Protocol

Communities Fighting COVID!: Returning our Kids Back to School Safely

ClinicalTrials.gov study number: NCT05150860

Funding: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NIH), award number: OT2HD108112-01

Protocol date: October 8, 2021

Clinical trial study period: October 2021-March 2022

Institutional Review Board (IRB) approval numbers:
San Diego State University Institutional Review Board: Protocol number: HS-2021-0208

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1. Background and rationale

Emerging data suggest minority individuals are at an increased risk of acquiring SARS-CoV-2 infection and experience worse clinical outcomes from COVID-19 compared to White individuals[1]. Geographic locations reporting data by race/ethnicity indicate that African American individuals and Latino individuals bear a disproportionate burden of COVID-19-related outcomes[2]. Blacks are experiencing a 2.7 times higher COVID-19 death rate as compared to whites, whereas Latinx are experiencing a 2.5 times higher rate[3]. In California, Asian Americans have been disproportionately affected by the COVID-19 pandemic accounting for at least 7% of COVID-19 cases and 15% of COVID-19 related deaths with a case fatality rate of 8.4% in California far exceeding that of the overall population (2.6%)[4].

The reasons for COVID-19 disparities among underserved minorities are complex and intertwined including a disproportionate burden of underlying comorbidities[5], being uninsured or having access issues[6], and holding public facing occupations with greater exposure risk[7]. It has been noted how minority status and language, household composition and transportation, are the greatest current predictors of COVID-19 case counts in the U.S.[8].

At this time, COVID-19 testing is predominantly comprised of diagnostic testing, where suspected positive cases, i.e. symptomatic individuals, are tested, with the primary aim of limiting further person-to-person transmission[9]. There is currently limited data on COVID-19 screening among asymptomatic individuals, especially among more vulnerable populations. Prior coronavirus outbreaks have shown asymptomatic spreaders to comprise a high proportion of infected individuals and identifying these individuals as important for containing further viral transmission. Contact tracing and testing of individuals of high-risk of COVID-19 exposure is the current public health focus for bending the curve.

Urban schools serving underserved communities (e.g., majority underrepresented minority students, > 50% qualifying for free/reduced price meals, those with high percentage of English language learners) lack the personnel and logistical support to implement robust COVID- 19 screening programs as part of their COVID prevention plans, even though they serve communities with some of the highest COVID infection and lowest vaccination rates.

Rapid antigen testing (results in <15 minutes) offers substantial advantages in the school setting, quickly identifying (and isolating) positive cases and significantly lowering cost relative to PCR testing. However, it requires significant logistical planning and staffing. Providing unvaccinated students and school staff with free at-home over the counter (OTC) antigen test kits would dramatically reduce the burdens of implementing school testing screening programs for disadvantaged school settings.

In particular, equitable access to simple, convenient, regular at-home COVID screening testing for unvaccinated middle school students, staff, and their families in disadvantaged schools can have substantial impact on reducing household, school, and community transmission. At-home testing timed right also reduces the economic consequences from school exposure quarantines. At-home antigen testing also promises broader testing access (in line with Presidential COVID response plan priorities[10]) and, in the school setting, can reduce within-school transmission and absenteeism from post-exposure group quarantine.

2. Specific objectives

Aim 1. We will determine if providing free at-home COVID-19 rapid antigen testing kits produces equivalent participation in and adherence to school screening testing as on-site school testing. In a non-inferiority trial, we will evaluate if, with appropriate educational materials and support (e.g., videos, a helpline, all in multiple languages, outreach,

reminders, follow-up support, etc.) providing at-home testing kits produces roughly equivalent weekly participation and adherence rates in the school screening testing program as on-site antigen testing.
Aim 2. We will evaluate if a family-based model of making testing available to family members enhances student and school staff participation.
Aim 3. [not part of clinical trial] We will also study implementation of the program to inform our scale-up to additional schools and identify resources needed to ensure ongoing high participation rates.
Aim 4. [not part of clinical trial] We will assess acceptability and feasibility of at-home COVID-19 testing.

3. Methodology

3.1 Setting and population.

Research setting.
This study will take place with Sweetwater Union High School District (SUHSD), a public school district in South San Diego County along the US-Mexico border, that serves 90% racial and ethnic minority students and a high proportion of socioeconomically disadvantaged students (66% of middle school students eligible for free/reduced meals). It is the second largest school district in San Diego County and the largest secondary school district in CA (>39,000 students). It includes middle schools, a junior high, and high schools. The proposed project will focus on ten middle schools and one junior high (10,160 students, 893 staff). The district serves one of the largest proportions of racial and ethnic minority students in the county and CA; 72.4% of students are Latino/a and 8.5% Filipino (vs. 54.9% Latino/a and 3.7% Filipino in San Diego County schools). Over a fifth (21.2%) of students are English-language learners and half speak a language other than English at home. The district's academic year begins on July 21, 2021.

