Project Title: PROmotion of COvid-19 VA(X)ccination in the Emergency Department – PROCOVAXED

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Study Procedures Manual for Specific Aims Three and Four – Cluster Randomized Trial:

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- **Overview**

This MOP addresses the following specific aims of the PROCOVAXED Study:

Specific Aim III: To determine whether implementation of PROCOVAXED trusted messaging platforms in EDs is associated with increased COVID-19 and influenza vaccine acceptance (i.e. converse of vaccine hesitancy) in ED patients.

At five safety net EDs (Zuckerberg San Francisco General, [San Francisco, CA], Thomas Jefferson University Hospital [Philadelphia, PA], Methodist Hospital [Philadelphia, PA], Harborview Medical Center [Seattle, WA], and Duke University Medical Center [Durham, NC]), we will conduct a cluster-randomized controlled trial of implementation of PROCOVAXED trusted messaging platforms, with COVID-19 and influenza vaccine acceptance rates on post-intervention ED surveys as the primary outcomes. *Hypothesis: Implementation of PROCOVAXED trusted messaging platforms in EDs will be associated with increased acceptance of COVID-19 and influenza vaccines in ED patients.*

Specific Aim IV: To determine whether implementation of PROCOVAXED platforms in EDs is associated with increased COVID-19 and influenza vaccine uptake in ED Usual Source of Care (USCARE) patients.

One month (28 to 32 days) after subjects' index ED visit enrollment in our PROCOVAXED implementation trial, we will conduct electronic health record (EHR) review and phone follow-up surveys to determine ED patient uptake (receipt) of COVID-19 and influenza vaccines. *Hypothesis: Implementation of PROCOVAXED platforms in EDs will be associated with greater COVID-19 and influenza vaccine uptake in ED patients.*

General Design: We will conduct a cluster-randomized controlled trial (RCT) of implementation of our PROCOVAXED trusted messaging platforms in 5 high-volume, safety net hospital EDs, testing two hypotheses that implementation of PROCOVAXED platforms will be associated with **increased acceptance** and **uptake** of COVID-19 and influenza vaccines in ED patients.

- **IRB**

The UCSF Committee on Human Research has approved this study. We will continue with multi-site reliance mechanism that we have used for Specific Aims I and II, as per NIH guidelines for randomized trials.

- **Deposition of Protocol into ClinicalTrials.Gov**

As per federal regulations, we will deposit our full study protocol into the repository https://clinicaltrials.gov/

- **Sites**

We will conduct this research at 5 high-volume EDs in four cities: 1) San Francisco: Zuckerberg San Francisco General Hospital [ZSFGH]; 2) Philadelphia: Thomas Jefferson University Hospital and Methodist Hospital; 3) Seattle: Harborview Medical Center; and 4) Durham, NC: Duke University Medical Center.

- **Randomization**

Within each of the 5 study sites, we will randomize 25 (one-week blocks) to the PROCOVAXED intervention and 25 (one-week blocks) to usual care using one-week periods with blocks of concealed size to ensure equal allocation to the two intervention settings. Our randomizations will be computer-based pseudo-random sequences of 7 days periods, stratified by study center. We will develop 60 random sequences separately for each center which will be enough to last the study for up to 14 months. We will stratify sequences by study week period so that 3 centers will be in the control condition for one week and 2 centers will be in the experimental condition for one week, or vice versa. This will minimize the effect of secular trends on the comparison of the intervention. We will generate a 60-week study calendar based on this randomization scheme. To try to maintain masking of allocation, sites will not be notified of their treatment assignment for the next week no more than 3 days prior to that week.

- **Site Orientation and Training**

The Core UCSF Site will develop orientation materials to familiarize the ED Sites with the study protocol. Each site will employ one or more Clinical Research Coordinators (CRCs), who will report to the Site PI and be responsible for day-to-day study implementation. We will develop and disseminate a manual of operating procedures (MOP) with standard personnel training methods, including education kits with scripts, summary cards, and PowerPoint presentations to assist coordinators in the orientation of site clinicians and other staff to our study protocol. We will convene ZOOM conference calls to review this summary and develop plans for optimization of PROCOVAXED platforms to improve usability and workflow. We will refine procedures with updates delivered to the site PIs during weekly ZOOM conferences.

