# A multilevel approach to understanding and reducing missed opportunities for vaccination among adolescents with chronic medical conditions

## C1. OVERALL GOALS AND OBJECTIVES

Vaccination coverage is suboptimal for all adolescents, yet particularly concerning for adolescents with chronic medical conditions who frequently fail to receive routinely recommended vaccines such as human papillomavirus (HPV) vaccine and other indicated vaccines such as pneumococcal polysaccharide (PPV23) vaccine. Vaccination of these adolescents is crucial from an individual perspective given their increased risk of infection and associated complications. It is also important from a public health perspective given the growing incidence of this population and need for high coverage levels to ensure a population-wide impact. Since many adolescents with chronic medical conditions receive health care services, yet remain under-immunized, further elucidation of the unique factors contributing to missed opportunities for vaccination is needed. In the proposed study, we seek to identify barriers to HPV and PPV23 vaccination in this population and address these using an innovative technology-based intervention. The ultimate goal of this initiative is to increase HPV dose 1 (HPV1) and PPV23 vaccination coverage among adolescents with chronic medical conditions.

**Objective 1: To examine missed opportunities for HPV1 and PPV23 vaccination of adolescents with chronic medical conditions.**

*Hypothesis: Missed opportunities for vaccination will be common, particularly for PPV23.*

To achieve Objective 1, we will examine missed opportunities for HPV1 and PPV23 vaccination of adolescents aged 11-17 years with chronic medical conditions receiving care at one of four primary pediatric clinics affiliated with NewYork-Presbyterian Hospital-Columbia University Medical Center (NYP-CUMC) during a 12-month period. We also will identify demographic, diagnostic, and visit characteristics associated with missed opportunities in this population.

**Objective 2: To assess parental and provider knowledge, attitudes, and experiences related to HPV and PPV23 vaccination of adolescents with chronic medical conditions.**

*Hypothesis: Many parents and providers will lack knowledge about HPV and pneumococcal infection risk, vaccine efficacy and safety, and vaccine recommendations/contraindications. Adolescents with chronic medical conditions whose parents have limited knowledge about infection risk and/or greater vaccine safety concerns will be less likely to be vaccinated.*

To achieve Objective 2, we will administer surveys to a sample of parents and providers of 11-17 year-old adolescents with chronic medical conditions in select pediatric clinics affiliated with NYP-CUMC. Parental survey responses will be linked to their adolescent's HPV1 and PPV23 vaccination status.

**Objective 3: To determine the impact of a provider vaccine alert and additional parental text message reminder on missed opportunities for HPV1 and PPV23 vaccination of adolescents with chronic medical conditions.**

*Hypothesis: Missed opportunities for HPV1 and PPV23 vaccination of adolescents with chronic medical conditions will be lower among those who visit a clinic when the provider alert is active (PA only group) compared to those who visit a clinic when it is inactive (baseline group). Missed opportunities for vaccination will be further reduced among those*

*who visit a clinic when the provider alert is active and their parent is sent a "priming" pre-appointment text message vaccine reminder (PA+TM group).*

To achieve Objective 3, we will design and implement an intervention comprised of an alert in the electronic health record for providers and an additional pre-appointment text message reminder for parents of 11-17 year-old adolescents with chronic medical conditions at four primary care clinics affiliated with NYP-CUMC. Missed opportunities for HPV1 and PPV23 vaccination of eligible adolescents with chronic medical conditions will be compared between (1) PA only *vs.* baseline groups and (2) PA+TM *vs.* PA only groups.

## C2. TECHNICAL APPROACH

### a. Assessment of Need

#### *i. Baseline HPV and PPV23 vaccination coverage of adolescents with chronic medical conditions*

The incidence of chronic medical conditions among adolescents has increased markedly in recent years, with estimates that one in every six to ten adolescents has a chronic medical condition.[1, 2] Many are at increased risk of HPV and *S. pneumoniae* infections with significant morbidity and mortality, including HPV-related cervical cancer and invasive pneumococcal disease such as meningitis.[3-6] Therefore, the Advisory Committee on Immunization Practices recommends that they receive all routine adolescent vaccines, including HPV vaccine, and, for some, additional vaccines such as PPV23 vaccine.[7]

