Assessing Testing Strategies for Safe Return to K-12 Schools in an Underserved Population

Short title: Safe Return to Schools

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TABLE OF CONTENTS

A. INTRODUCTION	**3**
B. BACKGROUND	**4**
C. STUDY DESIGN	**5**
D. STUDY PROCEDURES	**8**
E. STATISTICAL PLAN	**11**
F. STUDY MONITORING	**12**
G. REFERENCES	**13**
H. APPENDIX	**14**

A Introduction

African-American populations have been significantly and disproportionately impacted by the COVID-19 pandemic, experiencing a higher rate of cases, increased mortality, and deeper economic hardship.[1,2] Children and adolescents in these groups have been less likely to be offered an opportunity to attend in-person schooling.[3] As a result, the indirect impacts of the pandemic on children of color also include a greater likelihood of academic decline and significant social consequences, including food insecurity, missed recognition of child abuse and neglect, and increase in depression, anxiety, and suicide.[4,5] Public apprehension regarding return to in-person school is based on the concern that school-based transmission of COVID-19 will further spread the virus to high-risk and vulnerable individuals in students' homes and in the community, worsening the toll of death and suffering.

However, the available literature indicates that with proper COVID-19 mitigation strategies – masking, distancing, hand hygiene – school-based transmission of SARS-CoV-2 is low regardless of the community rate of disease.[6,7] The US Centers for Disease Control and Prevention (CDC) state that **"**screening testing" is "particularly valuable" as an additional mitigation strategy in areas with moderate, substantial, and high community transmission (currently most of the US).[8] Moreover, current CDC recommendations for types of instruction (virtual, hybrid, or fully in-person) are based in part on whether screening testing can be offered. For most middle and high schools in underserved communities, where resources to perform screening testing are unavailable, CDC recommends all-virtual schooling. However, no study has evaluated the impact of screening testing in schools as another mechanism to detect and prevent school-based COVID-19 transmission.

Since the beginning of the pandemic, Washington University in St. Louis (WUSTL) has worked closely with the St. Louis community, including many school districts and organizations that support underserved populations.[9] The PI, Dr. Newland, has met regularly with school superintendents throughout the region, including those in underserved school districts, since July 2020 to provide consultation on best practices for conducting in-person schooling. Additionally, he is co-PI on a current RADx-UP grant evaluating messaging strategies regarding performing weekly testing in schools dedicated to children with intellectual and developmental disability. Since November 23, 2020, we have performed approximately 4500 SARS-CoV-2 PCR tests in these staff and students. Furthermore, our team has collaborated with CDC to rigorously assess school-based COVID-19 transmission; we have performed another 500 tests in symptomatic students and asymptomatic contacts in that study (pilot data to be published in *MMWR* March 22, 2021). Finally, the faculty and staff of WUSTL Brown School of Social Work and Public Health have forged strong partnerships with community organizations to learn about barriers to SARS-CoV-2 testing, attending in-person school, and vaccination. These community partners have been essential in providing services, messaging, and support to our underserved communities. In summary, the research team and community partners have the experience and are well-positioned to implement the proposed work quickly and complete it successfully.

In this proposal, we will test the hypothesis that frequent screening testing will provide additional benefit, beyond current school-based mitigation strategies, to prevent SARS-CoV-2 transmission. We will complete a cluster randomized trial to compare the incidence of school-based SARS-CoV-2 transmission between weekly surveillance testing of students and school

staff versus testing only symptomatic students and staff. In this proposal, 12 middle and high schools from five predominantly African-American school districts in the St. Louis metropolitan area will be cluster randomized to screening testing plus symptomatic testing versus symptomatic testing alone. We will perform qualitative listening sessions and interviews with members of the school community including parents, teachers, administrators, and students to understand the facilitators and barriers to testing, the concerns regarding in-person school, and potential issues involving vaccine hesitancy evident in all populations and groups.

This study will provide critically needed, rigorous data to inform the utility of screening testing in schools and if it is important in aiding schools in the African-American community to return to in-person instruction. Additionally, the measurements of school-based transmission rates will help participating schools in the African-American community assess the impact of their mitigation strategies, demonstrate potential risk points for transmission that can be targeted for further intervention, and reassure the community on the safety of their schools. Finally, the study results will aid participating researchers, school districts and communities in understanding how to mitigate concerns about in-person schooling and the reliability of the mitigation strategies (with or without screening testing) in preventing COVID-19 transmission.

B Background

Investigators at WUSTL School of Medicine recognized early in the pandemic that establishing rapid and widespread SARS-CoV-2 testing would be essential to safe resumption of social, educational, and commercial activity. Therefore, the McDonnell Genome Institute (GTAC@MGI) deployed its expertise in high-throughput sequencing capabilities, enhanced technology development, and large-scale data processing to develop a saliva-based SARS-CoV-2 diagnostic test [Washington University SARS-CoV-2 Ultrasensitive-High-Throughput-Saliva assay (WUSC2-UHT-S)]. To address the limited supply of swabs and reagents needed for RNA isolation and the need for safe and acceptable collection method for use in children, we developed methods to detect virus directly from saliva. The non-invasive nature of saliva collection also facilitates its use in community settings (such as schools), because it does not require special training and minimizes potential aerosolization. Our preliminary data from the CDC project assessing K-12 transmission has noted 20% of participants would not have participated if a nasal specimen was required. This percentage would likely be higher if asked of individuals considering weekly screening testing. Because the WUSC2-UHT-S test methodology includes an inhibitor of viral reverse transcriptase (that might otherwise prevent detection of RNA genomes),[10,11] this innovative diagnostic allows viral detection directly from saliva without the need for RNA extraction.[12] In addition, saliva samples can remain for 5 days at ambient temperature without impacting assay sensitivity. This dramatically increases flexibility in the logistics of transport, storage, and handling of samples.

