This is an Accepted Manuscript for *Infection Control & Hospital Epidemiology* as part of the Cambridge Coronavirus Collection.
DOI: 10.1017/ice.2022.3

Article Type: Original Article

Real World Performance of SARS-CoV-2 Antigen Rapid Diagnostic Tests in Various Clinical Settings

Gili Regev-Yochay MD[1,2], Or Kriger MD[3], Michael J. Mina MD[4], Sharon Beni RN[1], Carmit Rubin PhD[1], Bella Mechnik RN[1], Sabrina Hason RN[1], Elad Biber[1], Bian Nadaf[1], Yitshak Kreiss MD[5,2] and Sharon Amit MD[3]

[1] Infection Prevention & Control Unit, Sheba Medical Center, Ramat-Gan, Israel

[2] Sackler School of Medicine, Tel Aviv University, Tel-Aviv, Israel

[3] Clinical Microbiology, Sheba Medical Center, Ramat-Gan, Israel

[4] Harvard Chan School of Public Health, Harvard, Boston, MA, USA

[5] Central Management, Sheba Medical Center, Ramat-Gan, Israel

Corresponding author: Gili Regev-Yochay, Bitan 16, Sheba Medical Center, Tel-Hashomer, Ramat-Gan, Israel, Tel: 972-3-5303372 email: gili.regev@sheba.health.gov.il

Running Title: **Real world performance of SARS-CoV-2 Ag Rapid Tests**

Abstract:

Objective: To assess the validity of Antigen rapid diagnostic tests (Ag-RDT) for SARS-CoV-2 as decision support tool in various hospital-based clinical settings.

Design: Retrospective cohort study among symptomatic and asymptomatic patients and Healthcare workers (HCW).

Setting: A large tertiary teaching medical center serving as a major COVID-19 hospitalizing facility.

Participants and Methods: Ag-RDTs' performance was assessed in three clinical settings: 1. Symptomatic patients and HCW presenting at the Emergency Departments 2. Asymptomatic patients screened upon hospitalization 3. HCW of all sectors tested at the HCW clinic following exposure.

Results: We obtained 5172 samples from 4595 individuals, who had both Ag-RDT and quantitative real-time PCR (qRT-PCR) results available. Of these, 485 samples were positive by qRT-PCR. The positive percent agreement (PPA) of Ag-RDT was greater for lower cycle threshold (Ct) values, reaching 93% in cases where Ct-value was <25 and 85% where Ct-value was <30. PPA was similar between symptomatic and asymptomatic individuals. We observed a significant correlation between Ct-value and time from infection onset ($p<0.001$).

Conclusions:

Ag-RDT are highly sensitive to the infectious stage of COVID-19 manifested by either high viral load (lower Ct) or proximity to infection, whether patient is symptomatic or asymptomatic. Thus, this simple-to-use and inexpensive detection method can be used as a decision support tool in various in-hospital clinical settings, assisting patient flow and maintaining sufficient hospital staffing.

Keywords: SARS-CoV-2, Antigen rapid diagnostic tests, sensitivity, positive percent agreement, testing strategy

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Introduction

Currently the benchmark standard test used for diagnosing and screening people suspected to be infected with SARS-CoV-2 is polymerase-chain-reaction (PCR). These tests have high analytic sensitivity, very high specificity but are costly, require mostly specialized laboratory technologists, and with relatively slow turn-around time (TAT) (Vogels et al. 2020). To efficiently break infection chains, rapid results enabling fast isolation and contact tracing is required. This necessitates frequent, fast, accessible and economical diagnostic tests.

Multiple antigen rapid diagnostic tests (Ag-RDT) for SARS-CoV-2 have been recently developed (Dinnes et al. 2020; Khairat et al. 2020; Mak et al. 2020; Organization 2020; Fenollar et al. 2021; Möckel et al. 2021; Pekosz et al. 2021) and few have received Emergency Use Authorization (EUA) from the US Food and Drug Administration (FDA). The tests typically use a sandwich immunodetection employing lateral flow test format and are designed to be point-of-care (POC), rapid and inexpensive.

The World Health Organization (WHO) (WHO 2020) and the European Center for Disease Prevention & Control (ECDC) (ECDC 2020) support the use of Ag-RDT to increase COVID-19 testing capacity and states that these tests can help reduce further transmission through early detection of highly infectious cases, enabling rapid contact tracing.

