Official Title: The VAX-MOM Study: Increasing Influenza and Tdap Vaccination of Pregnant Women

NCT #: NCT04444518

Protocol Document Date: Version 6/22/22 (the most recently approved protocol version for the study)

PLEASE NOTE: This protocol document has had some sentences/sections redacted in order to maintain the confidentiality of participating individuals and practice sites.

VAX-MOM Study: Protocol for Aim/Phase 2

[redacted]

NOTE: The VAX-MOM study is divided into 3 main aims/phases. Each aim/phase informs the next, and will be submitted separately for IRB approval, as we cannot predetermine details for each aim/phase until the prior aim/phase has been completed. Aim/phase 1 was previously submitted and approved. We are now (current protocol) on aim/phase 2, which is being submitted for single IRB review, with the University of Rochester RSRB acting as the IRB of record for all study sites.

1. PURPOSE OF STUDY (ALL AIMS/PHASES)

Infants under 6 months of age are at increased risk of both influenza (flu) and pertussis disease, and pregnant women who get influenza are more likely than non-pregnant women to have serious complications, including hospitalizations, death, preterm labor and premature birth. The Advisory Committee on Immunization Practices recommends that women receive a flu vaccine in flu season, and tetanus toxoid, reduced diphtheria toxoid, acellular pertussis (Tdap) vaccine during each pregnancy (ideally between 27-36 weeks) to lower the risk for flu and pertussis disease for both themselves and their infants. However, only half of pregnant women in the US receive a flu and Tdap vaccine, respectively; only 33% of women receive both vaccines. Lack of vaccination stems from a combination of patient (lack of knowledge, vaccine hesitancy), provider (suboptimal communication skills, missed opportunities), and system (e.g., lack of standing orders and patient reminders) factors. An effective intervention is needed to improve flu and Tdap vaccination rates for pregnant women.

This multi-site project has four key aims/phases. **Aim/Phase 1** is to measure baseline flu/Tdap vaccination coverage and provider knowledge, attitudes and behaviors for flu/Tdap vaccination in participating OB/GYN practices within 4 health systems in New York and California. **Aim/Phase 2** is to use a clustered randomized controlled trial (RCT) (practice-level randomization) to measure the effect of a multi-component quality improvement (QI) intervention (VAX-MOM: training in communication, provider prompts, standing orders + feedback on rates) on vaccination rates and provider attitudes, and to measure costs of the intervention. **Aim/Phase 3** is to develop a translational plan/toolkit for OB/GYN practices and health systems for maternal vaccination.

2. BACKGROUND AND RATIONALE (ALL AIMS/PHASES)

Burden of flu disease and pertussis

Infants <6 months of age are more likely than any other age group to have flu complications that lead to hospitalization. Our group has shown that the average annual rate of hospitalization attributable to flu was 4.5 per 1000 among children 0 to 5 months of age.[1,2]

Flu infection rates are similar in pregnant women to the general population, but pregnant women are at higher risk of severe flu complications, including hospitalization and death[3-6] and are at increased risk of adverse perinatal and neonatal outcomes.[7,8] According to CDC, from 1990–2016 infants <1 year of age consistently had the highest reported annual incidence of pertussis[9] as well as the greatest risk for serious disease and death from pertussis. Recently in the U.S., infants in the first 6 months of life had an age-specific pertussis incidence of 78 per 100,000; 43% of those with reported infection were hospitalized.[10] While infants start DTaP vaccine at 2 months and vaccination rates are high, they are not well protected until they complete their primary series at 6 months of age.

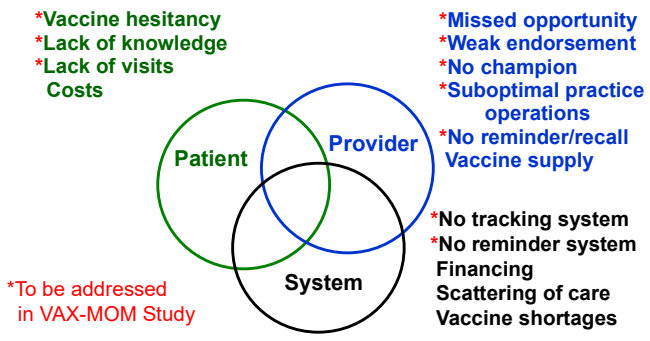
Effectiveness of maternal vaccination

A 2016 systematic review showed that maternal flu vaccination provided "substantial benefit for infants and mothers,"[11] with reduced rates of preterm birth and low birth weight. Infants <6 months of age whose mothers had received flu vaccine had a 63% reduction in laboratory-confirmed flu and a 29% reduction in respiratory illness with fever compared with controls; mothers had a reduction of 36% in the rate of respiratory illness with fever.[12] Maternal flu vaccination is 91.5% effective in preventing flu-associated hospitalization in newborns.[13] In a cohort study of mother-infant pairs, the rate of pertussis was 43% lower among infants whose mothers received prenatal Tdap than among infants whose mothers did not;[14] protection was seen only among infants whose mothers received Tdap at >27 weeks of gestation. These findings are consistent with earlier studies that showed maternal vaccination was associated with higher cord serum concentrations of pertussis antibodies[15] and, that maternal Tdap receipt at 30-32 weeks gestation was associated with significantly higher infant serum concentrations of Tdap antibodies at birth and 2 months of age.[16]

Barriers to Vaccination

There are many barriers to influenza and Tdap vaccination for pregnant women. Our team has conceptualized these barriers into a widely used model; the VAX-MOM study will address multiple components by focusing on provider and staff communication, prompts and/or standing orders, provider feedback, and patient education/reminders to overcome these barriers (Figure 1).

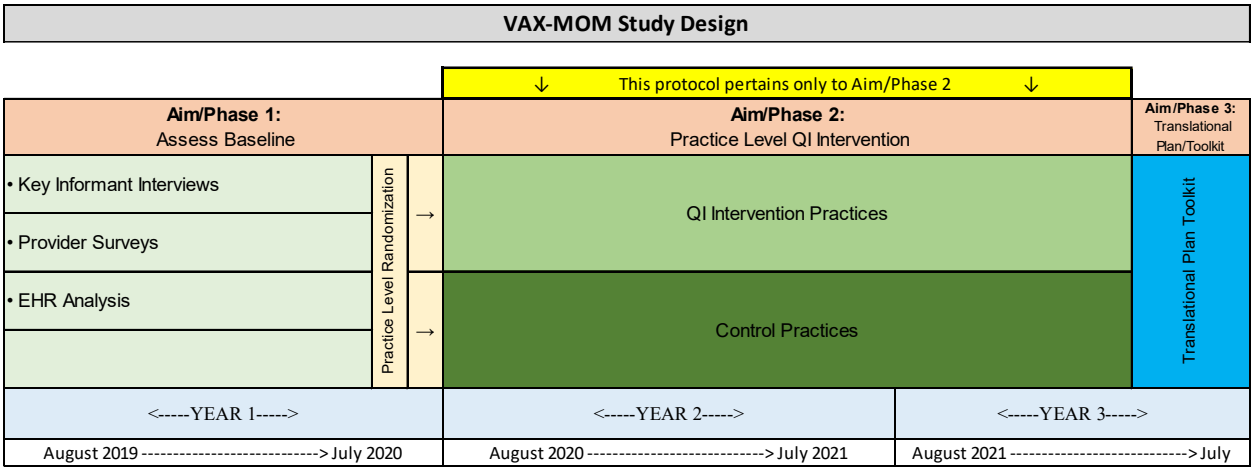
Figure 1. Barriers to Vaccination



Patient Barriers include vaccine hesitancy, lack of knowledge of the benefits and risks of flu or Tdap vaccine or protection for the baby, concerns about vaccine safety generally and during pregnancy, low perceived susceptibility to infection, and lack of access.[17,18] Vaccination rates are lower for younger women, Blacks, those with public insurance, lower income, and inadequate prenatal care.[19,20-22] *Provider Barriers* include missed opportunities for vaccination, lack of a vaccine recommendation or weak endorsements by health providers about needed vaccines (the most important predictor in many studies),[19,20-22] various suboptimal practice operations, insufficient knowledge, financial barriers, and lack of reminder recall.[23,24,25] *System Barriers* include the lack of a tracking or reminder system, as well as suboptimal staff training, and challenges with vaccine purchase and storage.[22,26]

3. ADMINISTRATIVE ORGANIZATION (AIM/PHASE 2 ONLY)

NOTE: As stated at the onset of the protocol, we are requesting that the University of Rochester RSRB serve as the IRB of record for all study sites during aim/phase 2 of the study. The remainder of the protocol will describe aim/phase 2 details only.