The WUSC2-UHT-S test is processed and run at the Cortex CAP/CLIA-approved laboratory on the WUSM campus with a turn-around time of <3 hours. The test has EUA status from the FDA and in the application had 100% positive and 100% negative agreement with gold-standard NP swab tests during validation. Application of microfluidics and adaptation of our existing sample-handling robotics has resulted in a capacity to test 20,000-30,000 samples per week. Through an industry partnership, the technology has been implemented

commercially (Advanta Dx SARS-CoV-2 RT-PCR Assay) and is available in other labs nationally.

As of June 1, 2022, the Washington University lab will be closed. In order to continue testing we have partnered with ShieldT3 and will use their saliva-based FDA approved (EUA#: EUA202555) covidSHIELD test. All coordinators and staff supervising the testing will complete the training module provided by ShieldT3.

We will use a standardized sample collection kit provided by Shield T3 project. Kits contain barcoded sample collection tube, CLIA/CAP-compliant label, and a zip-top biohazard bag. 500 µl of saliva will be collected from each subject under the supervision of a trained individual adhering to CAP/CLIA guidelines. For students unable to direct saliva into the tube because of poor motor control, we may use a sponge applicator or a pipette to obtain the saliva.

Barcode scanning and data entry into a HIPAA-compatible Research Electronic Data Capture (REDCap) database will occur at time of collection and will include all information needed for eventual National / County-level reporting and contact tracing (demographics, communal housing status, pregnancy status, etc.) (Appendix 4-6). Labeled samples are transferred to the zip-top bag which is externally sterilized with an alcohol wipe, then will be shipped by FedEx to the ShieldT3 lab in Kentucky.

The overall turnaround time (sample collection at a school, REDCap data entry to enable generation of the necessary order, and testing time) will be 24 to 48 hours. We have established the necessary reporting elements and mechanisms to send results to the State of Missouri, as well as a system to deliver test results by email to participants if they elect. All individuals with a positive test will be called by Dr. Newland (PI) or a member of the study team who are ideally suited to answer questions and provide additional information regarding treatment and appropriate isolation and quarantining for participants and their families.

C Study Design

Community partners

The St. Louis area school districts of University City, Normandy, Ferguson-Florissant, Pattonville, and Jennings will be our key partners throughout this project. These districts will collaborate with us by providing specific areas for testing in each participating school and by facilitating our engagement with their school communities. Additionally, they will provide input on the best messaging and communication strategies for study participation, barriers to testing, and how best to communicate test results and follow-up. The research team will conduct at least a monthly meeting with the superintendents to hear their concerns and feedback to provide them an update on the study progress.

The SPOT and CareSTL operate two school-based health clinics that will help us perform symptomatic testing for school staff, students, and families. People's Health Clinic has several locations within the boundaries of the study school districts and will aid in collecting additional saliva-based tests potentially using their mobile testing van to aid the screening testing program. These clinics will stock the saliva testing kits and will collaborate with the study team to properly obtain the tests and the required testing information.

Several community organizations are engaged with the study team who will be critical to ensuring the study design and implementation and the utilization of findings are responsive

and meaningful for the communities we are serving in the study. All three organizations (Beyond Housing, Better Family Life, and WEPOWER) are established and trusted leaders in their communities and will inform recommendations and improvements to the communication and application of testing and vaccination. They also provide important context and perspective to the design of the qualitative activities, assist with participant recruitment, co-facilitate some of the listening sessions, and actively engage in the interpretation and contextualization of the findings.

Community Advisory Board

Discussions have already occurred with the superintendents of the school districts regarding the importance of implementing SARS-CoV-2 testing immediately. University City has previously worked with our research team in establishing a drive-thru central testing site for families at their district office. Jennings High School has a school-based clinic, called the Supporting Positive Opportunities with Teens (SPOT) Youth Center, which will be able to start testing immediately. CareSTL, a federally qualified health center, also operates a school health clinic and other clinics in these school districts. The Betty Jean Kerr People's Health Center (People's Health Clinic) will also help in collecting the saliva-based test during the project.

The CAB will be comprised of members from each school district's parent-teacher organization, school administrators, teacher representatives from the appropriate unions and schools, and representatives from the community partners assisting with the project. Current community partners include Better Family Life, Beyond Housing, WEPOWER, People's Health Clinic, CareSTL and The SPOT Clinic (Table 1).

