Evaluation of qualitative and semi-quantitative cut offs for rapid diagnostic lateral flow test in relation to serology for the detection of SARS-CoV-2 antibodies: findings of a prospective study

Maddalena Peghin1,2,8*, Giulia Bontempo1, Maria De Martino3, Alvisa Palese4, Valentina Gerussi1, Elena Graziano1,2, Martina Fabris5, Federica D’Aurizio5, Francesco Sbrana6, Andrea Ripoli7, Francesco Curcio5, Miriam Isola3 and Carlo Tascini1

Abstract

Background: There is limited information to compare the qualitative and semi-quantitative performance of rapid diagnostic tests (RDT) and serology for the assessment of antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Therefore, the objective of the study was (a) to compare the efficacy of SARS-CoV-2 antibody detection between RDT and laboratory serology, trying to identify appropriate semi-quantitative cut-offs for RDT in relation with quantitative serology values and to (b) evaluate diagnostic accuracy of RDT compared to the NAAT gold standard in an unselected adult population.

Methods: SARS-CoV-2 antibodies were simultaneously measured with lateral flow immunochromatographic assays (LFA), the Cellex qSARS-CoV-2 IgG/IgM Rapid Test (by capillary blood), the iFlash-SARS-CoV-2 IgG/IgM chemiluminescent immunoassay (CLIA) (by venous blood) and the nucleic acid amplification test (NAAT) in samples from in- and out-patients with confirmed, suspected and negative diagnosis of coronavirus disease 2019 (COVID-19) attending Udine Hospital (Italy) (March-May 2020). Interpretation of RDT was qualitative (positive/negative) and semi-quantitative based on a chromatographic intensity scale (negative, weak positive, positive).

Results: Overall, 720 paired antibody measures were performed on 858 patients. The qualitative and semiquantitative agreement analysis performed in the whole sample between LFA and CLIA provided a Kendall's tau of 0.578 (p < 0.001) and of 0.623 (p < 0.001), respectively, for IgM and IgG. In patients with a diagnosis of COVID-19, accordance between LFA and CLIA was maintained as a function of time from the onset of COVID-19 disease and the severity of disease both for qualitative and semi-quantitative assessments. RDT compared to the NAAT gold standard
Background
Access to accurate and timely diagnostic test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection plays a major role to optimise clinical care and public health management worldwide. Since the beginning of the pandemic, market was flooded with several coronavirus disease 2019 (COVID-19) diagnostic tests of different classes with variable testing validation and regulatory oversight. The performance of nucleic acid amplification test (NAAT) in respiratory samples is currently the gold standard for confirming diagnosis, while rapid SARS-CoV-2 antigen diagnostic tests are used as an alternative to NAAT, with typically lower sensitivity than NAAT [1]. In addition, SARS-CoV-2 specific antibody detection is considered to complement NAAT, particularly in the late stages of disease (3–4 weeks post-symptom onset) to identify prior or late infection for clinical and epidemiological purposes [2]. The most common current diagnostic platforms utilised for SARS-CoV-2 specific antibody detection comprise rapid diagnostic tests (RDTs) with a qualitative (or semi-quantitative) antibody detection in COVID-19.

Methods
Aim, study setting and population
The aim of this extensive prospective study was to compare the efficacy of SARS-CoV-2 antibody detection between RDT and laboratory serology, trying to identify appropriate semi-quantitative cut-offs for RDT in relation with quantitative serology values and to evaluate diagnostic accuracy of RDT compared to the NAAT gold standard in an unselected adult population.

We completed this study at Udine Hospital (Italy), a 1,000-bed tertiary-care teaching hospital identified as a regional referral centre for COVID-19 patients and serving approximately 350,000 citizens. RDT and serology samples were simultaneously collected by trained nurses from a cohort of all consecutive adult in- and out-patients (≥18 years) attending the Infectious Disease Department with the diagnosis of confirmed COVID-19, suspicious COVID-19, and negative for COVID-19 (March–May 2020).

