Safer at School Early Alert Hub

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Principal Investigator: Rebecca Fielding-Miller

Sponsor: University of California San Diego

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CONFIDENTIALITY STATEMENT

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.]

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Principal Investigator or Clinical Site Investigator:

Signed:  Date: 4/25/24

Name: Rebecca Fielding-Miller

Title: Associate Adjunct Professor

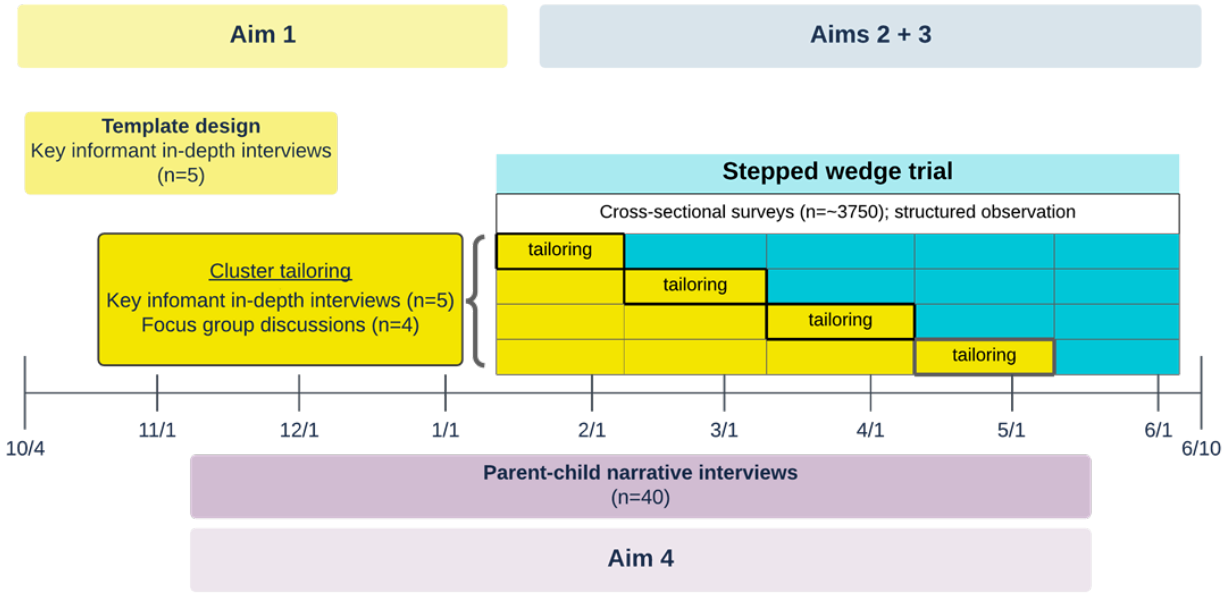
1 PROTOCOL SUMMARY

Protocol Title	Safer at School Early Alert Hub
Principal Investigator	Rebecca Fielding-Miller
Study Sites	University of California, San Diego
Study Activation Date	September 19, 2022
Planned Accrual	Total number of participants - 971
Planned Accrual Period	September 19, 2022 to December 17, 2022
Planned Duration	Data collection period: September 19, 2022 to December 17, 2022 Intervention period: October 3, 2022 to March, 2023
Study Design	Create the Safer at School Early Alert School Hub (SASEA Hub), a school-based environmental surveillance dashboard and diagnostic testing resource hub with an accompanying toolkit for rapid community tailoring to improve COVID-19 testing uptake in vulnerable and underserved communities using a Community Based Participatory Research (CBPR) framework and the Consolidated Framework for Implementation Research (CFIR). We will evaluate the ability of the saseahub.org to increase child and household diagnostic testing uptake via a step-wedge trial, with schools rotated onto the intervention arm (i.e., given access to the saseahub.org) at 2-week intervals. All schools will rotate into the intervention by the Thanksgiving holiday.

Study Objectives	**Aim 1:** Create the SASEA Hub, a school-based environmental surveillance dashboard and diagnostic testing resource hub with an accompanying toolkit for rapid community tailoring to improve COVID-19 testing uptake in vulnerable and underserved communities using a Community Based Participatory Research (CBPR) framework and the Consolidated Framework for Implementation Research (CFIR). **Aim 2**: Assess SASEA Hub's (intervention's) potential to increase diagnostic testing uptake and identify more asymptomatic cases than schools. We will assess this aim through a randomized stepped wedge cluster trial design. The primary outcome will be testing uptake within the past 14-day period, assessed through the SASEA bi-weekly community survey. **Aim 3**: Assess SASEA Hub's ability to increase risk mitigation behaviors (masking, physical distancing, increased hand hygiene) when the Hub notifies schools of a change in county level COVID-19 case rates or county level wastewater levels
Treatment Description	Intervention – receive access to the community tailored SASEA Hub website
Inclusion Criteria	Parent of a child or staff member attending one of 26 SASEA participating schools
Exclusion Criteria	All non SASEA school participating individuals or students of SASEA participating schools
Study Outcomes	Primary outcome – The primary study endpoint will be student diagnostic testing uptake in the previous 14-days, measured using household surveys distributed at 2-week intervals.

1.1 SCHEMA

Figure 5: Study design



1.2 SCHEDULE OF ACTIVITIES

Our timetable is shown below. Our partner schools will be enrolled as of August 2022, and we will already be implementing SASEA by the time this project begins. We anticipate completing all data collection by the end of Year 1 and will then work with our Community Advisory Board to develop the toolkit, with anticipated dissemination by the next academic school year. Throughout Year 2 we will continue analyzing data related to Aim 4, prepare manuscripts, lay summaries of findings to share with community partners, and applications for next-step work.