While studies indicate that many adolescents with chronic medical conditions fail to receive recommended vaccines such as influenza,[8, 9] national data describing HPV and PPV23 vaccination coverage of these adolescents are lacking. Thus, using the NYP immunization registry, EzVac (see Data Sources below), we recently examined HPV and PPV23 vaccination coverage of 11-17 year-old adolescents with select chronic medical conditions, defined per ACIP recommendations and existing literature,[2, 7, 10, 11] who received care at one of four primary pediatric clinics affiliated with NYP-CUMC during a 12-month period. Preliminary data indicate that only 47% had received three HPV vaccine doses, falling well short of Healthy People 2020 target levels of 80%,[12] and a meager 12% of eligible adolescents had ever received PPV23 vaccine. Even lower coverage may exist elsewhere given that our general pediatric and adolescent population typically has higher coverage than observed nationally,[13, 14] in part due to successful technology-based interventions.[15-18] With the rising incidence of chronic medical conditions among adolescents and the implications of under-vaccination of this vulnerable population, these findings are of critical public health importance.

#### *ii. Practice gaps underlying under-Immunization of adolescents with chronic medical conditions*

At present, there is insufficient understanding of the factors contributing to under-immunization of adolescents with chronic medical conditions. However, the few existing studies to date, primarily focusing on influenza vaccination, suggest that the main practice gaps include (1) insufficient understanding of vaccine-related issues among parents and providers; (2) inadequate communication between providers and parents caring for these adolescents; and (3) systems-based barriers to vaccination. Many parents and providers caring for children with chronic medical conditions may possess misinformation about infection risk, vaccine efficacy and safety, and vaccination recommendations and contraindications.[8, 9, 19] Perhaps consequently, providers often fail to recommend needed vaccines to these patients, and missed vaccination opportunities are common.[8, 19, 20] Reduced provider awareness of

vaccination status and time constraints during clinic visits could serve as additional challenges.[21-24] These adolescents may face other systems-based barriers, particularly since they often require care from multiple providers in a variety of clinical settings.[8, 9, 19, 25] Examining missed opportunities for HPV and PPV23 vaccination and further elucidating the parental, provider, and systems-based factors associated with under-immunization against HPV and PPV23 are critical first steps in designing an effective intervention to improve vaccine outcomes in this population.

***iii. Health technology strategies for vaccinating adolescents with chronic medical conditions***

Innovative strategies to target identified practice gaps and improve vaccination coverage of adolescents with chronic medical conditions are needed, and the use of health technology holds particular promise. Our previous qualitative work revealed provider interest in using provider vaccine alerts in our primary pediatric clinics.[26] In addition, we recently found strong parental, provider, and staff interest in using text message reminder/recall for vaccination in these clinics.[27] Importantly, we have also demonstrated that customized provider alert and text message reminder/recall systems, integrated with our EzVac immunization registry, significantly improve coverage levels for recommended pediatric and adolescent vaccines in our general patient population.[15-18] While we have yet to examine their impact on vaccination coverage of adolescents with chronic medical conditions, a few studies have demonstrated that they may rapidly and accurately identify high-risk children, primarily asthmatics, in need of influenza vaccine.[11, 28] Further examination of their impact on HPV and PPV23 vaccination coverage of adolescents with chronic medical conditions is warranted.

***iv. Primary target audience of intervention***

The primary target audience of our technology-based intervention will be parents and providers of adolescents with chronic medical conditions who receive care in one of four primary pediatric clinics affiliated with NYP-CUMC. We aim to directly benefit the health outcomes of these high-risk adolescents by reducing missed opportunities for HPV and PPV23 vaccination, thereby increasing their vaccination coverage levels.

**b. Intervention Design and Methods**

Overview: We will first clarify the practice gaps leading to the demonstrated poor HPV and PPV23 vaccination coverage among adolescents with chronic medical conditions using demographic, diagnostic, visit, and vaccine data from the EzVac immunization registry (Objective 1) as well as surveys of parents and providers caring for this high-risk population (Objective 2). We will then design and implement a technology-based intervention comprised of an electronic health record (EHR) vaccine alert for providers and an additional pre-appointment text message vaccine reminder for parents of adolescents with chronic medical conditions (Objective 3). Their impact on missed opportunities for HPV1 and PPV23 vaccination of eligible adolescents with chronic medical conditions will be determined. The Objective 1 protocol has been approved by the CUMC Institutional Review Board (IRB). Objective 2 and 3 protocols will be submitted for approval as detailed below (see Workplan below).

**Objective 1:** To examine missed opportunities for HPV1 and PPV23 vaccination of adolescents with chronic medical conditions.