The concordance between serological and rapid tests measurements were analysed considering paired measures (same patient at the same time). Samples were collected at various phases of the follow-up after onset of symptoms as explained by the patient and divided as follow: early stage (<15 days); late stage: between day 15 and day 30; between month 1 and 2, after month 2. A SARS-CoV-2 serological test and RDT follow-up test were performed for a subset of enrolled patients with a diagnosis of COVID-19 that accepted monthly serological controls (+/- 15 days), according to a previously established protocol. The details of this prospective cohort have been provided previously [2].

Acute COVID-19 and baseline definitions
Diagnosis of COVID-19 infection was established as confirmed (positive SARS-CoV-2 NAAT in nasopharyngeal swabs or bronchoalveolar lavage) or suspected (negative SARS-CoV-2 NAAT in respiratory tract samples but suggestive laboratory or imaging findings and/or positive SARS-CoV-2 serology) during the acute phase of the disease. Remaining patients were classified as negative for COVID-19 [4].

Patients were classified using the COVID-19 Disease Severity Scale and specifically, for the analysis, patients...
were classified into three groups: (1) asymptomatic, (2) mild, and (3) moderate to critical disease [5].

**Laboratory methods**

**NAAT test.** Respiratory samples were tested for SARS-CoV-2 using RT-PCR targeted that investigated the E gene for screening and then the RdRp and N genes of SARS-CoV-2 for confirmation (Roche Respiratory Panel Assay). The specimens were considered positive if the cycle threshold (CT) value for at least one of the three genes was ≤ 36 [4].

**Lateral flow immunoassays.** Samples for LFA were obtained from one capillary blood drop (10–20 µL) obtained from a finger stick sample. The Cellex SARS-CoV-2 IgG/IgM Rapid Test is a lateral flow qualitative chromatographic immunoassay to detect IgG/IgM s against SARS-CoV-2 N and S protein with a positive percent agreement and negative percent agreement of 93.75% and 96.40% respectively [6].

**Chemiluminescent immunoassay (CLIA).** Samples for SARS-CoV-2 serologies were obtained from venous blood samples. iFlash-SARS-CoV-2 (Shenzhen Yhlo Biotech Co. Ltd. China, distributed in Italy by Pantec SRL), is a paramagnetic particle CLIA for detection of IgG/IgM against SARS-CoV-2 N and (non-RBD) S protein (cut-off for IgG/ IgM positivity > 10.0 kAU/L. The test performance has been documented to have a sensitivity and specificity of 86.1% and 99.2% for IgM and 93.7% and 96.3% for IgG, respectively [7].

**Identification of semi-quantitative cut-offs for RDT**

An internal scientific committee consisting of three investigators (two infectious disease specialists and one laboratory medicine specialist) the hospital developed a chromatographic intensity scale (Fig. 1) and participated in the interpretation of qualitative (positive or negative) and semi-quantitative LFA results. A picture of every rapid test was taken at the manufacturer’s established time of reading (15 min), a photographic archive of LFAs was made for every test and test results were independently reviewed by three of these investigators. Results were based on full consensus among the experts. According to the expert panel chromatographic scale, the IgG and IgM band was classified as either N, Negative; WP, Weak positive; or P, Positive. Figure 1 shows three RDT displaying an example of each possible result observed in our study.

**Primary and secondary outcomes and data collection**

Primary endpoints of the study were assessed to compare the efficacy of SARS-CoV-2 antibody detection between RDT and CLIA serology in different phases and severity setting of COVID disease trying to identify appropriate semi-quantitative cut-offs for RDT in relation with quantitative serology values. The secondary endpoint was to evaluate the diagnostic accuracy of RDT compared to the NAAT gold standard.

**Statistical analysis**

Descriptive statistics for categorical variables are presented as number (percent) and for continuous variables as mean ± standard deviation (SD) or median (interquartile range (IQR)). Normality was assessed using the Shapiro-Wilk test.

The relation between serological measurements and semi-quantitative interpretation of RDT was estimated using the Kruskal-Wallis test, while the relation between serological measurements and qualitative interpretation of RDT was estimated using the Mann-Whitney U test. The agreement between serological and semi-quantitative interpretation of RDT was studied with Kendall’s tau. The performance of IgG serological measurements to discriminate between the two level of qualitative interpretation of RDT was determined using De Long’s non-parametric receiver operating characteristic (ROC) analysis. Sensitivity, specificity, positive and negative predictive values and their 95% confidence intervals (CI) were calculated to assess diagnostic performance of qualitative interpretation of RDT compared to NAAT. All analyses were performed by STATA 17 statistical software, and statistical significance was set at p < 0.05.