	Y1 Q1	Y1 Q2	Y1 Q3	Y1 Q4	Y2 Q1	Y2 Q2	Y2 Q3	Y2 Q4
Formalize CAB, hire and train staff								
Key informant interviews for template design (n=5)								
Pilot data analysis and dashboard template design with CAB								
Stepped wedge trial with cluster-level dashboard tailoring								
Parent-child interviews (n=40)								
CFIR data analysis and tailoring toolkit development								
Community data dissemination								
Parent-child narrative analysis								
Manuscript writing and dissemination, prepare follow-up applications								

2 INTRODUCTION

2.1 STUDY RATIONALE

The SARS-CoV-2 pandemic necessitated the closure of childcare and school sites around the world. Schools and childcare settings present a unique dilemma for epidemic abatement: As indoor settings where individuals who are not currently eligible for COVID-19 vaccines spend large amounts of time in close proximity to one another they can have very high potential for the virus to spread. Timely detection of asymptomatic infections in school settings is necessary to prevent outbreaks in school settings, particularly asymptomatic outbreaks that could lead to larger community outbreaks among the unvaccinated and/or the evolution of new variants of concern (VoCs) with increased vaccine escape potential. This project will create a unique public-facing dashboard and resource hub (SASEA Hub website) that provides school staff and parents immediate access to environmental testing results from their neighborhood with accompanying information about COVID-19 testing and other related resources. The project will also provide novel information about the potential impact of the dashboard and resource hub on testing practices among students, parents and the broader community.

2.2 BACKGROUND

Public schools are often cornerstones of their community. In historically marginalized communities in particular, they are often trusted providers for a range of support. The tradeoff between these crucial benefits of in-person learning versus the risk of SARS-CoV-2 transmission resulting from in-person learning has been hotly debated throughout much of 2020 and 2021. The stakes are particularly high in historically marginalized communities which rely most heavily on school services but have also been hit the hardest by COVID-19. Individual diagnostic testing combined with contact tracing and behavioral risk mitigation (masking, hand hygiene, ventilation, distancing) is key to reducing SARS-CoV-2 transmission and ensuring safe in-person learning.

The SASEA program was co-developed by the University of California, San Diego (UCSD), the County of San Diego, and 15 partner schools serving socially vulnerable students in 5 school districts. SASEA utilizes daily wastewater and surface (floor) environmental monitoring to detect asymptomatic SARS-CoV-2 infections. Responsive diagnostic testing is immediately triggered by positive environmental samples. In our pilot, SASEA was significantly associated with increased testing uptake among students and staff, and 75% of asymptomatic COVID-19 cases were preceded by a positive environmental sample.

The SASEA Hub intervention offers key innovations in school-community-public health partnership, utilizing anonymous, aggregate, and low-cost environmental surveillance strategies to trigger diagnostic testing, and rapid genetic surveillance with high spatial resolution. Because public schools serve families that reside within a specific geographic catchment area, and because children are likely to have the lowest levels of vaccine uptake even when vaccines become available for children under 12, SASEA Hub schools will provide community sentinel surveillance sites with a high degree of geographic resolution.

In addition to early warning data for students, staff, and parents, increased rates of environmental detection at a SASEA Hub neighborhood, even in the absence of diagnosed cases, can allow public health officials and community stakeholders to rapidly implement increased diagnostic testing and vaccine outreach, and to closely tailor these outreach efforts to the specific community. This project will create a unique public-facing dashboard and resource hub that provides school staff and parents immediate access to environmental testing results from their schools with accompanying information about COVID-19 testing and other related resources. The project will also provide novel information about the potential impact of the dashboard and resource hub on testing practices among students, parents and the broader community.

2.3 RISK/BENEFIT ASSESSMENT

There will be no risk in enrolling to receive text/email notifications for SASEA Hub website updates related to COVID-19 information.

We anticipate that the surveys sent to school parents and staff will hold minimal risk. There is a chance that participants may become emotional, uncomfortable, or bored when completing the survey due to topics concerning COVID-19. There is a small risk that survey data confidentiality could be breached and sensitive information may be exposed. We will not ask for personally identifiable information in these surveys.

2.3.1 KNOWN POTENTIAL RISKS

There will be no risk in enrolling to receive text/email notifications for SASEA Hub website updates related to COVID-19 information.

We anticipate that the surveys sent to school parents and staff will hold minimal immediate and long term risk. There is a chance that participants may become emotional, uncomfortable, or bored when completing the survey due to topics concerning COVID-19. There is a small risk that survey data confidentiality could be breached and sensitive information may be exposed. We will not ask for personally identifiable information in these surveys. No alternative procedures/methods have been considered as the surveys will hold minimal risk.

2.3.2 KNOWN POTENTIAL BENEFITS

Being part of a school enrolled in SASEA Hub will benefit school staff and parents by receiving environmental COVID-19 monitoring updates on their neighborhood along with additional COVID-19 related information on vaccination and testing locations.

ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

There is minimal risk in participating in the intervention – being part of a school receiving the SASEA Hub website. The surveys sent to the school families also hold minimal risk. Being part of a school enrolled in SASEA Hub will benefit school staff and parents by receiving environmental COVID-19 monitoring updates on their neighborhood along with additional COVID-19 related information on vaccination and testing locations.

OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
The primary outcome will be testing uptake among children within the past 14-day period, assessed through the SASEA bi-weekly community survey.	COVID-19 testing in past 14 days among children only	We will assess this aim through a randomized stepped wedge cluster trial design. The primary outcome will be testing uptake within the past 14-day period, assessed through the SASEA bi-weekly community survey. The SASEA Hub intervention offers key innovations in school-community-public health partnership, utilizing anonymous, aggregate, and low-cost environmental surveillance strategies to trigger diagnostic testing, and rapid genetic surveillance with high spatial resolution. In addition to early warning data for students, staff, and parents, increased rates of environmental detection at a SASEA Hub school, even in the absence of diagnosed cases, can allow public health officials and community stakeholders to rapidly implement increased	

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
		diagnostic testing and vaccine outreach, and to closely tailor these outreach efforts to the specific community (i.e., ensure properly translated materials, address testing barriers specific to the community as identified in Aim 1)	

STUDY DESIGN

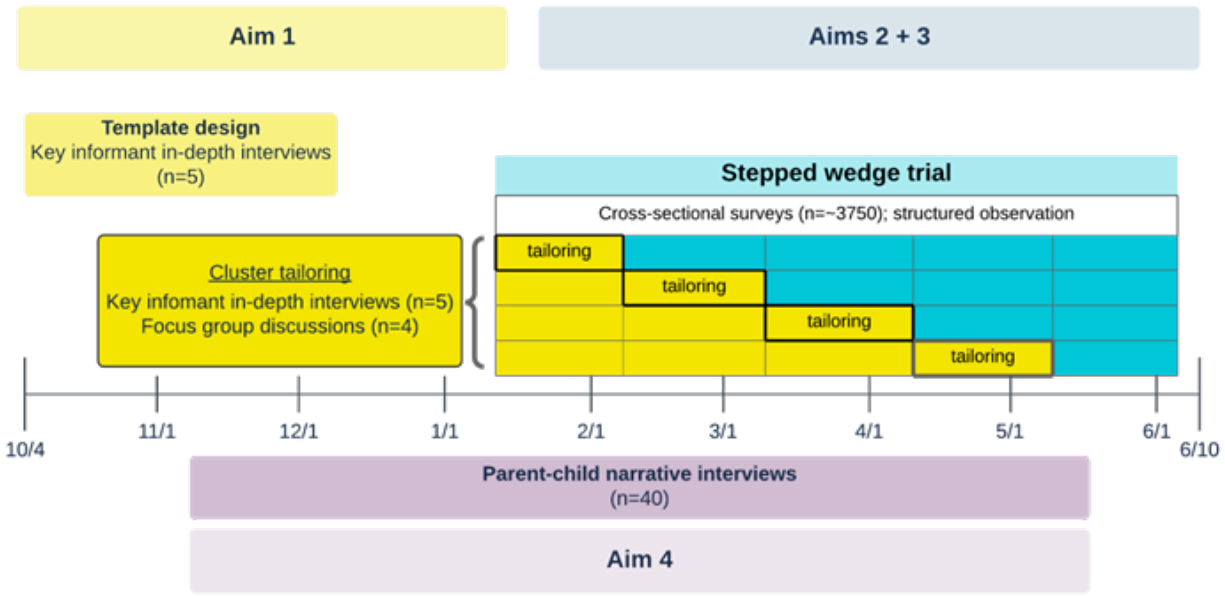
2.4 OVERALL DESIGN

This study uses a mixed-methods convergent participatory design[27] (Figure 5). Prior to the stepped wedge trial we will work with our CAB to develop a dashboard and resource hub template. We will then utilize a 20-week randomized stepped wedged trial in 48 school sites with approximately 24,000 students and staff to assess aims 2 and 3. During each 4-week step interval we will use key informant interviews and focus group discussions to tailor the dashboard template to each cluster's specific needs, preferences, and available community resources.

C.4 Aim 1: Create SASEA Hub, a school-based, public facing environmental surveillance dashboard and diagnostic testing resource hub, along with an accompanying toolkit for rapid community tailoring to improve access, acceptability, and implementation of COVID-19 testing in vulnerable and underserved communities using participatory action research to identify (1) core and (2) community-specific barriers to diagnostic testing within and across 4 low income and historically marginalized communities in San Diego County.

Background

Figure 5: Study design



Formative research is necessary to ensure that COVID-19 diagnostic testing, prevention, contact tracing, and isolation strategies are appropriately tailored to the unique needs of underserved and/or socially vulnerable communities. The objective of Aim 1 is to develop an environmental results dashboard and resource hub that can be rapidly tailored for diverse contexts to address COVID-19 diagnostic testing access and acceptability. The toolkit will contain the following components: (1)A customizable dashboard, developed using ArcGIS, for reporting school environmental surveillance results (2)Templates for online and print resources for schools to share with their community that address barriers to diagnostic testing access as well as the potential implications of a positive test; and (3)A toolkit to tailor the dashboard resource hub to specific communities.

C.4.1a Methods to create Product 1

Step 1: Dashboard Template Design

Figure 6: SASEA sample materials

After convening our CAB, we will host a participatory mixed methods data analysis workshop using data from 15 Focus Group Discussions (FGDs) in in English and Spanish with 49 parents and staff members from our pilot partner schools, as well as survey data collected from 299 parents and teachers in February of 2020. These data were collected during our pilot phase from November 2020 – March 2021. FGD domains included perceptions of diagnostic testing and contact tracing, barriers to testing access, and preferred strategies for notifications of environmental results. While our team has already reviewed these data internally and begun the process of preparing manuscripts for dissemination, a participatory workshop with our CAB will allow us to more fully incorporate community member insights, providing us with a richer understanding of the data that will support a more responsive public-facing dashboard template design. After the analysis workshop, we will conduct up to 5 additional key informant interviews with school administrators, parent leaders, and county leadership to ensure that our template is responsive to current district, county, and state guidelines.

We will build the dashboard template using ESRI's ArcGIS. This platform is easy to configure, can be embedded in a variety of websites (for example, school or district sites), and can provide real-time data updates on environmental monitoring results pulled from a central server maintained by our team at UCSD and/or the laboratory processing samples. We have already created a dashboard mockup, risk index, and a variety of printable resources as part of our pilot project (Figure 6). We will review and modify these with our CAB based on the data analysis workshop and current local and national guidelines.