While Ag-RDT have shown to have high specificity (>97%), they have been criticized to have sub-optimal analytic sensitivity compared to qRT-PCR detection of RNA (Osterman et al. 2021; Schildgen et al. 2021). However, the need for a high analytic sensitivity test for the use of successfully containing the ongoing COVID-19 pandemic, has been questioned (Mina et al. 2020). More importantly, early and rapid detection of highly infectious individuals, i.e. asymptomatic, or presymptomatic patients as well as early symptomatic patients (during the first days of symptoms), when viral load is typically high, should be the prior target. Thus, sensitivity for infectious individuals, rather than analytic sensitivity against detection of potentially non-infectious RNA is important for this aim.

Here, we present our initial real-world experience with several rapid antigen detection kits in a large tertiary medical center in Israel, utilizing the kits for Emergency Department (ED) triage, as well as in early detection of asymptomatic cases, mainly in support of outbreak investigations among HCW, ensuring operational continuity despite high prevalence of COVID-19 infections in the community.

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Methods:

Setting and Study Period: The Sheba Medical Center is the largest tertiary hospital in Israel, with 1600 beds, of these, 1400 acute care beds. Over 9000 HCW are occupied, of these, 1770 physicians and 3124 nurses. The study took place between September 2020 and January 2021, while Israel was going through an intensive 2nd COVID-19 surge, which peaked at the end of September and into the 3rd COVID-19 surge which peaked at the end of Jan 2021, and consisted mainly of the alpha variant of concern, both surges occurred in the pre-delta era.

Study population and Ag-RDT testing strategies: Three major testing strategies were used in this study: 1) As a decision support tool in the patient triage process, for a cohort of symptomatic patients or HCW, who visited the ED, and suspected as being infected with SARS-CoV-2 **(Figure 1).** 2) As a strategy for early detection of asymptomatic cases among two cohorts: i) asymptomatic patients screened for COVID-19, including women before delivery arriving to the obstetric ED (OB-ED), and ii) a cohort of HCW, who were screened following exposure to a detected COVID-19 case. In addition, for a small subset, these tests together were used as a decision support tool, to allow COVID-19 recovered HCW to return to work even if qRT-PCR was still positive (For mild infections with at least 10 days post-infection and asymptomatic for at least 3 days).

Inclusion criteria included 1) any patient (or HCW) who presented to the general or pediatric ED with symptoms suspected as COVID-19, including fever, dyspnea, unexplained cough or anosmia and ageusia, 2) all pregnant women admitted through the obstetric ED for labor and 3) all exposed HCW who were screened at the HCW clinic. Individuals who did not have both Ag-RDT and PCR results available, were excluded; Of a total of 4980 individuals screened, 87 without a valid PCR result and 40 without a valid Ag-RDT result were excluded.

Sample collection: A nasopharyngeal (NP) swab sample was collected by trained personnel following appropriate safety precautions and used in various Ag-RDT kits (Nowcheck COVID-19 Ag test (Bionote, S. Korea) (Haage et al. 2021), Panbio™ COVID-19 Ag rapid test, (Abbott Rapid Diagnostic Jena GmbH, Jena, Germany) (Fenollar et al. 2021), BD Veritor™ (Becton, Dickinson and Company Franklin Lakes, NJ) (Pekosz et al. 2020), GenBody COVID-19 Ag (GenBody Inc, S. Korea) (van Beek et al. 2020), STANDARD Q COVID-19 (SD-Biosensor Inc, S. Korea) (van Beek et al. 2020), following the manufacturer's instructions (**Supplementary Table**)). In addition, naso- and oropharyngeal

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

samples were obtained and tested for SARS-CoV-2 quantitative real-time polymerase chain reaction (qRT-PCR). For qRT-PCR, NP swabs were placed in 3mL of universal transport medium (UTM) or viral transport medium (VTM) and test was performed according to manufacturers' instructions on various platforms: Allplex™ 2019-nCoV (Seegene, S. Korea), NeuMoDx™ SARS-CoV-2 assay (NeuMoDx™ Molecular, Ann Arbor, Michigan), Xpert®, Xpress SARS-CoV-2 (Cepheid, Sunnyvale, CA, USA).

Data collection: Patient information was gathered through the hospital electronic database. Data included socio-demographic details, as well as duration, type of symptoms and laboratory tests including previous or proceeding SARS-CoV-2 qRT-PCR tests and SARS-CoV-2 IgG antibody levels when available. Day of COVID-19 infection onset was determined either by the first positive SARS-CoV-2 qRT-PCR or first day of symptoms, whichever was earlier. qRT-PCR cycle threshold (Ct) values of the N-gene were used as a correlate of SARS-CoV-2 viral load.