**Results**

**Study population and sample collection**

Overall, during the study period, 1292 patients were evaluated in our hospital and 858 were eligible: 639 (74.5%) with a diagnosis of COVID-19 infection (619 (72.1%) confirmed and 20 (2.3%) suspected) and 219 (25.5%) negative for COVID-19. The clinical and microbiological characteristics of patients with a diagnosis of COVID-19 are reported in Table 1.

The concordance between serological and rapid tests measurements were analysed considering 720 paired measures. The average time from the first day of reported symptoms to the performance of combined RDT and serological test has a median of 44 days (range 0–133).

Samples were collected at various stages of the follow-up after onset of symptoms as declared by the patient: 114/720 (15.8%) early stage (<15 days) and 71/720 (9.9%) at late stage (15–30 days), 311/720 (43.2%) between month 1 and 2, 224/720 (31.1%) between month 2 and 3.

**Diagnostic accuracy of qualitative interpretation of RDT compared to serology**

Overall, when the CLIA was used as the comparator, the median between the two groups (negative and positive) was significantly different for IgM (0.7 vs. 6.5, p < 0.001) and IgG (1 vs. 75.2, p < 0.001) (Table 2). Boxplots of IgM
and IgG serological measurements across the groups identified by the results of rapid tests in relation with a qualitative interpretation are described in Fig. 2A. Among patients with a diagnosis of COVID-19, qualitative RDT and serological measurements were evaluated as a function of time from the onset of COVID-19 disease and severity of disease and confirmed a significant association as described in Table 2. On the basis of the ROC curve for the association of qualitative RDT compared to serology, the AUC was 0.901 for IgM (95% CI 0.878–0.923) and 0.964 (95% CI 0.946–0.982) for IgG (Fig. 3).

**Diagnostic accuracy of semi-quantitative interpretation of RDT compared to serology**

Overall, the distribution of IgM and IgG and across the three levels of semi-quantitative interpretation of RDT in relation with serological response had a highly significant trend, as reported in Fig. 2B. The agreement analysis performed in the whole sample furnished a Kendall’s tau of 0.578 (p<0.001) and 0.623 (p<0.001), respectively, for IgM and IgG.

Among patients with a diagnosis of COVID-19, differences between the RDT measurement classes and CLIA test were statistically significant in relation to the time from symptoms onset (Table 2). Regarding the
Table 1  Patient’s baseline characteristics, clinical presentation in the subgroup of patients with diagnosis of COVID-19 at acute onset

| Category | N=639 |
|----------|-------|
| Gender, n (%) | 332 (52.0) |
| Female | 307 (48.0) |
| Male | 25 (3.9) |
| Age, median (IQR) | 52 (38–63) |
| Acute COVID-19 severity, n/N (%) | 75/631 (11.9) |
| Asymptomatic | 415/631 (65.8) |
| Mild | 97/631 (15.4) |
| Moderate | 27/631 (4.3) |
| Severe | 17/631 (2.7) |
| Critical | 0/631 (0.0%) |
| Management, n (%) | 470 (73.6) |
| Inpatients | 27/631 (4.3) |
| Outpatients | 144 (22.5) |
| Ward\^ | 25 (3.9) |
| ICU | 0 (0.0%) |

\^ Infectious Disease or Pneumology Department

measurement obtained during follow-up, the Kendall's tau was 0.392 (p<0.001) for IgM and 0.480 (p<0.001) for IgG between day 0–15 from the onset of the subgroup of patients with diagnosis of COVID-19 disease, 0.671 (p<0.001) for IgM and 0.574 (p<0.001) for IgG between day 15–30, 0.537 (p<0.001) for IgM and 0.524 (p<0.001) for IgG between day 30–60, and 0.534 (p<0.001) for IgM and 0.617 (p<0.001) for IgG after 2 months. Furthermore, considering the severity of disease, the Kendall's tau was 0.485 (p<0.001) for IgM and 0.623 (p<0.001) for IgG for asymptomatic patients, 0.537 (p<0.001) for IgM and 0.606 (p<0.001) for IgG for patients with mild disease and 0.355 (p<0.001) for IgM and 0.285 (p<0.001) for IgG for patients with moderate to severe disease (Table 2).

