Feasibility and Specificity of BinaxNOW for Diagnosis and Surveillance of Infection with SARS-CoV-2 in Schoolchildren

UW-Madison Health Sciences IRB #2020-1521

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A. Background

The Coronavirus Disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, is a worldwide pandemic that has resulted in large scale quarantines in cities, states and countries throughout the world. SARS-CoV-2 is a respiratory virus that is most commonly spread via contact with infective respiratory droplets and aerosols produced by coughing, sneezing, talking, and singing. Daycare centers and schools are known to be locations with high burdens of viral respiratory tract infections associated with horizontal transmission of infection to the children, teachers and their attendants. The role which children in daycare centers and schools play in the transmission of COVID-19 to each other as well as their parents and day care workers is unknown. Furthermore, the most effective strategies to limit those infections and thereby maintain children and their teachers/daycare workers within their educational setting and their parents at their place of employment have not been studied.

Disparities in health outcomes. Disparities in health outcomes to COVID-19 in minority populations have become evident in the United States. The burden of disease, both morbidity and mortality, experienced by Hispanics and Blacks has far exceeded their proportion in the general population. The CDC and other groups report that there are more COVID-19 cases, hospitalizations, and deaths in areas where racial and ethnic minority groups live and that community strategies to slow the spread of COVID-19 may cause unintentional harm, such as lost wages, reduced access to services, and increased stress for some racial and ethnic minority groups

Role of School Children. In most early investigations, the source of family outbreaks has been the adult members of the household. However, schools/daycares were closed very early as a reflexive response to the pandemic in most locations. Accordingly, the question regarding children has been, in large part, whether they will be a source of infection for each

other, their parents, teachers and daycare workers, therefore exerting a multiplier effect on the proportions of the pandemic.

The two-fold importance of daycare and school attendance. The importance of the availability of school and daycare to the ability to re-open the economy cannot be overemphasized. A substantial portion of the front-line work force, including both health care personnel and other essential workers, have families with children of school or pre-school age. Furthermore, the contributions of school attendance to the overall well-being of the physical and mental health of children in addition to their nutrition, guidance, emotional support, socialization and education is universally recognized.

Current strategies for prevention of infection in schools. Current strategies for the prevention of infection both in and outside of schools have included physical distancing, use of face masks, frequent handwashing and self-exclusion at the sign/symptoms of even minor illness. One of the difficulties imposed by infection with SARS-CoV-2 has been the consistent demonstration that transmission of infection precedes the development of symptoms, thereby allowing the "silent" transmission of infection in most cases even before the onset of symptoms. In addition, many children infected by SARS-CoV-2 are completely asymptomatic but nevertheless very effectively transmit the virus. Therefore, the key to maintaining attendance at school and daycare is **rapid identification of both symptomatic and asymptomatic children, teachers and other school staff for exclusion.** Many respiratory infections in the coming respiratory season will not be caused by SARS-CoV-2 but rather by other common respiratory viruses. Therefore, prompt diagnostic testing will be the key to documenting that children with mild respiratory symptoms, usually not qualifying for exclusion from school, actually do NOT have SARS-CoV-2 but rather another more benign respiratory viral infection.

BinaxNOW Covid-19 Ag Card. The means to rapidly identify and exclude symptomatic and asymptomatic children, teachers and other school staff from the classroom is potentially available as a rapid, easy to perform, relatively inexpensive test called BinaxNOW Covid-19 Ag Card manufactured by Abbott. The Food and Drug Administration (FDA) has

granted emergency use authorization for this test. We are requesting a Non-Significant Risk determination from the IRB for its use in this study, which is going to be outside of the EUA's indications. It works with a nasal swab sample and a credit card sized reactive card to detect the nucleocapsid protein antigen from SARS-CoV-2 (using a lateral flow assay) and results are available in 15 minutes. The emergency use authorization is for use of the BinaxNow Covid-19 card for symptomatic adult patients within 7 days of the onset of their illness. There is very good reason to believe that this technology will be effective in creating “safe schools”, however, there are no data to prove that. The ‘cards’ have been reported to be reasonably sensitive (85 to 95% as sensitive as polymerase chain assays for the spike protein of the virus) but have not been tested in children or broadly in the US. Accordingly, we are proposing a **two-step** investigation to establish the effectiveness of a strategy built on the availability of both diagnostic testing of symptomatic individuals and screening twice weekly of asymptomatic children and teachers. In step 1, we will demonstrate the feasibility and specificity of using BinaxNOW in school children and their teachers. In step 2, we will demonstrate the effectiveness of this strategy in maximizing school/work attendance for children and families receiving this intervention compared to students and teachers for whom this intervention is not available.