In cases with limited pre-detection data, to determine if the infection was in an early versus late phase of the infection, we used data from repeated testing within 48h, where available. If viral RNA load was dropping (i.e. higher Ct values) then virus was likely in the clearance phase at time of first detection, and vice versa.

Statistical analysis: Positive Percentage Agreement (PPA), Negative Percentage Agreement (NPA), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated for Ag-RDT compared with qRT-PCR results. Because the “ground-truth” is set as the result of a gold-standard which itself is imperfect, we discuss accuracy of the Ag-RDT not only in terms of overall biological sensitivity and specificity, but instead in terms of NPA and positive percent agreement PPA to indicate the fraction of negative and positive RT-PCR results, respectively, that are repeated on the Ag-RDT.

To estimate the association between Ct value, Ag-RDT and the number of days since SARS-CoV-2 infection (defined as the onset of symptoms or first detection), a mixed model was applied with the log transformed Ct value as the outcome. A random intercept was allowed for each subject to account for the correlation between repeated measurements of the same subject, assuming a similar correlation between each pair of measurements, i.e. Compound Symmetry. The model included number of days since SARS-CoV-2 infection as well as log transformed days, to capture the non-linear association between Ct value and time since infection, either as defined by symptoms or by first positive qRT-PCR. The predicted

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

association as well as its 95% confidence interval (CI) were calculated using the exact binomial method; p-values <0.05 were considered statistically significant.

A generalized linear mixed regression model was used to investigate independent predictors for a positive Ag-RDT test. Variables considered in the model included: whether the patient was symptomatic or asymptomatic, the number of days from disease onset to positive Ag-RDT (less or greater than 10 days), and Ct value (divided into 3 categories: lower then 30, 30-35 and greater than 35). Similar to the mixed model described above, we allowed a random intercept for each subject.

Ethical committee approval: The research protocol was approved by the Sheba Institutional Review Board and oral informed consent was obtained from study participants.

Results:

A total of 5172 samples were obtained from 4595 individuals who were tested by both Ag-RDT and qRT-PCR, including 3594 samples from symptomatic patients and HCW arriving to the ED, or patients hospitalized in COVID-19 wards, and 1548 samples from asymptomatic patients, with no previous COVID-19 detection, mainly women screened before labor and HCW screened post exposure. Among all samples collected, 30 were collected from 26 recovered COVID-19 patients of whom 25 had a positive qRT-PCR and one had a positive Ag-RDT (**Figure S2**). These recovered patients were excluded from analyses. Further demographic data is shown in **Table 1**.

Of all samples collected, 4656 were negative for SARS-CoV-2 by qRT-PCR. Three of 4656 negative qRT-PCR samples had a positive Ag-RDT, thus the overall NPA was 99.92%. A positive qRT-PCR was detected in 485 cases. In 79 (15%) cases, the samples were collected from patients who had a positive qRT-PCR or COVID-19 symptom onset starting before the preceding 10 days, and were thus excluded from the secondary analysis, since they were probably in the recovery stage.

The median Ct value of all 485 positive samples was 26 (interquartile range (IQR): 20.04-32.18). The median Ct was significantly higher for cases where Ag-RDT was negative (median 32.58, IQR: 28.9-35.75), vs. cases where it was positive (median 21.97, IQR: 18.1-26.8).

The PPA between Ag-RDT and qRT-PCR was greater for lower Ct values, reaching 93% in cases where Ct value was lower than 25. The overall PPA for all cases where Ct value was 35

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

or less, was 74%. Negative predictive value (NPV) was 96.8% and positive predictive value was 99.1%. When only newly detected cases were included, i.e. diagnosed within the preceding 10 days, overall PPA was 76% (for Ct<35), 85% for those with Ct<30 and increasing to 93% for those with Ct<25. (**Table 2**).

While symptomatic patients were older (mean age 56.7 years, median 50.1), mainly patients arriving at the ED, and asymptomatic patients were mainly younger HCW, or screened obstetric patients (mean age 43.8 years, median 36.4), the median Ct amongst the positive detected samples was not significantly different (24.9, IQR 19.2-31.4 vs. 26.7, IQR 21.5-33.3, respectively). The PPA was also similar amongst the two groups (**Table 2**).

In agreement with the above, a generalized linear mixed regression model identified that a positive Ag-RDT was significantly associated with lower Ct values (OR=0.04, 95%CI 0.018-0.095, P<0.0001) but not with age or symptomatic presentation (**Table 3**).