Diagnostic accuracy of RDT compared to NAAT

Overall, IgG RDT qualitative accuracy compared to the NAAT gold standard showed that RDT provided an overall agreement of 82.9%, sensitivity of 78.5% (95% CI 75.1%-81.7%), specificity of 94.1% (95% CI 90.4%-96.8%), a positive predictive value (PPV) of 97.2% (95% CI 95.3%-98.5%) and a negative predictive value (NPV) of 62.8% (95% CI 57.6%-67.9%). The accuracy of RDT was related to the delay between a positive NAAT and RDT showing a sensitivity of 37.2% (95% CI 23%-53.3%) and specificity of 97.8% (95% CI 94.6%-99.4%) between day 0–15 from the onset of COVID-19 disease, a sensitivity of 71.2% (95% CI 58.7%-81.7%) and specificity of 100% (95% CI 63.1%-100%) between day 15–30, a sensitivity of 84% (95% CI 79.4%-88%) and specificity of 76.9% (95% CI 56.4%-91%) between day 30–60, and a sensitivity

Table 2  Serological measurements of patients with diagnosis of COVID-19, among qualitative (negative-positive) and semiquantitative (N – Negative; WP – Weak positive; P – Positive) rapid diagnostic test in function of time from the onset of COVID-19 disease and severity of disease, described ad median (IQR)

| Time from the onset of COVID-19 | IgM, median (IQR) | IgG, median (IQR) |
|---------------------------------|------------------|------------------|
| Overall                         | 0.7 (0.4–1.2)    | 1 (0.4–14.7)     |
| 0–15 days                       | 0.7 (0.4–1.1)    | 0.6 (0.4–1.1)    |
| 15–30 days                      | 0.6 (0.3–1.4)    | 0.6 (0.3–1.4)    |
| 30–60 days                      | 0.6 (0.4–1.1)    | 0.6 (0.4–1.1)    |
| > 60 days                       | 0.7 (0.5–1.3)    | 0.7 (0.5–1.3)    |
| 0–15 days                       | 0.5 (0.3–1)      | 0.5 (0.3–1)      |
| 15–30 days                      | 1.45 (0.45–27.7) | 1.45 (0.45–27.7) |
| 30–60 days                      | 5.4 (0.5–22.8)   | 5.4 (0.5–22.8)   |
| > 60 days                       | 10.8 (1.3–20.6)  | 10.8 (1.3–20.6)  |

| Severity of disease | IgM, median (IQR) | IgG, median (IQR) |
|---------------------|------------------|------------------|
| Asymptomatic        | 0.6 (0.4–1.1)    | 2.8 (1.0–9.7)    |
| Mild                | 0.7 (0.5–1.3)    | 4.4 (1.7–13.9)   |
| Moderate-severe     | 0.6 (0.4–0.7)    | 21.9 (5.6–66.1)  |
| IgM, median (IQR)   | 0.6 (0.3–5.4)    | 77.7 (56.5–92.1) |
| IgG, median (IQR)   | 2.4 (0.5–20.6)   | 749 (55.9–91.3)  |
| Asymptomatic        | 1.3 (0.4–1.3)    | 773 (58.6–99.9)  |

\* Infectious Disease or Pneumology Department

Page 5 of 9
of 81.4% (95% CI 75.5%-86.4%) and specificity of 78.9% (95% CI 54.4%-93.9%) after two months.

**Discussion**

In this prospective real life cohort study, we compared the SARS-COV-2 diagnostic test accuracy of LFA and CLIA serologic tests and demonstrated that RDT can be a non-invasive and reliable alternative to laboratory tests and facilitate not only qualitative but also semi-quantitative antibody detection. In addition, RDT accuracy compared to the NAAT gold standard showed low sensitivity and high specificity, with variable rates depending on the delay between the positive NAAT and the RDT. The strengths of the present study reside in the large cohort analysed, paired systematic collection of capillary blood obtained by finger stick for RDT and venous samples for serology, clinical characterisation of study subjects with different grades of clinical severity and monitoring over time after disease onset compared to previous literature in this line [8].

