Self-sampling for SARS-CoV-2 Detection in Children

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On January 18, 2020, the Centers for Disease Control and Prevention (CDC) reported the first confirmed case of COVID-19 in the US.1 Since then, in only 2.5 years, the global pandemic has resulted in 588 757 628 confirmed cases of COVID-19 and 6 433 794 deaths (as of August 8, 2022).2 While the world is (once again) gradually reopening, the lingering social and economic effects of the pandemic are clearly felt, with national lockdowns and school closures still ongoing in 23 countries. Furthermore, the World Health Organization (WHO) recently forecasted a new wave of COVID-19, predicted to peak in the autumn and winter months, suggesting the potential need to reinstate disruptive measures in the northern hemisphere.

Preparing for the future, the WHO released its autumn/winter strategy for COVID-19, emphasizing the central role of diagnostics in countering the pandemic. Specifically, the organization recommended that countries should strengthen “laboratory capacities to ensure reliable rapid diagnostic SARS-CoV-2 detection and tracking of variants, complemented by continued population use of rapid diagnostic testing; [integrate] population-based surveillance systems for influenza, SARS-CoV-2 and other respiratory viruses to monitor the spread and intensity of respiratory viruses; [and prioritize] contact tracing and quarantining based on WHO recommendations for individuals, high-risk settings and situations of concern.”3

While reliable innovative diagnostic tests to detect SARS-CoV-2 were rapidly developed in the past 2 years, sampling has remained a major limiting factor, especially in settings where large-scale testing of symptomatic and asymptomatic populations are needed. The need for dedicated health care workers (HCWs), fitted with personal protective equipment, some of which has to be discarded between patients, has hampered implementation of mass screening. Sampling is time consuming, expensive, and exposes the HCW to potential transmission from patients. To address this barrier, several studies in adults have evaluated the use of self-collected samples for SARS-CoV-2 molecular testing and have demonstrated 93% to 97% concordance rates with standard swabs obtained by HCWs.4-7 In this issue of JAMA, the study by Waggoner et al8 further expands this knowledge by showing that school-aged children are capable of reliable self-sampling using nasal swabs.

The authors enrolled children from kindergarten through eighth grade who were referred for SARS-CoV-2 testing due to symptoms compatible with COVID-19. The participants were shown a short instructional video demonstrating how to self-swab and were provided with an instructional pictorial handout after which they proceeded to perform a nasal self-swab, followed by sampling by an experienced HCW. No assistance was provided by the HCW or the parents. Samples were tested by real-time reverse transcriptase–polymerase chain reaction, targeting nucleocapsid 1, nucleocapsid 2, and ribonuclease P, an abundant human nuclear endonuclease that serves as an internal control.

Among a total of 196 children included in the final analysis, 87 (44.4%) were SARS-CoV-2 positive, with 97.8% concordance between sampling modalities, and 105 (53.6%) were SARS-CoV-2 negative, with 98.1% concordance ($\kappa = 0.96$). There were 4 cases of disagreement between the self-collected swab and the HCW-collected swab: 2 negative self-collected swabs with a positive HCW-obtained swab, and 2 opposite cases. Overall, across age groups, the cycle threshold (Ct) values among the SARS-CoV-2–positive participants were similar between sampling methods. In addition, the 4 discordant sample pairs had relatively high Ct values in the single positive sample, perhaps indicating that lower viral shedding results in reduced agreement between modalities. Nevertheless, because the direction of disagreement was mixed, this should not detract from the utility of the self-testing.

Moreover, even though children younger than 8 years were more likely to be scored by the observing HCW as requiring assistance or not having completed the sample collection correctly, the proportion of concordant samples was similar to that of children aged 8 years or older. This might indicate that only partial adherence with the self-swab instructions is needed and superficial sampling is adequate, or it could be because children who have difficulties self-swabbing are more likely to have difficulties with proper sampling by the HCW as well. Another possibility is that the children who had positive test results for SARS-CoV-2 in this sample were highly infectious, as evidenced by the mean Ct value of about 26.

The strengths of the study are the balance in enrollment across test results and age groups, the simple structured instructions, the policy of “no intervention” even when the children seemed to have difficulty performing the swab, and the use of standardized molecular testing, including a quality control. Indeed, only 1 participant was excluded from the analysis based on a negative ribonuclease P test.

The potential to conduct repeated population-based screening in pediatric educational settings, without the need for labor-intensive sampling that disrupts children’s routines, is an important step in breaking the chain of transmission, and might help keep schools operating in times of high SARS-CoV-2 activity.

The study, however, also has several limitations. First, participants were all symptomatic, and it is unknown what
the performance characteristics of self-sampling will be in asymptomatic children. This is a major concern because the most obvious benefit of self-sampling would be in settings of screening in schools or other congregate settings, such as camps, where most individuals, hopefully, will be asymptomatic. Second, the study was performed in July to August 2021, and in the subset of patients who were tested for spike mutations 85.7% were of the Delta variant. The current COVID-19 wave is being propelled by sublineages of the Omicron variant, notably BA.2 and BA.5, and it is uncertain whether this variant will influence test results. Third, as with any voluntary participation in a study that includes some discomfort, especially when children are involved, there is an inherent selection bias because only the more cooperative children are enrolled, whereas parents of children who are reluctant to be tested might decline. These also are the children who might not perform the testing as instructed. Fourth, even though children self-sampled without adult help, the sampling procedure was individually supervised. Screening of large populations will require unsupervised sampling that is potentially prone to manipulation of samples and lower adherence with instructions.\(^5\)

The concept of self-sampling has been evaluated in the past for numerous conditions including sexually transmitted diseases,\(^9\) nasopharyngeal bacterial carriage,\(^10\) and, more relevantly, several respiratory viral pathogens, including influenza, human metapneumovirus, respiratory syncytial virus, and adenovirus.\(^7,11-15\) In these adult studies, self-collected swabs from the anterior nares resulted in high concordance rates with HCW-obtained samples. Considering the epidemiologic predictions regarding the upcoming active influenza season, combined with continued circulation of SARS-CoV-2, it is extremely important to develop strategies of population screening to facilitate isolation, prevention of continued spread, and when needed allow early treatment. Although children currently only constitute about 14.4% of all COVID-19 cases in the US, they are a major source of community transmission and should be included in any screening strategy.\(^16\)

The study by Waggoner and colleagues\(^8\) in this issue of JAMA is a first step toward development of policies based on convenient school-based self-sampling. However, further validation in broader populations is needed before pediatric self-sampling can be implemented, including asymptomatic children and patients with the newer circulating SARS-CoV-2 variants. If the preliminary results of this study are replicated in other studies, this simple intervention could be applied in a variety of settings in the community for different respiratory pathogens, without specialized personnel.

ARTICLE INFORMATION

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