Trusted Messengers: Intervention to Promote COVID-19 Vaccination

NCT04981392

Protocol and Analysis Plan

Version Date: August 1, 2022

INVESTIGATOR STUDY PLAN - REQUIRED

1. TITLE

Trusted Messengers: Supporting Physicians in Promoting COVID-19 Vaccination

2. EXTERNAL IRB REVIEW HISTORY*

N/A

3. PRIOR APPROVALS:

We have received prior approvals from the individuals at each of the clinical sites as follows:

1. University of Massachusetts Medical Center (UMMHC)
2. Family Health Center of Worcester (FHCW)
3. Edward M. Kennedy Community Health Center (EMKCHC)

4. OBJECTIVES*

This study aims to refine and test strategies to overcome COVID-19 vaccine hesitancy, particularly among vulnerable populations, through a community-engaged approach. We will accomplish our goals via the following specific aims:

Aim 1 (Focus Groups): To refine and adapt tools to support effective Primary Care Provider (PCP) recommendations for COVID-19 vaccination and information dissemination by PCPs and community organizations to vulnerable patients. Tools will include: (1) an online library of brief, culturally appropriate videos depicting PCP conversations with patients that address common concerns about the COVID-19 vaccine, to be disseminated by PCPs and community organizations; (2) automated PCP text messaging to patients recommending COVID-19 vaccination; and (3) educational materials for PCPs to support their conversations with patients about the COVID-19 vaccine.

Aim 2 (Intervention/Clinical Trial): To implement and assess the impact of the intervention on COVID-19 vaccine uptake through a large, pragmatic cluster randomized clinical trial in primary care clinics from 3 healthcare systems that serve populations vulnerable to both health disparities and COVID-19 vaccine hesitancy, including two federally qualified health center (FQHCs) and UMass Memorial Health Care (UMMHC). The primary outcome will be COVID-19 vaccine uptake among initially unvaccinated patients.

Aim 3 (Interviews): To evaluate the intervention according to the RE-AIM framework (Reach-Effectiveness-Adoption-Implementation-Maintenance[1]), incorporating the perspectives of patients, primary care providers, and clinic leaders, while characterizing the community environment and context. The findings of Aim 3 will be used to create an implementation guide to accompany the tools which will be made freely available for use by other physicians, healthcare systems, and community organizations.

We will submit two separate IRB applications for this study. This application is for Aim 2 (Intervention). The IRB application for Aim 1 (Focus Groups) and Aim 3 (Interviews) was submitted to the IRB on April 28, 2021 (IRB # H00023125).

5. BACKGROUND*

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and associated coronavirus disease 2019 (COVID-19) pandemic have been devastating. In the United States (US), more than 25 million people have been infected, resulting in more than 430,000 deaths. Black and Latino communities have borne a starkly disproportionate impact of COVID-19, compounding existing health disparities. The approval of multiple effective COVID-19 vaccines has raised hope that a return to "normal" life may be at hand. However, realizing the benefits of a vaccine requires widespread acceptance and vaccine uptake. Recent estimates suggest that as many as 90% of the population may need to be vaccinated to achieve herd immunity. Our work and that of others indicate a significant proportion of the US population are reluctant to be vaccinated. Overlap between factors associated with COVID-19 disease and COVID-19 vaccine hesitancy, including being of Black or Latino race/ethnicity, and socioeconomic disadvantage, threaten to severely exacerbate existing health disparities.

Our research hypothesis is that trusted messengers, such as PCPs and community organizations, are essential to increasing uptake of the COVID-19 vaccine, particularly for the most hesitant groups. Healthcare provider (HCP) recommendations for vaccination have consistently been associated with higher rates of vaccine uptake.[2-8] A recent poll in Massachusetts found that *people's own doctors* are the most trusted source of information regarding the COVID-19 vaccine, across all demographic groups.[9] In addition, a recommendation from a physician is highly influential in promoting uptake of other vaccines (e.g., influenza), underscoring the critical role of physicians in promoting COVID-19 vaccination. Like physicians, community organizations have been proven to be an essential component of outreach to promote vaccination, particularly among hard-to-reach populations. PCPs and community organizations need resources and tools to help them realize their potential role as trusted messengers to convey accurate, personalized recommendations for COVID-19 vaccination.

Building on strong community partnerships, we will refine, implement, and evaluate a multi-faceted intervention to support PCP outreach, and PCP and community organization dissemination of information to promote COVID-19 vaccination among vulnerable patients in and near Worcester. The intervention will include: (1) a library of videos addressing common vaccine concerns to be disseminated by PCPs and local community organizations; (2) tools to implement PCP outreach and COVID-19 vaccine recommendation; and (3) educational materials for PCPs to support their conversations with patients about the COVID-19 vaccine. We will implement and evaluate the intervention at three clinical sites via a large pragmatic clinical trial while simultaneously characterizing the community environment in which the intervention is situated. The clinical sites include two FQHCs and UMMHC which collectively serve large populations of racial and/or ethnic minority groups (Black, Latino, non-primary English speakers) and socioeconomically disadvantaged patients. We will work with community organizations to convene and engage community advisory boards to inform message and video development, implementation, and evaluation.

This research will generate crucial evidence of how to effectively promote COVID-19 vaccination among vulnerable populations. Our findings can be applied to promote uptake of other vaccines (including possible COVID-19 vaccine "boosters") among populations at risk of vaccine hesitancy and health disparities.