Subjects and Setting: Adolescents will be eligible if they 1) were 11-17 years-old; 2) had at least one pre-specified chronic medical condition; 3) required HPV1 and/or PPV23 vaccine; and 4) visited one of four primary pediatric clinics affiliated with NYP-CUMC during a 12-month period. Chronic medical conditions will be selected based upon ACIP recommendations and existing literature.[2, 7, 10, 11] They will be identified using ICD-9 codes, which have a 90% accuracy in detecting high-risk children with vaccination needs.[11]

Data Sources: Eligible children will be identified through the NYP registration system, which contains patient demographic (e.g., age, gender, language, insurance), diagnostic (e.g., ICD-9 code), and visit (e.g., site, date) data. HPV and PPV23 vaccine data will be collected from the NYP immunization registry, EzVac, of which Dr. Stockwell (co-I) and Dr. Vawdrey (co-I) are Medical and Informatics Director, respectively. EzVac holds active vaccine records for >135,000 children and adolescents receiving care at the hospital and affiliated clinics. It is estimated that EzVac captures >95% of all vaccines given at these sites. Data are extracted real-time from the EHR or entered directly by medical staff following administration. EzVac also synchronizes with the New York Citywide Immunization Registry, a population-based provider-mandated registry that includes >93% of vaccines given through the Vaccines for Children (VFC) program.[29, 30] Thus, doses administered at non-study sites in New York City will also be captured in EzVac data. Historical vaccine data are also routinely entered into EzVac/CIR by providers. We have significant experience examining vaccination coverage using these data.[13, 14, 31-35]

Analysis: A missed opportunity will be defined as a clinic visit during which a subject was eligible, yet failed to receive a needed vaccine. Demographic, diagnostic, and visit characteristics as well as missed opportunities for HPV1 and PPV23 vaccine during the 12-month period will be described. Bivariate and multivariable logistic regression analyses will examine the impact of demographic, diagnostic, and visit characteristics as well as seasonality on missed opportunities (dichotomized as 0 *vs.* ≥1) for HPV1 vaccination. These bivariate and multivariable analyses will also be conducted for PPV23 vaccine if permitted by the number of adolescents with/without missed opportunities.

Sample Size: Based upon preliminary data from the NYP registration system and EzVac, we anticipate that 466 adolescents will fulfill study criteria for HPV1 vaccination and 262 adolescents will fulfill study criteria for PPV23 vaccination. Assuming 80% power and a 5% Type I error, we estimate that the available sample size would allow us to detect ≥13% difference in select demographic, diagnostic, and visit characteristics between subjects with and without missed opportunities for HPV1 vaccination.

Objective 2: To assess parental and provider knowledge, attitudes, and experiences related to HPV and PPV23 vaccination of adolescents with chronic medical conditions.

For Objective 2, surveys addressing determinants of HPV and PPV23 vaccination of adolescents with chronic medical conditions will be designed and administered to parents and providers of these adolescents in select NYP-CUMC pediatric clinics.

Subjects and Setting: Parents will be eligible for participation if (1) their child is 11-17 years-old, has ≥1 pre-specified chronic medical condition(s), and receives care at one of four primary pediatric clinics affiliated with NYP-CUMC; and (2) they are fluent in English or Spanish. Chronic medical conditions will be selected and identified as described above (Objective 1). Providers (e.g., physicians, nurses, physician assistants, nurse practitioners) will be eligible for participation if they are working at one of the four primary pediatric clinics affiliated with NYP-CUMC. Given the potential influence of subspecialists on parental vaccination decisions, providers caring for adolescent patients in the 11 subspecialty pediatric clinics (e.g., allergy/immunology, cardiology, endocrinology, gastroenterology, hematology, infectious diseases, nephrology, neurology, oncology, pulmonology, rheumatology) affiliated with NYP-CUMC will also be eligible for participation.

Procedures: Medical records of adolescent patients will be reviewed on the day prior to a clinic visit to identify eligible parents. Recruitment will be performed on the day of the clinic visit in coordination with the adolescent's provider. After obtaining consent/assent, a survey will be administered verbally to the parent by the Project Coordinator in English or Spanish. The adolescent's HPV and PPV23 vaccine data will be obtained from EzVac and linked to their parent's survey data. Parents will receive a $10 gift card for their time.

For providers, mixed-mode survey administration will be used.[36, 37] The survey will be created using Qualtrics software. An email with personalization capabilities (e.g., name, clinic site) and embedded survey link will be designed. Email addresses will be obtained from departmental administrators. An initial email blast will be sent, followed by a reminder email blast to non-respondents two weeks later. Email and survey link opening rates will be tracked. Two weeks after the final email blast, site visits will be performed to request written survey completion by non-respondents. Providers who complete the survey will be entered into a lottery for a $100 gift card.