STUDY SITES & PROJECT STAFF OVERVIEW

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[redacted], study PI, will ensure study and regulatory compliance, by:

- Participating in routine prescheduled meetings with all project investigators and project staff for the duration of the study, including:
    - *Weekly Core Leadership Team Meetings* (State-level Investigators, study coordinators, all study consultants, data specialist): discussion of global project goals, timeline, regulatory requirements and adherence, protocol requirements and adherence, measure development, e-learning content, data analysis, workflow details, etc.

- *Weekly State-level Team Meetings* (State-level Investigators, study coordinators, data specialist as needed): discussion of day-to-day operations needed to support global study goals (including protocol and regulatory items).
- *Weekly Site-level Team Meetings* (State-level Investigators, study coordinators, Site Investigators, OB/GYN site liaisons, site EHR report builders): discussion of provider/nurse workflow, development of study measures specific to providers/nurses, optimal measure dissemination procedures, identification of possible vaccine champions.
- *Data Development & Analysis Meetings* (State-level Investigators, study coordinators, EHR report builders, data specialists): discussion of data collection methods, EHR data extraction methods, data analysis, data storage/management.

- Keeping all study personnel abreast of *prearranged study changes* and subsequent regulatory determinations (e.g., changes to study measures, workflow procedures, study personnel, etc.) via a predetermined communication chain:
  - Core Leadership Team discusses necessary study change→NY study coordinator submits amendment to RSRB→RSRB notifies Study PI and NY study coordinator of regulatory determination→ Study PI and NY coordinator notify Core Leadership Team→ As appropriate, both study coordinators will further notify site-level personnel and/or data specialists
  - Communication with study site personnel will most often take place during prescheduled meeting times, but in more urgent cases, will take place as soon as needed.
  - Communication will be both verbal (during or outside of weekly meetings depending upon level of urgency) and written as needed (via e-mail, e-mail attachments, or the secure shared Box folder).
- Keeping all study personnel abreast of *unforeseen study events* and subsequent regulatory determinations (e.g., protocol deviations, breaches in confidentiality, subject/site withdrawal, etc.) via a predetermined communication chain:
  - Study personnel reports study event to PI→ PI notifies NY study coordinator→ PI and NY study coordinator notify RSRB, as well as other study personnel as appropriate→ any action requested by RSRB is communicated to Core Leadership Team→ As appropriate, both study coordinators will further notify site-level personnel and/or data specialists
  - As described above, communication will be both verbal and written.
  - Also see section #16 “Data & Safety Monitoring Plan”

4. STUDY DESIGN & PROCEDURES (AIM/PHASE 2 ONLY)

Brief Overview of Aim/Phase 2:

Using a clustered RCT (randomizing practices), we will allocate half of the practices within each health system to the VAX-MOM intervention and the other half to standard of care. We will measure the impact of the intervention on vaccination rates (primary outcomes) and missed opportunities and process metrics (secondary outcomes) (see Table 4). Finally, if VAX-MOM is successful, we will provide the control practices the intervention during Year 3.

Design and Procedural Details of Aim/Phase 2: (also see Figure 2 for Timeline)

Step 1) Deliver VAX-MOM training/intervention to randomized practices:

Randomization Details:

Practices will be the unit of randomization. We will assign practices using a covariate constrained randomization strategy as follows: First, we will use data from Aim #1 to obtain key factors that we expect to affect the primary outcomes. We will perform constrained randomization to allocate practices within each health system to intervention/control arms and ensure each arm has similar baseline flu and Tdap vaccination rates, percent of patients covered by Medicaid, number of OB providers, and number of patients. Specifically, we will use these variables to construct and evaluate a balance criterion, which is the sum of the squared difference between standardized group means on these variables. We will generate randomization separately by health system. We will generate all possible combinations of eligible practices in 2 arms (using a SAS macro), and define an acceptable set of randomizations that result in balanced variables (generally the lowest 10% on the balance criterion). From this set of randomizations, we will select one set at random, and then randomly assign each practice to intervention vs control group.

Intervention Details:

Once randomization has been completed, and "intervention group" practices have been identified, multiple quality improvement (QI) techniques will be aimed at practice providers, nurses, and staff.

- **Identification of "vaccine champion" at each intervention site:** At each site, the affiliated medical director will select one "vaccine champion" for the practice. Each identified vaccine champion will be e-mailed an Information Sheet (see "*InformationSheetVaccineChampion…"* document) by their affiliated study coordinator, outlining the basic study goals as well as their involvement in tasks throughout the training and intervention adoption phases of the study (see "Consent Process" section). The position of vaccine champion is voluntary, and if they do not wish to accept the role, they may decline and another individual will be identified by the affiliated medical director. The vaccine champion will play a lead role throughout the study intervention, including:

- assisting with the dissemination of e-learning training modules and the scheduling of a follow-up site-specific meeting
- acting to ensure training content is being appropriately adopted into practice workflow procedures
- fielding questions from site personnel regarding the logistics of study interventions
- acting as an ongoing liaison between the site personnel and study staff
- leading bi-monthly discussions regarding immunization rate feedback with site personnel (see step 2 for further detail)
- planning for and completing monthly PDSA cycles (see step 2 for further detail)
- monthly completion of the "Practice Time/Cost Survey" (see step 4 for further detail)

- **Delivery/discussion of training modules**: Each site will receive training focused on 3 main areas of content (see Table 3). This training will be delivered first via an online e-learning platform, and next via an in-person or virtual site meeting.

Table 3: Training Module Content

Training Topic:	Training Content Details:
Flu & Pertussis 101	General information regarding prevalence/severity of influenza and pertussis disease
	General information regarding benefits of flu/Tdap vaccination
	Benefits of flu/Tdap vaccination within the pregnant population (e.g., benefits of passive immunity)
Communication	Understanding and applying a "Presumptive Recommendation"
	Brief introduction to Motivational Interviewing (MI) and application with vaccine hesitant pregnant women
	Communication Tips & Tricks: Responses to common concerns/questions about vaccines
Optimizing Office Workflow	Optimal methods and organizational/tracking tools
	• Pre-visit planning and nurse prompts
	• EHR prompts (Checklists/Text Fields)
	• Standing orders
	• Vaccine rate feedback
	• Vaccine champion and utilization of PDSA cycles
	• Optimal vaccine documentation (e.g., vaccines given offsite)
	Putting it all together
	• "Teamwork"- Ensure entire multidisciplinary team trained in utilization of new methods/tools
	• "Consistency"- Ensure all tools/methods used consistently
	• "Adjust as Needed"- Use feedback reports & PDSA cycles to reflect on progress and fine-tune accordingly

- E-learning platform: Module content will first be disseminated to practice site personnel via an online e-learning platform (i.e., Articulate). Study coordinators will obtain e-mail addresses for the site personnel from either the health system liaison or the associated vaccine champion, and will then e-mail a training content link to all appropriate site providers, nurses, and staff. Attached to this initial e-mail will be an Information Sheet describing the study goals and training phase details, as well as their involvement throughout the duration of the 12-month QI intervention (see *"TrainingPhaseEmail…"* and "*InformationSheetTrainingPhase…*" documents; also see "Consent Process" section for more detail). After reviewing the Information Sheet and discussing any questions/concerns with study staff, site personnel will be asked to access and complete the training lessons prior to their scheduled site meeting.