- **Study Hotline and Quality Assurance**

We will maintain a study hotline and encourage study personnel to contact the PI and Central Study Coordinator for all issues and queries. Hotline hours will be during primary study hours (weekday 8 a.m. to 5 p.m. PST).

We will enact rigorous methods for clinical trial quality assurance and performance improvement, including: 1) systematic review of enrollment logs, 2) quarterly audits of random samples of data for accuracy and missing elements, and 3) structured review of protocol deviations or violations. The Central Study Coordinator will prepare monthly summary report cards, tabulating individual site quality assurance metrics for review during scheduled Steering Committee calls. The overall study PI (Dr. Rodriguez) will discuss site-specific data with site PIs individually and summarize these data collectively during Steering Committee calls, with prompt dissemination of plans for process improvement.

- **Recruitment, Inclusions, Exclusions and Consent**

Practical budget considerations and limits on research personnel in patient care areas during the COVID-19 pandemic, preclude 24/7 delivery of the PROCOVAXED trusted messaging platforms and enrollment in this study. We will use a convenience sample technique to approach all eligible adult patients who present to our study EDs during 6-hour weekday blocks, typically beginning at approximately 10 a.m. and continuing to approximately 4 pm. Sites will have leeway choose their preferred daytime enrollment block period (i.e, 12 to 6 pm, as long as that block remains consistent throughout the study.

Inclusions will be:

- Adults
- Presenting to ED
- Not already vaccinated for SARSCOV2
- Able to provide informed consent
- Fluent in English or Spanish (Spanish only at SF General and Duke sites)
- Anticipated ability to complete study intervention in ED i.e., able to watch 5 minute videoclip

Reviewing ED triage information, we will exclude patients with the following characteristics:

1) Age < 18 years
2) Major trauma such that it will preclude survey
3) Inability to participate in a survey because of intoxication, altered mental status, or critical illness;
4) Incarceration
5) Psychiatric hold.
6) **We will also exclude patients who state that they have already received a COVID-19 vaccine and patients who are in the ED for suspected Covid.**

- **Study Procedures: Intervention Blocks**

The anticipated flow of the study during **Intervention Blocks** is summarized in Figure 1. CRCs and research personnel will begin by setting up their home base of Consents and platforms (video clips, printed materials and scripts for messaging).

Figure 1: <u>Intervention Blocks</u> Study Flow

PROCOVAXED Trial Workflow on <u>Intervention Blocks</u>

Introduction to ED Staff: Clinical Research Coordinators (CRCs) will set up their workstation in the ED and introduce themselves to ED staff (nurses, physicians and mid-levels), informing them that they will be doing the PROCOVAXED study that day. **They will avoid telling providers intervention vs non-intervention arms.**
Initial Screening and Scripted Consent for Surveys: CRCs will review ED dashboards for inclusion and exclusion information. When an eligible patient is identified, the CRC will ask the nurse or doctor caring for the patient whether it is Ok for them to approach the patient about the first survey. Whenever possible, the CRC will ask the provider to first ask the patient if they may speak to them.
For provider approved patients: CRCs will approach eligible patients and deliver a scripted consent for two short surveys (Pre-intervention) FIRST SURVEY and the (Post-Intervention) SECOND SURVEY. See Scripted Consent for the Intervention periods.
Complete PROCOVAXED Screening.Enrollment log for all patients.
First Survey in the ED: For patients agreeing to the above surveys, we will administer a short survey – a baseline survey to be complete after obtaining scripted consent at the beginning of their ED visit (before exposure to the messaging platform intervention – PROCOVAXED FIRST SURVEY). CRCs will have the option of inputting survey responses to REDCap on iPads in real time or using paper surveys (and later inputting into REDCap). **These surveys are to be delivered orally (CRC asks questions), not via handing them out.**
Covid Vaccine Flyer, Videos and Telling Provider to Deliver Message: At the end of the survey, the CRC will deliver the Covid vaccine information flyer and ask the patient if they will watch a short video about Covid vaccines. If they agree to watch the video, the CRC will show them the video on the iPad. After finishing with the video, the CRC will tell the subject that they will be back in about an hour for the second survey. The CRC will then leave the room and tell the patient's primary provider (doctor, mid-level practitioner, or nurse) to deliver the message (hand them the scripted message).
Intervention: The intervention will consist of three messaging platforms to reduce vaccine hesitancy that have been produced in Specific Aims I and II:

- Video clips – short (approximately 3 minute) Public Service Announcement type videos that we developed during Specific Aims I and II. These will be shown to the subjects on iPads.
- Printed materials – one page information sheets.
- Face to face messaging – short (< 1 minute), scripted message from the patient's providers in the ED (nurse or provider)

All of the above platforms have been reviewed and approved by the UCSF IRB

Each site will maintain a library of
A. 4-5 versions of the video clips - the particular version used in any particular patient

will be tailored to particular patients as guided by our previously conducted qualitative data analysis in Specific Aim I. See ***below
B. 4-5 versions of printed materials – likewise, particular versions will be tailored to particular patients. See ***below
C. 1 version of the scripted message

Delivery of Study Intervention: All surveys and interventions will be delivered in real-time patient visits in site EDs, during waiting times such that they will not interfere with patient care.

- Video clips will be delivered by iPads in patient's rooms.
- Printed materials will be handed to subjects by CRCs.
- CRCs will hand the patient's provider(s) the script for face-to-face messages and ask that they deliver it to the patient. These messages will be very short and should not significantly impact provider workflow. Notably, vaccine messaging is recommended in the ED by the American College of Emergency Physicians and other health care organizations (Centers for Disease Control).

***We will deliver messaging from our platform libraries in patients' preferred language (English, Spanish). To the extent possible, we will follow qualitative interview recommendations from Specific Aim 1 to choose platforms from site libraries that match video clip and printed material messengers with subjects' likely preferences for race, ethnicity, age and gender (e.g., Latino messenger on video clip with Latino subject).

At months 4 and 8 of the trial, we will review subject feedback regarding the most effective and least effective messaging tools and will consider modifying the choices and matching of messaging platforms, e.g., greater emphasis on video clips over printed materials. These changes will not entail true alterations in the overall PROCOVAXED intervention strategy; they will instead be minor adjustments to platform content.

Second Survey (Post-Intervention) in the ED: We will administer a short survey approximately one hour after the intervention (after all 3 platforms). See SECOND SURVEY: INTERVENTION GROUP.
Complete Master Data Flow Log after each patient enrolled.
NOTE: All of the above study procedures should be performed in patient waiting times and not interfere or disrupt patient care in any way.

- **Study Procedures: <u>Non-Intervention Blocks</u>**

The anticipated flow of the study during **Non-Intervention Blocks** is summarized in Figure 1.
Figure 2: <u>Non-Intervention Blocks</u> Study Flow

PROCOVAXED Trial Workflow on <u>Non-Intervention Blocks</u>

Introduction to ED Staff: Clinical Research Coordinators (CRCs) will set up their workstation in the ED and introduce themselves to ED staff (nurses, physicians and mid-levels), informing them that they will be doing the PROCOVAXED study that day.
CRCs will avoid telling providers intervention vs non-intervention arms.
Initial Screening and Scripted Consent for Surveys: CRCs will review ED dashboards for inclusion and exclusion information. When an eligible patient is identified, the CRC will ask the nurse or doctor caring for the patient whether it is Ok for them to approach the patient about the first survey. Whenever possible, the CRC will ask the provider to first ask the patient if they may speak to them.
For provider approved patients: CRCs will approach eligible patients and deliver a scripted consent for two short surveys: the Non-Intervention FIRST SURVEY and the Non-Intervention SECOND SURVEY. See Scripted Consent for the Non-Intervention periods.
CRCs will complete screening and enrollment log indicating whether or not they agreed to this survey. If they agreed to survey, CRC will assign a Study ID# and proceed to Master Data Flow form.
First Survey in the ED: For patients agreeing to the above surveys, we will administer a short survey – a baseline survey to be complete after obtaining scripted consent at the beginning of their ED visit (before exposure to the messaging platform intervention – PROCOVAXED FIRST SURVEY). CRCs will have the option of inputting surveys to REDCap on iPads in real time or using paper surveys (and later inputting into REDCap).
These surveys are to be delivered orally (CRC asks questions), not via handing them out. First Surveys are the same for intervention and non-intervention blocks.
Second Survey in the ED: We will administer a second short survey at some time (approximately 1 hour) after the FIRST SURVEY. See SECOND SURVEY: NON-INTERVENTION GROUP. These second surveys in the non-intervention group have the same key primary and secondary outcome questions as in the INTERVENTION GROUP second surveys. SECOND SURVEY: NON-INTERVENTION GROUP.