When we characterized the 87 false negative cases diagnosed within the 10 days of disease onset, in which Ct value was lower than 35, we found that 7 of these had been actually diagnosed with COVID-19 for over a week before testing at our institute. Yet, 73 cases were newly identified cases (tested on days 0-3 following COVID-19 diagnosis, which was defined either by date of symptom onset or dated of first positive qRT-PCR test). Of these 73 cases, 60 were identified on the test day (day 0). To determine if these were early versus late infection, we assessed a repeated test within 24-72 hours, where available. Lower Ct values on follow up measure were regarded as new infections, whereas stable or higher Ct values, were regarded as older infections, during recovery phase at time of first detection. For 18 of the 60 cases, we had follow up qRT-PCR tests with Ct values. Of the 18 cases for which we had day 0 and follow up data, 12 (67%) were recovering patients (**Figure 2**).

We observed a significant correlation between Ct value and time from infection onset; A mixed model using repeated measures with a random intercept for each subject indicated a significant non-linear relation between Ct value, and the log of number of day post SARS-CoV-2 infection (Regression coefficient of ln days post sars cov-2 infection: RR=0.18; p<0.0001). The variance of the observed Ct values was greatest on the day of SARS-CoV-2 diagnosis. During the first 10 days following the diagnosis, a logarithmic increase in Ct value was observed followed by a plateau. Following 20 days from infection, all cases had low viral loads, as defined by Ct value>30, apart from a single case of a patient with severe immunodeficiency (Common Variable Immuno-deficiency CVID) (**Figure 2**). A positive Ag-

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

RDT was observed only when the test was performed during the first 20 days after detection and in 89% when the test was performed within the first ten days. A single outlier was the CVID case, in which the test was positive after >20d.

Discussion:

We present real world use of SARS-CoV-2 Ag-RDT as an immediate clinical decision support tool in several clinical settings. RDT's had previously revolutionized the diagnosis and treatment of infectious diseases, most notable are malaria and streptococcal throat infections (Armengol et al. 2004; Dini and Bell 2008). In both these cases rapid diagnostics, performed by the primary care taker as a triage measure, may allow for a prompt rule-in/rule-out decision. Despite a relatively low analytic sensitivity compared to PCR, the advantages of RDT's are imminent: rapid result, simple operation and handling (size of kits, storage, use) allowing for point-of-care performance and minimal training, and low pricing. Large international health authorities (WHO, CDC, ECDC) have published papers referring to the use of RDT's for COVID-19 as a testing/screening tool in various settings, however real-life data regarding its performance beyond validation are lacking (Möckel et al. 2021).

In this study RDT's of various manufacturers were used for two main purposes – at the ED, as a triage measure for improving patient-flow and placement, and as a strategy for early detection of asymptomatic cases, at the personnel clinic for HCW following suspected exposures and at the obstetric ED for screening women before labor. In all settings, we tested patients/HCW with no symptoms or symptoms of various lengths, a design enabling an unbiased analysis of the performance of RDT's.

As expected, specificity of all kits tested in our study were very high (>99.7%), reassuring the strong positive predictive value of the assays, especially during peaking incidence. This may allow for prompt decision in all our study settings. At the ED – as an additional triage tool, allowing early differentiation between SARS-CoV-2 infectious patients and other suspected patients, enabling discharge of mild cases to home-care and isolation, or hospitalization in COVID-19 wards in more severe cases. At the obstetric ED, as a screening tool, permitting early detection and isolation of asymptomatic COVID-19 infectious patients. And last, at the personnel clinic – early detection of positive HCW, allowing exposed HCW to continue to work and avoid unnecessary isolation when Ag-RDT is negative and rapid and early epidemiological investigation, without awaiting PCR result, when Ag-RDT is positive.

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

As for the negative predictive value, in concordance with previous publications (Khairat et al. 2020; Mak et al. 2020; Fenollar et al. 2021), the overall analytical sensitivity of the kits is inferior to PCR, and correlates with the presumed viral load, represented by the Ct value (Table 2). However, the correlation between kit performance, Ct and the time since the onset of symptoms resembles the current knowledge regarding infectivity kinetics with respect to viral load and time (Gniazdowski et al. 2020; La Scola et al. 2020; Singanayagam et al. 2020). Moreover, the direct correlation between positive Ag-RDT and infectivity have been recently reported (Pekosz et al, 2021). Thus, for a patient with a given Ct value, there is a lower chance of being infective the more time elapsed since symptoms onset. This also explains the pattern of sensitivity gaps between symptomatic and asymptomatic cases, with similar sensitivity with high viral loads (Ct<25) yet lower in asymptomatic patients with lower viral loads (Ct>30). As most published data show similar infectiveness regardless of symptoms, and Ag-RDT's detect viral particles in the nasopharyngeal cavities, symptoms merely create a lead-time bias, allowing for early detection. Ag-RDTs perform well in both symptomatic and asymptomatic patients, as has been recently described (Mina et al. 2021).