Table 1: Community Partner Overview	
Better Family Life	Provides comprehensive, holistic services & supports to build strong communities & families www.betterfamilylife.org
Beyond Housing	Dedicated to creating, more equitable communities through community development www.beyondhousing.org
WEPOWER	Dedicated to activating community power to re-redesign education, economic, health, & justice systems to be just and equitable for all Wepowerstl.org
People's Health Center	An FQHC that Provides quality health care to metro St. Louis- phcenters.org
The SPOT	Provides comprehensive health and social services to youth- thespot.wustl.edu
CareSTL Health	An FQHC that provides comprehensive health care to the St. Louis- carestlhealth.org

In the initial CAB meeting, the best locations to perform symptomatic testing, both in the schools and in participating health centers was determined. Our CAB will be essential in addressing barriers to testing, follow-up care, and the importance of confidentiality. We will determine what information and resources are needed for individuals who test positive and address any concerns regarding confidentiality for these individuals. The CAB will meet at least monthly during the implementation of testing and more frequently if needed. Our team acknowledges that the success of this project will rely on these community partnerships and our maintenance of trust with these school communities. All of our community partners serve the families in the study school districts. In order to maintain the trust of the schools and the community, the research team will present study team updates to the CAB and superintendents at least monthly.

Description of milestones and timeline completion

The overall proposed project activities and timeline are shown in Table 2. Specifically, in the first-month post-award, the key dependencies include IRB approval, an initial meeting with the newly formed community advisory board (CAB), and development of the REDCap database structure required for saliva testing. Within 3 months, the key dependencies include schools returning to in-person learning and consenting of students and staff in the selected schools for screening testing. An important dependency for testing throughout the duration of this project will be the community case rate of COVID-19. Since the epidemiology and seasonality of this virus are still being defined, the volume of symptomatic testing could vary.

Table 2. Project Timeline (4/1/2021-3/31/2023)	**Year 1**				**Year 2**			
Milestones/Project Activities	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
Obtain IRB approval	●							
Submit to Clinicaltrials.gov	●							
Implement data coordination, collaboration, harmonization with RADx-UP CDCC	●	●	●	●	●	●	●	●
Convene Community Advisory Board meetings	●	●	●	●	●	●	●	●
Conduct monthly Superintendent meetings	●	●	●	●	●	●	●	●
Conduct symptomatic testing for all 12 schools	●	●	●					
Test & deliver messages for increasing uptake of SARS-CoV-2 testing	●							
Consent students and staff to receive surveillance testing	●							
Conduct surveillance testing in select schools	●	●	●	●				
Assess school-based transmission with use of testing	●	●	●	●	●			
Collect weekly number of school cases, contacts, and in-person enrollment	●	●	●	●				
Analyze testing data					●	●		
Conduct listening sessions & Interviews	●			●			●	
Conduct qualitative analysis		●			●			●
Share data with Duke coordinating center	●	●	●	●	●	●	●	●
Disseminate results			●			●		●

In this proposal, quantifiable milestones will be established in regards to testing. We propose that in the first 3 months post award (Q1), we will perform approximately 3,000 tests. In Q2 and Q3, we estimate approximately 5,000 and 8,000 tests will be performed. In Q4, forecasting a potential winter surge of COVID-19, we estimate a total of 10,000 tests. We estimate that approximately 50%-60% of the testing will occur in adult school staff members based on our current RADx-UP experience. Since we are primarily testing in middle and high schools, approximately 30%-40% of the tests will be done in students between the ages of 11 and 18 years of age.

We have established a process with our testing lab, informatics professionals, and study team to reliably obtain tests; however, trust in the test and the importance of testing will be important to maximize participation. We will work closely with our CAB, community partners, and messaging experts to mitigate this risk and maximize participation. Finally, we have identified additional schools to participate if one or more of the selected schools remain virtual, but could also include these additional schools if testing volume in the core schools proves to be lower than expected.

Study Setting and Populations.

The following five school districts in St. Louis County will be included: University City, Ferguson-Florissant, Normandy, Pattonville, and Jennings. Individuals who are students, staff, and household members of students and staff are eligible to participate in the various parts of the study. Sixteen middle and high schools from these school districts will participate. According to St. Louis County and regional hospital data, these districts are located in areas that have been most heavily impacted by COVID-19, especially in the early months of the pandemic. Additionally, all schools in this study receive Title 1 funding and have 100% of their students receiving free and reduced lunch. The percent of in-person attendance when available ranges from 20%-42%, and 18%-42% of families in these districts live below the poverty line.

D Study Procedures

D1 Testing Study Procedures

Recruitment and Consent

All research activities will occur among the students, parents/guardians, staff (teachers, aides, nurses, administrators) and household members of our participating school districts. All students (5-21 years old), school staff, and their household members (all ages) are eligible for inclusion in the study. Individuals will be excluded if they (or their parents/LAR) do not provide consent or are unable to provide saliva for testing.

Screening Testing Consent

Prior to starting screening testing, students, staff, and their household members will be consented or assented in-person (group or individual discussion), by phone, or by zoom. Middle and high school students under the age of 18 will provide assent (if cognitively able) for participation after we have obtained consent from their parent/LAR by phone, zoom or in person. Since household members/parents/LARs are not present in the school, they may receive a copy of the consent document prior to the consent discussion.

Symptomatic/Exposure Testing Consent

For symptomatic and/or exposure testing, we will obtain verbal consent and assent (when appropriate) prior to testing. A copy of the consent information will be provided. We will also have individuals sign an email communication form and note their email preferences. The email communication form might be in person or electronic since parents/LARs are not present at the school.