The easy-to-use SARS-COV-2 IgG/IgM combined RDT allow a valid, reproducible, cheap and non-invasive immunoassay device that can also be used in low income countries [9]. However, the usefulness and accuracy of
RDT for Ab detection has been widely questioned. Our data suggests that the RDT used in our study has a high estimated qualitative agreement compared with CLIA serology, which are significantly higher compared to variable data reported by the manufacturer and to previous literature in this line, testing various RDT [1]. Furthermore, in our cohort, this agreement was maintained as a function of time from acute disease onset and the severity of COVID-19. Contradictory results of previous studies on RDT performance may be explained by the heterogeneity of different factors, including the severity of the disease, the timing of detection after the disease.

Fig. 3 ROC curve for association of qualitative RDT compared to serology for IgM (1) and IgG (2)
onset and sample types. In addition, in our study, we used RDT and CLIA assays the detecting antibody response against a combination of the S and N proteins, which is expected to improve diagnostic accuracy [10, 11].

The quantity of Ab may condition the final immunological response [2]. Of interest that, although RDT are considered only qualitative (positive/negative) tests, on the basis of previous studies [12], we created a three-level chromatographic intensity scale and found that the overall semi-quantitative concordance rate of antibodies between the LFA and CLIA was high both for IgM and for IgG and maintained as a function of time from the onset and severity of acute COVID-19. Our study suggests that RDT semi-quantitative results could be an interesting and valuable tool to offer a simple POC strategy for large-scale assessments of previous SARS-CoV-2 infection and vaccination planning (for LFA with receptor binding domain S protein target), allowing for easy monitoring of the serological response, especially in areas with limited resources [13].

Accordingly, even if serological tests for SARS-CoV-2 should not be used to diagnose acute infection a combination of semiquantitative RDT and laboratory serological testing may be an alternative two-step algorithm, as recommended by international guidelines for maximising sensitivity and specificity of SARS-CoV-2 serological diagnostics [14]. Moreover pre-test probability should be considered in the execution and interpretation of the RDT [3]. A future prospective study could use artificial intelligence or mobile phone algorithm-based interpretation of the semi-quantitative results to decrease interobserver variability and perform population-wide testing [15].

RDT accuracy compared to the NAAT gold standard showed low sensitivity and high specificity. On the basis of international regulatory agencies, RDT must have at least 80% sensitivity and 98% specificity, as compared with a reference standard of laboratory-based RT-PCR testing to be approved [16]. Previous studies addressing the performance of RDTs compared to the reference NAAT have been published with variable results, depending on severity of disease and timing from acute onset [12, 17]. The timing of antibody detection after disease onset has a crucial role, since the sensitivity of serological tests depends heavily on the delayed humoral responses. In our cohort, most COVID-19 cases were submitted to Ab detection at a late (>15 days) stage of disease after the onset of symptoms [2]. In addition we evaluated a wide spectrum of individuals ranging from asymptomatic to severely infected who recovered from COVID-19 after the first wave [2]. Although NAAT is the gold standard, RDT allowed us to detect cases of suspected COVID-19 infection that were NAAT negative but antibody positive by RDT [1, 3].

Our study has several limitations. First, the performance and interpretation of RDT may be operator-sensitive. However, the health care professionals involved attended a training session prior to the beginning of the study and the test was read by three investigators who had to reach an agreement. Second, a relatively small sample of antibody was collected and reported in the early stages of infection, but most individuals were shown to have measurable antibody levels at late stages of infection [2]. Third, negative control samples were collected from patients with low clinical suspicion of COVID-19 and negative NAAT during the pandemic period, but not from serum samples retrieved from pre-pandemic period. Four, the RDT was performed on a finger stick blood sample; this assay has been approved for venous blood samples (a drop of plasma, serum or whole blood). However, previous studies showed that capillary blood shows similar sensitivity for detecting anti-SARS-CoV-2 IgM and IgG antibodies as venous blood samples, allowing the use of a non-invasive immunoassay device in daily practice [18]. Finally, our results only apply to one RDT and one CLIA test, which may have an assay-dependent rate of sensitivity, specificity and antibody decline. In addition, the emergence of SARS-CoV-2 variants of concern and vaccine-induced immunity may condition different humoral responses.

