HRP-503D - Protocol for Exemption Request
Version 2019-1

Protocol Title: AFIX-OB: A Customizable Quality Improvement Intervention to Increase Maternal Vaccine Uptake, AIM 1
Principal Investigator: Dr. Saad Omer
Version Date: January 27, 2020
NCT04678271

Instructions:

Certain research activities may be exempt from review, if confirmed by the IRB Chair or his/her designee and confirmed in writing to the Investigator. Research may be exempt from review when the only involvement of human subjects in the research falls into one or more of the categories noted below. The regulations allow for two additional exemption categories that are not currently implemented at Yale.

Note:

- **The IRB does not exempt studies that involve the Introductory Psychology Subject Pool.**
- **Exemption categories apply to research involving pregnant women.**
- **Exempt categories DO NOT apply to research with prisoners, except for research aimed at involving a broader subject population that only incidentally includes prisoners.**
- **Exempt categories generally apply to research with minors, except when specifically stated otherwise.**

Choose one of the following exemption categories for consideration and provide the information as requested under the corresponding category. **Delete all other categories that do not apply.** Upload the survey(s), instrument, or interview questionnaire/focus group guides to the Supporting Documents section of IRES IRB.

FOR HIPAA ONLY - The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

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CHOOSE YOUR CATEGORY(IES) OF EXEMPTION FROM FULL IRB REVIEW
Click here to enter text.

(*Category 2*) 45 CFR 46.104(d)(2) Research not regulated by the FDA that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (Please indicate which criteria applies)

☐(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

☒(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

☐(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination.

This exemption category applies to research with minors ONLY if the research involves educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.

Assessment
• Conduct chart review to establish pre-intervention immunization rates • Administer Immunization Delivery Scale to evaluate current immunization practices
Feedback
• Discuss baseline immunization rates • Compare rates between peer practices • Identify barriers to vaccine uptake at clinic • Select quality improvement interventions to implement
Incentive
• CME credit for completing VaxChat • MOC Part IV credit for participating in study • Recognition and award for practice with greatest improvement in rates
eXchange
• Conduct chart review to establish post-intervention immunization rates • Discuss post-intervention immunization rates • Compare immunization rates to peer practices • Establish sustainability plan for interventions

Table 1. AFIX-OB

1) Describe the purpose of the study. Click here to enter text.

An important milestone in the improvement of childhood vaccine coverage in the United States was the development of the Assessment, Feedback, Incentive, and eXchange (AFIX) model (Table 1). This model provides a framework for improving childhood vaccine delivery in pediatric practices by assessing practices' baseline immunization rates, sharing this information between peer practices to promote competition and engaging practices in selecting quality improvement measures to implement. AFIX is effective, sustainable and can be implemented on a large scale, increasing vaccination rates by four to seven percentage points on average.[1-3] Health departments have been utilizing this process for more than twenty years; however, the AFIX model has not been evaluated outside of pediatric and adolescent immunization

We will expand and evaluate the AFIX-OB model through two specific aims:

Specific Aim 1 (formative phase): Develop the AFIX-OB intervention package by identifying and refining a set of patient, provider, and practice-level quality improvement interventions.

Specific Aim 2 (intervention phase): Evaluate the AFIX-OB

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model. (We will be submitting a separate IRB proposal for this aim).
As with the original AFIX model, if efficacious the AFIX-OB framework has the potential to be widely implemented in a variety of obstetric care settings to improve vaccine uptake by supporting obstetric care providers as they address barriers at the practice, provider and patient levels.

2) **Describe the target population.** The study population will consist of pregnant women and providers.

Pregnant Women: Pregnant women will be recruited from obstetric care clinics within the Yale New Haven Health System. We will identify practices from socio-demographically diverse locations around the state of Connecticut. Inclusion criteria will include (a) between ages of 18-50 and (b) currently pregnant and at least 27 weeks gestational age. Study staff will approach women who appear eligible (based on age and trimester of pregnancy) in the clinic setting and administer a screening questionnaire, which will include the Emory Vaccine Confidence Index (EVCI)[4]. The pregnant women will be grouped into one of the following categories using the EVCI scale: 1) low-hesitancy, 2) medium hesitancy, or 3) high-hesitancy. We anticipate conducting 30 in-depth interviews or until we reach data saturation, about 10 women in each of the hesitancy categories.

Providers: Providers will be recruited from obstetric care clinics within the Yale New Haven Health System. We will identify practices from socio-demographically diverse locations around the state of Connecticut as well as practices with diverse immunization delivery practices. Clinics that do not stock the vaccines of interest (influenza and TDAP) will be excluded. We plan to interview a variety of providers (obstetrician-gynecologists (OBGYN), certified nurse midwives (CNM) and nurse practitioners (NP)) as well as clinic staff (practice managers, receptions, medical assistants, nurses) to identify and address barriers at all points of patient contact within a clinic. We anticipate conducting 30 in-depth interviews or until we reach data saturation, about 15 providers and 15 clinic staff members.