  Embedded at the conclusion of the online training module, will be a link to a brief REDCap survey (see *"TrainingModuleCompletionSurvey…"* document) to obtain information regarding those who have fully completed the training. A list of practice personnel who have successfully completed the online training will be stored in a password-protected Excel/Word file by each study coordinator. The names will not be linked with any other study data. The list will be accessible only by study staff for the purposes of confirming those who should receive CME/CNE credit.

  Note: For intervention sites that have completed the e-learning training during the first half of the calendar year (i.e., prior to July), site personnel may be asked to additionally complete an abbreviated "flu booster" e-learning module just prior to flu season of that same year (e.g., in Aug/Sept). This abbreviated version (approx. 15 minutes to complete) will contain content (see table 3) only applicable to influenza.

- Site Meeting: Following the online training, all site personnel will meet with study staff either in-person or via a virtual Zoom meeting. The meetings (both virtual and in-person) will be audio and video recorded using a laptop or handheld recording device (in-person meetings) or via the Zoom recording option (virtual meetings) (see "Audio/Video Recording" and "Privacy and Confidentiality" sections for more detail). These archived video files will allow for the review of meeting content by site personnel who were unable to attend the meeting live, or by those who simply wish to review the meeting discussion for a second time.

  During the site meeting, study staff will briefly review online training content, allow time for the sharing of comments/questions from site personnel, and lead a discussion regarding the application of training content ideas specifically to that practice site. During this meeting, study staff will also present site personnel with their current immunization rates.

Each designated vaccine champion will track meeting attendance, and a list of practice personnel who have attended the site meeting will be e-mailed to the study coordinators and stored in a password-protected Excel/Word file. The names will not be linked with any other study data. This list will be accessed for the purposes of confirming those who should receive MOC credit.

Note: For intervention sites that have completed their site meeting during the first half of the calendar year (i.e., prior to July), site personnel may be asked to participate in a second abbreviated "flu booster" site meeting just prior to flu season of that same year (e.g., in Aug/Sept). This abbreviated meeting (approx. 15 minutes) will discuss content (see table 3) only applicable to influenza.

- MOC/CME/CNE Credit: To encourage the completion of online trainings and the attendance at site meetings, providers and nurses will be offered CME/CNE credit for completing learning modules, and MOC/QI credit for attending office systems change meetings and reviewing practice rates.

Step 2) Monitor adoption of VAX-MOM training content at randomized practices:

To monitor the adoption of VAX-MOM training content (changes in communication techniques, workflow optimization, etc.) at each practice site, each vaccine champion will participate in the following activities in an ongoing basis:

1. *Lead a discussion regarding immunization rate feedback* with practice providers, nurses, and staff on a bi-monthly basis (every-other month). The champion will monitor the site personnel attending each feedback discussion as well as their role (e.g., Ob/Gyn, nurse, desk staff, etc.) within the practice. They will e-mail study staff with a list of individual attendees for the purposes of tracking those receiving MOC credit. They will also report aggregate numbers on a monthly basis using the "Practice Time & Cost Survey."

   The site-specific flu and Tdap vaccination rates will be obtained from either: 1) the EHR report builders for each health system (*possible for all 4 health systems*), or 2) manual chart review (*possible for only NY health systems*). Obtained rates will be sent either via secure e-mail directly to the study coordinator in each corresponding state, or uploaded to the secure shared Box folder. The study coordinator will then disseminate the vaccination rates for each site to all corresponding site personnel (see *"RateFeedbackTemplate…"* document).

2. *Develop PDSA cycles/goals* on a monthly basis utilizing knowledge about current workflow efficiency and data from vaccine rate reports. Vaccine champions will utilize the PDSA template (see *"PDSASurvey…"* document) to guide progress with their respective teams. The template will help them decide upon specific

intervention activities appropriate for their setting, track those involved with each activity, compare results from the activity to previous performance, and focus on changes that may need implementation during future cycles. PDSA cycle logs will be shared with study staff via a secure REDCap survey (same *"PDSASurvey…"* document formatted on the REDCap platform) sent to the vaccine champion each month by the appropriate study coordinator.

During the final quarter of the 12-month intervention phase, a study team member will observe a subset of NY intervention sites in-person in order to collect qualitative data regarding workflow and communication techniques as described in the sites' submitted PDSA cycle logs. Specifically, the study team member will observe select OB/GYN practice nurses and staff for 1-2 days per site, and will document the ways in which the targeted intervention techniques are implemented within the practice (see "*InterventionObservationNotes*…" document). Observation notes will then be compared with submitted PDSA cycle log information and analyzed for consistency.

Of Note: Although study staff will observe OB/GYN practice nurses and staff during patient encounters, practice patients will NOT be the target of the observation, and no identifying patient information will be collected. Rather, the focus of observation will be the select practice personnel only. Any patient-level information recorded during the observation will be done so in a generic manner such that the patient could not be identified on the basis of the notes (e.g., *"…when patient indicated that they did not want a Tdap vaccine, the nurse stated, 'The doctor may talk to you more about that when she comes in.'"*). The study staff will only observe the initial nurse/staff interaction with the patient, and will not continue to observe once the provider (doctor or midwife) enters for the visit.

3. *Complete the "Practice Time/Cost Survey"* on a monthly basis (see step 4 for further detail).

To monitor study staff effort during this phase, study staff will participate in the following activity in an ongoing basis:

4. *Complete the "Study Staff Time/Cost Survey"* on a monthly basis (see step 4 for further detail).

Step 3) Compare intervention vs. control practices:

Using the "RE-AIM" framework (see Table 4) we will compare intervention practices to control practices using multiple data sources. We will focus on one primary outcome and multiple secondary outcomes.

Primary Outcome: Following the conclusion of aim/phase 2 (12-month duration), we will assess the "Effectiveness" of the intervention by comparing intervention group flu and Tdap vaccination rates against control group flu and Tdap vaccination rates.

Secondary Outcomes: Following the conclusion of aim/phase 2 (12-month duration), we will assess the remaining "RE-AIM" domains including "Reach," "Adoption," "Implementation," and "Maintenance."

Table 4: Summary of Outcome Measures and Tools

RE-AIM Category	Outcome Measure(s)	Data Source
Reach	• Number of patients seen in the practice within study period. • Number of providers/nurses/staff completing the training modules.	EHR data & training attendance records
Effectiveness	• Primary Outcome: Rate of flu and Tdap vaccination • Secondary Outcomes: Flu and Tdap vaccination rates by subgroups including (i) insurance groups, (ii) race/ethnicity, (iii) number of pregnancy, (iv) flu vaccine in prior year	EHR data
Adoption	• Missed opportunities by (i) provider characteristics and (ii) patient characteristics • Number and proportion of personnel involved in the VAX-MOM office changes (receiving MOC credit, attending in-office meetings)	Provider Surveys, EHR data, training attendance records
Implementation	• Provider and office staff perceptions of feasibility, acceptability, barriers and facilitators to implementation, adherence to intervention, perceived time and cost, and impact on patient flow. • Missed opportunities for flu/Tdap vaccination. • Perceived strength of vaccine recommendations. • Perceived adherence to staff checking whether flu/Tdap is due. • Costs of implementing interventions	Provider Surveys, EHR data & *Time/Cost Survey
Maintenance	• Sustainability	Provider Survey

*See Step 4 for more details

Details for EHR data extraction:

- Measure Description (also see *"EHRDataExtraction …"* document)
  We will work with our experienced [redacted] analysts (initial planning of required data fields and subsequent analysis of data output) and health system report builders (algorithm development) to extract EHR data for the purposes of evaluating basic flu and Tdap vaccination rates and additional secondary outcomes (see Table 5).

