, specificity, positive and negative predictive values of SARS-CoV-2 antigen tests compared to RT-PCR must be known before recommending their use for such purpose.

2. Objectives

This retrospective diagnostic case control study using a large number of frozen NPS aimed to evaluate the performance of 6 commercially available rapid diagnostic tests (RDT) for SARS-CoV-2 antigen detection and to describe their potential integration into diagnostic algorithms adapted to health systems and epidemiological contexts.

2.1. Study design

The performance of 6 SARS-CoV-2 antigen RDT has been assessed in 634 symptomatic hospitalized patients or outpatients from the Henri Mondor university hospital. They included: (i) 297 patients found to be positive for SARS-CoV-2 RNA by means of RT-PCR between March and April 2020; (ii) 337 patients presumed to be SARS-CoV-2 RNA-negative because they had been sampled between April and August 2019 (i.e., before the emergence of SARS-CoV-2), including some who were positive for one or more other respiratory pathogen(s) (Table 2). The following SARS-CoV-2 antigen RDT were evaluated: (i) CORIS Respi-Strip (Coris BioConcept, Gembloux, Belgium), also known as (aka) CORIS Respi-Strip; (ii) Standard™ Q COVID-19 Ag (SD Biosensor, Inc., Suwon, Korea), aka BIOSENSOR Standard Q; (iii) Panbio™ COVID-19 Ag Rapid Test (Abbott Rapid Diagnostics, Jena, Germany), aka ABBOTT Panbio; COVID-VIRO® Antigen Rapid Test (AAZ, Boulogne-Billancourt, France), aka AAZ COVID-VIRO; NG-test® SARS-CoV-2 Ag (NG-Biotech, Guipry, France), aka NG-test; Biosynex COVID-19 Ag BSS (Biosynex, Illkirch-Graffenstaden, France), aka BIOSYNEX COVID-19 (Table 1).

The NPS had been collected by the medical staff for nucleic acid extraction in viral transport media (VTM), including Xpert® Nasopharyngeal Sample Collection kit (Cepheid, Sunnyvale, California), Media for virus (Deltalab, Barcelona, Spain), or saline buffer (0.9% NaCl). Part of the suspension was used to initially diagnose the etiological agent of the symptoms. The remaining part was stored at -70°C until use in the present study.

In NPS collected in March and April 2020, SARS-CoV-2 RNA was sought by means of an "in-house" assay based on the Charité protocol targeting the *E* gene or the RNA-dependent RNA polymerase (*RdRp*) gene [2], or of a commercially available RT-PCR assay targeting the *E* or *S* genes (RealStar® SARS-CoV-2 RT PCR Kit 1.0, Altona Diagnostics GmbH, Hamburg, Germany) [3]. Samples with cycle threshold (Ct) value ≤40 were interpreted as positive. In NPS collected in April to August 2019, respiratory viral and bacterial pathogen testing was performed by the BioFire® Respiratory Panel 2 (BRP2) (bioMérieux, Marcy-l'Étoile, France), according to the manufacturer's instructions. This assay targets 17 viruses and 4 bacteria that commonly cause upper and lower respiratory tract infections.

All of the 634 included patients NSP were tested with CORIS Respi-Strip, BIOSENSOR Standard Q, Abbott Panbio, AAZ COVID-VIRO, NG-test, and Biosynex COVID-19. One hundred microliter of frozen medium (VTM or NaCl buffer) was mixed with the extraction buffer provided with each RDT and then processed according to the manufacturer's instructions. The results were read after 15-30 min by two independent laboratory investigators. Discrepancies were solved by a third individual.

Quantitative variables were expressed as medians, interquartile range [IQR] and ranges [minimum-maximum]. Qualitative data were expressed as raw numbers (%). The diagnostic performance analysis of rapid antigen test was conducted considering RT-PCR results as the reference gold standard, computing sensitivity and specificity along with their 95% confidence intervals (95%CI) calculated using the exact method. To illustrate the clinical significance of our result in real-life setting, positive and negative predictive values were calculated for a range of hypothetical prevalence values. All statistical analyses were performed with Stata® 15 (StataCorp LP, College Station, Texas). *p* values <0.05 were considered as statistically significant.