3) **Describe the location of the study.**

For aim 1, we will recruit two obstetric clinics within the Yale New Haven Health System (YNHHS). The Yale New Haven Health System consists of four Connecticut hospitals (Yale New Haven Hospital, Bridgeport Hospital, Lawrence & Memorial Hospital and Greenwich Hospital) which encompass 45 obstetric and gynecologic care practices across the state and nearly 300 obstetric care providers. Between the four locations, the health system sees approximately 12,000 live births a year, which is roughly a third of all live births in Connecticut in a given year.[5] The health system serves the entire state of Connecticut, including the five largest cities, and covers a socio-demographically diverse patient population. New Haven in particular is one of the poorest cities in the United States, with more than a quarter of its residents living in poverty. The Yale New Haven Hospital location and surrounding clinics serve a majority minority patient population (58% non-White). The YNHHS is dedicated to participating in research to improve the quality of care they can deliver to their patients with all hospitals and more than 25% of associated community practices already participating in clinical research. The entire health system utilizes a single Electronic Health Record system (EHR), improving the ease of conducting quality improvement and immunization studies. The current overall maternal influenza vaccine uptake rate in the YNHHS is 34% and the maternal Tdap uptake rate is 42%, which are approximately in line with national averages(Table 2a and 2b).[6] The diverse patient population increases the generalizability of our findings, making the YNHSS an ideal health system for this trial. Additionally, the low baseline rates indicate that there is room for improvement in maternal immunization delivery, unlike in other health systems, like Health Maintenance Organizations (HMOs), which typically have higher immunization coverage.

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Practices will be identified from socio-demographically diverse locations around the state of Connecticut. Selected clinics will include both private and non-private practices as well as practices with diverse immunization delivery practices. Practices that do not stock the vaccines of interest will be excluded. Interviews will be conducted in a private area of the clinic in order to protect privacy.

Campus	Total Deliveries (Oct. 2017 – Apr. 2018)	Received Flu Vaccine – N (%)
Yale New Haven (St. Raphael Campus)	529	300 (57)
Yale New Haven (York Street Campus)	2,227	1,104 (50)
Greenwich	1,225	110 (9)
Lawrence & Memorial	670	125 (19)
Bridgeport	1,141	335 (29)
Totals:	**5,792**	**1,974 (34)**

(a) Influenza Vaccine

Campus	Total Deliveries (Jan. – Dec. 2018)	Received Tdap Vaccine – N (%)
Yale New Haven (St. Raphael Campus)	1,086	693 (64)
Yale New Haven (York Street Campus)	4,791	2,777 (60)
Greenwich	2,719	423 (16)
Lawrence & Memorial	1,348	363 (27)
Bridgeport	2,512	865 (35)
Totals:	**12,456**	**5,121 (42)**

(b) Tdap Vaccine

Table 2. 2017/2018 Vaccine Coverage Rates at YNHSS Hospital Systems

a. Does this study include an international location? ☐ Yes ☒ No
If yes, specify location: Click here to enter text.

4) Describe the procedures that will be used to recruit subjects.

Pregnant Women: Pregnant women will be recruited from obstetric care clinics within the Yale New Haven Health System. Providers will identify women who are eligible and ask them if they are willing to participate in the study. Those women who express interest in participating in the study will then be approached by research staff who, following a recruitment script, will confirm eligibility and administer a screening questionnaire. Women may withdraw at any time by stopping the interview with no adverse consequences. If a woman is found eligible and interested in participating, the research staff member will go through the informed consent process with the patient and obtain written informed consent after the participant has been given time to read the form and ask questions. Consent will include permission to conduct and record the interview. We will recruit 30 women total and categorize them by hesitancy category (high, medium, and low vaccine hesitancy) from two clinics in the system. The number of interviews per site will depend on the size of the site.

Providers: Two clinics will be recruited from the Yale New Haven Health System. We will contact practice managers to request participation in the formative phase of the study. Providers and clinic

staff within practices that agree to be in the study will then be asked if they are willing to participate. If a provider is interested in participating, the research staff member will go through the informed consent process with the them and obtain written informed consent after the participant has been given time to read the form and ask questions. We will recruit providers and clinic staff members until we reach data saturation, about 15 providers and 15 clinic staff members.

5) Describe how subjects will provide consent (and/or research authorization) to participate in the study.