Taken together, as the viral-load curve of SARS-CoV-2 shows a short, sharp incline and a long, moderate decline, with a relatively short infectious period with respect to PCR positivity (Mina et al. 2020; Turner et al. 2021) our findings suggest that at a given time point, an RDT-negative PCR-positive patient, will likely present a non-infective individual.

The study has several limitations. First, day of infection onset is defined as either day of first positive qRT-PCR, or day of symptoms onset, yet for some patients this may not be the precise day of infection, and we suspect that many of those diagnosed on day 0, were actually already infected for several days (Menkir et al. 2021). This may be particularly pertinent to asymptomatic patients, whom are likely more frequently recovering and no longer infectious by the time they are detected (Mina et al. 2021). Second, we do not test a single specific Ag-RDT, but rather combined the results of several kits. Since our objective is to show the potential use of the method, rather than the performance of a specific kit the study included several available kits. But, since the performance of each kit in similar settings did not differ significantly, we believe that for our objective this is not a significant limitation. Last, the population tested were very diverse ranging from symptomatic patients or HCW to asymptomatic HCW and pre-labor screening of women. This may potentially impact the predictive value of the test. Yet, we report very similar PPA, NPV and PPV among symptomatic and asymptomatic individuals. While prevalence of COVID-19 in the

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

population changed along the study period, it included increasing, decreasing and peak periods in which screening of both populations (symptomatic and asymptomatic) took place simultaneously.

In conclusion, this report of a real-life experience with SARS-CoV-2 Ag-RDT's offers several usage settings. The very high specificity enables immediate rule-in of positive SARS-CoV-2 infectious cases, be it symptomatic ED patients, exposed or early-recovered HCW. Despite the lower analytic sensitivity, accumulating bulk of data suggest that Ag-RDT may be a better surrogate for infectivity than PCR, as it represents translated viral proteins rather than RNA remnants. For example, Pekosz et al, 2021, show a better correlation between infectivity and Ag-RDT+/PCR+ cases than Ag-RDT-/PCR+ cases. In a hospital setting, an Ag-RDT is always backed by a PCR which will minimize the chance of missing a very early disease in the case of presymptomatic or asymptomatic patients. However, our data support its prudent use as a rapid decision-support tool allowing for an efficient ED flow and management of hospital staff during peaking COVID-19 prevalence.

Acknowledgements: We would like to thank Efrat Steinberger for her devotion in coordinating the study, Amir Grinberg and Amit Gotkind for administrative and management assistance.

This study used own funding of the Sheba Medical Center. GRY has received a research grant on an unrelated topic (pneumococcal infections) from Pfizer and honorariums for talks, unrelated to the subject of the current manuscript, by Teva and MSD. None of the other authors have any conflict of interests to report.

References:

Armengol CE, Schlager TA, Hendley JO. Sensitivity of a rapid antigen detection test for group A streptococci in a private pediatric office setting: answering the Red Book's request for validation. Pediatrics. 2004 Apr;113(4):924–926.

Dini L, Bell D. Malaria rapid diagnostic tests: A revolution and challenge for management of febrile disease. CME: Your SA Journal of CPD. 2008;

Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev. 2020 Aug 26;8:CD013705.

European Centre for Disease Prevention and Control. Options for the use of rapid antigen tests for COVID-19 in the EU/EEA and the UK. 19 November 2020. ECDC: Stockholm; 2020

Fenollar F, Bouam A, Ballouche M, Fuster L, Prudent E, Colson P, et al. Evaluation of the Panbio COVID-19 Rapid Antigen Detection Test Device for the Screening of Patients with COVID-19. J Clin Microbiol. 2021 Jan 21;59(2).

Gniazdowski V, Morris CP, Wohl S, Mehoke T, Ramakrishnan S, Thielen P, et al. Repeat COVID-19 Molecular Testing: Correlation of SARS-CoV-2 Culture with Molecular Assays and Cycle Thresholds. Clin Infect Dis. 2020 Oct 27

Haage V, de Oliveira-Filho EF, Moreira-Soto A, Kühne A, Fischer C, Sacks J, et al. Impaired performance of SARS-CoV-2 antigen-detecting rapid tests at elevated temperatures. medRxiv. 2021 Jan 6

Khairat SM, Guindy NEL, Motaleb M. Evaluation of two rapid antigen tests for detection of SARS-CoV-2 virus. International Journal of Microbiology and Biotechnology 2020

Mak GC, Cheng PK, Lau SS, Wong KK, Lau CS, Lam ET, et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. J Clin Virol. 2020 Jun 8;129:104500.