The 297 SARS-CoV-2 RNA-positive NPS were randomly selected from patients found positive during the study period and stratified according to the number of days from symptom onset, the viral load estimated by the cycle threshold value (Ct), and the severity of the symptoms (mild/moderate *versus* severe/critical requiring oxygen therapy and admission in the intensive care unit). Similarly, the 337 patients presumed to be SARS-CoV-2 RNA-negative were randomly selected during the study period.

The COVID-19 disease severity was defined according to the definition of the Chinese Center for Disease Control and Prevention and the World Health Organization (WHO) [4, 5]. Mild disease are symptomatic patients meeting the case definition of COVID-19 without evidence of

Table 1
SARS-CoV-2 antigen RDT evaluated in the study.

Test	Manufacturer	Abbreviation	Volume of extraction buffer (μL)	No. of drops of extracted specimen dispensed to the device[a]	Time to read
COVID-19 Respi-Strip	Coris BioConcept	CORIS Respi-Strip	100 μL	8 drops (200 μL)[b]	15 min
STANDARD™ Q COVID-19 Ag Test	SD Biosensor, Inc.	BIOSENSOR Standard Q	350 μL	4 drops (100 μL)	30 min
Panbio™ COVID-19 Ag rapid Test	Abbott Rapid Diagnostic SAS	ABBOTT Panbio	100 μL	5 drops (150 μL)	15-20 min
COVID-VIRO® Antigen Rapid Test	AAZ	AAZ COVID-VIRO	100 μL	3 drops (100 μL)	15 min
NG-test® SARS-CoV-2 Ag	NG-Biotech	NG-test	100 μL	4 drops (120 μL)	15 min
BIOSYNEX COVID-19 Ag BSS	Biosynex SA	BIOSYNEX COVID-19	150 μL	5 drops (150 μL)	15 min

[a] Corresponding to an approximate volume of extracted VTM (viral transport medium)
[b] Strip is directly immersed in the tube containing VTM and the LY-S dilution buffer

pneumonia or hypoxia. Moderate disease was characterized by clinical signs of pneumonia without signs of severe pneumonia, including oxygen saturation (SpO_2) in ambient air $\geq$90%. Severe pneumonia was defined by fever, cough, dyspnea, fast breathing plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress or SpO_2 <90% on room air. Critical disease is characterized by the presence of acute respiratory distress syndrome (ARDS), sepsis, septic shock or acute thrombosis.

3. Results

3.1. Characteristics of the study population

Table 2 summarizes the baseline characteristics of the population studied. In total, 297 samples from patients with confirmed COVID-19 based on SARS-CoV-2 RNA detection were tested. Among these patients, 203 (68.4%) had mild or moderate disease at admission, whereas 94 (31.6%) had severe disease requiring intensive care. The median age of SARS-CoV-2 RNA-positive patients was 51 years (interquartile range [IQR]: 38-65 years), with a difference between patients with severe and non-severe disease (67 *versus* 45 years, respectively), and 55.2% of them were female. There was a median of 5 days (IQR: 3-8 days) between symptom onset and sample collection. Ct values ranged from 10.7 to 39.0 (median: 26.3) with the *E* gene target. Ct values correlated with the time since symptom onset (*p*<0.001).

Samples from 337 patients were considered as SARS-CoV-2 RNA-negative because they had been collected before December 2019. The median age of the patients was 67 years and 57.8% were males. Respiratory viral pathogens were detected in 20.2% of them, including, human rhinovirus/enterovirus (n=23), coronavirus other than SARS-

CoV-2 (n=18), parainfluenza virus (n=15), influenza A virus (n=8), respiratory syncytial virus (n=4), human metapneumovirus (n=3), and mixed infections (n=4, including coronaviruses HKU1 and 229E) (Table 2).