**Conclusion**

The selected RDT may be a useful qualitative and semi-quantitative tool for diagnosis assessing SARS-CoV-2 serology and provides valuable information on past exposure and monitoring for patients with different grades of clinical severity and variable follow-up after disease onset. Further studies are necessary to validate RDT to understand its value in establishing determining the general population’s immunological status and in assessing immunity after vaccination.

**List of abbreviations**

| Abbreviation | Definition |
|--------------|------------|
| C            | control    |
| CLIA         | chemiluminescent immunoassays |
| COVID-19     | coronavirus disease 2019 |
| ELISA        | enzyme linked immunosorbent assays |
| IQR          | Interquartile range |
| HP           | High positive |
| LFA          | lateral flow assays |
| N            | negative   |
| NAAT         | nucleic acid amplification tests |
| NPV          | negative predictive value |
| P            | positive   |
| POC          | point of care |
| PPV          | positive predictive value |
| RDT          | rapid diagnostic test |
| SARS-CoV-2   | severe acute respiratory syndrome coronavirus 2 |
| SD           | standard deviation |
| WP           | weak positive |
Acknowledgements
The authors would like to thank all clinical and nursing staff who cared for the patients at Udine Infectious Disease Clinic during hospitalisation and ambulatory management.

Authors' contributions
MP conceptualisation, methodology, formal analysis, investigation, writing—review and editing. MF methodology, laboratory analysis. MDM conceptualisation, methodology, formal analysis, writing. AP review and editing. GB data collections and methodology. EG data collections. VG data collection. AR formal analysis. FS formal analysis. MI conceptualisation, methodology, formal analysis, writing. FDA laboratory analysis. FC laboratory analysis and review. CT methodology, formal analysis, investigation, writing—review and editing. All authors read and approved the final manuscript.

Funding
This research was funded by PRIN 2017 n.2017854EK9—“Innovative statistical methods in biomedical research on biomarkers: from their identification to their use in clinical practice.” The funding body had no role in the design of the study, in the collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and materials
All datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
This study was approved by the Ethics Committee of the Friuli Venezia Giulia Region (CORMOR 3–4 protocol; CEUR-2020-OS-219 and CEUR-2020-OS-205). All procedures were carried out in accordance with the ethical standards of the University of Udine and the Agenzia Sanitaria Universitaria Friuli Centrale and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Patients gave their written consent prior the participation on the study and informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
MP reports receiving grants and personal fees from Pfizer, MSD, Menarini and Dia Sorin outside the submitted work. CT has received grants in the last two years from Correvio, Biotest, Biomerieux, Gilead, Angelini, MSD, Pfizer, Thermofisher, Zambon, Shionogi, Avir Pharma and Hikma outside the submitted work. The other authors have no conflict of interest to declare.

Author details
1 Infectious Diseases Division, Department of Medicine, University of Udine and Agenzia Sanitaria universitaria Friuli Centrale (ASUFC), Udine, Italy
2 Infectious and Tropical Diseases Unit, Department of Medicine and Surgery, University of Insbruck-ASST-Sette Laghi, Varese, Italy
3 Division of Medical Statistics, Department of Medicine (DAME), University of Udine, 33100 Udine, Italy
4 Department of Medical Sciences, School of Nursing, University of Udine, Udine, Italy
5 Institute of Clinical Pathology, Agenzia Sanitaria Universitaria Friuli Centrale, Udine, Italy
6 I.O.O Lipoapheresis and Center for Inherited Dystlipidemias - Fondazione Toscana Gabriele Monasterio, Pisa, Italy
7 Bioengineering Department, Fondazione Toscana Gabriele Monasterio, Pisa, Italy
8 Infectious Diseases Division, Agenzia Sanitaria universitaria Friuli Centrale (ASUFC), Presidio Ospedaliero Universitario Santa Maria della Misericordia, Piazzale Santa Maria della Misericordia 15, 33010 Udine, Italy
9 Pfizer, Thermofisher, Zambon, Shionogi, Avir Pharma and Hikma outside the last two years from Correvio, Biotest, Biomerieux, Gilead, Angelini, MSD,
and Dia Sorin outside the submitted work. CT has received grants in the MP reports receiving grants and personal fees from Pfizer, MSD, Menarini