Purpose and Research Goal

The overall purpose and research goal of this project is to understand how the virus SARS-CoV-2 is spread in the K-8 setting, decrease secondary cases of COVID-19, improve attendance and educational opportunities for children, teachers and other school staff, and decrease time away from work for parents (with threat of loss of employment and other benefits).

Inclusion Criteria:

- Children aged 5 - 15 years inclusive
- Currently attending school K-8 at one of the designated schools of the Madison Metropolitan School District
- Teachers and other school staff aged 20-65 years

Exclusion Criteria:

- Children < 5 years or $\geq$ 16 years
- Teachers and other school staff < 20 years or > 65 years

We hypothesize that prompt diagnostic testing for SARS-CoV-2 in symptomatic children and twice weekly surveillance of asymptomatic children (with appropriate exclusion of children with positive tests) will be effective as a strategy to achieve maximum attendance in school and minimal disruption of the associated workforce.

STEP 1: Determine feasibility of using BinaxNOW COVID19 cards for diagnosis and surveillance of infection with SARS-CoV-2 in teachers, other school staff, and school children.

The specific aims are to determine:

a. if it is feasible to obtain nasal samples to be used with the BinaxNOW COVID-19 for diagnosis of COVID-19 in children or teachers/other school staff with symptoms compatible with a diagnosis of COVID-19.
b. if it is feasible to obtain nasal samples twice weekly to be used with BinaxNOW COVID-19 for surveillance of infection with SARS-CoV-2.
c. The specificity of positive tests for SARS-CoV-2 obtained for diagnosis or surveillance compared to traditional PCR diagnostic testing.

STEP 2: Determine effectiveness of prompt diagnostic testing and twice weekly surveillance for SARS-CoV-2 among children and school faculty/staff to reduce the rate of positive cases (symptomatic) of COVID-19 in an elementary school setting resulting in an ultimate decrease in absenteeism for students and an increase in attendance for their parents at the workplace.

We propose to implement STEP 1 now as a pilot study and STEP 2 at a later date.

B. Methods for STEP 1.

240 students and 80 teachers/other school staff will be recruited from schools within the Madison Metropolitan School District. The schools will email families and teachers a letter explaining the study and inviting them to participate in a virtual information session which

includes a question answer opportunity. The virtual information sessions will describe the process of sample collection so that students and teachers know what to expect. If parents, teachers and other school staff are interested in enrolling in the study, they can contact the school at which time they will be asked if they agree to have study staff contact them. Research personnel will not directly contact parents, students, teachers or other school staff regarding initial recruitment for the study. All subjects will agree to the performance of nasal swabs samples to be used for diagnosis or screening. Samples will be obtained by research staff in the school setting. The Madison Metropolitan School District has obtained a CLIA waiver for collection of samples. When there is a positive test, a saliva sample will be collected for testing with a standard PCR method. The standard PCR samples will be processed at UW Clinical Laboratory.

All subjects will be followed for 8 weeks. Children and staff will not receive compensation for their participation in the study. Subjects are free to withdraw from the study at any time.

At the conclusion of this portion of the study, we will understand the feasibility and specificity of the testing procedures.

Data Collection:

We will collect the following data elements from subjects; name, address, date of birth, and gender.

Confidentiality

Electronic data will be stored in a password protected database on a password protected server. Subjects will receive a study ID. The key code linking the subject's name and study ID will be stored separately on the Department of Pediatrics password protected server and only available to research staff. Samples sent to the UW Clinical Laboratory will be labeled with the subject/study ID, date of birth and date of collection.

Reporting of test results

Research personnel who are on site at the schools will report positive results from the BinaxNOW test to the subjects. School nurses will then notify parents of positive results immediately by phone and offer information about available resources, next steps and respond to questions.

In accordance with the Wisconsin Department of Health infectious disease reporting requirements, research staff will notify the local health office immediately with all positive results. In addition to the immediate report, research staff will complete and submit a case report form within 24 hours of a positive result.

The standard PCR samples that are processed at UW Clinical Laboratory will be labeled with a subject ID, date of birth and date of collection. The UW Clinical Laboratory will report positive test results to research staff who will then notify the school nurse.