3.2. Performance of SARS-CoV-2 antigen RDT

The rate of success of the 6 RDT was high, comprised between 99.1% and 100%. All of the 6 specimens with invalid results were from the SARS-CoV-2-positive group with severe disease (Ct values: 18 to 33). Two specimens had invalid results with 4 tests (CORIS Respi-Strip, BIOSENSOR Standard Q, ABBOTT Panbio and AAZ COVID-VIRO), 3 specimens with 2 assays (CORIS Respi-Strip and BIOSENSOR Standard Q), and 1 specimen was indeterminate with BIOSENSOR Standard Q only. A total of 111 results (2.9%) were discrepant and required a third independent reading. The proportion of discrepant result was similar between the 6 RDT tested.

As shown in Table 3, all RDT but one had high specificity, comprised between 98.5% and 100% for the detection of SARS-CoV-2 antigen. Five SARS-CoV-2 RNA-negative NPS tested antigen-positive with the NG-test. None of them contained another respiratory viral pathogen. The specificity of BIOSENSOR Standard Q was lower than that of the other tests (93.2%, 95%CI: 89.9%-95.6%). Among the 22 falsely positive NPS with this test, 6 contained another respiratory viral pathogen, including human rhinovirus/enterovirus (n=3), parainfluenza virus (n=2) or coronavirus NL63 strain (n=1).

The overall sensitivity of the 6 RDT was variable, from 32.3% (95%CI: 27.0%-38.0%) for NG-test up to 61.7% (95%CI: 55.9%-67.3%) for AAZ COVID-VIRO. As shown in Table 4, the sensitivity of the RDT correlated with the delay of sampling after the onset of symptoms and the viral load estimated by the Ct value in RT-PCR. For NPS collected during the first 3 days following symptom onset, 4 RDT out of 6 achieved sensitivities $\geq$80%, including BIOSENSOR Standard Q, ABBOTT Panbio, AAZ COVID-VIRO and BIOSYNEX COVID-19 (Table 4). In addition, the association between sensitivity and the delay of sampling after the onset of symptoms was maintained after adjustment the viral load estimation (Supplementary Table).

In samples with Ct value $\leq$25, sensitivities were 71.1% (95%CI: 62.4%-78.8%) for CORIS Respi-Strip, 92.9% (95%CI: 87.0%-96.7%) for BIOSENSOR Standard Q, 86.9% (95%CI: 79.9%-92.2%) for ABBOTT Panbio, 96.2% (95%CI: 91.3%-98.7%) for AAZ COVID-VIRO, 62.3% (95% CI: 53.4%-70.7%) for NG-test, and 93.8% (95%CI: 88.2%-97.3%) for BIOSYNEX COVID-19. The detection rates of BIOSENSOR Standard Q and AAZ COVID-Viro were 100% for samples with a Ct value $\leq$20, and decreased to 92.5%, 61.3% and 12.0% (BIOSENSOR Standard Q) and to 94.4%, 65.8% and 9.1% (AAZ COVID-VIRO) for Ct values 21-25, 26-30 and $\geq$31, respectively (Table 4).

The severity of the disease (mild *versus* severe/critical) did not appear to affect the sensitivity of antigen detection compared to RT-PCR (Table 4).

Table 2
Baseline characteristics of the study population, including 297 symptomatic patients with positive SARS-CoV-2 RNA detection by RT-PCR and 337 patients sampled prior to the identification of SARS-CoV-2.

	SARS-CoV-2 RNA-positive (N=297)	SARS-CoV-2 RNA-negative (sampled prior to emergence) (N=337)
Median age (min-max), year	52 (20-98)	67 (17-100)
% male gender (n/N)	44.8% (133/297)	57.8% (194/337)
Severity of COVID-19 disease[a]		
Mild/moderate [% n/N)]	68.3% (203/297)	-
Severe disease [% n/N)]	31.7% (94/297)	-
Days from symptom onset [median (Q1-Q3)] (N=289)	5 (3-8)	unknown
Days 0-3 [n(%)]	96 (33.2%)	-
Days 4-7 [n(%)]	105 (36.3%)	-
Days $\geq$8 [n(%)]	88 (30.5%)	-
PCR Ct value [median (Q1-Q3)] (N=296)	26 (22-31)	-
Ct $\leq$20 [n(%)]	58 (19.6%)	-
Ct 21-25 [n(%)]	85 (28.7%)	-
Ct 26-30 [n(%)]	73 (24.7%)	-
Ct $\geq$31 [n(%)]	80 (27.0%)	-
Other pathogen detected		
No pathogen detected [% (n/N)]	unknown	79.8% (269/337)
Viral pathogen detected [% (n/N)][b]	unknown	20.2% (68/337)