Pregnant Women: Providers or nurses (depending on the practice), will refer patients who are interested in the study to research staff who will screen them for eligibility, provide them with an explanation of the study's purpose and procedures, give them an opportunity to ask questions, and obtain written consent. Study personnel will receive training in assessing a person's ability and capacity to obtain consent. First, they will complete all human subjects training. Second, they will meet and work with clinic nurses and providers to learn how to handle situations in which capacity is of concern. Clinic staff will also be able to help identify patient participants for whom capacity may have been a concern during routine clinical care. Third, they will attend informed consent training sessions as appropriate to learn more about the consent process. Consent will include permission to conduct and record the interview. Participants will be given a copy of the consent form for their records. The entire process will be non-coercive. Participants will be given the name and phone number of the Principal Investigator to contact if they have any concerns.

Providers and Clinic Staff: The research staff member will go through the informed consent process with clinic staff and providers that are interested in participating in the study. Consent will include permission to conduct and record the interview. Participants will be given a copy of the consent form for their records and the entire process will be non-coercive. Participants will be given the name and phone number of the Principle Investigator to contact if they have any concerns.

6) Describe the procedures that will be used to conduct the research. ***(NOTE - If using enumerators, include the name of the agency, training provided to individuals at the agency, and the specific role in this research. If using a survey platform, name the platform.)***

This formative phase will combine evaluation data from our previous trials with additional in-depth interviews with pregnant women and providers to refine the quality improvement interventions that will be offered to participating practices.

Data Safety and Risks: The risks involved in this study include potential invasion of privacy, discomfort with discussion of reasons for non-vaccination, and the potential for release of protected health information. Invasion of privacy will be minimized by conducting interviews in a private area. Data protections, using Yale Secure Box, will be used to ensure security and confidentiality of findings (interview transcripts, surveys, and automated data). Access to protected health information, from electronic medical records will be conducted only by authorized users of the systems. Data abstracted from these databases will be stored on Yale Secure Box, with access limited to permitted research staff. We are studying maternal vaccine uptake, but vaccine administration is not a component of the intervention. Vaccines will be administered as part of standard medical care.

Pregnant Women:

In-depth Interviews: Those women who express interest in participating in the study will then be approached by research staff who will confirm eligibility and administer a screening questionnaire, which will include the Emory Vaccine Confidence Index(EVCI).[4] The pregnant women will be grouped into one of the following categories using the EVCI scale: 1) low-hesitancy, 2) medium hesitancy, or 3) high-hesitancy. We will also collect self-reported information on the woman's

maternal vaccination status, whether the woman is a first-time mother and the vaccination status of any previous children.

We anticipate conducting 30 in-depth interviews or until we reach data saturation, about 10 women in each of the hesitancy categories. Invasion of privacy will be minimized by conducting interviews in a private area.

Semi-structured interviews using a standardized interview guide will be conducted. Interview guides will include questions exploring maternal immunization attitudes as well as feedback on the existing patient level interventions. Sample questions about maternal immunization attitudes include: what are the most important factors you consider when making a health decision during pregnancy? What are the most important sources of health information for women during pregnancy? For feedback on existing patient level interventions, participants will be shown sample flyers, content or videos and asked questions like if you came across this information, what thoughts come to mind? Do you feel like you received enough information? Do you have any questions regarding the language?

Interviews will last approximately 20 to 40 minutes, depending on the extent of the discussion, and will be audio recorded, pending interviewee consent to be recorded. Interview recordings will be transcribed, and all audio recordings and transcriptions will be stored on a password-protected Yale Secure Box. Participants will receive $20 for their participation in the interview.

Qualitative Analysis: At the end of the in-depth interviews, we will have elicited beliefs and attitudes about recommended immunizations, barriers to immunization and specific feedback on the patient-level interventions. Based on our experience conducting qualitative studies, we anticipate reaching data saturation at approximately 30 interviews with our segmented recruitment strategy. Using thematic and logical analysis, we will identify common themes and patterns through NVivo 11.0 for transcript analysis.[7,8] Thematic analysis identifies themes articulated directly by participants or identified by the team during analysis, which will be helpful in condensing data and identifying subtle patterns or themes while simultaneously considering outlier opinions. All in-depth interview transcripts will be coded according to emerging patterns and these codes will be further refined through a series of iterative cycles used in team-based qualitative analysis.[9] Coding of these qualitative data will be conducted by two members of the research team, with comparisons for consistency, enabling us to ensure high inter-coder reliability. We will use both the structural and content coding techniques for developing our codebook and to describe our resulting thematic observations. Results from the in-depth interview will be used to inform the updates to the patient-level interventions, the patient survey that will be administered during the trial as well as the implementation of the specific quality improvement measures in the intervention phase.