Menkir TF, Chin T, Hay JA, Surface ED, De Salazar PM, Buckee CO, et al. Estimating internationally imported cases during the early COVID-19 pandemic. Nat Commun. 2021 Jan 12;12(1):311.

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Mina MJ, Parker R, Larremore DB. Rethinking Covid-19 Test Sensitivity - A Strategy for Containment. N Engl J Med. 2020 Nov 26;383(22):e120.

Mina MJ, Peto TE, García-Fiñana M, Semple MG, Buchan IE. Clarifying the evidence on SARS-CoV-2 antigen rapid tests in public health responses to COVID-19. Lancet. 2021 Feb 17

Möckel M, Corman VM, Stegemann MS, Hofmann J, Stein A, Jones TC, et al. SARS-CoV-2 antigen rapid immunoassay for diagnosis of COVID-19 in the emergency department. Biomarkers. 2021 May;26(3):213–220

Osterman A, Baldauf H-M, Eletreby M, Wettengel JM, Afridi SQ, Fuchs T, et al. Evaluation of two rapid antigen tests to detect SARS-CoV-2 in a hospital setting. Med Microbiol Immunol. 2021 Feb;210(1):65–72

Pekosz A, Parvu V, Li M, Andrews JC, Manabe YC, Kodsi S, et al. Antigen-Based Testing but Not Real-Time Polymerase Chain Reaction Correlates With Severe Acute Respiratory Syndrome Coronavirus 2 Viral Culture. Clin Infect Dis. 2021 Jan 20

Schildgen V, Demuth S, Lüsebrink J, Schildgen O. Limits and Opportunities of SARS-CoV-2 Antigen Rapid Tests: An Experienced-Based Perspective. Pathogens. 2021 Jan 5;10(1)

La Scola B, Le Bideau M, Andreani J, Hoang VT, Grimaldier C, Colson P, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. Eur J Clin Microbiol Infect Dis. 2020 Jun;39(6):1059–1061

Singanayagam A, Patel M, Charlett A, Lopez Bernal J, Saliba V, Ellis J, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. Euro Surveill. 2020 Aug;25(32)

Turner F, Vandenberg A, Slepnev VI, Car S, Starritt RE, Seger MV, et al. Post-Disease Divergence in SARS-CoV-2 RNA Detection between Nasopharyngeal, Anterior Nares and Saliva/Oral Fluid Specimens - Significant Implications for Policy & Public Health. medRxiv. 2021 Jan 26

van Beek J, Igloi Z, Boelsums T, Fanoy E, Gotz H, Molenkamp R, et al. From more testing to smart testing: data-guided SARS-CoV-2 testing choices. medRxiv. 2020 Oct 14

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Vogels CBF, Brito AF, Wyllie AL, Fauver JR, Ott IM, Kalinich CC, et al. Analytical sensitivity and efficiency comparisons of SARS-CoV-2 RT-qPCR primer-probe sets. Nat Microbiol. 2020 Jul 10;5(10):1299–1305.

World Health Organization: SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide. 2020