[a] Among the SARS-CoV-2 positive patients, 203 were referred to an outpatient clinic whereas 94 patients were hospitalized

[b] Respiratory viral pathogens included human rhinovirus/enterovirus (n=23), coronavirus other than SARS-CoV-2 (n=18), parainfluenza virus (n=15), influenza A virus (n=8), respiratory syncytial virus (n=4), human metapneumovirus (n=3), and mixed infections (n=4, including coronaviruses HKU1 and 229E). Other coronaviruses than SARS-CoV-2 were detected in 18 patients, including HKU1 (n=8), NL63 (n=3), 229E (n=6) and OC43 (n=1) strains

Table 3
Specificity of RDT for SARS-CoV-2 antigen detection in NSP (n=337).

Test	Manufacturer	Abbreviation	Specificity (95%CI)
COVID-19 Respi-Strip	Coris Bioconcept (Belgium)	CORIS Respi-Strip	100% (98.9%-100%)
STANDARD™ Q COVID-19 Ag Test	SD Biosensor (South Korea)	BIOSENSOR Standard Q	93.2% (89.9%-95.6%)
Panbio™ COVID-19 Ag rapid Test	Abbott (Germany)	ABBOTT Panbio	100% (98.9%-100%)
COVID-VIRO® Antigen Rapid Test	AAZ (France)	AAZ COVID-Viro	100% (98.9%-100%)
NG-test® SARS-CoV-2 Ag	NG Biotech (France)	NG Test	98.5% (96.6%-99.5%)
BIOSYNEX COVID-19 Ag BSS	Biosynex (France)	BIOSYNEX COVID-19	100% (98.9%-100%)

95%CI: 95% confidence interval

Table 4

Sensitivities (95%CI) of SARS-COV-2 antigen RDT according to the number of days from symptom onset, the viral load, as assessed by the cycle threshold value (Ct) in RT-PCR and the severity of the COVID-19 disease.