6. INCLUSION AND EXCLUSION CRITERIA*

Patient Participants

Inclusion criteria

- Patient at a participating clinic site
- Age ≥ 18 years

Exclusion criteria

- None

Provider Participants

Inclusion criteria

- PCP at a participating clinic site
- Age ≥ 18 years

Exclusion criteria

- None

Children

This study will not include children. The study is restricted to adults aged 18 and over.

Prisoners

Prisoners will not be included in the study. We will not knowingly collect data on prisoners.

Pregnant Women

It is possible that data will be collected on pregnant women who meet inclusion criteria, however pregnant women are not a focus of recruitment and the intervention itself is not experimental.

Non-English Speaking Subjects

Non-English speaking subjects will be included in the study. Patient participants will be recruited from primary care clinics which collectively serve a large population of non-primary English speakers.

7. STUDY-WIDE NUMBER OF SUBJECTS*

Patient Participants

The intervention will be implemented at approximately 16 primary care clinics selected from three healthcare systems, including UMMHC, the Edward M. Kennedy Community Health

Center (EMKCHC), and the Family Health Center of Worcester (FHCW). Eligible patients seen at a study clinic are at least 18 years of age or older. Based on the most recent data, there were approximately 152,110 adult (age ≥ 18) patients seen in the selected primary care clinics at UMMHC, EMKCHC, and FHCW.

Provider Participants
Eligible providers are those who currently work at one of the primary care clinics selected from the three healthcare systems (UMMHC, EMKCHC, FHCW). Using information available on each healthcare system's website, we estimated that there are approximately 250 providers employed across the selected primary care clinics who will be eligible to participate in the provider education portion of the intervention. We will collect data from a subset of these providers, covered in IRB docket #H00023125.

8. STUDY-WIDE RECRUITMENT METHODS*

Patient Participants
Patient participants will not be recruited as there are no study-specific activities for them to engage in.

Provider Participants
All sites will follow local recruitment methods. Please see Section #24. Local Recruitment Methods for more information.

9. STUDY TIMELINES

The implementation of the intervention will start after all study materials have been finalized using feedback from focus groups (Aim 1) and community advisory boards. The intervention will be implemented in stages. This will allow for coordinated delivery of a physician education session approximately 1-2 weeks prior to each clinic starting the intervention. The intervention will be implemented in blocks of matched clinics, approximately one block every 1-3 months. We anticipate it taking approximately 6-12 months to complete the intervention at all sites. Patient participants will receive intermittent text messages over a period of approximately 3 weeks. We will examine vaccination status 12 weeks (primary outcome) and 6 months after the last text message to allow for possible lag between the intervention and vaccination. Because the vaccination status in the electronic health record is not immediately updated, these outcomes will be ascertained approximately 3 months after the timepoint in question to allow time for lag in the clinical system updating vaccination status. Therefore, the entire duration of the intervention for an individual patient participant will be approximately 52 weeks.

Provider participant involvement will occur over approximately 2 months.

This study is planned to take place over the course of 3 years, but may be extended if needed until all the tasks and deliverables are complete (see Table 1).

Table 1: Study Timeline

	Year 1				Year 2				Year 3			
Task	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Convene advisory panel, quarterly meetings	X	X	X	X	X	X	X	X	X	X	X	X
IRB approval	X											
Focus groups to refine messages & videos	X	X										
Video production & website creation		X										
Baseline data collection, including interviews	X	X	X									
Identification of study cohort		X										
Randomization of clinics		X										
Intervention – phased start			X	X	X	X	X	X				
Intervention data collection			X	X	X	X	X	X	X	X		
Intervention evaluation						X	X	X	X	X		
Data analysis		X				X			X		X	X
Manuscript preparation	Ongoing											
Implementation guide creation & dissemination									X	X	X	X

10. STUDY ENDPOINTS*

Primary Endpoint

The primary endpoint is the receipt of a complete COVID-19 vaccination series (2 doses for vaccines that require 2 doses) 12 weeks after the last text message, among patients who are unvaccinated at the time of clinic entry into the study.

Secondary Endpoints

Secondary endpoints include receipt of incomplete (1 dose for vaccines that require 2 doses) COVID-19 vaccination series; receipt of a complete COVID-19 vaccination series 6 months after the last text message; racial/ethnic differences in vaccination rates; and the percentage of intervention clinic patients who initiate vaccination after the first batch of provider texts, after the second batch of provider texts, and after the third batch of provider texts.

11. PROCEDURES INVOLVED*

Please see Figure 1 for study activities.