Step 2: Community Tailoring

Once we have developed the initial template, we will tailor the dashboard to each school cluster in the 3-4 weeks before a site rotates into the intervention (SASEA Hub) condition using rapid community needs and asset mapping based on the methods developed by Lazarus et al. We will conduct 4 focus group discussions (FGDs) of approximately 8 parents and staff in each cluster. Focus group participants will be asked to participate in a series of activities to identify community needs and assets related to

COVID-19 diagnostic testing uptake and health disparities in their community. The final activities and focus group domains will be determined together with our CAB. Likely activities are shown in table 1.

Table 1: Community mapping exercises

Exercise	Details
1: Community mapping	Participants draw maps of their community to identify needs and assets related to COVID-19 diagnostic testing uptake and related health disparities
2: Health and safety within the (school) community	Participants identify key factors in their community that support or undermine diagnostic testing and/or contribute to related health disparities
3: Contribution of school and community assets to (school) community health and diagnostic testing uptake.	Participants synthesize needs, assets, and factors identified in exercises 1 and 2 to create a community needs and asset ranking matrix.
4: Local action / resource creation	Using the matrix developed in exercise 3, participants identify pre-existing resources that should be included in SASEA-HUB and/or resources that should be created by the CAB and study team (i.e., translations or summaries of key information.)

Step3: SASEA Hub documentation and tailoring toolkit

Throughout the study, we will collect formative process data by meeting regularly with our CAB. We will document the tailoring and academic-community collaboration process using the Consolidated Framework for Implementation Research (CFIR)[29] and the Community Based Participatory Research (CBPR) model developed by Belone et al[30] as shown in Table 2. Both models recommend regular team meetings and debriefings to reflect on the process of implementation. We will hold regular study team and CAB check-in meetings in which we will reflect on (1) the complexity and logistics of the process, (2) the potential cost of the project and sources for long-term funding (i.e., state grants) (3) the organizational capacity necessary to conduct tailoring data collection and implement the project, and (4) the climate of the project and whether all team members feel equally heard and valued. Similarly, the CBPR model advises study teams to systematically reflect on (1) context, (2) partnership process, and (3) processes and outputs of research. These CBPR and CFIR guided reflections will be recorded using a standardized data collection sheet.

C.4.2.c Analyses for Product 1: We will analyze data for steps 1 and 2 in real time as part of the workshops and focus group discussions. Members of the study team will also record these conversations and take extensive notes throughout to verify any discrepancies that emerge later. After all 4 tailored dashboards (one per school cluster) have been deployed, we will conduct a second round of participatory data analysis workshops with our CAB to identify core similarities and key differences in

the 4 different community need and asset mapping exercises and use these to further refine the dashboard template. We will also analyze the data collected from team debriefings to create a shareable toolkit of best practices for dashboard tailoring.

C.4.3 Expected outcomes and products of Aim 1: The dashboard template and toolkit we generate will be made available on our project website (*www.SASEAsystem.org*), which already hosts open access laboratory and project implementation protocols for school environmental monitoring.

Table 2: Constructs to create rapid tailoring toolkit

Context • Resource checklist to identify the knowledge, skills, and capacity necessary to execute project and where they exist within a team • Context checklist to assess the political, historical, institutional, and socio-economic issues which are likely to affect the execution of the project. • Ethical considerations
Partnership • Researcher and CAB "bill of rights" • Best practices for working with, convening, and reimbursing CAB members • Other considerations for ensuring partner equity • Ethical considerations
Research • Logic model identifying which aspects of a program will likely need to be uniquely tailored for a given community and which needs or preferences are likely to be similar across communities • Research protocol and field guides for focus group discussions and key informant in-depth interviews • Analytic plans for qualitative data • Ethical considerations

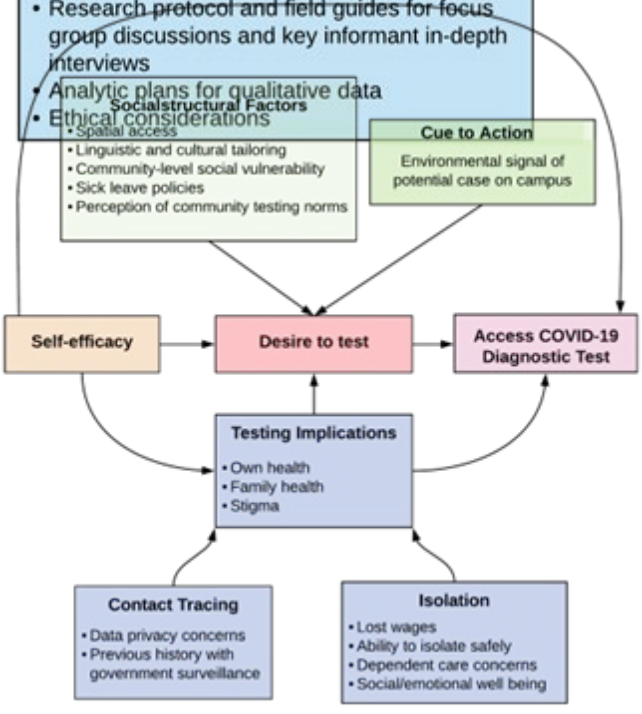


Figure 4: Testing conceptual framework

C.4.4 Potential problems and contingency plans We recognize that school administrators, parents, and other key stakeholders are likely to have significant time constraints. We have very strong relationships with school districts across the county, as well as the San Diego County Health and Human Services Agency (see letters of support). However, if time constraints do not permit the opportunity for live IDIs, we will instead email our proposed toolkit and questions for written feedback.