Abbreviation	No. of samples tested	COVID-19 Respi-Strip CORIS Respi-Strip	STANDARD™ Q COVID-19 Ag Test BIOSENSOR Standard Q	Panbio™ COVID-19 Ag rapid Test ABBOTT Panbio	COVID-VIRO® Antigen Rapid Test AAZ COVID-VIRO	NG-test® SARS-CoV-2 Ag NG Test	BIOSYNEX COVID-19 Ag BSS BIOSYNEX COVID-19
Days from symptom onset							
Days ≤3	97	53.6% (43.2-63.8)	80.4% (71.1-87.8)	79.4% (70.0-86.9)	81.4% (72.3-88.6)	52.6% (42.2-62.8)	81.4% (72.3-88.6)
Days 4-7	103	37.3% (27.9-47.4)	61.8% (51.6-71.2)	52.4% (42.4-62.4)	61.2% (51.1-70.6)	30.1% (21.5-39.9)	56.3% (42.6-66.1)
Days 8-11	63	12.9% (5.7-23.9)	40.3% (28.1-53.6)	33.3% (22.0-46.3)	42.9% (30.5-56.0)	14.3% (6.7-25.4)	42.9% (30.5-56.0)
Days ≥12	26	20.8% (7.1-42.2)	30.4% (13.2-52.9)	37.5% (18.8-59.4)	37.5% (18.8-59.4)	15.4% (4.4-34.9)	42.3% (23.4-63.1)
Ct value categories							
Ct ≤20	40	89.7% (75.8-97.1)	100% (91.0-100)	95.0% (83.1-99.4)	100% (91.2-100)	80.0% (64.4-90.9)	97.5% (86.8-99.9)
Ct 21-25	90	62.9% (52.0-72.9)	89.8% (81.5-95.2)	83.3% (74.0-91.4)	94.4% (87.5-98.2)	54.4% (43.6-65.0)	92.2% (84.6-96.8)
Ct 26-30	74	15.3% (7.9-25.7)	65.3% (53.1-76.1)	57.5% (45.4-69.0)	65.8% (53.7-76.5)	18.9% (10.7-29.7)	63.5% (51.5-74.4)
Ct ≥31	89	1.1% (0.0-6.2)	11.4% (5.6-19.9)	8.0% (3.3-15.7)	9.1% (4.0-17.1)	1.1% (0.0-6.1)	9.0% (4.0-16.9)
Ct ≤25	130	71.1% (62.4-78.8)	92.9% (87.0-96.7)	86.9% (79.9-92.2)	96.2% (91.3-98.7)	62.3% (53.4-70.7)	93.8% (88.2-97.3)
Disease severity							
Mild/ moderate	203	37.1% (30.5-44.2)	59.9% (52.8-66.7)	58.4% (51.3-65.3)	62.4% (55.3-69.1)	34.7% (28.1-41.7)	60.4% (53.3-67.2)
Severe/ critical	94	31.5% (22.0-42.2)	61.4% (50.4-71.6)	47.8% (37.3-58.5)	59.8% (49.0-69.9)	27.7% (18.9-37.8)	58.5% (47.9-68.6)

Supplementary Tables and Figures show simulations of the calculated negative and positive predictive values (NPV and PPV) of the 6 RDT according to the prevalence of infection in the tested population.

4. Discussion

In the present study, we assessed the performance of SARS-CoV-2 antigen RDT in NPS from 667 patients with or without infection. Indeed, SARS-CoV-2 antigen detection appears as an attractive alternative to RT-PCR for early diagnosis and interruption of transmission chains through targeted isolation and cohorting of the most infectious cases and their close contacts.

All of the 6 RDT tested but one had high specificity (≥98-100%) for the detection of SARS-CoV-2 antigen. The lower specificity of the BIOSENSOR Standard Q assay was also reported in recent results from a cross-sectional unblinded prospective study using fresh nasal swabs [6]. However, other studies conducted with fresh nasopharyngeal and/or oropharyngeal swabs or with viral transport media reported better specificity values for this assay [7-10]. Low specificity implies a reduced positive predictive value in low-pre-test probability population, such as asymptomatic individuals targeted by large-scale screening campaigns. In such context, confirmation of positive results by means of nucleic acid testing is mandatory to avoid negative prejudices at the individual or public health levels. In contrast, the positive predictive value of the assay markedly improves when the pre-test probability of the infection in the tested population exceeds 20%. Because rapid antigen tests may not have similar performance in asymptomatic populations, large-scale studies are needed for further evaluation.

In our study, SARS-CoV-2 antigen detection using lateral flow assay was globally less sensitive for the diagnosis of infection than nucleic acid detection by means of a 2-target molecular method. When compared to RT-PCR, antigen detection using RDT was more sensitive when the viral load was high (Ct ≤25, reported to correspond to SARS-CoV-2 RNA levels higher than 10^6 copies/mL, a proposed threshold of transmissibility [11]) and for samples collected during the first 3 days following the onset of symptoms. Patients tested more than 5-7 days after the onset of symptoms are more likely to have low viral loads, thus a high likelihood of a false-negative result with an antigen RDT. Four out