Table 5. EHR Data Extraction Categories	
Primary	• Flu vaccines received during flu season (Sept-April) • Tdap vaccines received during 27-36 weeks of pregnancy
Secondary	• Vaccine refusal (as documented in EHR) • Missed opportunities for flu and Tdap • Flu vaccine in prior season • Covid vaccination
Patient Demographics	• Race/ethnicity • Insurance • Parity • Age • Language
Practice Demographics	• Site • Provider type (resident, midwife, MD)

- Measure Procedures

  Each health system [redacted] will have its own "report builder." The report builder will be in charge of collecting the electronic health record (EHR) data from their own health system and putting it into a format (report) that can be easily understood and analyzed by study staff.

  Bi-Monthly Feedback Reports: The report builder for each health system will create vaccine rate feedback reports utilizing extracted EHR data for intervention sites on a bi-monthly basis. These reports will be sent either via secure e-mail directly to the study coordinator in each corresponding state, or uploaded to the secure shared Box folder. The study coordinator will then disseminate the vaccination rates for each site to all corresponding site personnel.

  For NY health systems, in the event an automated EHR feedback report cannot be generated in time for any given month, the identified vaccine champions or study personnel will estimate flu and Tdap vaccine rates via manual chart review. All vaccine champions and/or study personnel conducting manual chart review will have completed all appropriate eRecord training prior to accessing patient charts. Of those patients who delivered during the identified month, at least 20% will be reviewed. For each chart reviewed, the vaccine champion or study personnel will document the receipt (or lack thereof) of influenza and Tdap immunization as well as Covid vaccination when possible, and will share results with the study team via secure e-mail.

  Final EHR Data Analysis: Additionally, at the conclusion of aim/phase 2 (12-month duration) each health system report builder will create a final EHR report for both the intervention sites as well as the control sites capturing updated baseline information from 2019 and 2020 (now needed due to COVID pause), as well as detailed intervention information from 2021 and 2022 (information indicated in Table 5 that was not captured during monthly reports). These final reports will be uploaded to a shared folder on the secure Box platform, accessible by select study staff [redacted]. This report will allow for the comparison of vaccination rates and secondary outcomes

between intervention and control sites. In the event that the final automated EHR reports cannot be generated in a timely manner by the report builders, study personnel and/or a medical student (after being added to the study protocol) will conduct manual EHR chart reviews to collect the data. They will be appropriately trained in the EHR system requiring access, prior to conducting the chart reviews.

Details for Provider & Nurse Survey:

- Measure Description
  The Provider & Nurse Survey (see *"ProviderNurseSurvey…"* document) is an 86-question survey consisting of Likert scale, multi-option and open-ended questions. The survey takes approximately 20 minutes to complete. The survey assesses opinions regarding flu, Tdap and COVID-19 vaccinations, patient refusal of those vaccinations, barriers to those vaccinations, policies and procedures within provider offices as they relate to vaccinations, and basic demographic information.

- Measure Procedures
  At the conclusion of aim/phase 2, all providers (MD, residents, NPs, PAs and CNMs) and select nurses from both the intervention and control sites will be asked to complete the survey. Surveys will be e-mailed (see *"ProviderNurseSurveyInviteEmail…"* document) to providers and select nurses by the appropriate Study Coordinator, using the secure web application REDCap. E-mail addresses will have previously been obtained from the health system liaisons or vaccine champions and uploaded to the REDCap platform by the Study Coordinators. An Information Sheet (see "Consent Process" section for more details) will be embedded in each e-mail.

  After initial survey distribution, if the subject does not click on the survey link embedded within the e-mail, the REDCap platform will automatically disseminate a reminder e-mail to the subject (identical content as initial invite e-mail). They will receive this reminder e-mail every 3 days, up to a maximum of 5 reminders. Once the subject clicks on the survey link, they will be redirected to the secure survey site where they may answer survey questions at their own pace. Subjects may stop and restart at any time, and may skip any questions they do not wish to answer. At the conclusion of the survey, they will receive an automated confirmation message to assure them that the process is complete.

Details for Practice Culture Survey:

- Measure Description
  The Practice Culture Survey (see *"PracticeCultureSurvey…"* document) is a 15-item Likert scale survey which takes approximately 5 minutes to complete. The survey assesses opinions regarding communication, decision making, stress/chaos and leadership domains within a practice site.

- Measure Procedures
  At the conclusion of aim/phase 2, select providers (MD, residents, NPs, PAs and CNMs), nurses and staff from the intervention sites will be asked to complete the survey. Surveys will be e-mailed (see *"PracticeCultureSurveyInviteEmail…"* document) to personnel by

the appropriate Study Coordinator, using the secure web application REDCap. E-mail addresses will have previously been obtained from the health system liaisons or vaccine champions and uploaded to the REDCap platform by the Study Coordinators. An Information Sheet (see "Consent Process" section for more details) will be embedded in each e-mail.

After initial survey distribution, if the subject does not click on the survey link embedded within the e-mail, the REDCap platform will automatically disseminate a reminder e-mail to the subject (identical content as initial invite e-mail). They will receive this reminder e-mail every 3 days, up to a maximum of 5 reminders. Once the subject clicks on the survey link, they will be redirected to the secure survey site where they may answer survey questions at their own pace. Subjects may stop and restart at any time, and may skip any questions they do not wish to answer. At the conclusion of the survey, they will receive an automated confirmation message to assure them that the process is complete.

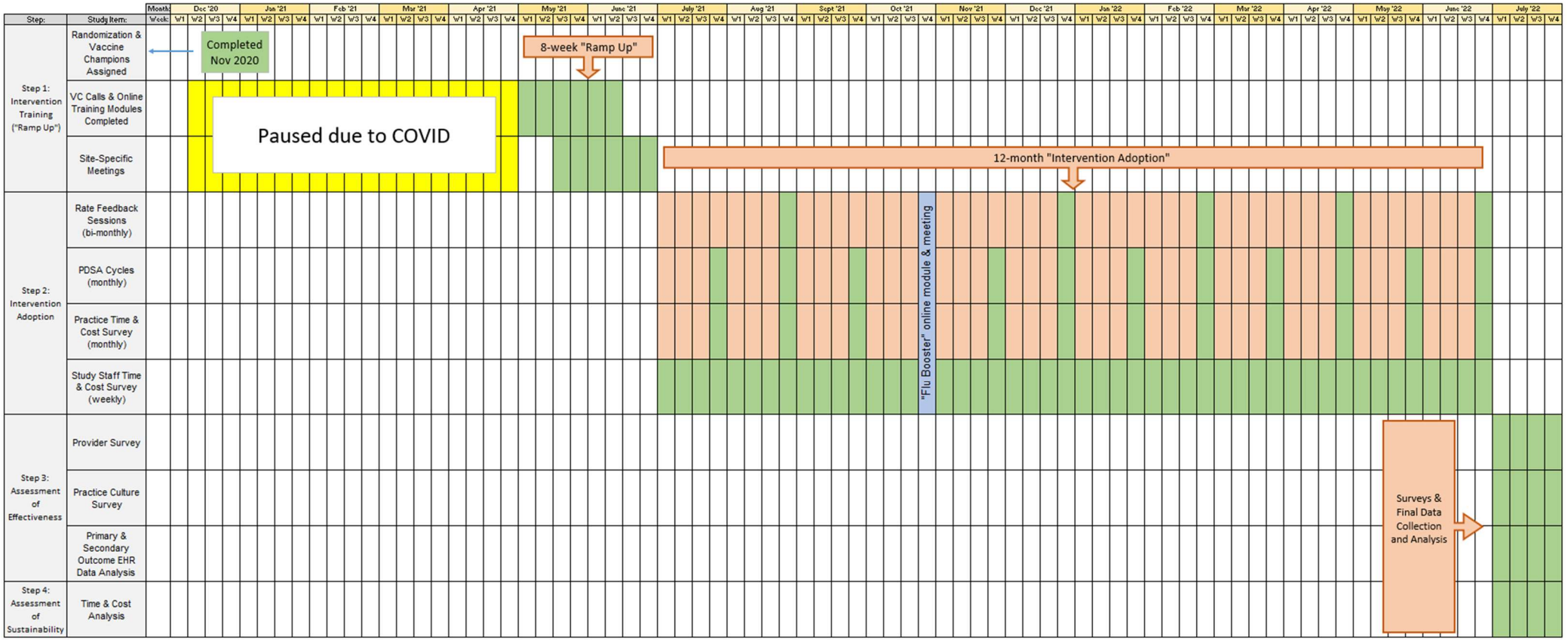
Step 4) Evaluate cost of the VAX-MOM intervention:

Practice Time & Cost Survey (see *"PracticeTime&CostSurvey…"* document): A survey aimed at evaluating the amount of time and money devoted to VAX-MOM intervention activities will be sent by the study coordinators via REDCap to the vaccine champion for each site on a monthly basis. The survey will be completed by the vaccine champion using their best time/cost estimates pertaining to the month prior.

Study Staff Time & Cost Survey (see *"StudyStaffTime&CostSurvey…"* document): A survey aimed at evaluating the time and cost efforts of VAX-MOM study staff will be sent to study personnel on a weekly basis via REDCap.

Final Time & Cost Analysis:
Upon completion of aim/phase 2 we will conduct a final time/cost analysis. Our two-fold cost measures are (a) total intervention cost to implement the VAX-MOM program aggregated at the four health-system level under a cost analysis and (b) cost per additional flu or Tdap vaccination under a subsequent cost-effectiveness analysis.

Figure 2: Timeline of Aim/Phase 2 Study Procedures



5. SUBJECT POPULATION

During aim/phase 2, we will utilize subjects from a total of 37 participating practices across both NY and CA. "Subjects" refers to both a) the providers, nurses, and staff at the participating OB/GYN practice sites and b) data from practice patients (pregnant women) gathered via electronic health record (EHR). A list of all participating practices and corresponding demographic information is below (Table 6).

Table 6: Participating Practice Sites and Demographic Information (Total Subject Pool)

NEW YORK PRACTICES:		
[redacted]		
Participating Practice	**Total Number of Providers**	**Annual Deliveries**
[redacted]	35	800
[redacted]	9	100
[redacted]	12	200
[redacted]	18	300
[redacted]	16	500
[redacted]	2	200
[redacted] **Insurance (% Private/Public/Other)**		45/55/5
[redacted] **Race/Ethnicity (% White/ Black/Hispanic)**		65/25/10
[redacted]		
Participating Practice	**Total Number of Providers**	**Annual Deliveries**
[redacted]	10	511
[redacted]	4	130
[redacted]	6	144
[redacted]	3	13
[redacted]	7	415
[redacted]	4	110
[redacted]	4	17
[redacted]	3	0
[redacted]	5	256
[redacted]	1	16
[redacted]	5	392
[redacted]	6	353
[redacted]	3	309
[redacted]	3	298
[redacted]	6	143
[redacted]	3	128
[redacted] **Insurance (% Private/Public/Other)**		55/45/5
[redacted] **Race/Ethnicity (% White/ Black/Hispanic)**		65/15/20

CALIFORNIA PRACTICES:		
[redacted]		
Participating Practice	**Total Number of Providers**	**Annual Deliveries**
[redacted]	13	1792
[redacted]	8	300
[redacted]	8	1500
[redacted]	5	157
[redacted]	1	80
[redacted]	4	472
[redacted]	2	180
[redacted] **Insurance (% Private/Public/Other)**		89/1/10
[redacted] **Race/Ethnicity (% White/ Black/Hispanic)**		52/7/13 & 14% Asian
[redacted]		
Participating Practice	**Total Number of Providers**	**Annual Deliveries**
[redacted]	5	≈800
[redacted]	7	≈1000
[redacted]	3	≈450
[redacted]	3	≈450
[redacted]	2	≈250
[redacted]	1	≈150
[redacted]	9	≈1000
[redacted]	3	≈500
[redacted] **Insurance (% Private/Public/Other)**		20/75/5
[redacted] **Race/Ethnicity (% White/ Black/Hispanic)**		15/25/55 & 5% Asian

Inclusion of Women and Minorities

Every effort will be made within this project to ensure that women, racial and ethnic minorities will be included in all aspects of the research. Practices selected from two states include a broad spectrum of size, regional location as well as public and private practices. These variables will ensure racial/ethnic diversity among study subjects that will mirror the state of New York and California's racial and ethnic distribution as shown in the enrollment table. In New York and California, an estimated 57% of Obstetrician/Gynecologists are female. Therefore, we anticipate a slightly higher percentage of females among the provider study subjects. Patient study subjects will all be female.

Inclusion of Pregnant Women

Although the research project involves OB/GYN practice sites, study staff will not have direct contact with pregnant patients, nor do study efforts place the patients' pregnancy at risk. All pregnant patients, at both the intervention and control sites, will continue to receive their expected standard of care for the entirety of their pregnancy.

Inclusion of Children

Pregnant patients receiving care at eligible practices will be considered part of the study population. As the Advisory Committee on Immunization Practices (ACIP) recommends influenza and Tdap vaccination during pregnancy, the intervention, performed by primary care physicians within the study clinics, will include pregnant patients that are aged less than 18 years of age.

Inclusion of Employees

Employees of [redacted] will be included as subjects. All Information Sheets disseminated to study subjects during this study phase will emphasize that the decision to participate will have no impact upon: performance evaluations, job advancement, or the loss/gain of benefits (e.g., salary increases, time off).

6. INCLUSION/EXCLUSION CRITERIA & RECRUITMENT METHODS

All Participating Sites (Intervention & Control)

During aim/phase 1 of the study, health systems ([redacted]) within each state were chosen because a) their size allowed for an ample sampling of patients and practitioners (i.e., large subject pool) and b) they allowed for a broad spectrum of geographic and socio-economic diversity (e.g., privately and publicly insured, ethnic multiplicity, rural and urban locations, etc.). Prior to the start of the project, [redacted] contacted leadership within each health system, and letters of support were obtained (see attached Letters of Support for each system).

Intervention Sites

As described in the "Randomization" subsection of the "Study Design & Procedures" portion of the protocol, study sites from the larger pool were selected to be part of the "intervention group" using specific constrained randomization procedures within each health system (see section 4 of protocol for more details). All remaining sites were allocated to the "control group."

Practice-Level Personnel

Criteria/Recruitment Method for Vaccine Champion:

At each site, the affiliated medical director will select one "vaccine champion" for the practice. The vaccine champion will be selected due to their perceived ability to play a lead role throughout the study intervention, including their ability to complete all monthly and bi-monthly tasks listed in "Step 1" of the "Study Design and Procedures" section. The position of vaccine champion is voluntary, and if they do not wish to accept the role, they may decline and another individual will be identified by the affiliated medical director.

Criteria/Recruitment Method for Remaining Site Personnel:

By default (and with the support of health system and practice site leaders) all remaining providers, nurses, and practice staff employed by the practice location, are able to participate in the quality improvement initiative.

Patient-Level Study Subjects

Criteria for EHR Data from Practice Patients (Pregnant Women):
Baseline vaccine rates for each practice site were established during aim/phase 1 of the study, and contained EHR information from practice patients who were identified as having a live birth within the time period of summer 2018 to summer 2019. Due to a COVID-19 related pause in study activity, updated baseline vaccine rates will also be obtained during aim/phase 2 for the 2019-2020 time period. All subjects are female and some are <18 years of age.