SCIENTIFIC RATIONALE FOR STUDY DESIGN

Our conceptual framework is based on our pilot data and behavioral theory (figure 4)

Drawing from both Social Cognitive Theory (SCT) and the Social Ecological Model (SEM), we assume that accessing a COVID-19 diagnostic test is affected by individual self-efficacy and desire to learn one's COVID-19 status, as well as social and structural factors such as geographic access to a testing site, linguistic and cultural tailoring of health outreach efforts, and community level social vulnerabilities (including any local, state, or municipality regulations related to COVID-19 sick leave, unemployment insurance, or rent relief). Desire to test will also be influenced by the perceived implications of testing, whether a desire to know one's status is to protect one's own health and one's community, or a fear of stigma and blame upon diagnosis. Testing implications are also directly related to perceived implications of a positive diagnosis – contact tracing has been linked to fears of data privacy, particularly for those who are undocumented or living in households with mixed documentation status – and tracking and

tracing efforts seem to echo previous alleged government surveillance efforts by the FBI for many ethnic minority Muslim communities. Similarly, a positive test implies the need to isolate with attendant concerns about lost wages, the ability to isolate safely, dependent care, and mental and emotional health during isolation.

In addition to providing resources to address these social and structural factors (i.e., providing downloadable materials in a user's preferred language, linking local to income-replacement or other economic support services) SASEA Hub is also designed to serve as a cue to action via environmental testing data. Environmental testing results and a community risk indicator that incorporates the percentage of students and staff who have consented to responsive testing will be part of the public facing dashboard.

SASEA Hub posits that specific cues to test as a result of concrete risk information (i.e., higher concentrations of COVID-19 particles in wastewater), along with resources to address social and structural barriers to diagnostic testing, is more likely to result in diagnostic testing uptake than (1) offering routine diagnostic testing in the absence of environmental cues, and (2) environmental cues alone with no resources to offset structural barriers.

JUSTIFICATION FOR INTERVENTION

Formative research is necessary to ensure that COVID-19 diagnostic testing, prevention, contact tracing, and isolation strategies are appropriately tailored to the unique needs of underserved and/or socially vulnerable communities. The objective of Aim 1 is to develop an environmental results dashboard and resource hub that can be rapidly tailored for diverse contexts to address COVID-19 diagnostic testing access and acceptability. The toolkit will contain the following components: (1)A customizable dashboard, developed using ArcGIS, for reporting regional environmental surveillance results (2)Templates for online and print resources for schools to share with their community that address barriers to diagnostic testing access as well as the potential implications of a positive test; and (3)A toolkit to tailor the dashboard resource hub to specific communities.

We will utilize a 20-week randomized stepped wedged trial in 48 school sites with approximately 24,000 students and staff to assess aims 2 and 3. During each 4-week step interval we will use key informant interviews and focus group discussions to tailor the dashboard template to each cluster's specific needs, preferences, and available community resources. The stepped wedged trial will allow all participants to eventually access this COVID-19 tool to help them assess their risk and choose mitigation strategies. It would be unethical to restrict information of this kind from some participants.

END-OF-STUDY DEFINITION

A participant is considered to have completed the study if she or he has completed the community survey.

STUDY POPULATION

INCLUSION CRITERIA

NIH Protocol Template for Behavioral and Social Sciences Research

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Parent with children enrolled at any of the 50 schools across the San Diego County that participated in the study during the 2021-2022 school year.
2. School staff working at any of the 50 schools across the San Diego County that participated in the study during the 2021-2022 school year.
3. Provision of signed and dated informed consent form
4. Access to necessary resources for participating in a technology-based intervention (i.e., computer, smartphone, internet access)

EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Not affiliated with participating sites as parents or staff.
2. No access to necessary resources for participating in a technology-based intervention (i.e, computer, smartphone, internet access)

LIFESTYLE CONSIDERATIONS

N/A

SCREEN FAILURES

N/A

STRATEGIES FOR RECRUITMENT AND RETENTION

This study will consist of a 20-week randomized stepped wedge cluster trial. Parents will be invited to participate in a 5–10-minute self-administered survey conducted at 4-week intervals. Prospective parent participants will be identified using a sampling frame provided by schools, at the beginning of the school year, consisting of classroom, classroom size, and grade level. etween 40 participating schools clustered and 8 childcare sites within 4 district clusters (approximately 12 sites per district cluster) will be enrolled during the study; for a total of 48 sites and 4 district clusters. The average size of school and childcare sites is 500. From the sampling frame, three classrooms within each school will be randomly selected. Within the randomly selected classroom, teachers will distribute a survey invitation to all students. Average class size is 25 and we anticipate a 25% response rate per class, resulting in approximately 20 surveys per site or approximately 150 surveys per cluster. Random samples of classrooms will be selected every 2-weeks with replacement using a randomization schedule generated by the study

biostatistician. All parents will be notified of the study and the possibility of receiving a survey invitation by school administrators at the beginning of the school year, with periodic reminders.

This is a one time survey that does not require participant retention. Participants who complete the survey will be entered into a 1 of 3 $250 raffle gift card as an incentive.

STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Assess SASEA Hub's potential to increase diagnostic testing uptake and identify more asymptomatic cases than schools with SASEA environmental and response testing alone (control); and

Assess SASEA Hub's ability to increase risk mitigation behaviors (masking/double masking, physical distancing, increased hand hygiene, enhanced ventilation) when a potential case is signaled but not identified.

Intervention schools will have higher rates of diagnostic testing than control-arm schools. We will test this hypothesis using self-reported survey data

Diagnostic testing among household members of students will be higher in the control arm. We will test this hypothesis using self-administered survey data. Survey participants will be asked if they (1) have learned of any positive cases at the school site in the previous 14 days, and (2) whether or not they and their household members accessed a diagnostic test as a result of that notification.

School staff and families will use more behavioral risk mitigation strategies in the three days following a potential case signal compared to times when there is no signal. We will test this hypothesis using biweekly surveys and structured systematic observations at school sites.