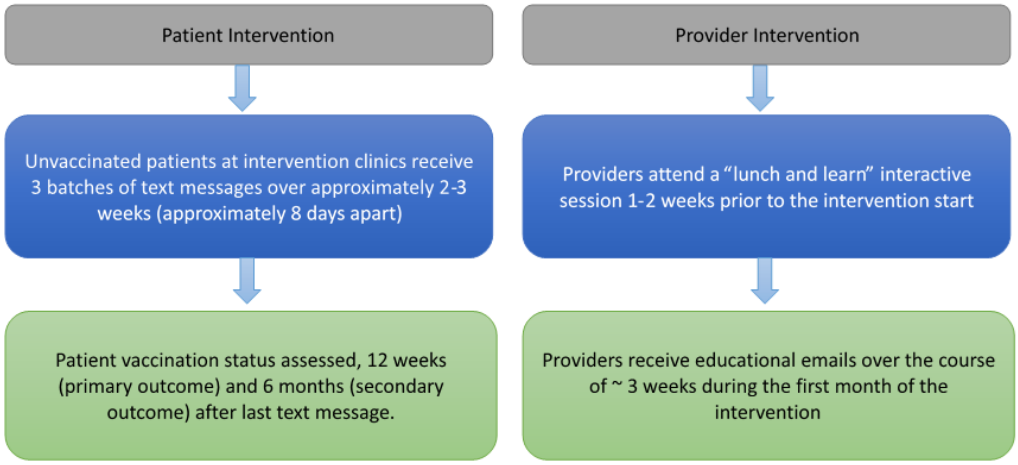
Randomization

Participating clinics will be randomized to the intervention. Clinics will be matched by site (UMMHC, EMKCHC, FHCW), baseline COVID-19 vaccination rates, and availability of COVID-19 vaccines in the clinic, based on advice of the statistician and feasibility. Within each pair, clinics will be randomly allocated to intervention/control condition using a randomization generated by the study statistician. Matched clinics will be grouped into blocks, balancing the blocks regarding sites and baseline vaccination rates.

Intervention Implementation

The details and timing of intervention components at a given study clinic are shown in Table 2.

Figure 1. Aim 2 Study Activities



<u>Patient intervention</u>

Eligible patients seen at a study clinic randomized to the intervention will receive text messages in up to 3 different batches using the clinical text messaging platform at each study site. These messages will be delivered over approximately 2-3 weeks. Patients will have the option to reply "NO" to the text messages to decline further participation at any point during the intervention. Patients at FHC will also have the option to respond "VAXED" or "SCHED" (or some phrasing like these) if they have already been vaccinated and would like their records to reflect that, or if they would like someone to reach out to them to schedule a vaccination appointment. The texting at FHC will all be performed through their secure clinical texting system, HealthTalk AI (HTAI), which is fully HIPAA compliant. HTAI software is hosted in a HIPAA compliant cloud instance and their secure bi-directional communication is encrypted at rest and in transit. If a patient does respond that they would like to schedule a vaccination appointment, the Local Site Champion for the study at FHC will triage their information to a scheduler. All correspondence, updating of medical records, and vaccine scheduling will be performed at FHC by staff performing their typical duties as required by their role. We are requesting a waiver of consent from the IRB. We will collect patient text communication preferences ('yes', 'no', or 'null') and filter out those whose text communication preference is 'no' so that they do not receive any texts. We will follow the clinical system policy for patients whose preference is 'null'.

The first batch of text messages will be delivered at the start of the intervention at a study clinic. Patients who have not been vaccinated against COVID-19 will receive messages from their PCP recommending the COVID-19 vaccine, with information on how and where to schedule a vaccination, and a link to a website with additional information and resources. The message content for each batch will be broken up into separate messages to ensure that the content is readable and not truncated by the texting system. Text message batches #2 and #3 (if applicable) will be sent approximately 1 week after the prior batch and will remind patients of the study website. The message content is included in appendix 1.

Text messages sent out in each batch will be professionally translated into multiple languages and provided in the patient's preferred primary language, according to the capabilities of the clinical text messaging systems. Although messages will be automatically sent via a centralized

system, they will indicate they are from the patient's PCP where possible. If it is not possible to include the PCP's name, the message will refer to the organization where the patient receives care. (See **Appendix 1** for text message content).

The website patients are directed to will be available in multiple languages via an embedded automatic translation feature. The provider videos will also be available in multiple languages via an automatic translation feature embedded in the website or video hosting platform.

Provider intervention

Providers at a study clinic randomized to the intervention will be asked to participate in a "lunch and learn" interactive session approximately 1-2 weeks prior to the start of the intervention. The session will be conducted either via video conference (e.g., Zoom) or in-person, depending on the state of the pandemic. An email inviting providers to these sessions is included in **Appendix 2**.

Providers will be introduced to the study and presented with underlying research supporting message content, as well as the importance of provider recommendations for vaccination. They will be provided with an orientation to the materials on the study website during these sessions. Material to be presented to providers in these sessions is included in **Appendix 3**. This material is intended to be a guide for these sessions. Because these will be interactive sessions with opportunities for questions and discussions, they will necessarily not follow this PowerPoint verbatim.

Providers at intervention clinics will be given the opportunity (separate from participation in a lunch-and-learn session), to decline to have text messages sent to their patients, and/or to identify specific patients to not send text message to. We will ask providers if they are willing to explain their decisions and record that information in a de-identified manner. We are requesting a waiver of consent from the IRB for this aspect of the intervention.

During the first month of the intervention, providers will receive several emails over the course of approximately 3 weeks (the number and timing of emails received may slightly vary depending on feedback received during the focus groups we will conduct; we will not send more than 4 emails over a 4 week period). The draft emails are included in **appendix 2**. The emails will remind providers of the availability of the website and the resources included on the website, and will include an attached "tip sheet" offering tips for talking with vaccine hesitant patients (**appendix 4**). We will email providers periodically with updates as new professional resources or evidence related to COVID-19 vaccines or communicating with patients about COVID-19 vaccination becomes available, as is common practice within the clinical system. Providers will have the option to request not to receive further emails at any point. We will give providers in intervention clinics prescription pads with a link to our website so that they can give "a prescription for trustworthy information" to vaccine hesitant patients. We have included two versions of this prescription pad to be used based on provider preference (**appendix 5**). We are requesting a waiver of consent from the IRB for this aspect of the intervention.