If a student is 18 to 21 years of age and is not cognitively able to provide consent/assent, consent will be obtained from the legally authorized representative. Children 8-17 years of age who are developmentally able will provide assent. Children age 5-7 will not be providing

assent due to their age and development. The consenting/assenting process will be done virtually, in person or by phone.

Contact/Data Elements Survey Consent

Interviews might be eligible for a contact interview if they are a known contact in the school. Additionally, all parents are eligible for the data elements survey regardless of type of testing (screening vs symptomatic/exposure). Prior to completing contact interviews, verbal consent and assent will be obtained from students, staff, and household members as appropriate. Prior to completing the data elements survey, consent will be obtained from the individual completing the survey. Assent will not be obtained for the data elements survey due to lack of student participation in the survey and nature of the questions. As appropriate, a copy of the consent and assent information will be emailed.

Strategy for Sample Collection and Processing.

At the testing site(s), 500 uls of saliva will be collected from each subject under the supervision of a trained research team member. For those in surveillance testing, participants will also have the option of providing the sample at home and bringing it to the school. These individuals might also provide their sample to a family member to bring to the school for drop off. We will provide what is needed to obtain the sample at home. If a participant becomes symptomatic while at school, a study team member may be able to obtain additional samples from those individuals in addition to their weekly testing. If a study team member is not available at the school, these indivduals will be referred to outside testing facility.

Symptomatic and/or Exposure Testing: All schools participating in the study will have access to ShieldT3 saliva SARS-CoV-2 PCR testing for students, staff, family members, and/or household members who exhibit symptoms of COVID-19 or have a known exposure. This testing will be provided for both virtual and in-person staff and students. Test samples will be collected in a designated area in each school building for those individuals attending or working in the in-person environment.. For those in virtual learning, or those who are family members and/or household members a drive-up testing area will be available at each site. In situations where transportation is limited, home visits will be offered.

Contact/Data Elements Survey:

Case/Contact Interviews

If any of these individuals or other students/staff present in the school setting are positive for COVID-19, contact tracing will be performed by their school districts per local/state guidance. As part of their contact tracing, individuals will be informed that that they may be contacted by a member of the study team to see if they would like to provide additional information via participating in our research. Our research team will contact any cases and their known contacts in the school setting, as provided by the schools. After consent and assent (for those 8-17) is obtained, we will ask them the types of questions listed below. A separate case interview will also be conducted for any known contacts that have a subsequent positive COVID test.

Data Elements Survey

Those who have signed a consent for screening testing will be asked these data elements. Additionally, anyone who has symptomatic testing performed for the purpose of this study and/or was identified during contact tracing, will be asked to provide additional information via participating in our research. Once consent [consent information sheet 14Apr2021] is obtained via phone, Zoom, email or in person, we will ask them questions. Individuals who have agreed to referral and indicate certain needs or resource limitations will be referred to community partners. This will be done through information being provided to the community partner for follow up with the individual.

The questions in both of these include those related to: housing, employment, health insurance, languages spoken in the home, family income, work PPE and distancing, vaccinations, reasons for getting/not getting a COVID-19 vaccine, alcohol and tobacco/nicotine use, previous COVID-19 testing, accessibility to testing, perceived accuracy of testing, perceived benefits of testing, perceived risks of testing, intention to be testing, food insecurity, trust of sources to provide correct information about COVID-19, height, weight, health status, teacher or student, grade taught/ grade student is in, type of learning, classroom setting, sports/ band/choir/drama/clubs participation, before or after school program, percent of time spent closer than 6 feet to others, percent of time mask is worn, percent of time able to social distance, access to handwashing, COVID symptoms, quarantine status/length, COVID test results, type of test,last day in person school, mitigation strategies by the individual/case at school, exposures outside school setting in the 14 days prior to exposure (contact) or 2 days prior to symptom onset (COVID sample if asymptomatic) (case) up until isolation, mask/social distance used at outside school settings. To reduce the length of the interview, these individuals will also be asked to complete some questions via RedCap.

Screening Testing: Schools will be randomized to perform or not perform weekly saliva-based screening testing for students and staff in addition to symptomatic testing. Eight of the sixteen schools will be randomized to screening testing.

Students, staff, and household members attending in-person school will be offered weekly screening testing if they (or their household member) are attending a school randomized to this strategy. Prior to the start of screening testing, participants will provide informed consent/assent and demographic information. The saliva-based testing method will allow for staff and students to obtain the sample at home or school, then give it to school personnel; study team members will label and transport the specimens for testing to the WUSTL laboratory. Weekly screening testing will be available whenever in-person school is provided for schools randomized to this strategy, including during summer sessions.

Follow-up Protocols: Testing results will be available within 24 to 72 hours. All students, staff, and household members with positive results will be notified by Dr. Newland and/or a member of the study team and information regarding appropriate isolation and quarantining for contacts will be provided to comply with prevailing National/County health department recommendations. Additional financial and social services needed for the student and family due to isolation and/or quarantine procedures may be coordinated with the school and community partners. Finally, all positive individuals may have a 3-week phone call follow-up to inquire about the outcome of their illness including the need to seek medical attention and/or be hospitalized. For those in the contact arm, there might be additional questions if the

individual tests positive related to: activities, behaviors, and potential school based exposures.