NOTE: All of the above study procedures should be performed in patient waiting times and not interfere or disrupt patient care in any way.

- **Research Staff Informing of ED Providers when Participants will accept Covid vaccine**

At this time all of our EDs have the capability of administering COVID19 vaccines in some manner, and we expect that this will continue for at least the first 6 months of the trial. The last question in the SECOND SURVEY **in both arms** of the study is "*Would you accept the Covid vaccine in the emergency department today if your doctor asked*

you?" When a participant says they will accept the vaccine, the CRC or research staff will ask the patient if they can notify the patient's providers (nurse and/or physician) that they said they will accept the vaccine. They will also ask the patient if they (the CRC) can check to see if the patient receives the vaccine in the ED.
Other than this question and notification, research staff will not push that they get vaccinated.

- **Consent for 1- Month Follow Up Surveys for patients saying No to Vaccine in ED**

For all patients saying **no** to the question "*Would you accept the Covid vaccine in the emergency department today if your doctor asked you?*", research staff will ask if they can contact them and review their records in a month for follow up via full written consent. If patient says yes, then the CRC will get full **written** informed consent, including a separate HIPAA form, for review of their records and phone call. See FOLLOW UP Consent. Patients will not be compensated for participation. We will then ask Subjects for their best phone number(s) to reach them for a follow-up phone call. Sites will maintain a separate password protected database of subject IDs and follow up phone #s. Patients may agree to a phone call and not the EHR review, or vice versa. In those cases obtain the relevant consent, and note that they have accepted only one or the other.
We will also ask for 1-month follow up in those subjects who said YES to accepting the Covid vaccine in the ED and did not get the vaccine in the ED. We will attempt to get full **written** informed consent for review of their records and phone call at 1 month in the same manner as above.

- **Community Covid Vaccine Information for patients saying No to Vaccine in ED**

Additionally, if the patient says no to accepting the vaccine in the ED today, the CRC will also ask, "*Would you like some information about where you can get a Covid vaccine outside of the emergency department?"* If the patient says yes, then the CRC will provide information about where they can get a Covid vaccine outside of the ED (community locations).

- **Primary Outcomes and Ascertainment**

Our primary outcome for Specific Aim III is **vaccine acceptance at the time of SECOND SURVEY** (the converse of vaccine hesitancy) defined as a response of "*yes*" to the question "*Would you accept the Covid vaccine in the emergency department today if your doctor asked you?*" This and other outcomes for Specific Aim III will be ascertained during the SECOND SURVEYS at the end of their index ED visit. **If the patient says yes, the CRC will then ask the patient if it is acceptable for them to notify the provider and confirm their receipt of the vaccine. If the patient says yes, the CRC will notify the provider that they are willing to get the vaccine. CRCs will later confirm with the provider that the patient received the COVID-19 vaccine in the ED.**
Our primary outcome for specific aim IV will be **uptake (receipt) of a COVID-19**

vaccine (at any vaccination location) within 28 to 32 days after their index ED visit. For ascertainment of this primary outcome:

- As above, for patients who stated they would accept it in the ED today, CRCs will confirm whether the patient received the vaccine directly from providers or by review of that patient's EHR the following day.
- For those who do not accept the vaccine in the ED **and consent to follow up**: We will conduct EHR review and follow-up phone calls (*Have you received a COVID-19 vaccine?)* one month after index ED visits.