ADMINISTRATION AND/OR DOSING

Forty-eight participating schools (approximately 24,000 student and staff) clustered within 4 geographic areas will be enrolled during the study. The average size of school/childcare site is 500. Implementation of the intervention (SASEA Hub) will be conducted using a cluster randomized stepped wedge design, where the schools will be randomized by the study biostatistician, Dr. Gaines, into 4 clusters (with 12 schools per cluster). Clusters will receive the intervention in a randomized order over 4 successive waves (see Figure 5) during a 20-week period (from mid-January 2022 to beginning of June 2022).

A random cross-sectional sample of parents and caregivers (hereafter referred to as "parents") will be selected to participate in a 5–10-minute self-administered survey conducted at 4-week intervals (see Table 3). Prospective parent participants will be identified using a sampling frame provided by schools, at the beginning of the school year, consisting of classroom, classroom size, and grade level. From the sampling frame, three classrooms within each school will be randomly selected. Within the randomly

selected classroom, teachers will distribute a survey invitation to all students. Average class size is 25 and we anticipate a 15% response rate per class, resulting in approximately 12 surveys per school or approximately 144 surveys per cluster; equating to 2,880 parent surveys during the 20-week period. Random samples of classrooms will be selected every 4-weeks with replacement using a randomization schedule generated by the study biostatistician, Dr. Gaines. To increase generalizability, we will randomly select serial cross-sectional samples with replacement since serial samples will allow for greater representation given the likelihood of student absences on the day of recruitment (e.g., potential for individual students to be absent and/or classrooms to be quarantined due to COVID-19 exposure). All parents will be notified of the study and the possibility of receiving a survey invitation by school administrators at the beginning of the school year, with periodic reminders.

The primary outcome, diagnostic testing before and after implementation of the SASEA Hub will be examined using a mixed effects logistic regression with fixed effects for Time, SASEA Hub, and the interaction of Time x SASEA Hub. The mixed effects model will include a random component for school-level intercepts (to account for students nested within schools) and district-level intercepts (to account for schools nested in districts). Potential confounders will be controlled for in the model (e.g., baseline COVID-19 diagnostic testing and vaccination rates within communities encompassing schools, school size, race/ethnicity, % receiving free/reduced lunch).

FIDELITY

INTERVENTIONIST TRAINING AND TRACKING

All schools will be receiving the same SASEA Hub website as the intervention with minimal modifications based on their region. Region specific wastewater results and vaccine locations will be provided.

MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Because of the stepped wedge trial, all schools will be receiving the intervention (SASEA HUB). There is no randomization occurring in intervention rollout. As schools do not receive the website before the intervention, schools will not be in communication with other schools and will not find out about the website before the intervention is introduced to their campus.

STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

N/A

CONCOMITANT THERAPY

N/A

RESCUE THERAPY

N/A

STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Because the website traffic and survey participation are voluntary, there will be no need to remove participants from the study.

PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue a participant from the study for the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

LOST TO FOLLOW-UP

There will be no follow up in this study. Participants are completing a one-time survey. Participants may decide to discontinue the survey at any time. Participants receiving notifications to the SASEA Hub website may also choose to discontinue the notifications.

STUDY ASSESSMENTS AND PROCEDURES

ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

No safety end point procedure was provided to participants since there was minimal risk in participating in a SASEA Hub school and completing the surveys.

SAFETY ASSESSMENTS

1. Physical risk management plan
    a. We do not anticipate any physical risks from participating in this study.
2. Psychological risk management plan
    a. Adverse Emotional Reaction: Following administration of screeners or surveys, if discomfort is evident. Significant discomfort will be study PI, Dr. Fielding-Miller, or her designee, and recommendation for continued monitoring by staff or for referral, as appropriate, for further evaluation and treatment will be made.
3. Social/political risk management plan
    a. Adverse Community/Social impact from publication of study results: Significant rates of COVID-19 as well as other risk behaviors and psychiatric disorders occur in most ethnic groups. The specifics of the rates of these disorders and behaviors, their relationship to risk, protective, and resilience factors, and the effects of individual and environmental intervention remain to be determined. However, it seems unlikely that specific rates or characteristics of these factors in historically marginalized school communities in San Diego County or differences as compared to other groups will lead to stigmatization. Nevertheless, we plan to take the following steps to minimize this risk:
    b. Ongoing community feedback to school communities about the nature, purposes, and results of the study. This will afford an opportunity for community feedback on issues that might represent potential risk of stigmatization prior to publication of results.
4. Confidentiality risk management plan
    All identifiable PHI data will be stored on a secure REDCap server and shared with the CDCC using appropriate protocols. Paper documents and digital recorders containing names and other identifying information (i.e., paper consent forms, focus group transcripts) will be kept in a locked file drawer in a locked office. All digital files will be deleted after transcription. Transcripts will be de-identified and kept on a password protected computer.

Assessment of adverse events. PI, Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying with the reporting requirements. All Serious Adverse Events will be reported to the UCSD IRB and to NIH within two business days.

ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

DEFINITION OF ADVERSE EVENTS

Mild adverse event (AE is transient and usually self-limited, requires no more than minimal intervention, monitoring, or treatment, does not interfere with the participant's daily activities, usually does not require discontinuation from the study).

Moderate adverse event (AE may or may not be transient and self-limited, requires more than minimal intervention, monitoring, or treatment, interferes with daily activities, usually does not require discontinuation from the study).

DEFINITION OF SERIOUS ADVERSE EVENTS

Severe adverse event (AE usually not transient and self-limited, requires significant intervention, monitoring, or treatment, any AE resulting in hospitalization, prolongation of existing hospitalization, or significant disability/incapacity).

Life-threatening adverse event, persistently disabling adverse event, or a congenital anomaly/birth defect.

Fatal adverse event.