Assessment of School Mitigation Strategies: Ascertaining the mitigation practices in place for each school is essential for evaluating the impact of additional testing on school transmission. A school-based mitigation strategy survey (Appendix 1), developed in conjunction with the CDC and utilized in prior school-based investigations, may be completed by each school at the beginning of the project. Questions in this survey will include: method of instruction (e.g., hybrid, type of hybrid, fully in-person) and date implemented, masking recommendations and perceived compliance, distancing in classrooms, use of physical barriers (e.g., Plexiglas), location and processes for eating lunch, and mitigation strategies used in extracurricular activities (e.g., sports, choir, band). Schools will also be asked about their quarantine rates and new school based cases/contacts on a weekly basis. This will help understand the rates of transmission in the schools.

Assessment of School-based Transmission: The primary outcome for this study will be the average of the secondary attack rate of school-based transmission per case at each school. For example, if a case has 10 contacts and 2 become infected, the secondary attack rate for that case would be 20%.

School-based transmission will be determined by two methods. First, all close contacts of an infectious case in the school, identified through contact tracing by school staff and administrators, will be approached to participate in the study (as described above). Those electing to participate will undergo a contact interview (Appendix 2) to understand their behaviors and potential other COVID-19 exposures. Furthermore, the school contact tracer will complete a survey on the relationship of the case to each contact that provides information on the location of the exposure (e.g., classroom, lunch, extracurricular activity), distance between case and contact, use of barriers, masking adherence, and total amount of time the contact was exposed to the case (Appendix 3). The contacts will be offered testing 5-7 days after a school exposure. All contacts testing positive will undergo an independent review by five study team members using the information obtained from the case interview, contact interview, and contact tracing interview to determine whether a school-based transmission has occurred. These transmission events will be classified into the following categories with standardized definitions that were developed in conjunction with the CDC: probable, possible, unlikely, and unable to determine.

The second method to evaluate school-based transmission will be to collect weekly data from the schools, as participation in the above individual assessments is unlikely to reach 100%. The additional data to be collected will include total number of new staff and student cases, total number of new contacts, and number of school-based contacts that become new cases during their quarantine period. The secondary transmission rate will be calculated based on the number of positive school-based contacts per positive case. This method will provide the most conservative/greatest estimate of school-based transmission without knowledge of an individual's exposure to a potential household or community case.

While schools have continued to operate safely even during the highest community COVID-19 case rates, new surges in cases could result in some schools within participating districts ceasing to offer an in-person option. If most schools in our proposal forgo an in-person option, we will continue to offer testing through our community partners to the entire school community in these districts. Testing strategies will be discussed with our school partners to determine if, for example, providing screening testing for all schools would aid in returning to

in-person instruction. Research questions related to school-based transmission could then be addressed within these schools in the context of frequent screening testing. If one district elects not to offer in-person instruction, we can leverage one of the many existing collaborations we have built during the pandemic with superintendents and other community leaders, to add additional school districts comprised of underserved population. One such school district (Pattonville), in which we are currently conducting a school-based transmission study in collaboration with CDC, has agreed to participate in the present study if other participating schools are not in-person when this project begins (see letter of support). As we have extensive experience already performing surveillance testing in St. Louis schools with our current RADx-UP project, adding additional schools if necessary will not hinder this proposal. Second, for schools that remain virtual we can continue to provide symptomatic testing for the school community.

D2 Evaluation/Messaging Study Procedures Timepoint 1

A. Timepoint 1

Recruitment and Consent

Enrollment/Consent Process: Focus Groups / Listening Sessions:

The participating school districts will share project description through multiple methods (e.g., email, electronic platforms, meetings) with parents/caregivers and school staff. One of the methods will be to share project description handout. [Newland flyer 01Apr2021] Evaluation Center and community partners will recruit participants via phone call [attachment: 02 Recruitment Phone Script 16Jun2021].

Individuals interested in participating in discussion sessions will contact the research team to enroll or complete the Qualtrics survey displayed in recruitment flyer. [attachment: RecruitmentFlyer 16Jun2021 -- Note: there is a placeholder here to insert the respective stakeholder group and school district name (there will be 15 separate flyers)]. [attachment: 03 LSSignupSurvey 16Jun2021].

Within approximately 1-2 business days after initial contact the research team will follow-up with a phone call [attachment: DSInfoPhoneScript 09Apr2021]. If agree to participate, research team will follow up with discussion session information email, text message, and/or phone call. [DSConfirmation 09Apr2021 and DSDemographicForm 09Apr2021. Reminders will be sent between 2-7 days prior to the discussion session date via email, text message and/or phone call.

Participants that attend discussion sessions will provide verbal consent at the beginning of the session.

Discussion sessions will be conducted virtually (via Zoom), over a phone call, or in person with approximately 1-15 participants. Sessions will be led by at least one facilitator and at least one note taker. Facilitators will use a guide to assist with facilitating the discussion session. [Attachment: DSGuide 09Apr2021]

Enrollment/Consent Process - Qualitative Overview: Administrator Interviews

The Evaluation Center will host listening sessions with both district-level leadersip (superintendents and assistant superintendents), as well as school-level leadership (principals and assistant principals). The Evaluation Center project team members will share project

description and recruitment of school administrators via email [Attachments:03 Admin Recruitment Email; 04 Principals Recruitment Email].