- **28 to 32 Day Follow-Up for Ascertainment of Primary Outcomes**

CRCs will review Master Data Flow daily (workdays) to determine which subjects have reached the 28-day follow-up time period. The CRC will conduct the first follow-up EHR review and, if necessary, follow up phone call attempt on that 28th index day. For the subsequent second and third EHR reviews and follow-up phone calls, CRCs will use the following weekday calendar, which will ensure no greater than 32 days between the index visit and final outcome ascertainment:

Index Study Visit Day of Week	First Call (Same day of week as index study visit – 4 weeks later)	Second Call	Third Call
Monday	Monday	Tuesday	Wednesday
Tuesday	Tuesday	Wednesday	Thursday
Wednesday	Wednesday	Thursday	Friday
Thursday	Thursday	Friday	Monday
Friday	Friday	Monday	Tuesday

Study subject's medical record #s and telephone #s will be accessed from the **PROCOVAXED Follow up** sheet. **The CRC who conducts this EHR and phone follow-up will be blinded to the subject's study group assignment (intervention vs non-intervention), i.e., a separate CRC who does not recruit at that site will conduct this phone follow-up.**

- The CRC will first review the EHR to determine whether there is any record of a Covid vaccination in the preceding time period from the study index visit. If there is a record of vaccination, the CRC will record what date and where the study received it. See **Follow up Data Collection** form.
- If there is no record of vaccination in the EHR, the CRC will proceed with a phone call to the study subject. See **Follow up Data Collection** form. CRCs will enter follow up data on both the Master Data Flow and Follow up spreadsheets

via REDCap links.

- If the patient does not answer the phone that morning, the CRC will place two more calls to the study subject over the next 2 workdays. They will vary the time of these calls to improve response.
- If the patient does not answer the phone by the third call, the CRC will leave a message with the phone # of the study team. No more calls will be initiated by the study team after this third call.
- If there is no call received from the study subject one week after the 3rd call, the phone follow up will be considered as incomplete.

Of note, CRCs will only review EHR and conduct phone follow-up with study subjects who have given written consent for these follow-up techniques.

In terms of final ascertainment of Specific Aim 4 (uptake of Covid Vaccine within 28 to 32 days of index ED visit), we will use the following scheme:

Yes, Covid vaccine received	**Any of the following:** • **Confirmed receipt of Covid vaccine during index ED visit** • **Confirmed receipt of Covid vaccine via EHR review** • **Confirmed receipt of Covid vaccine via phone follow-up call**

No, Covid vaccine not received	**All of the following:** • **Did not receive Covid vaccine in ED during index visit** • **Did not receive Covid vaccine on EHR review** • **Did not receive Covid vaccine on phone follow-up call** ****If subject did not receive Covid vaccine in the ED, these 2 scenarios will also qualify as Covid vaccine not received:** • **Did not received Covid vaccine on EHR review but unable to complete phone follow-up** • **Did not received Covid vaccine on phone follow-up but unable to complete EHR review**
Indeterminate	**Unable to review EHR and Unable to contact subject via phone call**

- **Data Recording and Entry**

CRCs will record survey responses and other data via two mechanisms:

- Direct entry into the PROCOVAXED Study REDCap database in real time during surveys via secure links
- Recording onto paper forms first. Then entry of survey information and data after each participant enrollment.

CRCs will keep a running log of all study flow and enrollment, recording on REDCap forms the following data for all patients approached: study date, study arm, “Yes” and “No” to having received a Covid vaccine, “Yes” and “No” agreeing to first surveys, delivery or non-receipt of messaging platforms, agreeing to receipt of study vaccines, receipt of vaccines in the ED, “Yes” and “No” agreeing to follow-up calls and EHR review. See Enrollment Log and Master Data Flow. CRCs will also record First and Second Survey responses on REDCap. Sites are allowed to use either one of two methods for REDCap data entry: recording of survey response on printed sheets and later entering on REDCap, or recording responses in real time directly on REDCap via iPads.

- **Data Analysis**
- **Primary Analysis**

We will compare primary outcomes in patients seen on PROCOVAXED intervention dates with those seen on non-intervention dates to test our 2 study hypotheses. We will measure outcomes in all ED patients surveyed as our group of primary outcome

analysis.