CLASSIFICATION OF AN ADVERSE EVENT

N/A

2.4.1.1 SEVERITY OF EVENT

Mild adverse event (AE is transient and usually self-limited, requires no more than minimal intervention, monitoring, or treatment, does not interfere with the participant's daily activities, usually does not require discontinuation from the study).

Moderate adverse event (AE may or may not be transient and self-limited, requires more than minimal intervention, monitoring, or treatment, interferes with daily activities, usually does not require discontinuation from the study).

Severe adverse event (AE usually not transient and self-limited, requires significant intervention, monitoring, or treatment, any AE resulting in hospitalization, prolongation of existing hospitalization, or significant disability/incapacity).

Life-threatening adverse event, persistently disabling adverse event, or a congenital anomaly/birth defect.

Fatal adverse event.

2.4.1.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Related – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and

the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.

Not Related – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

EXPECTEDNESS

The likelihood of the incidence of the occurrence of each adverse event during a participant's involvement in the study is estimated using the following categories:

Likely: incidence equal to or greater than 10%

Less Likely: incidence equal to or greater than 1% to less than 10%

Rare: incidence less than 1%

1. Physical Risk: rare, no biological samples will be collected from human subjects in this study
2. Psychological Risk: Adverse emotional reaction to the information collected in screeners or surveys. This includes an adverse emotional reaction to reporting substance use, related morbidity, or other associated problems (mild, rare).
3. Social/Political Risk: Adverse community/social impact from publication of study findings (moderate, rare).
4. Legal Risk: Lawsuits arising from the testing intervention (moderate, rare).
5. Confidentiality Risk: Loss of confidentiality in any of the studies, but particularly those obtaining Identified PHI (private health information) (moderate, rare).
6. Other Risks: None

TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying with the reporting requirements. All Serious Adverse Events will be reported to the UCSD IRB and to NIH within two business days.

2.4.2 ADVERSE EVENT REPORTING

Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying with the reporting requirements. All Serious Adverse Events will be reported to the UCSD IRB and to NIH within two business days.

2.4.3 SERIOUS ADVERSE EVENT REPORTING

Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying with the reporting requirements. All Serious Adverse Events will be reported to the UCSD IRB and to NIH within two business days.

2.4.4 REPORTING EVENTS TO PARTICIPANTS

N/A

2.4.5 EVENTS OF SPECIAL INTEREST

N/A

2.4.6 REPORTING OF PREGNANCY

N/A

2.5 UNANTICIPATED PROBLEMS

2.5.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

2.5.2 UNANTICIPATED PROBLEMS REPORTING

[The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the Data Coordinating Center (DCC)/lead principal investigator (PI). The UP report will include the following information:

Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying

with the reporting requirements. All Serious Adverse Events will be reported to the UCSD IRB and to NIH within two business days.

2.5.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

3 STATISTICAL CONSIDERATIONS

3.1 STATISTICAL HYPOTHESES

- Primary Endpoint(s):

For the primary outcome, we hypothesize that diagnostic testing among household members of students will be higher in the control arm. We will test this hypothesis using self-administered survey data. Survey participants will be asked if they (1)have learned of any positive cases at the school site in the previous 14 days, and (2)whether or not they and their household members accessed a diagnostic test as a result of that notification.

- Secondary Endpoint(s):

N/A

3.2 SAMPLE SIZE DETERMINATION

Power was computed for a randomized stepped wedge design with 48 schools, 4 clusters (12 schools per cluster), and 5 steps with 1 cluster per step (or 4-week interval) based on diagnostic testing uptake in response to a positive environmental signal (see 1, responsive testing). Power is based on the primary outcome, on-site COVID-19 diagnostic testing uptake in response to a positive environmental signal in schools (see section A.4.1 and C.5.2). Published studies on the uptake of COVID-19 diagnostic testing among school-aged children and their household members in the presence of environmental surveillance are non-existent. We relied on testing rates observed in San Diego County schools during the latter half of the 2020-2021 academic year. Assuming a baseline COVID-19 testing rate of 2%, intra-class correlation ICC=0.10, Type I error rate of 0.05, and an average of 500 staff/students per school, we will have more than 80% power to detect a minimal difference of 0.06% in weekly testing uptake (2.0% pre SASEA-SNAP vs. 2.6% post SASE-SNAP). Using similar assumptions for the secondary outcome, COVID-19 diagnostic testing uptake within household members of students, we will have over 80% power to identify a minimal detectable difference of 2.8% in testing uptake with a serial cross-sectional sample of 2,880 parents (2.0% pre SASEA-SNAP vs. 4.8% post SASEA-SNAP). Power was calculated in STATA 16.1 using a method described by Hemming and Girling

3.3 POPULATIONS FOR ANALYSES

A random cross-sectional sample of parents and caregivers will be selected to participate in a 5–10-minute self-administered survey conducted at 4-week intervals (see Table 3). Prospective parent participants will be identified using a sampling frame provided by schools, at the beginning of the school year, consisting of classroom, classroom size, and grade level. From the sampling frame, three classrooms within each school will be randomly selected. Within the randomly selected classroom, teachers will distribute a survey invitation to all students. Average class size is 25 and we anticipate a 15% response rate per class, resulting in approximately 12 surveys per school or approximately 144 surveys per cluster; equating to 2,880 parent surveys during the 20-week period. Random samples of classrooms will be selected every 4-weeks with replacement using a randomization schedule generated by the study biostatistician, Dr. Gaines. To increase generalizability, we will randomly select serial cross-sectional samples with replacement since serial samples will allow for greater representation given the likelihood of student absences on the day of recruitment (e.g., potential for individual students to be absent and/or classrooms to be quarantined due to COVID-19 exposure).