District-level individuals interested in participating in a discussion will complete a Doodle poll to identify a time that works for the group. School-level individuals interested in participating in a discussion will fill out the signup link provided via a recruitment email sent by the Evaluation Center team [Attachment: 05 Principal Qualtrics]. Within approximately 3 business days of contacting research team, interested individuals will be emailed a confirmation of their schedule interview time, along with the following: Emailed consent cover page [attachment: 01 Listening Session Cover Page] and emailed consent information sheet [attachment: 02 Listening Session Consent Form]. They might receive a phone call or text confirmation of the interview time as well.

Reminders will be sent 1 day prior to the interview via email, text message, and/or phone by a member of the Evaluation Center team. Interview participants will provide verbal consent at the beginning of the session. Interviews will be conducted virtually via Zoom or phone depending on interviewee preference. Interviews will be led by one facilitator and one note taker.

Listening Session Questions and Objectives

These interviews and group sessions will occur amongst students, staff, and household members in all five school districts identified for the project. The overall purpose is to understand if frequent screening testing will provide additional benefit, beyond current school-based mitigation strategies, to prevent SARS-CoV-2 transmission in schools. Individuals will be asked to give their insight to understand the social, behavioral, and ethical factors driving testing and in-person school participation. They will also be asked about experiences returning to school and during COVID. The research team will also ask about the facilitators and barriers to SARS-CoV-2 testing, attending in-person school, and vaccination. The sessions will be recorded and the recordings will be transcribed.

Listening Session Objectives

1. To understand what resources and supports superintendents and principals have needed throughout the return to in-person learning
2. To understand from the perspective of a school leader the successes and challenges their district/school has experienced throughout the return to in-person learning Understand the potential risks of COVID-19 for teaching staff (teachers and teaching assistants), nurses and students at district when going to school (in-person)
3. Identify what additional COVID-19 information district and school leadership would like to help address concerns about in-person school participation
4. To understand the facilitators and barriers to testing, attending in-person school, and vaccination
5. To understand the social, behavioral, and ethical factors driving decision-making about in-person school participation.

1.4.22 The pre-message interviews and focus groups have been completed as outlined above. The first round of messages have been developed to increase communications within the schools. This is targeted at increasing participation in testing.

B. Timepoint 2

Recruitment and Consent

Enrollment/Consent Process: Focus Groups / Listening Sessions:

The participating school districts will share project description through multiple methods (e.g., email, social media, electronic platforms, meetings) with students, parents/caregivers and school staff. One of the methods will be to share a listening session recruitment flyer. [attachment:01 Recruitment Flyer Mar22] Evaluation Center and community partners will share a recruitment flyer through multiple methods (e.g., email, social media, PeachJar, meetings) and will also recruit participants via phone call [attachment: 02 Recruitment Phone Script Mar22].

Individuals interested in participating in discussion sessions will contact the research team to enroll or complete the Qualtrics survey displayed in recruitment flyer. [attachment: 03 LSSignupSurvey Mar2021].

Within approximately 1-2 business days after initial contact the research team will follow-up with a confirmation email, including a project overview flyer, consent documents based on age group, and a link to a demographics survey [attachments: 04 LSConfirmationEmail Mar22, 05 DemographicsSurvey Mar22, 06 ConsentForms Students Mar22, 07 ConsentForms TeachersParents Mar22, 08 ProjectOverview Mar22]. Please note: the Project Overview includes a QR code, which directs interested participants to a schedule of available COVID-19 testing [attachment: 09 QRLandingPage Mar22]. Reminders will be sent one day and one hour prior to the listening session date via email, text message and/or phone call [attachment: 10 SessionReminder Mar22].

Participants who are 18 years and over that attend listening sessions will provide verbal consent at the beginning of the session. Research team members will obtain parent/guardian consent for student participants who are under 18 years old prior to the session.

Discussion sessions will be conducted virtually (via Zoom), over a phone call, or in person with approximately 1-15 participants. Sessions will be led by at least one facilitator and at least one note taker. Facilitators will use a guide to assist with facilitating the discussion session. All sessions will be recorded and subsequently transcribed. See below for listening session objectives and topics to be covered.

Enrollment/Consent Process - Qualitative Overview: Administrator Interviews

The Evaluation Center will host listening sessions with both district-level leadersip (superintendents and assistant superintendents), as well as school-level leadership (principals and assistant principals). The Evaluation Center project team members will share project description and recruitment of school administrators via email [Attachments:03 Admin Recruitment Email; 04 Principals Recruitment Email].

District-level individuals interested in participating in a discussion will complete a Doodle poll to identify a time that works for the group. School-level individuals interested in participating in a discussion will fill out the signup link provided via a recruitment email sent by the Evaluation Center team [Attachment: 05 Principal Qualtrics]. Within approximately 3 business days of contacting research team, interested individuals will be emailed a confirmation of their schedule interview time, along with the following: Emailed consent cover page [attachment: 01 Listening Session Cover Page] and emailed consent information sheet [attachment: 02 Listening Session Consent Form]. They might receive a phone call or text confirmation of the interview time as well.

Reminders will be sent 1 day prior to the interview via email, text message, and/or phone by a member of the Evaluation Center team. Interview participants will provide verbal consent at the beginning of the session. Interviews will be conducted virtually via Zoom or phone depending on interviewee preference. Interviews will be led by one facilitator and one note taker.

