RESEARCH BRIEF

Screening for SARS-CoV-2 in close contacts of confirmed cases

Performance and operational considerations

Background

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, which causes COVID-19, has significantly burdened health systems globally, with over 22 million confirmed cases in Brazil alone as of 2021. A key challenge of the pandemic response is diagnostic testing, which is critical to inform public health strategies. The reference standard for SARS-CoV-2 testing is RT-PCR. While accurate, this method has many practical limitations, including cost, laboratory infrastructure requirements, and often invasive sampling. RT-PCR testing is typically centralized, which can lead to delays in reporting results to patients. Such delays have important public health implications, including increased risk for transmission during the period before results are available. Expanded access to decentralized and point-of-care (POC) testing is essential to identify cases early and limit community transmission, particularly where RT-PCR is unavailable. Data on test performance in priority use cases are needed to understand trade-offs in test selection and inform screening strategies.

Methods

From July to September 2021, a prospective diagnostic accuracy study was conducted among close contacts of COVID-19 positive index cases at the Centro de Pesquisa em Medicina Tropical de Rondônia (CEPEM) in Porto Velho, Brazil. The objective of the study was to evaluate the performance of three rapid antigen tests and one molecular method for performance against a reference RT-PCR in the detection of SARS-CoV-2. The following tests were evaluated in this study:

- The STANDARD Q COVID-19 Ag Nasal and Saliva tests (SD Biosensor, Republic of Korea)
- The SARS-CoV-2 Ag Test (LumiraDx™ Limited, United Kingdom)
- The SalivaDirect™ PCR protocol (Yale School of Public Health, United States)

Figure 1. The STANDARD Q COVID-19 Ag Test (SD Biosensor).

Figure 2. The SARS-CoV-2 Ag Test (LumiraDx).

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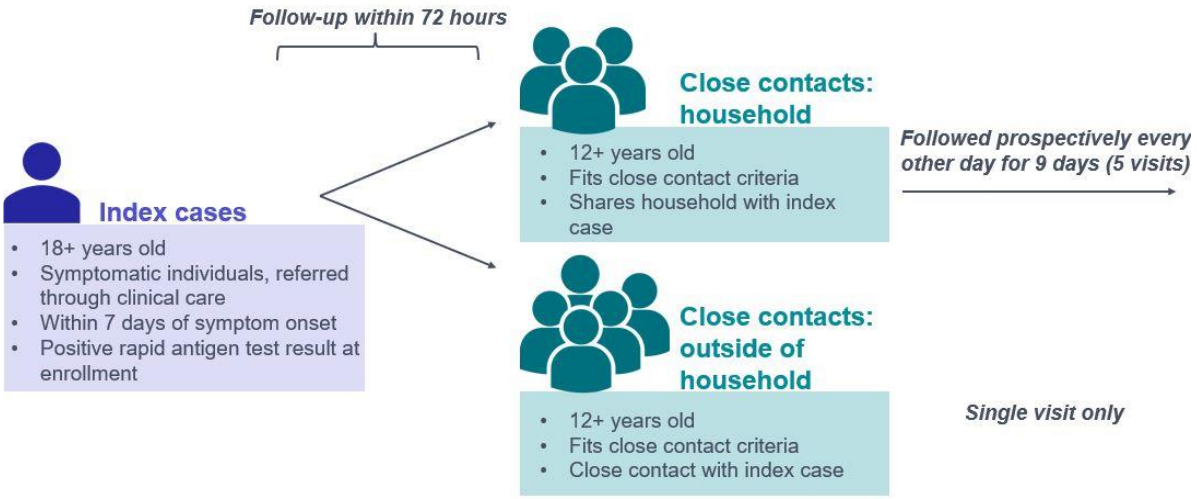
The study was designed to identify individuals at high risk of infection by enrolling close contacts of confirmed COVID-19 positive index cases. Symptomatic adults within seven days of symptom onset who screened positive on a rapid SARS-CoV-2 antigen test were enrolled as index cases through clinical platforms. Close contacts were then identified through a contact elicitation interview. A subset of only household close contacts (close contacts who shared the same primary residence as the index case) were followed longitudinally every other day over a period of nine days for clinical evaluations and testing (Figure 3). All study participants provided informed consent to participate.