Table 2. Intervention components and timing at an individual clinic.

Intervention Component	Details (what)	Recipient (who)	Timing (when)
Provider intervention			
Provider education	"Lunch and learn" **interactive session** to introduce study, underlying research supporting message content, and importance of provider recommendation for vaccination (**appendix 3**)	Providers at study clinic randomized to intervention	-~ 1-2 weeks prior to intervention start at study clinic
Provider education	• **Emails** with brief educational content (**appendix 2):** • Reminder of the study website and the resources available there • Tip sheet for responding to patient questions and concerns (**appendix 4**) • New scientific information as available	Providers at study clinic randomized to intervention	~ Weekly x 3 during month that intervention starts at study clinic and if new resources or information is available thereafter
Patient intervention (appendix 1)			
Text message batch #1	Text messages from patient's PCP or organization recommending COVID-19 vaccine and the study website (which contains the video library and information on how and where to get vaccinated).	Patients who have not been vaccinated against COVID-19 at time of study clinic entry	Delivered in a set at start of intervention at study clinic
Text message batch #2	Text messages from patient's PCP or organization encouraging the patient to access the study website.	Patients who were unvaccinated at the start of the intervention	Delivered as a set approximately one week after first message
Text message batch #3	Text messages from patient's PCP or organization encouraging the patient to visit the study website	Patients who were unvaccinated at the start of the intervention	Delivered as a set approximately one week after the second message

Control

Eligible patient participants seen at a study clinic randomized to the control group will receive usual care with no text intervention. Providers at a study clinic randomized to the control group will be not be invited to attend the education session or sent any education materials. We are utilizing the Cluster Randomized design in an effort to control cross-group contamination.

EHR Data Collection

All Electronic Health Record (EHR) data pulls will be requested following the UMMS Data Science Core processes (currently located here: https://www.umassmed.edu/research-informatics/data_services/how-to-obtain-data/). EHR data will be pulled at non-UMMS sites according to their local institution-specific processes.

COVID-19 vaccination status will be assessed via EHR on all patients seen at a study clinic to allow clinic matching by vaccination rate at study start. Prior to sending a batch of text messages, the COVID-19 vaccination status of patients in the intervention clinic will be re-assessed to identify those eligible to receive text messages, and their text communication preference will be extracted to allow those who have indicated they do not want to receive text messages to be filtered out.

Data related to the primary and secondary outcomes will be obtained via the EHR system following the completion of the intervention.

We will obtain additional data on all patients via the EHR to conduct supplemental analyses, including demographics (e.g., age, sex, race/ethnicity), text communication preference, text delivery status (delivered/undelivered), any response to study text messages, primary insurer, receipt of influenza vaccine, social vulnerability index (determined using patient address), and selected co-morbid medical conditions associated with risk of COVID-19 disease (e.g., hypertension, diabetes, obesity, congestive heart failure, chronic lung disease).

For additional details, see section 13. Data Analysis and Management.

Screenshots of the website, transcripts of the videos to be hosted on the website, factsheets that include video content adapted for print, and biographical sketches of the providers featured in the videos can be found in **appendices 6, 7, 8, and 9.** The factsheets were professionally translated and submitted to the IRB for review.

12. DATA AND SPECIMEN BANKING*

No specimens are being collected as part of the research. A limited data set will be securely stored for potential future use by the Principal Investigator. We acknowledge that we will be collecting address information which cannot be included in a limited data set. This information will be used to determine the social vulnerability index and then it will be removed from the study data set. The address information will not be stored for future use. A de-identified data set will be shared upon request in accordance with NIH requirements for data sharing.

13. Data Analysis and Management*

SAMPLE SIZE

For details related to sample size, please see #7 Study-wide Number of Subjects.

POWER ANALYSIS

Power calculations employ two-sided hypothesis testing, 80% power, 0.05 Type I error, and account for within-clinic clustering and between-clinic variation in size. If 25% of patients are unvaccinated at the start of the intervention and 5% of control-clinic patients go on to receive a

vaccination during the intervention period, we can detect an intervention-control difference of 2.96%, i.e., 7.96% of intervention-clinic patients become vaccinated. This is consistent with the effect size of other studies using a similar approach.[10-12]

DATA ANALYSIS PLAN

The primary outcome of this study is receipt of a complete COVID-19 vaccination series (2 doses for vaccines that require 2 doses) among patients unvaccinated at a clinic's entry into the study, a binary outcome. We hypothesize that intervention-clinic patients receiving text messages from their provider will be more likely to receive a complete vaccination series than control-clinic patients. We will compare vaccination in patients from the two randomization arms using generalized linear mixed modeling,[13] with a random effect for clinic to account for within-clinic clustering. In addition to estimating unadjusted between-randomization arm differences, we will adjust for key covariates, including study block as well as variables reflecting possible secular trends such as vaccine availability at the time of a clinic's entry into the study. Patient-level covariates will be available from the electronic health record (EHR), including age, sex/gender, insurance type, and address which will be used to determine the social vulnerability index; separate models also will adjust for race/ethnicity and relevant clinical diagnoses, both of which may be subject to more missing data than age and sex. In order to fully describe the population who did not receive the intervention (text messages), we will collect text communication preference, any responses to study text messages (to capture any patients responding "NO" to opt out of receiving further study text messages), and text delivery status (delivered/undelivered). We also will adjust for provider type (e.g., resident, attending, nurse practitioner) and time since last visit. In supplemental analyses, we will assess effect modification of the intervention-control difference by a) block, to explore whether intervention-control differences change over time; and b) provider type, to examine whether the impact of text message receipt varies by a patient's provider type. Analyses will be intention-to-treat.