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

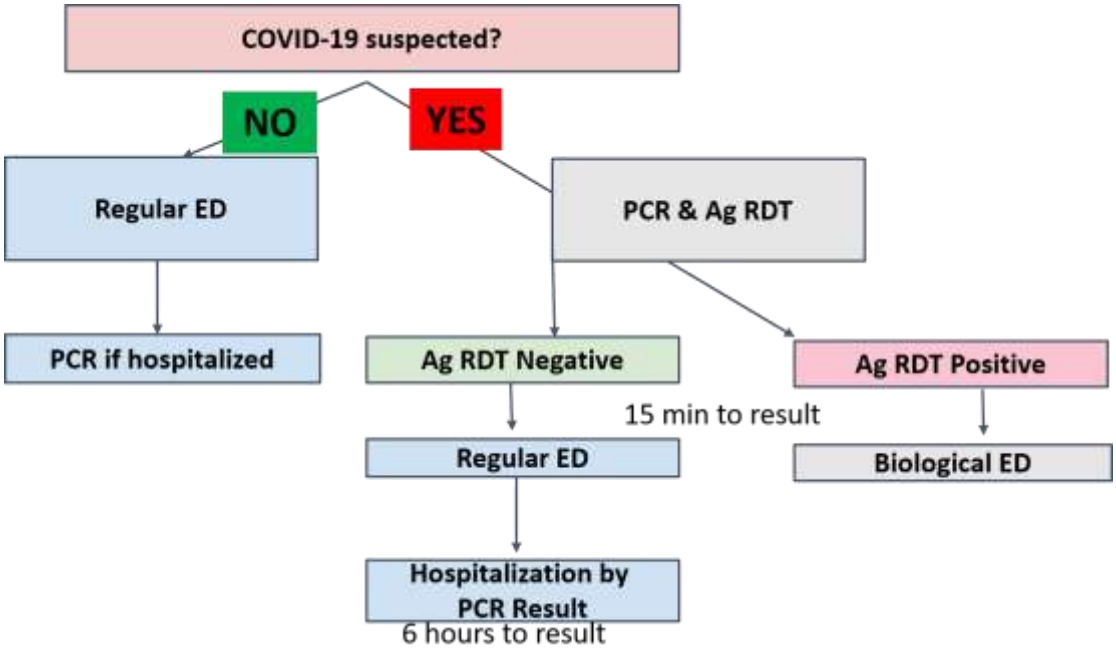


Figure 1: Testing strategy in the Emergency Department

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

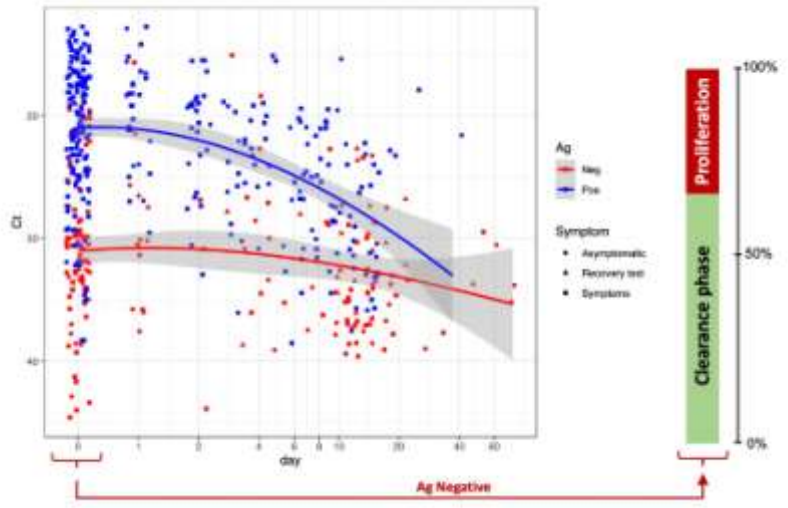


Figure 2: Correlation between Ct value and days from COVID-19 diagnosis by Ag-RDT. Red – denotes negative Ag-RDT, Blue – denotes positive Ag-RDT. Square denotes symptomatic patient on test day, circle denotes asymptomatic patient, and triangle denotes a recovery test.

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Table 1: Study population

		Total		Symptomatic		Asymptomatic	
		N	%	N	%	N	%
Total number of individuals tested		4827		3429		1398	
Total number of samples		5142		3594		1548	
Sex (Male)		2026	41.97%	1751	48.72%	275	17.76
Age	Mean	56.7		61.9		43.8	
	Median	50.1		61.0		36.4	

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Table 2: PPA, NPA, NPV and PPV

n	Neg PCR	Pos PCR	Pos Ag	PPA	NPV	PPV	NPA
The full Cohort							
5142	4656		3		96.8%		99.9%
All		485	329	67.8%		99.1%	
Unknown Ct		15	13	86.7%			
Ct <35		412	305	74.0%			
Ct <30		317	267	84.3%			
Ct <25		227	210	92.5%			
Ct <20		121	116	95.9%			
Excluding patients with documented disease onset >10d before sample							
5055	4649		3		97.6%		99.9%
All		406	292	71.9%		99.0%	
Unknown Ct		11	10	90.9%			
Ct <35		363	277	76.3%			
Ct <30		295	252	85.4%			
Ct <25		217	201	92.6%			
Ct <20		118	113	95.8%			
Symptomatic patients (within 10 days of disease onset)							
3529	3213		0		97.5%		100%
All		316	234	74.1%		100%	
Unknown Ct		11	10	90.9%			
Ct <35		285	221	77.5%			
Ct <30		233	202	86.7%			
Ct <25		175	162	92.6%			
Ct <20		100	95	95.0%			
Asymptomatic patients (within 10 days of disease onset)							
1527	1436		3		97.9%		99.8%
All		91	60	65.9%		95.2%	
Unknown Ct		1	1	100%			
Ct <35		79	57	80.4%			
Ct <30		63	51	81.0%			
Ct <25		42	39	92.9%			
Ct <20		21	21	100%			