Listening Session Questions and Objectives

These interviews and group sessions will occur amongst students, staff, and household members in all five school districts identified for the project. The overall purpose is to understand if frequent screening testing will provide additional benefit, beyond current school-based mitigation strategies, to prevent SARS-CoV-2 transmission in schools. Individuals will be asked to give their insight to understand the social, behavioral, and ethical factors driving testing and in-person school participation. They will also be asked about experiences returning to school and during COVID. The research team will also ask about the facilitators and barriers to SARS-CoV-2 testing, attending in-person school, and vaccination. The sessions will be recorded and the recordings will be transcribed.

Listening Session Objectives

1. Understand the perceived risks of COVID-19 for staff and students while being at school since T1.
2. Understand what role, if any, testing and vaccination plays in mitigating perceived risk.
3. Identify information and resources that are needed to keep students and staff in school.
4. Understand the social, behavioral, and ethical facilitators and barriers to testing, attending in-person school, and vaccination in the school community.

C. Empowerment (CDE) listening sessions:

Sessions will be conducted with school parents/caregivers and school staff, community partner staff, and residents of St. Louis City and St. Louis County. These sessions will occur either on zoom or in person. Individuals will be asked questions about the common data elements in a semi-structured interview fashion. They will be asked questions about their thoughts on the CDEs, which questions they would like asked, and how the team can be better informed regarding the data collection process and resulting information. Individuals will read a consent information sheet prior to participating. These sessions will be audio-recorded for transcription and data analysis. Prior to the sessions participants will be sent a brief demographic form to complete.

D. Implementation Evaluation

Anyone who has participated in either/both forms of testing, as well as individuals in the school who did not participate in the study, will be asked to complete a survey and participate in a focus group evaluating the study implementation. The surveys will be distributed over REDCap with a consent information sheet to read before completing. Following completion of the survey participadnts will be contacted by phone to schedule participation in a focus group or interview. A phone, text, or email reminder will be sent for focus groups and interviews in advance of the scheduled time. Individuals will read a consent information sheet prior to participating in the focus groups, which will occur over zoom or in person. These sessions will be audio-recorded for transcription and data analysis.

Individuals who aided in the implementation of the testing protocol, such as research team members or community partners, will asked to participate in a discussion session. A phone, text, or email reminder will be sent for focus groups and interviews in advance of the scheduled time. Individuals in this group will not be asked to complete a survey prior to the discussion session. Participants that attend discussion sessions will review a consent information sheet at the beginning of the session

before participating. They will be given time to review the information and ask questions. Discussion sessions will be conducted virtually (via Zoom) or in person. These sessions will be audio-recorded for transcription and data analysis.

E Statistical Plan

Power calculation: A cluster randomized trial (CRT) will be conducted at 12 schools that provide symptomatic SARS-CoV-2 testing to students and staff. Schools will be randomized 1:1 to either screening testing plus symptomatic testing, or symptomatic testing only. All participants including students and staff will receive the same assignment within a given school. The primary outcome is transmission rate, defined as the ratio of the number of contacts testing positive for SARS-CoV-2 to total number of contacts for each school-based case. We hypothesize that schools performing screening testing will have lower transmission rates than routine symptomatic testing. We expect that transmission rates with screening testing or routine symptomatic testing will be 2% and 8%, respectively. With the assumptions that the intracluster correlation coefficient (ICC) is 0.02 and the standard deviation of transmission rate is 0.22, 6 schools in each arm with an average of 117 participants per school will achieve 80% power to detect a difference in transmission rates between the two study arms using a two-sided t-test at a significance level of 0.05 (Table 3). PASS 15.0 was used to conduct this power analysis.

Table 3. Sample Size

ICC	Standard deviation	# of participant per school
0.01	0.25	83
	0.30	188
	0.33	376
	0.35	803
0.02	0.22	117
	0.23	164
	0.24	252
	0.25	486
0.03	0.20	221
	0.21	806

Analysis plan: The generalized estimating equation (GEE) model with appropriate link function (e.g., identity for primary outcome) will be used to analyze the CRT data, in which the correlation among participants within each school needs to be considered. The autoregressive of first order as a working correlation structure will be used, and participants with missing values will be excluded from the GEE analysis. The GEE model includes the group indicator and other potential factors, including: race/ethnicity, insurance status, age, gender, underlying diagnoses, masking, distancing, ventilation, location of transmission. Least square means for the primary outcome per group will be estimated, and the standard errors will be calculated with the GEE sandwich method when accounting for within-school correlation. All analyses will be conducted using SAS (SAS Institute, Cary, NC) at the two-sided significance level of 0.05.

Data Management.

All testing data are maintained in a secure, password-protected REDCap database. Information collected on paper forms is stored in locked filing cabinets on a restricted-access floor at WUSM. Prior to undergoing testing, participants will complete a HIPAA authorization form and/or informed consent to allow SARS-CoV-2 testing data to be shared with the State of Missouri. All participants are assigned an ID number, and testing information is kept separate from the demographic data. Subjects who test positive are contacted by phone to

be given their results. This information will be shared only with the participant unless an informed consent is signed that will allow sharing of their data with the RADx-UP Coordination and Data Collection Center. For students and staff who complete informed consent, their positive results will be shared with the relevant school, after the individual has been notified and provides verbal re-confirmation of their permission to share that information.