Analyses for the secondary outcome of 1+ dose – also binary – will parallel the above analyses.

For the additional secondary outcome of racial/ethnic differences in vaccination rates, we will add an interaction between randomization arm and race/ethnicity to the above model. This will allow estimation of race/ethnic- specific vaccination rates in each arm and corresponding pairwise racial/ethnic differences in the intervention-control differences, as well as testing the statistical significance of this effect modification; we hypothesize thatthe beneficial impact of the intervention (versus control) will be larger in patients self-identifying as in minority racial groups than in patients self-identifying as white; that is, the gap in vaccination percentage between minority and non-minority patients will be smaller in the intervention arm.

Additional secondary analyses will estimate the percentage of intervention-clinic patients who initiate vaccination after the first provider text, after the second provider text, and after the third provider text. Related analyses will compare patients in each of these three subgroups with each other and with those not initiating vaccination after three texts, using generalized mixed models for categorical characteristics[13] and linear mixed models for continuous characteristics such as age.[14]

DATA SECURITY

All research staff collecting, or handling data will be trained in human subjects' procedures, confidentiality, and privacy protection. All investigators and project staff are required to receive and complete Human Subjects and HIPAA training. All research personnel will hold a current Human Subjects Training Certificate. Clinical staff will access data to send text messages to eligible patients, consistent with their role and current activities in the clinical system. They will provide a report of patients who the text messages were delivered to.

All Electronic Health Record (EHR) data pulls at UMMHC will be requested following the UMMS Data Science Core processes (currently located here: https://www.umassmed.edu/research-informatics/data_services/how-to-obtain-data/). We will follow institution-specific processes at the other clinic sites. We will transfer data from participating sites to UMMS using UMMS MoveIT to transfer the information securely. We will only transfer data after a data sharing agreement has been executed between the three organizations (UMMHC, EMKCHC, FHCW).

We are requesting a waiver of HIPAA authorization for the entire conduct of the intervention.

All computerized data will be kept on secured computers or network servers at Meyers Primary Care Institute/UMMS and/or the respective clinic sites. These data will be accessible only to research staff with approved access, using confidential usernames and passwords.

Patient participants will be assigned a numerical code (Study ID) for identification in study files. Names, addresses, and other direct identifiers will be removed from study data sets once data collection is complete and data accuracy is verified. The research data set used for study analysis will be a limited data set (containing only date and age identifiers); the Study ID will be retained for researcher communication about subjects.

Analyses will be performed using only limited data sets and only aggregate data will be reported. All data will be used for research purposes only; published data will not contain any individual identifiers and will be reported in the aggregate.

See also #14 Provisions to Monitor the Data to Ensure the Safety of Subjects, #26 Confidentiality and #27 Provisions to Protect the Privacy Interests of Subjects.

DATA MANAGEMENT

The study database will be programmed and maintained by study staff (e.g. Research Assistant, Project Manager, Principal Investigator). Handling and storage of all data will be conducted as described above under Data Security.

DATA QUALITY ASSURANCE

The PI of the study will be responsible for oversight of the clinical trial and will review study data on a periodic basis to monitor and ensure the safety of study subjects.

Data quality control will include regular data verification and protocol compliance checks by the PI and Project Manager. Reports detailing the study progress and subject status, any adverse

events, and any protocol deviations will be generated and reviewed by the PI and additional study team members as necessary.

14. PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS*

The proposed study involves no more than minimal risk to participants. Therefore, we believe that an intensive data and safety monitoring plan is not needed. However, we will take steps to ensure the integrity of the data and to detect any adverse effects of the study on the participants.

See #16 for details related to the protection against risks to study subjects.

15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT*

Patient Participants
No patient participants will be recruited as there are no study-specific activities for them to engage in. As a result, there is no need to withdraw patient participants without their consent. No further text messages will be sent to patients who reply "STOP" to a text message.

Provider Participants
Provider participants will engage in a one-time education session and will receive approximately 4 emails with educational information about communicating with patients about COVID-19 vaccination. No further emails will be sent to any provider who asks not to receive further educational emails.

16. RISKS TO SUBJECTS*

Risk to Subjects
Patient participants
The proposed study poses minimal risks to patient participants. The risks that do exist are associated with potential loss of confidentiality.

Risks associated with potential loss of confidentiality
There is a slight risk that research records (EHR data) might be obtained by persons not authorized to do so. There is a slight risk that research data files might be compromised, and obtained or viewed by unauthorized persons. Our procedures for protecting against such risks are described below.

Provider participants
The proposed study poses minimal risks to provider participants. The risk that do exist are associated with participating in an educational session.

Risks associated with participating in an educational session

Providers will be recruited to participate in a one-time education session. This activity can be time-consuming to complete and inconvenient to attend. Our procedures for protecting against such risks are described below.

Protections Against Risk for Patient and Provider Participants

Minimizing risks
The training and monitoring of all study staff performance in accordance with an IRB-approved study plan will be the responsibility of the Principal Investigator. All efforts will be made to minimize risks and participant inconvenience.

Protection for risks associated with potential loss of confidentiality
The organization proposing this study has systems, oversight, experienced personnel, and an organizational culture that supports the appropriate use, access and storage of confidential information. All persons collecting or handling data will be trained in human subjects' procedures, confidentiality and privacy protection. All investigators and project staff are required to receive and complete IRB and HIPAA training.