of the 6 RDT tested including BIOSENSOR Standard Q, ABBOTT Panbio, AAZ COVID-VIRO and BIOSYNEX COVID-19 achieved over 80% of sensitivity for samples with ≤25 Ct in RT-PCR. Three of them were over 90% sensitive for these highly contagious samples. According to the World Health Organization guidance, sensitivities of ≥80% or ≥90% are acceptable or desirable, respectively for use as decentralized standalone point-of-care tests in symptomatic patients and their close contacts with or without symptoms (WHO, R&D Blue Print; COVID-19: Laboratory and diagnosis, 28 September 2020). Even higher sensitivities (≥95% acceptable, ≥98% desirable) are theoretically required for diagnosis of confirmation acute or subacute SARS-CoV-2 infection. Thus, the sensitivity of COVID-19 antigen RDT should be further improved, while specificity is maintained, through optimization of their chemistry and of signal detection by means of digital reading equipment [12]. COVID-19 antigen RDT would be of benefit in a triage scenario (short turnaround time, cost-saving, alleviating central testing) [10, 13].

Our study had some limitations. First, the study included exclusively symptomatic individuals recruited during the first wave of the COVID-19 epidemic in France in March and April 2020. Therefore, performance in other populations of infected individuals was not assessed. However, there is unlikely that the correlation between viral load and assay sensitivity would be any different in asymptomatic individuals. Second, detections of SARS-CoV-2 RNA in NPS were not all performed with the same molecular assay, due to the stepwise implementation of different technologies in the laboratory at the beginning of the pandemic. Ct values at a given input concentration of target RNA may slightly vary across different RT-PCR assays and they are not strictly quantitative. Third, the performance of the 6 SARS-CoV-2 antigen RDT has been assessed on leftover sample materials frozen at -70°C after the initial RT-PCR analysis and stored at this temperature for several weeks. However, we recently observed with an ELISA-based COVID-19 antigen assay that congelation and conservation at -70°C does not affect antigen detection for Ct values ≤33, a threshold considered by the French Society of Microbiology as "compatible with significant viral excretion". Fourth, the delay between sample collection and freezing, as well as the use of different frozen viral transport media and dilution of the sample, may have had an impact on the overall performance of the RDT. Fifth, lot-to-lot variation is a well-known challenge for immunoassays that

may affect their performance. Only one batch was tested for all RDT but one, and we observed a significant difference in sensitivity between 2 different batches of CORIS Respi-Strip (overall sensitivity: 43.2% [IC95%: 35.6%-51.0%] *vs* 26.8% [IC95%: 20.0%-34.5%]). Finally, RDT were tested in a university hospital laboratory by highly qualified and trained personnel, which may not reflect the situation with less well-trained operators in the real world. The technical handling is however extremely simple after minimal training. The use of fresh dry swabs with bigger cellular loads may increase the sensitivity of these assays in proportions that need to be determined. Rapid assays were not conducted within manufacturer requirements.

In conclusion, our study, based on a large number of well-characterized hospitalized patients and outpatients with or without SARS-CoV-2 infection, shows that rapid diagnostic tests are reliable tools for the rapid diagnosis of COVID-19 and the control of this pandemic. These tests are easy and rapid to perform in the context of patient care. However, the specificity and sensitivity of COVID-19 antigen RDT may widely vary across different tests and must therefore be carefully evaluated before releasing these assays for real-world applications, including the diagnosis of early symptomatic infection, contact tracing and large-scale screening campaigns. Our study indicates that some tests may lack specificity, exposing to the risk of a high number of falsely-positive results. Some assays showed excellent sensitivity for NSP with high viral loads, indicating that these tests will be able to identify the most contagious individuals without requiring RT-PCR and access to biology laboratories, thereby playing a key role in interrupting the chains of contamination. Four of the tested RDT qualified for these indications on the basis of our experiments, including BIOSENSOR Standard Q, ABBOTT Panbio, BIOSYNEX COVID-19 and AAZ COVID-VIRO.

Declaration of Competing Interest

SF has served as an advisor and/or speaker for Abbott. EA has received personal fees from GBT and Hemanext. JMP has received grants from Roche and Gilead Sciences and served as advisors and/or speaker for Roche, Gilead and Bristol-Myers Squibb. S.C. has received research grant from Gilead and has served as an advisor and/or speaker for Abbott, Cepheid, Hologic. All others authors have nothing to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcv.2021.104930.

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