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Table 3: Predictors of positive Ag-RDT multiple logistic regression:

		Adjusted OR	95% CI	P-value
Time from infection	0-10d			
	11+ d	0.356	0.09-1.28	0.098
Ct value	<30			
	≥30	0.052	0.01-0.28	0.004
Indication	Asymptomatic			
	Symptomatic	0.383	0.05-2.64	0.285
Age (per year)		1.027	0.99-1.06	0.092
Gender	Female			
	Male	1.263	0.38-4.16	0.657

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Author contributions:

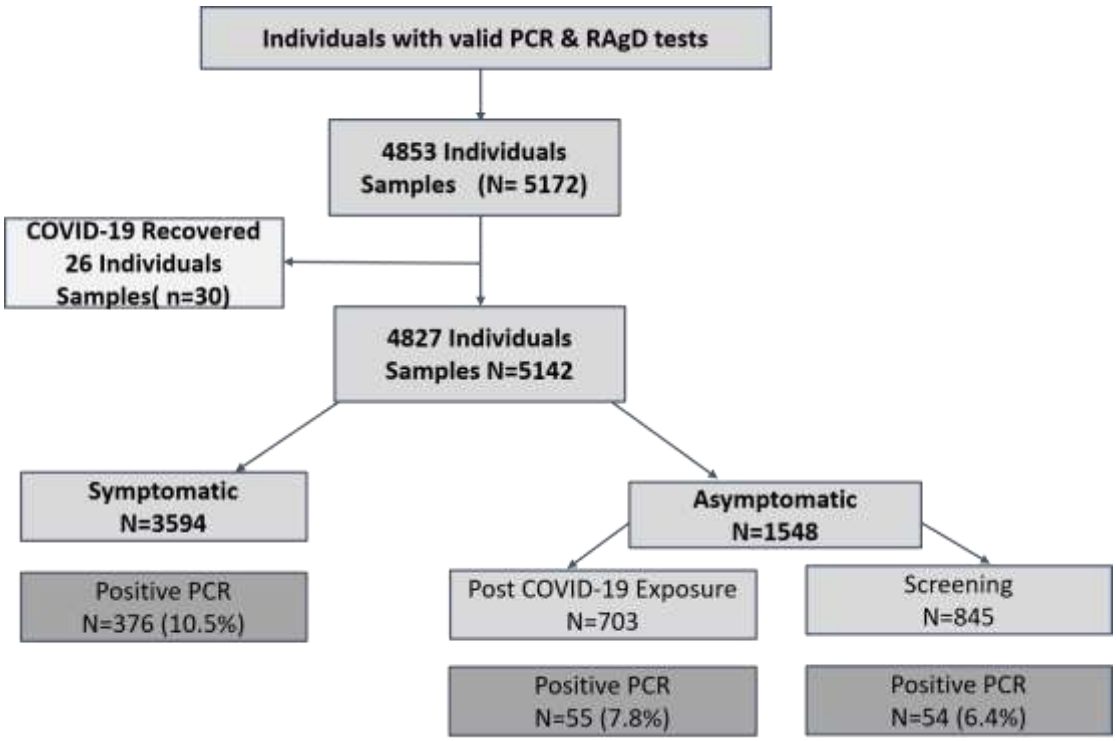
GRY and SA conceived and planned the study, interpreted the results. GRY supervised the project and prepared and lead the writing of the manuscript. SA supervised the laboratory work and contributed to the final version of the manuscript. OK, SB, BM, SH, EB and BN performed the screening, collected the data and contributed to the final version of the manuscript. MJM analysed and interpreted the results, reviewed the final version of the manuscript. CR performed the statistical analyses. YK conceived the idea and contributed to the final version of the manuscript

Supplementary Table S1

RAD test name	Manufacturer	Number of samples
Nowcheck COVID-19 Ag test	Bionote, S. Korea	3038
Panbio™ COVID-19 Ag rapid test	Abbot laboratories, Germany	582
BD Veritor™	Becton, Dickinson and Company Franklin Lakes, NJ	150
GenBody COVID-19 Ag	GenBody Inc, S. Korea	207
STANDARD Q COVID-19	SD-Biosensor Inc, S. Korea	288

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press

Supplementary Figure S1:



Supplementary Figure S1: Study population

https://doi.org/10.1017/ice.2022.3 Published online by Cambridge University Press