Study population. There are 10 middle schools and 1 junior high school eligible for inclusion, all in the Sweetwater Union High School District. Three will be selected to participate in the noninferiority trial. Schools will be excluded from possible selection if they have a lower proportion of students from households receiving Supplemental Nutrition Assistance Program benefits, a lower proportion of underrepresented minority students compared with other schools, have ongoing school-wide testing programs with a commercial provider, cannot be matched to other schools by population size, or are geographically close to another school.

Study participants will be students or staff at the selected SUSHD schools.

Inclusion criteria: SUHSD school staff member or student at a school selected for inclusion in the trial. Able to speak English or Spanish.

Exclusion criteria: Not a SUHSD student or staff member at a school selected for inclusion in the trial. Not able to speak English or Spanish.

3.2 Study design and procedures

Recruitment, eligibility screening, and informed consent.
Recruitment into the research study will be multi-modal. We will leverage SUHSD communication channels to reach district parents and inform them about the study. This will include email, SMS, presentations at events, and Community Health Worker-staffed tables at drop-off and pick-up times at each of the three schools. All of the aforementioned communications will be informational in nature. The "call to action" will be for parents and

students to visit the study website to review study eligibility and informed consent documents. After confirming eligibility, informed consent will take place through Qualtrics, with appropriate affirmations throughout the document to ensure understanding and a field to record signature. Study participants will be emailed a copy of the consent forms including the study details, benefits and risks, and information they may opt-out of the study at any time without risk of repercussions or loss of benefits provided outside of this study. In addition, a phone number and email address to reach SDSU study staff will be available for individuals with further questions. The study participant will be informed over the phone/email if they contact us that there are no repercussions for refusing to consent.

Consented participants will complete a 30-minute questionnaire via Qualtrics or verbally or on their own phone if registering on site.

Research design

Aim 1. At-home rapid antigen COVID-19 testing vs. on-site rapid antigen testing. Pragmatic non-inferiority trial, randomizing middle schools to either the on-site or the at-home COVID testing model. Trial duration about 5 months weeks. We will compare participation rates (percentage of the school population participating in testing) and adherence to the testing schedule (percentage of scheduled tests completed).

Aim 2. Family-based model to increase student and staff participation in testing
Quasi-experimental trial pre-post control group design. To establish a baseline (pre-test), all three schools will implement the respective testing program without the family-based model for 4 weeks. At the end of the 4 weeks the two schools in Aim 1 will implement the family-based model promoting the availability of testing for unvaccinated family members whereas the control school will not. We will track participation rates (overall and testing schedule adherence) in the three schools for 12-15 weeks post implementation of opening up testing to family members.

Study variables

Primary outcomes:

- Aim 1. At-home testing vs. on-site rapid antigen testing (testing rate)
    - Participation rate: weekly percentage of students and staff (school population) who participate in testing
    - Adherence to testing schedule: percentage of scheduled weekly tests completed once a participant enrolls in the trial
- Aim 2. Family -based model to increase student and staff participation in testing
    - Participation rate over time: percentage of students and staff who participate in testing
    - Adherence to testing schedule: percentage of scheduled tests completed

Other variables assessed:

- Sociodemographics
- Housing characteristics, household employment
- Health insurance and health care access
- Health status and risk factors for severe COVID
- Prior COVID testing and beliefs about testing
- Other risk factors for COVID (smoking, vaping, alcohol use - brief)
- Disability/Functional status
- Pandemic Impacts: Economic, Housing, Food Insecurity
- COVID vaccine receipt and perceptions.
- COVID prevention, testing experience, and challenges.
- COVID symptoms and exposure

- [not part of clinical trial] Implementation outcomes[11] and CFIR[12] constructs
    - Acceptability: Perception that the testing approach is agreeable or satisfactory
        - recipients of testing: client satisfaction scale,[13]
        - testing program staff: 4 item acceptability scale[14]
        - Meeting notes from staff.
        - Stakeholders: listening sessions with parents/guardians, meeting notes from stakeholder meetings
    - Appropriateness: Perceived fit, relevance, or compatibility of the COVID testing program for a given individual or staff and/or the perceived fit of the approach to address problems with alternative COVID testing approaches and aspects of safe return to school programs
        - recipients of testing: 4 item appropriateness scale[14] collected after testing.
        - staff: 4 item appropriateness scale[14] completed after training and 1 month into implementation.
        - Meeting notes from staff meetings
        - Stakeholders: listening sessions with parents/guardians, meeting notes from stakeholder meetings
    - Feasibility: Extent to which the testing approach can be successfully implemented
        - stakeholders: listening sessions with parents/guardians; meeting notes from stakeholder meetings
        - testing program staff: 4 item feasibility scale[14] & staff notes
    - Fidelity: Testing program implemented as intended
        - Review of study records.
        - Throughout implementation
- Assessment of modifiable factors which can enhance implementation efficacy during scale-up
    - Intervention Characteristics: Relative advantage, adaptability, complexity/perceived difficulty, design quality & packaging
    - Outer Setting: Student/parent/staff needs & resources, policies and incentives, peer pressure
    - Inner Setting: Structural characteristics, implementation climate, tension for change, relative priority, leadership engagement, available resources, learning climate, networks and communication
    - Characteristics of individuals: Knowledge and beliefs about testing approach, self-efficacy
    - Process: Executing, reflecting and evaluating, external change agents, champions, key stakeholders

3.3 Data collection

Aims 1 and 2. Baseline Questionnaire: Upon enrollment into the study, we will collect RADx-UP Tier 1 Common Data Elements (including demographics, household characteristics, pandemic effects on household employment, pandemic effects on access to health care, risk factors for severe COVID, COVID vaccination status, intentions, hesitancy, prior COVID testing and beliefs about testing, other COVID risk factors, and contact information.