Data are stored using HIPAA-compliant encryption to comply with all local, state, and national regulations for health-related data. Consent will be obtained from participants for future use of biospecimens (saliva), and these biospecimens will be stored in a -80°C freezer. The consent form will allow participants to opt-out of having their saliva specimens stored and being contacted for future research studies including COVID-19 vaccination trials in children.

Our existing Consortium Data Reporting Unit (CDRU), in collaboration with our data manager, will coordinate the submission of common evaluation metrics on SARS-CoV-2 testing-related outcomes to the RADx-UP CDCC at Duke University. We will comply with data sharing as mandated by the NIH and follow guidance provided by the CDCC for data acquisition, collection, and curation, including appropriate consent for data sharing and implementation of the schemas proposed under the ABOUT ML effort. The CDRU will also ensure compliance with federal, state, and local requirements and policies for testing, reporting, and surveillance. The CDRU will also work closely with the CDCC to employ a common set of tools to promote collection of comparable data on social determinants of health, including measures from the PhenX Toolkit. Effective implementation strategies for rapid adoption will be disseminated through the CDCC.

We will work collaboratively with the Duke CDCC in reviewing and revising our data collection tools to ensure we are collecting the appropriate CDEs. We will share our data with Duke CDCC. Finally, we will share our findings with the participating school districts and community partners at regular intervals throughout the project.

Publicly Available Information. We will make the aggregate results of the surveys, discussion sessions, and testing results publicly available on the following website: https://safereturntoschoolstudy.wustl.edu/. Additionally, we will provide a flyer at the end of the study to participants sharing aggregate results, provide study updates, and include relavent information regarding the pandemic.

F Study Monitoring

Study Monitoring Plan

A plan is in place to monitor for emerging differences in school based-transmission between the two testing strategies. Quarterly, Dr. Newland (PI), Fritz (Co-I), and two independent monitors, Drs. David Hunstad (Division Chief of Pediatric Infectious Diseases) and Greg Storch (Pediatric Infectious Diseases physician and virologist), and the trial statistician, Dr. Lu, will review the data. Drs. Newland and Fritz will monitor the volume of SARS-CoV-2 tests being obtained at the schools, rates of SARS-CoV-2 positivity in all schools, and the number of potential transmission events within the schools on a continuous basis.

Important to this study is the monitoring of the social, ethical, and equity implications associated with the testing implementation in these underserved communities. All participants will be given the opportunity to express their concerns and identify barriers to participating in the study at time of enrollment. Additionally, a study email and phone number will be available for participants to provide feedback and voice any concerns about the project.

G References

1. Van Dyke ME, Mendoza MCB, Li W, et al. Racial and Ethnic Disparities in COVID-19 Incidence by Age, Sex, and Period Among Persons Aged <25 Years — 16 U.S. Jurisdictions, January 1–December 31, 2020. *Morbidity and Mortality Weekly Report.* 2021;70.
2. Johnson A, Buford T. Early Data Shows African Americans Have Contracted and Died of Coronavirus at an Alarming Rate. *Propublica.* 2020. https://www.propublica.org/article/early-datashows- african-americans-have-contracted-and-died-of-coronavirus-at-an-alarming-rate. Accessed March 11, 2021.
3. Henderson MB, West MR, Peterson PE. Pandemic Parent Survey Finds Perverse Pattern: Students are More Likely to Be Attending School in Person Where COVID Is Spreading More Rapidly. *Education Next.* 2021;21(2). https://www.educationnext.org/pandemic-parent-surveyfinds- perverse-pattern-students-more-likely-to-be-attending-school-in-person-where-covid-isspreading- more-rapidly/. Accessed March 11, 2021.
4. Bryant DJ, Oo M, Damian AJ. The rise of adverse childhood experiences during the COVID-19 pandemic. *Psychol Trauma.* 2020;12(S1):S193-S194.
5. Benner AD, Mistry RS. Child Development During the COVID-19 Pandemic Through a Life Course Theory Lens. *Child Dev Perspect.* 2020;14(4):236-243.
6. Zimmerman KO, Akinboyo IC, Brookhart MA, et al. Incidence and Secondary Transmission of SARS-CoV-2 Infections in Schools. *Pediatrics.* 2021.
7. Falk A, Benda A, Falk P, Steffen S, Wallace Z, Hoeg TB. COVID-19 Cases and Transmission in 17 K-12 Schools - Wood County, Wisconsin, August 31-November 29, 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(4):136-140.
8. Centers for Disease Control and Prevention. Schools and Child Care Programs: Plan, Prepare, and Respond. 2021; https://www.cdc.gov/coronavirus/2019-ncov/community/schoolschildcare/ index.html. Accessed March 11, 2021.
9. Orscheln RC, Newland JG, Rosen DA. Practical School Algorithms for Symptomatic or SARSCoV- 2-Exposed Students Are Essential for Returning Children to In-Person Learning. *J Pediatr.* 2021;229:275-277.
10. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis.* 2020;20(5):565-574.
11. Wylie AL, Fourneir J, Casanovas-Massana A, al. e. Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs. *medRxiv.* 2020.
12. Lalli MA, Langmade SJ, Chen X, et al. Rapid and extraction-free detection of SARS-CoV-2 from saliva with colorimetric LAMP. *medRxiv.* 2020.
13. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res.* 2005;15(9):1277-1288.

H Appendices