3.4 STATISTICAL ANALYSES

3.4.1 GENERAL APPROACH

As a guide, the following should be addressed, as appropriate:

- *For descriptive statistics, describe how categorical and continuous data will be presented (e.g., percentages, means with standard deviations, median, range.*
- *For qualitative research, describe how procedural and interpretive rigor will be monitored and maintained*
- *For inferential tests, indicate the p-value and confidence intervals for statistical significance (Type I error) and whether one or two-tailed*
- *Indicate whether covariates will be pre-specified in the sections below or later in a SAP*
- *State whether checks of assumptions (e.g., normality) underlying statistical procedures will be performed and whether any corrective procedures will be applied (e.g., transformation or nonparametric tests)*

<Insert text>

3.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

Descriptive statistics will be calculated for all primary outcomes, which will be assessed through the collection of weekly diagnostic testing surveillance data (provided by SDHHSA) and serial cross-sectional parent surveys. The primary outcome, diagnostic testing before and after implementation of the SASEA program will be examined using a mixed effects logistic regression with fixed effects for Time, SASEA program, and the interaction of Time x SASEA program. The mixed effects model will include a random component for school-level intercepts (to account for students nested within schools) and district-level intercepts (to account for schools nested in districts). Potential confounders will be controlled for in the

model (e.g., baseline COVID-19 diagnostic testing and vaccination rates within communities encompassing schools, school size, race/ethnicity, % receiving free/reduced lunch).

3.4.3 SAFETY ANALYSES

N/A

3.4.4 BASELINE DESCRIPTIVE STATISTICS

Include content in this section if applicable, otherwise note as "N/A."

Intervention groups should be compared on baseline characteristics (e.g., demographics, laboratory measurements, behavioral characteristics) using descriptive statistics. Discuss planned baseline descriptive statistics, and indicate whether inferential statistics will be used.

<Insert text>

3.4.5 PLANNED INTERIM ANALYSES

N/A

3.4.6 SUB-GROUP ANALYSES

N/A

3.4.7 TABULATION OF INDIVIDUAL PARTICIPANT DATA

State whether individual participant data will be listed by measure and time point.

N/A

3.4.8 EXPLORATORY ANALYSES

All planned exploratory analyses should be specified in the protocol.

<Insert text>

4 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

4.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

4.1.1 INFORMED CONSENT PROCESS

4.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Any consent forms will be approved by the IRB prior to research activity onset. Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and written documentation of informed consent will be completed prior to starting the study intervention. The following consent materials are submitted with this protocol: consent form for community survey.

4.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Consent forms will be required to be completed prior to starting the community survey. Consent forms will be available in English and Spanish. An email address and phone number will be provided if individuals have questions.

STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (ie, significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency and IRB

4.1.2 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

There will be no medical records collected for this study.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored on a secure server at UCSD. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by UCSD research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at Redcap.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal

statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.]

Survey data will be securely stored in UCSD's REDCap database. Study personnel accessing the data will be required to access UCSD's VPN and Active Directory log in to enter REDCap. We take care to ensure that participants cannot be identified on the basis of a combination of metadata values (e.g zip code). Qualitative data transcripts will be stored in UCSD's Microsoft One Drive.

4.1.3 FUTURE USE OF STORED SPECIMENS AND DATA

Survey data collected for this study will be analyzed and stored at Duke University using the RADxUp database. After the study is completed, the de-identified, archived data will be transmitted to and stored at the RADxUp database, for use by other researchers including those outside of the study. Permission to transmit data to the RADxUp database will be included in the informed consent.

When the study is completed, access to study data will be provided through the RADxUp database managed by Duke University. There will be no specimens collected for this study.

4.1.4 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator
Rebecca Fielding Miller, PHD, Professor
University of California San Diego
9500 Gilman Drive, La Jolla CA 92093
(858) 534-2230
rfieldingmiller@health.ucsd.edu

Rebecca Fielding-Miller, PhD MSPH, or her designees, who will constitute the committee responsible for monitoring the safety of this study, executing the Data and Safety Monitoring Plan (DSMP), and complying with the reporting requirements.

4.1.5 SAFETY OVERSIGHT

As required by the FOA, Dr. Fielding-Miller, PhD, MSPH, PI of the study, will establish a Data and Safety Monitoring Board (DSMB) to monitor data and oversee participant safety. Members of the DSMB who have expressed their willingness to participate include Dr. Natasha Martin, DPhil, Dr. Nanda Ramchandar, MD, and Dr. Laramie Smith, PhD. At the first meeting, the DSMB will review the study's protocol. Thereafter, the DSMB will monitor and review recruitment, adverse events, data quality, outcome data,

and overall awardee performance. The DSMB has the responsibility to review interim data and final data, and recommend whether the protocol should be modified, and, at each meeting, whether the study should be continued or should be terminated early. The significance of the DSMB's ethical responsibilities, to the participants as well as to the integrity of the study, are of paramount importance to individual members of the proposed research alliance of UCSD, SDCOE, our school district partners, and to the National Institutes of Health.

4.1.6 CLINICAL MONITORING

The study is collecting survey data, there is no clinical monitoring

4.1.7 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed*.*

Source documents and the electronic data --- Data will be initially captured on source documents (see **Section 10.1.9, Data Handling and Record Keeping**) and will ultimately be entered into the study database. To ensure accuracy site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

4.1.8 DATA HANDLING AND RECORD KEEPING

4.1.8.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the stepped-wedged study staff under the principal investigator's supervision. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data.

Survey data will be collected through REDCap, and entered into RADxUp database. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

4.1.8.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

4.1.9 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within days of identification of the protocol deviation. All deviations will be addressed in study source documents, reported to the NIH. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements.

4.1.10 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 3 years after the completion of the primary endpoint by contacting Duke University RADxUP database. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

4.1.11 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the RADxUp has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

4.2 ADDITIONAL CONSIDERATIONS

N/A

4.3 PROTOCOL AMENDMENT HISTORY

N/A. 1 protocol write up version