Survey Instruments: Two survey instruments will be designed for parents and providers based upon existing literature and investigator expertise. The surveys will include both open- and close-ended questions. Key content areas may include, but are not limited to: demographics, knowledge (e.g., HPV and pneumococcal infection risks, HPV and PPV23 vaccine efficacy and safety, ACIP recommendations and contraindications), attitudes (e.g., medical home *vs.* alternative sites for vaccination; provider perceptions of vaccination responsibilities); experiences (e.g., HPV and pneumococcal infections, adverse events, parent-provider communication about vaccine-related issues), practice attributes (e.g., type, hours of operation, vaccine availability), and medical home indicators (e.g., accessibility, family-centeredness). Survey instruments will be pretested by five parents and five providers; they will be revised accordingly to improve clarity and content.

Analysis: Distribution frequencies will be used to describe parental and provider responses. Bivariate and multivariable analyses will be used to identify key parental determinants of HPV1 and PPV23 vaccination. Bivariate and multivariable analyses will also be used to compare survey responses between primary and subspecialty providers.

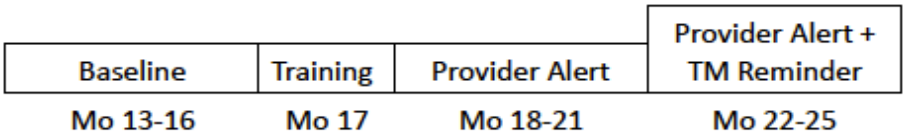
Sample Size: We will conduct purposeful sampling in order to be sufficiently powered to detect differences in survey responses with a reasonable sample size. We aim to enroll at least 50

parents of HPV1-vaccinated and at least 50 parents of HPV1-unvaccinated adolescents with chronic medical conditions who have a clinic visit during the study period. We also aim to enroll at least 30 parents of PPV23-vaccinated (i.e., fewer due to lower baseline coverage levels) and at least 120 parents of PPV23-unvaccinated adolescents with chronic medical conditions who have a clinic visit during the study period. These sample sizes will allow us to detect ≥30% difference in survey responses between groups (stratified by vaccine), using 80% power at a 5% significance level. This effect size has been reported previously in a study examining determinants of influenza vaccination of children with chronic medical conditions.[9] For providers, we anticipate a 68% response rate based upon physician response rates using a mixed mode approach.[36, 37] We anticipate combining all subspecialty providers into one analytic group, although we recognize the importance of comparing vaccine-related knowledge, attitudes, and experiences across subspecialties. Of note, we are currently investigating these in a separate national sample of pediatric subspecialists, which will enable us to assess differences across disciplines and identify national issues, thereby facilitating dissemination of our proposed study findings.

Objective 3: To determine the impact of a provider vaccine alert and additional parental text message reminder on missed opportunities for HPV1 and PPV23 vaccination of adolescents with chronic medical conditions.

For Objective 3, we will design and implement an educational/order vaccine alert in the EHR for providers and additional "priming" pre-appointment text message vaccine reminder for parents of eligible adolescents with chronic medical conditions seen in four primary pediatric clinics. The intervention will be comprised of four sequential time periods: 1) 4-month baseline period with no provider alert or text message reminder; 2) 1-month training period; 3) 4-month provider alert period (*PA only*); and 4) 4-month provider alert plus pre-appointment text message vaccine reminder period (*PA+TM*) (**Figure 1**).

**Figure 1. Study Design**




Study Setting: This intervention will be conducted in four primary pediatric clinics affiliated with NYP-CUMC. These clinics provide >55,000 visits annually to children and adolescents living primarily in a HRSA–designated health professional shortage area in northern Manhattan, where community residents are predominantly Latino and foreign born and many receive federal income assistance.[24] Sites are centrally administered and staffed by one pediatric group practice. Provider alerts and text messaging reminder/recall interventions for routine pediatric and adolescent vaccination have been conducted previously at these sites.[15-18] More than 90% of patients at these sites are eligible to receive vaccine free through the VFC program.