The two primary outcomes are the verbal acceptance (Second Survey response) of a Covid vaccine in the ED and the receipt of at least one dose of a Covid vaccine dose within 30 to 32 days after the index ED visit. Both outcomes will be compared using mixed logistic regression with a fixed effect for randomization assignment, a random slope to allow for clustering by enrolling center, and a random slope to allow for secular trends. The treatment effect will be tested by the coefficient for the fixed effect of intervention along with 95% confidence intervals

- **Sub-analyses**

Another focus of this research is on the ED Usual Source of Care group, defined on the FIRST SURVEY questions as

- An answer of "No" or "Unsure" to the question: "*Do you have a regular clinic or doctor for medical care?"*

OR,

- *If they say "Yes" to* the question: "*Do you have a regular clinic or doctor for medical care?", an answer of > 2 years to the question "*If YES to regular doctor, when was the last time you saw this doctor or went to this clinic?"

We will conduct subgroup analyses of the same primary outcomes of this ED Usual Source of Care group.

We will additionally stratify outcomes by study site (representing different regions of the country and different communities), age, gender, and race/ethnicity. We will also analyze outcomes according to patient-level experience characteristics, such as having already had COVID-19.

- **Rationale for time (1 week unit) cluster and consideration of Alternative Study Designs:**

Our primary goal with this research is to determine whether real-world implementation of PROCOVAXED as an ED-site level intervention results in greater acceptance and uptake of COVID-19 vaccines in vulnerable ED populations. Each site sees approximately 150-250 patients per day and applying or not applying the intervention (delivery of PROCOVAXED messaging) *for individual patients* in this high workflow, rapid patient turnover ED environment is simply impractical. Patient level randomization may also result in high risk of cross-contamination between intervention and control arms in terms of the messaging flyer and direct ED provider messaging platforms. Therefore, removal of the intervention from the site completely during specified time periods (1-week units) of non-intervention is the optimal approach. Although a single switch of the intervention at each site (i.e., stepped-wedge trial design) is easier to enact, changes in general population attitudes over time introduce bias that limit the validity of this trial method. We expect gradually increasing acceptance of the COVID-19 vaccine over time, which would introduce substantial bias toward the intervention. These practical and methodological benefits of the 1-week unit cluster RCT far outweigh the smaller sample size and easier analysis with an individual patient unit RCT or a stepped-wedge design.

Statistical approach: In terms of statistical approach, this is a superiority trial in which we seek to verify our central study hypothesis that provision of PROCOVAXED will

result in greater acceptance and uptake of the COVID-19 vaccine. Following the recommendations of Hussey and Hughes, our statistical analyses of AIMS III and IV will focus on comparing the vaccine and uptake rates during the time periods when PROCOVAXED is in place (intervention) and when the system is not in place (usual care) using mixed effects logistic models.[122,123] The outcomes of interest are the binary indicators of whether a patient will accept the COVID-19 vaccine ("*Will you accept the COVID-19 vaccine if it was offered to you*" – yes/no) and whether they have received a COVID-19 vaccine (uptake - yes/no) upon follow-up. Models will include a random center effect to accommodate potential within-center characteristics (e.g., case mix, demographics), as well as terms for time and intervention. Hypothesis tests will focus on the statistical significance of the intervention indicator. We will fit the mixed effects models using maximum likelihood and routines in Stata or SAS.
We will test our primary hypothesis and analyze outcomes according to the study arm (index visit in intervention month vs non-intervention month) to which patients were allocated, regardless of whether they received PROCOVAXED messaging or not - ***intention to treat analysis***. We will also conduct a ***per-protocol analysis****,* in which we assess results that would occur if they actually did or did not receive PROCOVAXED messaging (e.g., viewed the video clip given to them) during their index visit (ascertained by direct questioning in the Outcome Survey). When compared to the primary analysis, the per-protocol analysis will allow us to dissect the reasons for success (or failure) in demonstrating improved vaccine acceptance and uptake with PROCOVAXED. For example, if we find better acceptance and uptake in the per protocol analysis and not in the intention to treat allocation analysis, we would subsequently seek ways to improve delivery of PROCOVAXED messaging. Conversely, if both analyses fail to improve acceptance, then the PROCOVAXED intervention truly fails and other efforts to improve delivery would not be indicated. In addition to the effects on *total* vaccine acceptance, we will also examine the effect of PROCOVAXED on acceptance in patient sub-groups, especially African Americans and Latinos. PROCOVAXED may work for one patient sub-group and not others - these additional analyses will guide future directions and modifications of PROCOVAXED messaging.