Data for all participants will be kept strictly confidential. All hard copies of research files will be kept in locked file cabinets or a locked file room. Participants will be assigned a numerical code (Study ID) for identification in the files. Names and other identifiers will be kept in separate locked files. Individual identifier information will be removed from study data files as soon as possible in the data processing steps. All computerized data will be kept on secured computers or networks. These data will be accessible only to research staff, using confidential usernames and passwords. Data sharing will only occur between sites with appropriate consent/waiver of consent, authorization/waiver of authorization, and an executed Data Use Agreement. Statistical analyses will be performed using only limited datasets and only de-identified data will be reported. All data will be used only for research purposes only; published data will not contain any individual identifiers.

Protection for risks associated with participating in an educational session
Providers will be recruited to participate in an education session. This can be time-consuming to complete and inconvenient to attend. We will minimize the inconvenience by offering to hold the education session at a convenient time for most providers of a given study clinic (e.g., lunch break) and via Zoom. Providers will be told that participation is voluntary and that participation in the study will have absolutely no bearing on their employment.

17. POTENTIAL DIRECT BENEFITS TO SUBJECTS*

It is uncertain whether individual participants will directly benefit from participation. Some participants may learn something new about vaccination (or specifically, about the COVID-19 vaccine). Some participants may be motivated to specifically discuss their concerns related to vaccination with their providers and/or patients. Some participants may become motivated to be vaccinated against COVID-19 which has substantial health

benefits. Subjects may enjoy participating and may feel that doing so contributes to scientific knowledge in general.

18. VULNERABLE POPULATIONS*

Please refer to our answers to section #6 Exclusion and Inclusion Criteria.

We will not be targeting any specific vulnerable population for this study. Children and prisoners will not be included. It is possible that a pregnant woman may meet inclusion criteria and it is not an explicit exclusion criterion. However, the risks involved in participation are no more than risks typically associated with general care. While we are not providing COVID vaccinations as part of the study, we are promoting its use. Currently, there are no recommendations against vaccination for pregnant women. Further, PCPs can exclude patients from participation.

In the event of inclusion of pregnant women, the following three statements will hold true:

1. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
2. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.

While we will ask providers to participate in an education session and send them emails with brief educational content, providers will be informed that their decision not to participate or to unsubscribed from our mailing list will not impact their employment in any way.

19. MULTI-SITE RESEARCH*

This study and all participating sites will comply with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-16-094). All identified participating sites have agreed to rely on the University of Massachusetts Medical School IRB. The PI and Project Manager at the University of Massachusetts Medical School will be responsible for managing all communications between participating sites and the IRB. The University of Massachusetts Medical School will maintain records of the authorization/reliance agreements and of the communication plan. All participating sites will, prior to initiating study activities, sign an authorization/reliance agreement that will clarify the roles and responsibilities of the IRB and participating sites.

The central project office will be located at the Meyers Primary Care Institute (MPCI) at the University of Massachusetts Medical School (UMMS). The Principal Investigator, Dr. Fisher, will oversee all project activities. The MPCI project manager, with support from the MPCI research assistant, will coordinate all meetings, conference calls, dissemination of materials, and

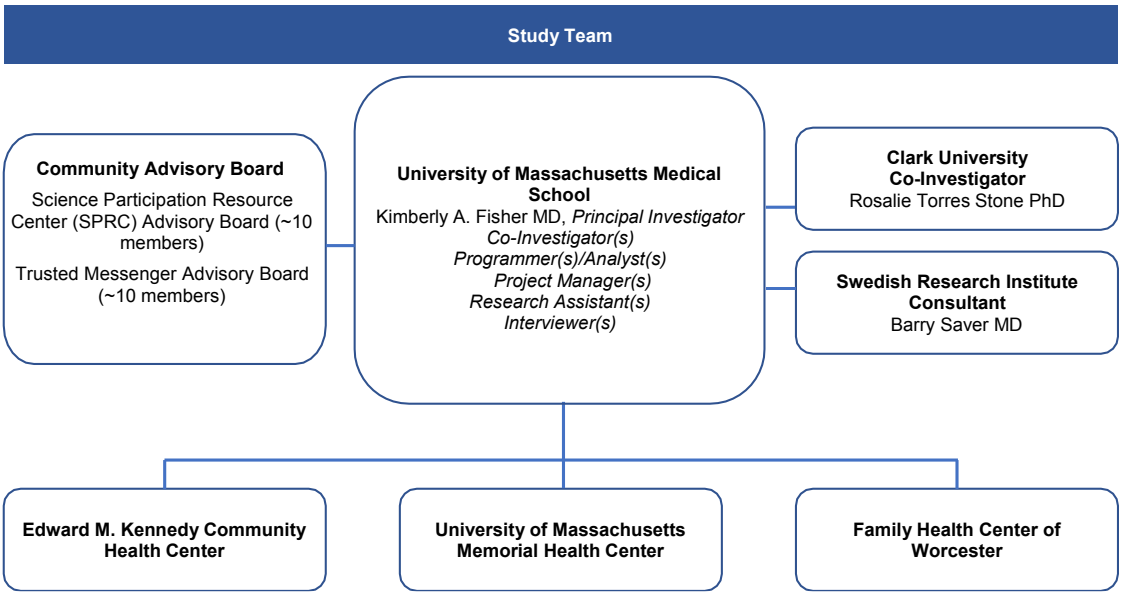
tracking of task completion. As we have in previous multi-site studies, to maximize clear communication and efficient study management, we will utilize the following procedures: (1) a cross-site working group will be established for investigators and project managers; this group will hold regularly scheduled conference calls coordinated by staff from the central project site who will develop and distribute agendas and action-oriented minutes; Dr. Fisher will participate in these calls; (2) detailed timelines will be developed and distributed for each aspect of the project; (3) tracking systems will monitor study progress. Additional meetings will be coordinated regularly with study leadership and study sites for planning of implementation of study activities.