Subjects: This intervention will include all providers (e.g., physicians, physician assistants, nurse practitioners, nurses) at the four participating clinics. It will also include parents who fulfill the following eligibility criteria: (1) their child is 11-17 years-old, has ≥1 pre-specified chronic medical condition(s), requires HPV1 and/or PPV23 vaccine, and receives care at a participating

site during the study period; (2) have an active cell phone number listed in the NYP registration system; and (3) have English or Spanish listed as their primary language in the NYP registration system. Chronic medical conditions will be selected and identified as described above (Objective 1). A study conducted at these sites in 2011 found that 89% of parents had a cell phone with text messaging capabilities.[27]

Procedures: During the baseline period, there will be no provider alert or pre-appointment text message vaccine reminder. During the training period, five training sessions will be held to educate providers and staff about the provider alert system and issues related to HPV and PPV23 vaccination of adolescents with chronic medical conditions. Site visits with individual provider instruction will also be conducted in order to reinforce this teaching. During the two provider alert periods, the educational/order alert will "fire" when a provider opens a note in the EHR for any adolescent aged 11-17 years with a pre-specified chronic medical condition. For those who are not up-to-date with HPV1 and/or PPV23 vaccine, providers will be alerted to either, through the alert, order the needed dose(s) or document reasons for not ordering vaccine. During the provider alert plus text message reminder period, a text message reminder will also be sent in the parent's primary language (English or Spanish) via the customized text message reminder platform to eligible parents two days before their adolescent's scheduled appointment at a participating clinic site.

Provider Alert Design*:* The customized provider alert will be designed based upon our prior provider alert experience, expertise in adolescent medicine, chronically ill populations, and vaccination issues such as vaccine safety, and existing literature. This alert aims to address practice gaps by disseminating accurate HPV and PPV23 vaccine information to providers, prompting them to communicate this information with their patients and families and facilitating vaccination eligibility determination and vaccine ordering/documentation. We will modify our existing provider alert system, which is integrated with the NYP registration system, EzVac immunization registry, and the EHR (Eclipsys Ambulatory Care Coordinator), for the proposed intervention. The alert will be tailored to the individual patient, displaying his/her relevant medical information (i.e., eligible chronic medical conditions, allergies) and HPV1 and PPV23 vaccination status (including date(s) of prior vaccine receipt). The alert will also include talking points addressing common misconceptions (e.g., infection risk, vaccine efficacy, vaccine safety)—printable for parents in English/Spanish—and a summary of ACIP recommendations for HPV and PPV23 vaccination (including target populations, contraindications). A vaccine eligibility algorithm for HPV and PPV23 vaccines will be developed and integrated within the provider alert and EHR ordering system. Based upon our prior qualitative research of provider preferences, the provider alert will not included forced actions.[26] Alert content and implementation will conform to the best practices of health information technology clinical decision support. Implementation will be coordinated with clinical sites so as not to impede workflow; real-time feedback will be exchanged to optimize intervention success.

Text Message Reminder Design: A pre-appointment text message will be designed based upon our previous experience with text messaging, expertise in adolescent medicine, chronically ill populations, and vaccination issues such as vaccine safety, and existing literature. The text message vaccine reminder aims to address practice gaps by (1) "priming" parents to receive vaccination information from their adolescent's provider and (2) serving as an appointment

reminder. We will personalize the message—a feature requested by the majority of parents in our recent study.[27] The message will address general vaccine needs and include specific appointment information (e.g., date/time, clinic site) (**Figure 2**). We will modify our current text message reminder/recall platform, which is integrated with the NYP registration system and EzVac registry, to obtain necessary demographic, diagnostic, clinic visit, and vaccine information for assessing vaccine eligibility and generating the reminder message.

Translation and Pretesting: The provider alert talking points and text message reminder will be targeted to a third-grade reading level and will be forward- and back-translated into Spanish by a certified Spanish translator to ensure linguistic and cultural equivalency. Five parents fulfilling eligibility criteria will be recruited at participating clinic sites to pretest these materials in English and Spanish; content will be adapted accordingly. Parents will receive a $10 gift card for their time. The provider alert will also be pretested by five providers at participating sites in order to optimize content and functionality.

**Figure 2. Text Message Content Example (English Version)** [a]

| |
|---|
| Jose has an appointment at 10am on August 15 at Rangel Clinic (212-754-6754). The doctor will discuss needed vaccines to protect him from harmful infections! |

[a] *Also available in Spanish; message to be modified after pretesting with parents.*

**c. Evaluation Design**

***i. Addressing practice gaps using a provider alert and text message reminder for vaccination***

Data Sources: Demographic, diagnostic, visit, and vaccine data will be obtained from the NYP registration system and EzVac registry (see Objective 1).