To establish vaccine rates for the ongoing feedback reports, EHR information will be collected bi-monthly (every 2 months) from intervention sites during the entirety of the intervention phase (see timeline depicted in Figure 2). EHR information will reflect practice patients who are identified as being eligible for flu or Tdap vaccine within the specified 2-month time period. Again, all subjects will be female and may be <18 years of age.

To establish the final vaccine data reports (for intervention vs. control comparison), detailed EHR information (see Table 5) will be collected from both intervention and control sites for the 2021-2022 time period.

7. CONSENT PROCESS

Health System, Practice Site, & Site Personnel Level

Health System & Practice Site Consent:

Health System support (and subsequently site-level support) was previously obtained during aim/phase 1 of the study, as described in the "Inclusion/Exclusion Criteria & Recruitment Methods" section of the protocol.

Site Personnel Consent:

Delivery of Training Content & Involvement in 12-Month QI Intervention
(All site personnel: completion of e-learning module, attendance of follow-up site meeting, and participation in monthly/bi-monthly discussions of rate feedback and PDSA cycles)

This study involves commonly accepted quality improvement efforts aimed to improve upon the standard of care in medical settings, such as the completion of e-learning modules and in-person trainings specifically related to practice goals, the review of practice metrics (vaccine rates) by site personnel, discussion of office workflow procedures/efficacy, and trainings in optimal communication techniques.

We are therefore seeking a *waiver of documentation of consent and a waiver of HIPAA authorization* for the training portion of the study. More specifically, we are requesting this waiver because: **a)** the training portion of the study is no

greater than minimal risk, **b)** the purpose of the study/intervention and a basic framework of the trainings will be clearly outlined for participants in the Information Sheet (see *"InformationSheetTrainingPhase…"* document) e-mailed to them at the onset of the intervention phase, **c)** ample time will be given to personnel to review the Information Sheet in full and ask questions of study staff regarding the quality improvement effort and/or specific tasks involved in the training phase, and **d)** PHI will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

We will attach an Information Sheet (cited above) to the first e-learning invite e-mail, describing the study goals and training phase details, as well as site personnel involvement throughout the duration of the 12-month QI intervention (e-mailed to site personnel just prior to the training phase). Study staff will field any and all questions from potential study subjects prior to their module training and subsequent site meeting.

Assessment of Intervention Adoption: Surveys & Rate Feedback
(Selected Vaccine Champions: completion of bi-monthly rate feedback discussions and monthly PDSA cycles and Practice Time & Cost Surveys)

The assessment of intervention adoption by study sites involves commonly occurring procedures within a medical setting, including the ongoing review of practice metrics (vaccine rate feedback sessions), the development and assessment of practice goals (PDSA Cycles), and the evaluation of personnel efforts to achieve these goals (Time & Cost Survey).

We are therefore seeking a *waiver of documentation of consent and a waiver of HIPAA authorization* for the training portion of the study. More specifically, we are requesting this waiver because: **a)** the assessment portion of the study is no greater than minimal risk, **b)** the purpose of the study/intervention and a description of the assessment tasks will be clearly outlined for vaccine champions in the Information Sheet (see *"InformationSheetVaccineChampion…"* document) e-mailed to them at the onset of the assessment phase, **c)** ample time will be given to each vaccine champion to review the Information Sheet in full and ask questions of study staff regarding the quality improvement effort and/or specific tasks involved in the assessment phase, and **d)** PHI will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

As soon as they are selected, each identified vaccine champion will be e-mailed (see *"VaccineChampionEmail…"* document) an Information Sheet (cited above) by their affiliated study coordinator, outlining the basic study goals as well as their involvement in tasks throughout the training and intervention adoption

phases of the study. After the Information Sheets have been disseminated, study coordinators will conduct a follow-up phone call with each vaccine champion, reviewing their role within the project and fielding any and all questions they may have. The position of vaccine champion is voluntary, and if they do not wish to accept the role, they may decline and another individual will be identified by the affiliated medical director.

Assessment of Intervention Adoption: In-Person Observation
(Select Nurses and Staff: observation of workflow and communication techniques)

The in-person observation of intervention adoption involves commonly occurring procedures within a medical setting, including the ongoing documentation and review of daily workflow and communication procedures.

We are therefore seeking a *waiver of documentation of consent and a waiver of HIPAA authorization* for the in-person observation portion of the study. More specifically, we are requesting this waiver because: **a)** the observation portion of the study is no greater than minimal risk, **b)** the purpose of the observation will be clearly outlined for nurses and staff in the Information Sheet (see *"InformationSheetInPersonObs…"* document) e-mailed to them prior to the scheduled observation, **c)** ample time will be given to each nurse/staff to review the Information Sheet in full and ask questions of study staff regarding the observation, and **d)** PHI will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

Prior to in-person observation, the study coordinator will contact each site's vaccine champion to determine 1-2 days that would be optimal for study staff to be onsite. Once the observation schedule has been determined, all nurses and staff who are scheduled to work on the specified day(s) will be e-mailed an Information Sheet (see *"InformationSheetInPersonObs…"* document) by the study coordinator, which they may review at their own pace prior to the observation date. They may e-mail the project coordinator with any questions, or bring questions to the attention of the study staff on the scheduled visit day prior to the start of any observation. The content of the Information Sheet will be reviewed again by study staff with practice nurses/staff on the visit day prior to the start of any documented observation (any nurses/staff not previously known to be working that day will be given a hard copy of the Information Sheet upon arrival by the study staff and given ample time to review).

As stated previously, although study staff will observe OB/GYN practice nurses and staff during patient encounters, practice patients will NOT be the target of the observation, and no patient information (in either individual or aggregate form) will be collected. Rather, the focus of observation will be the select practice personnel only. Information recorded during the observation session will be

written in a generic manner such that specific nurses/staff/patients will not be identifiable. Notes will describe the general workflow processes and communication methods used, rather than specific unique behaviors or exact dialogue. For example, study staff may document *"…when patient declined to receive the Tdap vaccine, the practice nurse gave them an informational handout and told them the doctor may speak with them further*." The study staff will only observe the initial nurse/staff interaction with the patient, and will not continue to observe once the provider (doctor or midwife) enters for the visit. Although the patient is <u>not</u> the study subject, prior to each observation, study staff will explain to the patient in simple language the purpose of the observation (i.e., to take notes regarding the nurse/staff work routine), and any patient that communicates discomfort or preference to not be observed, will not be observed.

<u>Provider & Nurse Survey and Culture Survey Dissemination</u>

We are seeking a *waiver of documentation of consent and a waiver of HIPAA authorization* for the Provider & Nurse Survey and Culture Survey portion of the study. We are doing so because: **a)** the surveys are no greater than minimal risk (a brief online survey with unobtrusive questions), **b)** a detailed Information Sheet (see *"InformationSheetProviderNurseSurvey…"* and *"InformationSheetPracticeCultureSurvey…"* documents) will be made available to each subject prior to the start of the survey, **c)** ample time will be given to each subject to consider participation (subjects are notified of the survey via e-mail and can review the information sheet and/or ask questions of study staff for as long as necessary before deciding about survey completion), **d)** no identifiers will be included on the survey form (only subject IDs), and the separate document linking subject name to subject ID will only be made available to a limited number of study staff, will be kept under double-locked conditions, and will be destroyed three years after study completion, and **e)** PHI will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

<u>Patient (EHR) Level</u>

EHR Data Extraction: We are seeking a *waiver of consent and a waiver of HIPAA authorization* for the EHR data extraction portion of the study. We are doing so because: **a)** we believe that this research cannot be practicably conducted without such a waiver, as we cannot feasibly obtain consent and HIPAA authorization from all potential subjects ($10{,}000^{+}$ in total subject pool), **b)** site liaisons and report builders have routine access to patient records, **c)** a minimal number of patient-level data fields will be extracted from the EHR (just enough to complete analysis) **d)** a plan to protect EHR data during all data transfers will be implemented (see "Privacy & Confidentiality" section for details), **e)** any individual-level data will be destroyed three years after study completion, and **f)** PHI will not be reused or disclosed to any other person or entity except (i) as required by law, (ii)

for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

8. AUDIO/VIDEO RECORDINGS

All site meetings (both virtual and in-person) held during the training phase may be audio and/or video recorded using a laptop or handheld recording device (in-person meetings) or via the Zoom recording option (virtual meetings) (see "Privacy and Confidentiality" section for more detail). These archived audio/video files will allow for the review of meeting content by site personnel who were unable to attend the meeting live, or by those who simply wish to review the meeting discussion for a second time.