References
1. Dines J, Deeks JJ, Berhane S, Taylor M, Adriano A, Davenport C, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev. 2021;3:CD013705.
2. Peghin M, De Martinis M, Fabris M, Palese A, Visintini E, Graziano E, et al. The fall in antibody response to SARS-CoV-2: a longitudinal study of asymptomatic to critically ill patients up to 10 months after recovery. J Clin Microbiol. 2021;59:e0113821.
3. Diam PK. Rapid diagnostic testing for SARS-CoV-2. N Engl J Med. 2022.
4. World Health Organisation. Clinical management of COVID-19: interim guidance, 25 January 2021. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1. Accessed 21 Nov 2021.
5. World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases interim guidance, 14 January 2020 (No. WHO/2019-nCoV/laboratory/2020.2). 2020. https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200211. Accessed 21 Nov 2021.
6. Cellex sSARS-CoV-2 IgG/IgM rapid test. https://www.ifa.gov/media/136625/download. Accessed 17 Feb 2022.
7. Johns Hopkins Center for Health Security. Serology tests for COVID-19: https://www.centerforhealthsecurity.org/resources/COVID-19/serology/-Serology-based-tests-for-COVID-19.html (2022). Accessed 17 Feb 2022.
8. Hansson KE, Calendino AM, Arias CA, Englund JA, Hayden MK, Lee ML, et al. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: serologic testing. Clin Infect Dis. 2020.
9. Jacobs J, Kuhne V, Lunguaya O, Affolabi D, Hardy L, Vandenberg O. Implementing COVID-19 (SARS-CoV-2) rapid diagnostic tests in Sub-Saharan Africa: a review. Front Med (Lausanne). 2020;7:57797.
10. Rosadas C, Randell P, Khan M, McClure MO, Tedder RS. Testing for responses to the wrong SARS-CoV-2 antigen? Lancet. 2020;396:e23.
11. Andrey DO, Cohen P, Meyer B, Torriani G, Yerly S, Maaza L, et al. Diagnostic accuracy of AugurX COVID-19 IgG serology rapid test. Eur J Clin Invest. 2020;50:e13357.
12. Prazuck T, Colin M, Grache S, Gubavcu V, Seve A, Ropeczci V, et al. Evaluation of performance of two SARS-CoV-2 Rapid IgM-IgG combined antibody tests on capillary whole blood samples from the fingertip. PLoS ONE. 2020;15:e0237694.
13. Fulford TS, Van H, Gherardin NA, Zheng S, Cula M, Drummer HE, et al. A point-of-care lateral flow assay for neutralising antibodies against SARS-CoV-2. Ebiomedicine. 2021;74:103729.
14. Centers For Disease Control and Prevention. Interim guidelines for COVID-19 antibody testing. 2022. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html. Accessed 17 Feb 2022.
15. Mendels DA, Dortet L, Emeraud C, Oueslati S, Girlich D, Ronat JB, et al. Using artificial intelligence to improve COVID-19 rapid diagnostic test result interpretation. Proc Natl Acad Sci U S A. 2021;118.
16. European Centre for Disease Prevention and Control. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA – first update. 2021. https://www.ecdc.europa.eu/en/publications-data/options-use-rapid-antigen-tests-covid-19-eueea-first-update. Accessed 16 Jan 2022.
17. Dortet L, Ronat JB, Vauloup-Fellous C, Langendorf C, Mendels DA, Emeraud C, et al. Evaluating 10 commercially available SARS-CoV-2 rapid serological tests by use of the STARD (Standards for Reporting of Diagnostic Accuracy Studies) method. J Clin Microbiol. 2021;59.
18. Black MA, Shen G, Feng X, Garcia Beltran WF, Feng Y, Vasudevareva V, et al. Analytical performance of lateral flow immunosassay for SARS-CoV-2 exposure screening on venous and capillary blood samples. J Immunol Methods. 2021;489:112909.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.