The Principal Investigator also assures:

- All collaborators have the most current version of the protocol.
- Consent (where applicable) will be conducted by trained research staff listed on the IRB.
- All required approvals will be obtained prior to the initiation of study activities.
- Any and all modifications will be communicated to collaborators, and approved before the modification is implemented.
- All engaged collaborators will safeguard data as required by local information security policies.
- All local site investigators will conduct the study appropriately.
- All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

An organizational chart detailing the sites involved (and the preliminary study team) is included below (**Figure 2**).

Figure 2. Study Team and Organization



20. COMMUNITY-BASED PARTICIPATORY RESEARCH*

The study team will meet at least quarterly with each of two diverse community advisory boards throughout the study duration. The advisory board meetings will serve as a forum for dialogue and bidirectional exchange of information with communities at risk of COVID-19 vaccine hesitancy and health disparities. The advisory boards will convey up-to-date local community concerns regarding the COVID-19 vaccine to the study team and will provide input on all aspects of the study, including physician message content and delivery, and video content and dissemination. Advisory boards will assist with identification of influential community leaders who are willing to appear in videos and assist with disseminating the link to the online video library via social media and other channels. We will host continuing community forums based on guidance provided by the community advisory boards regarding the need and level of interest for ongoing dialogue about the COVID-19 vaccine among their members.

The first board, the standing University of Massachusetts Medical School's Science Participation Research Center's Community Advisory Board (SPRC CAB) includes clergy who lead local Black and Hispanic churches, a leader in the African immigrant community, a leader in the local Indian community, and leaders of community organizations (e.g., Elder Services, the YWCA, and the United Way)

We will convene a second advisory board to provide further advice and input on the proposed study; this board will include additional community members, both leaders and "regular" community members to comprise a Trusted Messengers Community Advisory Board (TMCAB) to complement the existing board. Members of the TMCAB will be drawn from the community organizations our study team is currently working with as part of the Worcester COVID-19 Vaccination Campaign. These presently include but are not limited to CENTRO (the largest minority led, community based, multiservice, multicultural, multilingual, nonprofit organization in Central MA), the Southeast Asia Coalition, the African Community Education Program, the Massachusetts Women of Color Coalition, and Black Families Together.

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*

There are no specific plans to share results with study subjects; study procedures do not include any type of diagnostic testing. All results shared in published research will be in aggregate or summary format and will not include identifiable information about participants. Published results will be available to the greater community at large, including study subjects.

22. SETTING

The study will be conducted in primary care clinics across three health systems in central Massachusetts, including UMMHC, EMKCHC, and FHCW.

The intervention will be carried out at 16 primary care clinics across three healthcare systems (UMMHC, EMKCHC, FHCW). Data entry and analysis will be conducted at the Meyers Primary Care Institute offices.

23. RESOURCES AVAILABLE

All research personnel listed on this study will read the protocol and receive the appropriate supervision and possess the appropriate experience (both higher education and related work experience) needed to fulfill their roles and complete their responsibilities for this study. All investigators and project staff are required to receive and complete IRB and HIPAA training.

The **Principal Investigator (PI)** will oversee all personnel and all research activities conducted within this study. She will have responsibility for the overall conduct of the project at this study site. She will have primary oversight of all study personnel. She will participate in the design and the execution of the respective study analyses and will be responsible for the reporting of study results.

The **Co-Investigator(s)** will participate in all aspects of the research and help to ensure the accomplishment of all study goals. They will participate in designing, developing, and implementing study procedures and materials. They will participate in project-related calls and meetings and help to develop deliverables and participate in manuscripts. The Co-Investigators will assist the PI in research design and intervention development as well as analytic aspects of the study. The Co-Investigators include clinicians and researchers with varied expertise including: healthcare services research, qualitative and quantitative research design, health communication and health literacy, and biostatistics.

The **Programmer/Analyst(s)** will perform a range of programming and data management activities essential to conduct of the project. S/he will perform analyses under the direction of the PI.

The **Project Manager(s) (PM)** will assist the PI and the Co-Investigators in implementing all aspects of the project. Under the direction of PI, the PM will be responsible for day-to-day coordination and oversight of the project, including: developing timelines, work allocation, workflow plans, monitoring project progress and task completion, monitoring spending and effort allocation, and managing correspondence and administrative tasks. S/he will monitor/manage ethics and regulatory approvals (IRB, HIPAA/DUA). The PM will attend and plan for all project-related meetings as needed. S/he will work under the direction of the PI to assist with all study activities, preparing IRB submissions and reports, and developing study materials, such as development of data collection instruments and intervention-related tools. S/he will be responsible for maintaining communications with all parties participating in the project. S/he will maintain project documentation and will assist in developing and filing required project reports. PMs at the Meyers Primary Care Institute all hold graduate-level degrees and have vast experience working on healthcare services research projects.