Patient Level Intervention Refinement: The ‘core’ patient level intervention utilized in the study will be a tablet-based interactive app and will include both written and audio/video content covering the benefits of antenatal flu and Tdap vaccination. The basis for the app will be the Elaboration Likelihood Model-guided interactive iBook-based tutorial utilized in our P3 “MOMVAX” Trial.[10] Refinements of the app may include but are not limited to updates to the content (i.e. updated information on the benefits of vaccination), to the framing of the messages and to the design of the app. In addition to the app, practices will also have option of selecting flyers and/or posters to distribute to their patients or post in their offices during the intervention phase. Updates to all patient level interventions will be guided by feedback from our previous trials and in-depth interviews with pregnant women.

Providers and clinic staff

In-Depth Interviews: Semi-structured interviews using a standardized interview guide will be conducted. Interviews will be conducted in a private area in order to minimize invasion of privacy.

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Interview guides will include questions on the type of provider (OB/GYN, nurse midwife, physician's assistant, nurse practitioner), their age and sex. For staff, we will ask what their role at the clinic is and make sure that we interview the clinic manager in each of the two clinics samples. We will include questions exploring current immunization recommendation practices as well as provider perspectives on the implementation of the included quality improvement measures. It is well documented that a strong provider recommendation is the best predictor of vaccine receipt among pregnant women, however, there is no consistent understanding of what a strong provider recommendation is.[11,12]

Sample questions about current immunization practices for providers include how do you initiate vaccine conversations? Do you feel that vaccination is a priority in your clinic? For feedback on the implementation of the quality improvement interventions, participants will be asked about barriers to implementation and strategies for implementing in their clinic. Interviews will last approximately 20 to 40 minutes, depending on the extent of the discussion, and will be audio recorded, pending interviewee consent to be recorded. Interview recordings will be transcribed, and all audio recordings and transcriptions will be stored on a secure, password-protected account at Yale Secure Box. Providers and clinic staff will receive $30 for their participation in the interview

Qualitative Analysis. Analysis of the provider and clinic staff interviews will be conducted in a similar manner to patient interviews. Using thematic and logical analysis, we will identify common themes and patterns through NVivo 11.0 for transcript analysis. Coding of these qualitative data will be conducted by two members of the research team, enabling us to ensure high inter-coder reliability. We will use both the structural and content coding techniques for developing our codebook and to describe our resulting thematic observations.
Results from the in-depth interview will be used to inform the updates to the quality improvement interventions, the provider survey that will be administered during the trial as well as the implementation and monitoring of the chose quality improvement interventions.

Provider and Practice Level Intervention Refinement: The in-depth interviews with providers will be used to refine the following quality improvement interventions for the intervention phase. The 'core' provider level intervention will be "VaxChat: Helping Obstetric Care Providers Confidently Discuss Maternal Vaccination," which is currently an hour-long webinar that tutors obstetric providers on evidence-based methods to discuss vaccinations with their pregnant patients. VaxChat was developed and tested as part of our P3+ trial (PI Omer). Potential improvements to VaxChat include but are not limited to updating the content (e.g. updating for any change in recommendations), reducing the length of the tutorial and adding additional interactive elements. In addition to VaxChat, practices will be able to select whether they would like to implement provider-to-patient talking points as another quality improvement intervention.
The 'core' practice level interventions are reminder/recall systems and standing orders. Reminders refer to messages before a patient is due for a vaccine, whereas recall refers to messages when a patient is overdue for a vaccine and have been demonstrated to be very effective at improving vaccine uptake, both broadly[13-16] and specifically in the context of maternal immunization.[17]
Standing orders represent a policy where medical assistants (MA) or nurses can administer a vaccine without an order from a provider and are considered one of the most effective evidence-based practices for improving vaccine uptake.[18] Practices will be asked to select one or the other to implement as part of their quality improvement effort.
In addition to standing orders and reminder/recall systems, practices will also be able to select from the following interventions: educational information to post on their practice website, highlighted and laminated Vaccine Information Statement sheets for use in the clinic and training the study champion as an immunization champion.

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7) **If subjects' identity can be readily ascertained directly or through identifiers linked to them, could any disclosure of their responses outside the research reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, educational advancement, or reputation? ☐ Yes ☒ No ☐ NA**

   If YES –provide the list of identifiers and describe how data will be secured to protect the privacy of subjects and maintain the confidentiality of the data, and, if applicable, the coding system that will be used.:

8) **If you are from Yale School of Medicine, School of Nursing, or another HIPAA covered entity (such as Psychology clinics) and wish to collect PHI without obtaining written HIPAA authorization, – a HIPAA waiver must be obtained. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data:**

N/A

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