Each time they test, participants (parent/guardians for participants under age 11) will self-report COVID symptoms to determine if post-antigen PCR confirmatory testing is needed (see “symptom and exposure report at the time of testing” document). We will observe the number of COVID cases at participating schools by grade and among staff each month from cases diagnosed outside our testing program.

Adult participants (school staff) aged 18 and above including any students aged 18 and above will complete the questionnaires themselves. Participants aged 11-17 will answer the majority of the questions in the questionnaires themselves with some questions about the household and background health history being completed by a parent/guardian who is asked to report about the child. For participants below age 11, a parent or guardian will complete the questionnaires reporting about the child.

COVID-19 testing approach and frequency of testing. Weekly screening testing with rapid antigen tests will be available for students and staff. We will follow CDC antigen testing algorithms and any changes (current: confirmatory PCR in asymptomatic antigen+ and symptomatic antigen- cases).[15] We will use the Quidel Quickvue COVID-19 antigen tests, available as both a point-of-care CLIA waived test and an at-home OTC test with results in 10 minutes. For the at-home OTC test an adult collects the sample of children <14 years. In the current EUA, the OTC test is used as a serial test to improve sensitivity, with a first test followed 24-36 hours later by a second test. However, a mobile app to interpret the test results with a smartphone or tablet camera is expected to be released soon and per the 03/31/21 EUA will change the testing procedure from serial testing to a single test. Although we expect the updated EUA to be issued prior to our project start date, we will use serial testing if needed to begin.

Monitoring of safety and mitigation measures. Although SUHSD’s 2021-22 COVID-19 safety/mitigation plan has not yet been finalized, we anticipate indoor mask requirements, HVAC system ionizers, engineering controls (e.g., ventilation modification), cleaning/disinfection practices, and physical distancing with possible daily temperature checks. We will document plan details and modifications and account for them in our testing program impact analyses.

COVID-19 onsite results, case reporting, and follow-up support. All test results in onsite antigen testing are provided in individual privacy tents to maintain confidentiality and to provide a place for students with positive results to wait until a parent or guardian arrives to pick them up. School-affiliated antigen+ cases in onsite testing are reported immediately to the school nurse and District COVID-19 response team lead, and to the County of San Diego (CoSD) Epidemiology team at the end of the day, which satisfies County and State reporting requirements. Site-related close contacts are evaluated by the District COVID-19 team during a support call with the parent/guardian, which also functions to provide isolation instructions, procedures to safely return to campus, and referrals for resources (food, medical, social support, academic support). Support calls are repeated partway through the isolation period. Additional steps such as close contact quarantine are taken as necessary. Confirmatory PCR results are also communicated by the District COVID-19 response team.

3.4 Statistical Analysis Plan

Aims 1 and 2. All analyses will follow the intention-to-treat principle.

This study is designed to determine if at-home COVID-19 testing is noninferior to onsite testing for participation rates and adherence to weekly testing. We selected a noninferiority margin of 6%, because of the significant advantages of an at home COVID-19 testing program in implementation resources and reducing at-school exposures.

The necessary sample size was calculated as 324 per arm (type I error rate 0.05, power 80%) for both outcomes.

We plan to use generalized estimating equations models with a logit link and will evaluate correlation structure selecting correlation structure based on model fit. We anticipate a first-order autoregressive correlation structure to account for the time dependence within each participant. Models including covariates, such as participant type (student, staff), race and ethnicity, primary language spoken at home, gender identity, COVID-19-vaccination status, and prior COVID-19 testing among interaction terms, will be evaluated.

The first outcome, participation rate in testing over time, utilizes the school population sample of both enrolled and non-enrolled participants using school demographic data. Therefore, models for this outcome will only have basic demographic covariates of participant type, race and ethnicity, and gender identity since these demographics were available by school. Estimated marginal means (model predicted probabilities) and standard errors for the outcomes for each study arm, controlling for covariates, will be generated for testing the noninferiority hypotheses. Exploratory subgroup analyses will be conducted for covariates that showed differences between the arms. One-sided noninferiority tests for participation rates and adherence proportions between the 2 study arms will be assessed. One-sided 95% confidence intervals for all models will be constructed.

4 Ethical considerations

IRB approval (#HS-2021-0208) was granted by the San Diego State University Institutional Review Board (FWA00003782). Written informed consent and child assent/parental consent will be obtained from all individual participants included in the study.

5. References

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