The **Research Assistant(s) (RA)** will work under the direction of the Principal Investigator and

Project Manager to assist with all study activities. S/he will assist in the development and submission of IRB and HIPAA materials, and in IRB reporting over the course of the project. S/he will help to coordinate meetings related to the study, and record meeting minutes, products and action items. S/he will assist in recruitment of participants and interviewees, consenting participants and scheduling interviews. Under the direction of the PI and PM, s/he will assist with developing REDCap forms for data collection and management, and for tracking study activities. S/he will assist in managing transcription and checking the quality of the automated transcription. Under the PI's direction and supervision, s/he will assist in the analysis of qualitative data, reviewing and coding transcripts and interviews.

The **SPRC CAB and TMCAB members** (see #26. Community-Based Participatory Research) will be engaged in an advisory capacity only. These members are neither considered study subjects nor study personnel, but rather an expertise resource for the study team. They will neither interact with subjects nor access private identifiable information about them.

All study personnel are required to undergo Human Subjects Training and hold a current CITI Human Subjects Training Certificate and will familiarize themselves with the study protocol and IRB documents.

24. LOCAL RECRUITMENT METHODS

Patient Participants

Patient participants will not be recruited as there are no study-specific activities for them to engage in. The participating healthcare systems will implement the intervention in a fashion that is consistent with other healthcare system patient reminders. Patients not vaccinated for COVID-19 will be sent a series of text messages that will include a message from their Primary Care Provider, a link to schedule an appointment (if they choose to), and a link to an online library of videos and educational materials that they can access if they choose. Patient participants will be given the option to reply "NO" to the text messages.

Provider Participants

Primary care providers at study clinics randomized to the intervention will be sent an invitation to participate in the "lunch and learn" interactive session via email. The invitation email will inform clinic leaders and providers that their primary care clinic has been randomized to receive the intervention, briefly introduce the intervention, and explain their involvement in the intervention (**appendix 2**).

The invitation will make it clear that participation in the education session is voluntary. Providers will be given the option to decline the invitation. We will send a reminder email 1-2 days before each session to providers who have not yet attended one of the sessions for their clinic. Should a provider decline the invitation or indicate that they do not want to be contacted again for this study, they will be removed from our mailing list.

The invitation email and subsequent reminder emails will be submitted to the IRB for review and approval prior to use in the study (**appendix 2**).

25. LOCAL NUMBER OF SUBJECTS

Please see #7. Study-Wide Number of Subjects.

26. CONFIDENTIALITY

A major risk of any research is the accidental disclosure of information; however, precautons will be taken to prevent this and the study team has an excellent track record of protection of confidential data. The organizations proposing this study have systems, oversight, experienced personnel, and an organizational culture that supports the appropriate use, access and storage of confidential information. All persons collecting or handling data will be trained in human subjects' procedures, confidentiality, and privacy protection. All investigators and project staff are required to receive and complete IRB and HIPAA training.

See details related to data security under section #13 Data Analysis and Management.

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

Privacy

Please see section #16. Risks to subject, section #26. Confidentiality, and section #30 Consent Process for how participant data will be protected and information on informed consent.

HIPAA Authorization

We are requesting a waiver of HIPAA Authorization for the entire conduct of the study. See HIPAA waiver request for details.

28. COMPENSATION FOR RESEARCH-RELATED INJURY

Not applicable; we do not anticipate any research-related injuries. We believe the research poses no more than minimal risk to subjects.

29. ECONOMIC BURDEN TO SUBJECTS

N/A

30. CONSENT PROCESS

Patient Participants

We are requesting a waiver of consent for patient participants as there are no study-specific activities for them to engage in. The participating healthcare systems will implement the intervention in a fashion that is consistent with other healthcare system patient reminders. Patients not vaccinated with the COVID-19 vaccine will be sent a series of text messages that

will include a message from their Primary Care Provider, a link to schedule an appointment (if they choose to), and a link to online educational materials that they can access if they choose. Subjects will be given the option to "STOP" the text messages.

Waiver of Consent

We believe the intervention meets the following criteria to obtain a waiver of consent. We attest that the following statements are all true:

1. The research involves no more than Minimal Risk to the subjects.
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
3. The research could not practicably be carried out without the waiver or alteration.
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation. In this event, we will seek the guidance of the IRB.
5. The research could not practicably be carried out without using Identifiable Private Information which is necessary to identify unique participants as participation unfolds over time.
6. The research does not involve Non-Viable Neonates as subjects.

Provider Participants

We are requesting a waiver of consent for provider participation in the educational component of the intervention (attending a one-time educational session and receiving a series of emails with educational information about communicating with patients about the COVID-19 vaccine). Providers will be informed that participation in these activities is voluntary. Any provider who does not want to take part in the education session can simply not attend. Providers can choose not to open and read the emails with no consequences, or to request not to receive further emails.

Waiver of Consent

We believe the intervention meets the following criteria to obtain a waiver of consent. We attest that the following statements are all true:

1. The research involves no more than Minimal Risk to the subjects.
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
3. The research could not practicably be carried out without the waiver or alteration.
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation. In this event, we will seek the guidance of the IRB.
5. The research could not practicably be carried out without using Identifiable Private Information which is necessary to identify unique participants as participation unfolds over time.
6. The research does not involve Non-Viable Neonates as subjects.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

N/A: We are requesting a waiver of consent for patient and provider participants.

32. DRUGS OR DEVICES

N/A

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