Figure 3. Description of study populations.



At each study visit, all participants provided two paired anterior nares swabs (ANS), one nasopharyngeal swab (NPS), and a saliva sample. The STANDARD Q COVID-19 Ag Nasal Test was run at the point of care, and all other tests were performed at the laboratory. RT-PCR conducted on NPS was used as the reference assay. For household contacts in the longitudinal sample, if the POC antigen test was positive for SARS-CoV-2, only one additional study visit took place, during which NPS were not collected to minimize study staff exposure. Participants were considered lost to follow-up after two missed visits. Clinical case definitions from the US Centers for Disease Control were applied to assign PCR-confirmed, infected individuals as symptomatic, oligosymptomatic, or asymptomatic.

Findings

Fifty symptomatic COVID-19-positive index cases and 214 of their associated close contacts were enrolled. Sixty-four contacts shared a primary residence with an index case and were therefore included in the longitudinal sample. 65 of the 214 (30%) close contacts were SARS-CoV-2 positive by NPS RT-PCR during at least one study visit. In total, 42 paired samples were collected at unique visits with oligo/asymptomatic close contacts who were positive for SARS-CoV-2, from 32 individual participants.

Study participants were either fully vaccinated (27%, 70/264), partially vaccinated (45%, 118/264), or un-vaccinated (29%, 76/264) at enrollment. The available vaccines were AstraZeneca, CoronaVac, Johnson & Johnson, and Pfizer. No statistical difference was observed in viral loads between vaccinated and unvaccinated individuals, although the study was not powered to measure this. Sequences were available for 84 positive samples: 68 Gamma and 16 Delta. The Delta strain became more prevalent among samples collected later in the study.

The two POC ANS antigen tests demonstrated comparable performance. Excluding cases with Ct values >34, above which transmission is less likely, the tests performed with sensitivity in the ranges of 90% and 60% for symptomatic and oligo/asymptomatic cases, respectively. In all scenarios, the rapid antigen test conducted on saliva had a sensitivity in the range of 50% or less. The SalivaDirect PCR assay showed

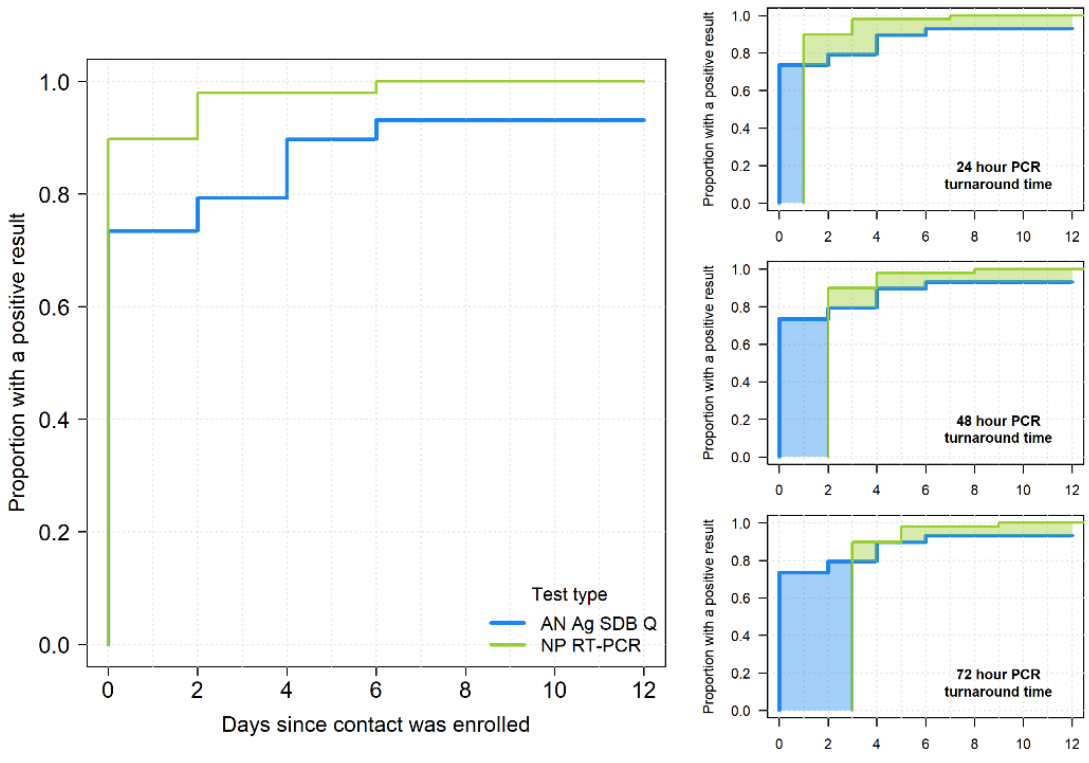
the highest overall performance among close contacts at 76% sensitivity, which increased to 90% among contacts with Ct<34.