- **Data management plan**

We will manage data using REDCap, hosted by the core site (UCSF) for secure data entry and management. Patient identifiers (medical record numbers and phone numbers) only link will be to unique study ID numbers, which will be housed in files that are kept separate from other study data. We have developed a detailed data dictionary to ensure consistent standards across sites. We will reduce missing or erroneous data using the REDcap data quality tool.

- **Sample Size Considerations**

The sample size calculations for this research are governed by hypothesis testing of Specific Aims III and IV -- *Implementation of a trusted messenger informational program will be associated with increased acceptance and uptake (receipt) of COVID-19*

vaccination in ED USCARE patients. Considering the commonality of hesitancy (non-acceptance), the high benefit of increasing acceptance and the negligible risk of the intervention (a trusted messaging program), even a small effect size of increased acceptance would be a clinically important difference. By investigator consensus and in consultation with a panel of health policy experts, we have determined that PROCOVAXED would be clinically useful if it increased acceptance by 7%. Similarly, with the same considerations of negligible risk, we have determined that PROCOVAXED would be useful with an effect size on vaccine uptake of 7%.
Our sample size calculations accommodate the randomization of clusters design consisting of 1 week periods (implementation of PROCOVAXED months and non-implementation) to the intervention at each of six sites. To avoid period effects, we will assign sites using a Latin square design S2. This design is more efficient than either the randomization of site for the study period or for individual subject randomization. We base the sample size calculation on the comparison of the proportion of patients who accept the vaccine between the PROCOVAXED and usual care time periods using standard formulae for individual randomization. We have verified that these sample sizes are conservative by simulation of data using a mixed random effects model.
When our protocol was originally written in February 2021, vaccines were not widely available and the degree of baseline vaccine acceptance and uptake was unknown. We therefore calculated sample sizes for a wide range of vaccine acceptance and uptake rates with a plan to measure these in the non-intervention (control) group during the first month of the trial. After the first month, we estimate that our baseline vaccine acceptance and uptake rates (without intervention) will be approximately 15%. With this baseline uptake rate of 15%, we find that at an alpha=0.05 level and a power of at least 0.9, we will need to enroll 1,290 patients (645 in each arm) in the study to detect the difference of interest (a setting in which the vaccine acceptance rate will increase by 7% in PROCOVAXED weeks).
With this same baseline 15% rate of uptake and the same specifications for power, we will need to enroll 1,290 patients (645 in each arm) to detect a vaccine uptake difference (the primary outcome of Specific Aim IV) of 7%. Thus, our target enrollment for this implementation trial is 1290 subjects across all sites.
In terms of total projected time for enrollment, we expect a minimum enrollment of 1 subject per site per day (6 hour block) at the 5 sites, or 25 enrollees per 5 day work week. We therefore expect to attain our target enrollment of 1290 subjects in approximately 50 weeks.

- **Consents and Rationale**

Survey Consent We will obtain scripted verbal consent for the surveys in the usual manner that we have conducted other survey studies of similar design and scope - (CHR. See 2 versions of this Scripted consent for the Intervention periods and for the Non-intervention periods. (Intervention and Non-Intervention).
We will obtain written consent for follow up chart review and phone calls. See FOLLOW UP Consent.
With regards to consent for delivery of the intervention (Covid vaccine

messaging) during intervention periods, we must emphasize that messaging for vaccine hesitancy is firmly a part of standard best-practice emergency department care (messaging of this type is currently be enacted in EDs across the US). Delivery of all of the vaccine messaging platforms is therefore an accepted common best practice not requiring consent. To add an extra layer of consent could even lead to greater vaccine hesitancy. We therefore plan the following processes with verbal assent during the PROCOVAXED FIRST SURVEY **in intervention months:**

- Handing patients the Covid vaccine message information sheet at the end of the first survey.
- Informing the patient's provider(s) of the short scripted vaccine message to deliver to the patient sometime after the FIRST SURVEY
- At the end of the FIRST SURVEY, asking patients if they are willing to watch the vaccine messaging video(s). If the patient says *Yes*, then we will play the video. If the patient says no, we will not play the video.