The archived site meeting audio/video files will be stored on a secure Box platform, accessible only to study staff and site personnel from the corresponding practice site (each site will have their own Box folder ensuring meetings from other sites are not viewable to outside personnel). Invites to the secure Box folder will be e-mailed from study coordinators directly to site personnel. As soon as the video files have been uploaded to the secure Box platform, they will be deleted from the laptop or handheld recording device. Once the study has been fully completed, all video files will be deleted from the shared Box folder.

9. RISKS TO SUBJECTS

Practice Level Risk: This project involves QI trainings/interventions which aim to improve upon the existing communication techniques and workflow procedures at each intervention practice site. Planned study trainings/interventions are widely accepted among medical practices (e.g., practice providers/nurses/staff attending an informational meeting regarding the risk of influenza in the pregnant population), and do not involve any novel high-risk changes to practice structure or procedures. Practice sites in the control group will continue to utilize "best-practice" guidelines. Thus, at the practice level, anticipated overall study risk is very low.

Site Personnel & Patient Level Risk: The primary risk to site personnel and practice patients is the risk of a breach of confidentiality, though overall risk remains low.

To reduce risk, personal information being collected from site personnel or practice patients (EHR data) has been minimized, and when possible is being collected in aggregate form.

A number of policies, procedures, and technical safeguards (described in the "Privacy & Confidentiality" section of this protocol) will be in place to ensure that there is no breach of confidentiality as a result of this study.

10. POTENTIAL BENEFITS TO SUBJECTS

Practice personnel will receive targeted training related to: influenza and pertussis disease as it pertains to the pregnant population, communication, and optimization of office workflow as it relates to the improvement of immunization rates within their practice. As such, practice personnel who participate in both the training and ongoing QI portions of the study will have the opportunity to apply for MOC, CME, or CNE credit.

There are no anticipated benefits for practice patients beyond those inherent to the overarching study goals (i.e., an improvement in flu and Tdap immunization rates).

11. COSTS FOR PARTICIPATION

There will be no costs incurred by participants.

12. PAYMENT FOR PARTICIPATION

For completing each "PDSA Cycle" survey and "Practice Time & Cost" survey, each vaccine champion will receive $5. Payment will be in the form of a gift card or check, and will be mailed to the vaccine champion at the conclusion of the 12 month intervention phase. Payment made will be the cumulative total of all completed monthly surveys (12 PDSA surveys + 12 Time & Cost surveys = 24 total surveys), for a maximum payout of $120 (24 surveys x $5 = $120). Additionally, if manual chart review is necessary for any NY practice sites, each vaccine champion will receive $20 for each monthly review. As with the above listed surveys, payment will be in the form of a gift card or check, and will be mailed as a cumulative payment to the vaccine champion at the conclusion of the 12 month intervention phase. To receive payment, subjects will enter their home address information into a secure REDCap field at the conclusion of the last online survey. This address information will be accessible only by study staff, and will be deleted as soon as the payment has been mailed.

For completing the "Provider & Nurse Survey" portion of the study, each subject will receive $40. For completing the "Practice Culture Survey" portion of the study, each subject will receive $10. For both surveys, payment will be in the form of a gift card or check, and will be mailed or e-mailed to the subject within 6 weeks of survey completion. Subjects will enter their home address and e-mail information into a secure REDCap field at the beginning of each online survey. This information will be accessible only by study staff, and will be deleted as soon as the payment has been sent.

Additionally, subjects completing the above surveys will be entered into a drawing for a $75 gift card for each survey completed. Health systems will have the ability to opt out of this additional drawing incentive if it conflicts with their institutional policy. Disclosure of the approximate chances of winning, and when required per institutional policy, procedures for the inclusion of those who do not wish to complete the survey will be included in the survey invite e-mail and Information Sheets. Winners will be chosen at random using a secure computer-generated randomization program containing the names of all participating subjects. Winners will be notified within 48 hours of being selected. Payment will be sent to the winners using the contact information collected in the address/e-mail field of their REDCap survey.

For serving as an intervention site, a single practice-level payment will be offered in the amount of $250. This payment will be in the form of a gift card or check, and will be disseminated to the vaccine champion from each intervention location. Payment may be used for any practice-wide item(s) deemed beneficial by the vaccine champion. If manual chart review is necessary at a practice site (and thus additional payment to the vaccine champion is made), the $250 practice-level payment for that site will be reduced by the total payout amount for the manual chart review.

13. SUBJECT WITHDRAWALS

During aim/phase 1 of this study (August 2019-July 2020) all health systems and affiliated practice sites agreed to participate in this quality improvement effort. While we do not anticipate a high level of subject/site withdrawals, any site wishing to end their involvement in the quality improvement initiative may do so at any time. Any practice personnel wishing to abstain from participation in quality improvement activities (trainings, ongoing meetings, adoption of new workflow procedures) are free to do so. Any vaccine champion who does not fully complete all monthly study activities during the 12 month intervention period, will still receive payment for all completed surveys prior to their withdrawal. All subjects (practice personnel) are free to discontinue participation at any time, without consequence.

14. PRIVACY AND CONFIDENTIALITY OF SUBJECTS AND RESEARCH DATA

The following data collection and storage procedures will be implemented at each study site, to ensure that subject privacy and confidentiality are maintained throughout the entirety of the research process:

Data obtained via e-mail and REDCap during the training phase:
(Site personnel names collected during the e-learning modules and site meetings)

Study coordinators will maintain a list of site personnel who have successfully completed their e-learning modules and who attended follow-up site meetings. These names will be obtained via e-mails from the vaccine champions and/or REDCap surveys. The lists will be stored in password protected Excel/Word files on a password protected computer for the purposes of confirming requests for MOC, CME and CNE credit. No additional study information (e.g., future survey responses) will be contained within this file. All files will be stored on a secure server within each university system ([redacted]). These individual-level training completion files will be deleted once they are no longer necessary (i.e., once all credit applications are in). Only aggregate data, not individual names, will be stored long-term by study staff regarding the completion of online training content by site personnel (i.e., the total number of providers, nurses, and staff who did/didn't complete the training).

Data Obtained via REDCap during the intervention adoption & assessment phase:
(PDSA cycles, Time & Cost Surveys, Provider & Nurse Survey, Practice Culture Survey)

For study measures completed via a REDCap survey, all subject names and corresponding e-mail addresses will first be collected by the study coordinators from either the previously

identified health system liaisons ([redacted]) or the assigned vaccine champions (not yet determined) for each site. The names, e-mail addresses, site locations, and an assigned subject ID for each person, will be stored in a password protected Excel/Word file on a password protected computer. No additional study information (e.g., survey responses) will be contained within this file. All files will be stored on a secure server within each university system ([redacted]).