The time-to-positivity from days since enrollment for close contacts with a positive reference result (Ct<34) at any timepoint was assessed by comparing the proportion of participants with positive results by reference RT-PCR and a POC ANS antigen test (STANDARD Q Nasal) under different scenarios for RT-PCR result turnaround time (Figure 4). The study shows that even with a relatively rapid RT-PCR result turnaround of 24 hours, >70% of contacts would have been identified by a POC test. At 48 hours, cumulative sensitivity is 80%, increasing to nearly 90% at four days.

Public health implications

Overall, the observed positivity rate among close contacts in this study (30%) highlights the importance of contact tracing and testing as a public health strategy. Additionally, POC rapid antigen tests for SARS-CoV-2 are highly versatile and useful tools for combatting the COVID-19 pandemic. The lower cost and near immediate time-to-result of rapid antigen tests is a significant benefit that offsets reduced sensitivity by decreasing diagnostic delays and onward viral transmission. Here, we demonstrate that POC ANS antigen tests for SARS-CoV-2 perform adequately to provide prompt, actionable information to both the health system and individuals. In this study, we show that in settings where RT-PCR is unavailable due to financial or infrastructure limitations, or where time-to-results is >4 days, close to 90% of individuals with Ct<34 could benefit from an earlier result via a POC test. Even in settings where PCR results are available within 24 hours, cumulative sensitivity of a POC test is >70%. In many settings, limited RT-PCR testing capacity—especially during high demand—can lead to delays in results. Immediate results can impact behavior of potentially infectious individuals, encouraging earlier isolation and signaling where additional testing is warranted. The emergence of antiviral therapies—which are more effective the sooner they are taken—further underscores the value of timely results.

Figure 4. Time to positivity from time of first visit for close contacts with a positive NPS RT-PCR result (Ct<34) at any time. The blue line represents the proportion of NPS RT-PCR positive cases identified as positive by the POC antigen test on nasal samples, and the green line represents those identified by the reference NPS RT-PCR. Four different scenarios for RT-PCR result turnaround time are presented.



Limitations

Limitations of the study include its modest sample size, reflected in the 95% CIs reported with performance indicators. Further, the STANDARD Q Nasal and LumiraDx tests are among the best-in-class commercial POC antigen tests. Other tests with lower performance may increase the risk of missing infections against the benefit of identifying cases, to the extent that other strategies may be needed if PCR is unavailable. Lastly, future research should investigate implications of new variants on diagnostic performance across sample types.

Collaborators

For more information

Please see the full publication from this study:

> Zobrist S, Oliveira-Silva M, Vieira AM, et al. Screening for SARS-CoV-2 in close contacts of individuals with confirmed infection: performance and operational considerations. *medRxiv*. Preprint posted online January 28, 2022. https://doi.org/10.1101/2022.01.27.22269904.

For questions, please contact Dr. Gonzalo Domingo (PATH) or Dr. Dhélio Pereira (CEPEM).

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