Once e-mail addresses have been obtained, each study coordinator will upload the e-mail addresses onto the secure REDCap platform. Surveys will automatically be disseminated to the appropriate subjects in the appropriate timeframe (weekly, monthly, bi-monthly) through previous REDCap programming completed by the study coordinator. Completed REDCap survey data will be exported in an Excel/Word file and stored under double-locked conditions on a secure server within each university system ([redacted]), before transfer to the [redacted] Health Sciences Box platform (a regulated platform frequently used by [redacted] for data storage and transfer online) for analysis by the project's [redacted] data specialists.

Surveys for which payment (gift card or check) is given will request home address information within the survey questionnaire. This information will temporarily remain on the secure REDCap platform and/or secure university server, and will be utilized by the study coordinators during the payment mailing process. All personal address information will be destroyed once payments for phase 2 have been fully completed.

Data Obtained via EHRs:

EHR data reports will be generated only by the specified EHR report builder for each health system. A minimal number of patient-level data fields (only those needed for analysis) will be extracted from the EHRs. For data verification purposes, identified study staff will check a small percentage of patient eRecord files to ensure the accuracy of generated EHR reports. The identified individuals will have access to EHR files and will complete all appropriate eRecord training prior to conducting data verification. All individual level data will be stored in encrypted form on the secure Box platform. Whenever possible, data will be stored in aggregate form. "Rate Feedback" reports received by site personnel will present immunization rate information in aggregate form only (no individual patient information), and the recipient of the report will be identified by a study ID# rather than a name.

All Research Data: All individual-level research data (saved in encrypted form) will be stored on the secure [redacted] Health Sciences Box platform (a regulated platform frequently used by [redacted] for data storage and transfer online). Aggregate data will be stored on secure university servers and/or the secure Health Sciences Box platform. Analyzed data reports from the [redacted] data specialist will be sent in a de-identified form via secure e-mail to the project PI for review. Any files linking subject name to subject ID# (e.g., REDCap survey files, personnel ID files for feedback reports) will be password protected and stored on secure university server systems accessible only by study staff.

15. DATA / SAMPLE STORAGE FOR FUTURE USE

Hard copy data: Due to the online (e.g., REDCap) nature of data collection during phase 2 of the study, no hard-copy documents will be created or stored.

Electronic data:

Site Meeting Attendance:
Files containing site meeting attendance records will be stored in password protected Excel/Word files on password protected computers. No additional study information (e.g., survey responses) will be contained within these files. All files will be stored on a secure server within each university system ([redacted]). Once all MOC, CME and CNE credit requests have been completed, attendance records will be destroyed.

E-learning modules, PDSA cycles, Time & Cost Surveys, Provider & Nurse Survey, Practice Culture Survey:
Survey data is stored immediately upon completion by the REDCap website. Study staff will then access the secure password-protected survey site to generate data reports when needed. These data reports will be stored on password-protected computers within the locked offices of study staff (double-locked conditions) using the secure university servers. Any *personal address information* obtained from study subjects for the purposes of payment will be destroyed once payments for phase 2 have been fully completed.

As we are seeking a waiver of documentation of consent and a waiver of HIPAA authorization for the survey portions of the study, there will be no need to store consent forms with subject names.

EHR data output:
Individual-level EHR data reports (saved in encrypted form) and aggregate EHR data reports will be stored on the secure [redacted] Health Sciences Box platform (a regulated platform frequently used by [redacted] for data storage and transfer online). Analyzed data reports from the [redacted] data specialist will be sent in a de-identified form via secure e-mail to the project PI for review. All data will be stored 3 years beyond study completion.

16. DATA AND SAFETY MONITORING PLAN

This study presents no more than minimal risk, however there is still a risk to privacy and confidentiality. Prior to the start of aim/phase 1, the research team from both NY and CA met to create a data safety monitoring plan. PIs, team members, and representatives from each study clinic regularly discuss communication and action plans in the unlikely event that an adverse event occurs. Information on how to contact the study team via phone, mail or email is readily apparent to all participating providers and care team members. Though adverse events are not anticipated, should any occur they will be reported to the site PI ("team leader") in each state and then to the IRB at the time of the event, and copies of all correspondence regarding the event with the IRB will be shared with the CDC, as needed.

17. DATA ANALYSIS PLAN

Primary outcomes (receipt of Flu and Tdap vaccines) are binary and our main explanatory variable will be an indicator for study arm. We will employ intent-to-treat analyses using generalized linear mixed models (GLMMs) with practice random effects, an approach recommended for group-randomized RCTs in which the goal is to estimate the causal effects of interventions on individuals, adjusted for clustering within groups. This method performs well in situations where the number of observations per cluster is large and for unequal cluster sizes. Models will assume a binomial distribution and a log link function in order to compare vaccination rates between study arms in terms of risk ratios. We will adjust for all practice-level variables included in the randomization balancing criterion, as well as patient-level race/ethnicity (and prior year vaccination status for the flu analysis). Hypothesis tests will be two-sided with alpha = 0.025, reflecting a 2-fold Bonferroni correction for the co-primary endpoints of Flu and Tdap vaccination status, ensuring a familywise type I error rate of 0.05. Analyses will be performed using SAS v. 9.4 (SAS Institute Inc., Cary, NC).

Power Analysis: We assume national vaccine rates for flu (49%) and Tdap (54%). Adjusting for clustering of patients in practices, and assuming an intraclass correlation (ICC) of 1% (consistent with previous work), this sample size provides >80% power to detect an overall increase of 6.3 percentage point increase in vaccination rates between the QI intervention and control arms. This assumes a chi-squared test (a simplification of the planned mixed model analysis described above), a test-level alpha of 0.025, and a sample size of 5,000 pregnant women organized into 16 practices per study arm.

Final Time/Cost Analysis:

Upon completion of aim/phase 2 we will conduct a final time/cost analysis. Our two-fold cost measures are (a) total intervention cost to implement the VAX-MOM program aggregated at the four health-system level under a cost analysis and (b) cost per additional flu or Tdap vaccination under a subsequent cost-effectiveness analysis. To derive a policy implication regarding the sustainability of programs, we will estimate costs and ICER estimates from the health system perspective.

Total Cost: To make these cost measures comparable to similar past interventions of reminders and educational programs, we will estimate cost with one-year time horizon, excluding the cost to purchase, store and administer vaccines. We will estimate the total intervention cost, summing non-personnel costs (e.g., EHR hardware, software, and materials) and personnel costs. The personnel costs will distinguish research costs from intervention costs (e.g., practice-level meeting and collecting EHR data). The dollar values of these personal costs will be calculated by multiplying “time efforts” (weekly reported by study personnel using a REDCap email survey) with the nationally representative “hourly-wage rates” by occupation codes of study personnel, derived from the Bureau of Labor Statistics.

Cost-Effectiveness: We will develop a standard decision model for our cost-effectiveness analyses. The effectiveness measures are the rates of flu and Tdap vaccination estimated under Aim 2b.

As explained above, this intervention cost will exclude the cost to purchase, store and administer vaccines, which is assumed to be identical among all practices. Applying the same assumption, the average cost for the control group (costControl) is zero. To make separate ICER estimates for flu and Tdap vaccination, the Tdap-vaccination-specific costStudy will be estimated during non-flu season (April to September) first and applied for calculating the flu-vaccination-specific costStudy during a flu season (October to March), assuming the Tdap-vaccination-specific costStudy is constant throughout a year. Using the developed standard decision model, we will conduct probabilistic analyses to generate point estimates and 95% CIs for ICERs and one-way sensitivity analyses to determine conditions for being lower than the thresholds of cost-effectiveness, e.g., healthcare-system based quality improvement interventions to improve flu vaccination uptake targeting general populations (median ICER $51 among 23 interventions) and healthcare workers (median ICER $125 among 6 interventions) reported by a systematic review.

Hyp. : Cost per additional flu or Tdap vaccination under the VAX-MOM is lower than past similar interventions.

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