Variables: The primary outcome measure of the intervention will be a missed opportunity for vaccination. This will be defined as a clinic visit during which a subject was eligible, yet failed to receive a needed vaccine (HPV1 and/or PPV23). A secondary outcome measure will be the documented reasons for not ordering HPV1 and/or PPV23 vaccine for eligible adolescents with chronic medical conditions. Independent variables will include demographic characteristics (e.g., age, gender, language, insurance), diagnostic (e.g., select/common ICD-9 codes), visit characteristics (e.g., clinic site, number of visits), and seasonality (if found to be associated with missed opportunities in Objective 1 findings).

Analysis: Descriptive analyses will be performed for demographic, diagnostic, and visit characteristics as well as missed opportunities and documented reasons for not ordering vaccine. We will then use bivariate analysis on an intention-to-treat (ITT) basis to compare the proportion of subjects with a missed opportunity for vaccination between (1) those seen at a participating clinic during the provider alert only period (*PA only group*) and those seen during the baseline period (*baseline group*); and (2) those seen at a participating clinic during the provider alert plus text message reminder period (*PA+TM group*) compared to those seen during the provider alert only period (*PA only group*). We will then examine missed opportunities between groups, adjusting for select demographic, diagnostic, and visit characteristics as well as seasonality using multivariable logistic regression. Of note, eligible adolescents will be included only in the first period during which they have a clinic visit; missed opportunities will be assessed only at their first visit within that period. Adolescents whose

parents received a pre-appointment text message reminder, but failed to attend the appointment will be excluded from the primary analyses. In a sub-analysis, we will compare no-show rates among eligible adolescents with an appointment at a participating clinic during the PA+TM *vs.* PA only periods. We will also compare missed opportunities between groups separately for HPV1 and PPV23 vaccines.

Sample Size: Based upon EzVac data, we anticipate that approximately 728 adolescents with a chronic medical condition who require HPV1 and/or PPV23 vaccine will visit a participating clinic during the 12-month study period; thus, we estimate that there will be 243 eligible adolescents with visits during each 4-month study period (i.e., baseline, PA only, PA+TM). Preliminary EzVac data indicate that 57% of eligible adolescents with chronic medical conditions with a visit to a participating clinic during a 12-month period fail to receive HPV1 vaccine and 98% fail to receive PPV23 vaccine. Assuming 80% power and a 5% Type I error, we anticipate that the available intervention sample size will allow us to detect a ≥12% difference in the proportion of subjects with a missed opportunity for HPV1 or PPV23 vaccine between the PA only and baseline groups and a ≥13% difference between the PA+TM and PA only groups.

***ii. Expected change***

We previously showed that provider alerts used during the peak of influenza activity increased influenza vaccination by 5.4%[18] and text message reminders increased adolescent vaccination by 11-18%.[15, 16] We expect that our proposed intervention will lead to similar, if not greater, changes in our study population given the low baseline coverage levels and since it will address the unique educational/communication barriers to vaccination in this high-risk population.

***iii. Target audience engagement***

We will track all provider actions in response to the alert—either vaccine order or documentation of reason for not ordering in order to assess their engagement in the intervention. For parents, we will capture undeliverable text messages and replies to the text message reminder. In addition, after the intervention, we will recruit parents in the PA+TM group whose eligible adolescent had no prior HPV1 or PPV23 receipt and, during the clinic visit of interest, received both vaccines (n=5); received HPV1, but not PPV23 vaccine (n=5); received PPV23, but not HPV1 vaccine (n=5); or received neither vaccine (n=5). They will be requested to participate in a semi-structured interview focusing on vaccine-related issues (e.g., knowledge, perceived risks/benefits, barriers to vaccination) and the intervention itself (e.g., text message content/delivery, provider alert talking points, provider vaccine communication during the visit). Overall satisfaction, concerns, and suggestions will be elicited. Descriptive analyses will be conducted. Participants will receive a $10 gift card for their time.

***iv. Dissemination***

Our findings will be presented at scientific meetings (e.g., Pediatric Academic Societies, Society for Adolescent Health and Medicine) and published in peer-reviewed journals. We will develop a workshop for health care professionals focusing on vaccination of adolescents with chronic medical conditions, including use of innovative health technology to improve vaccination coverage in a variety of clinic settings. We will also disseminate results to public health departments since our approach should be easily adaptable.

***v. Methodological Considerations***

Why focus specifically on HPV1 and PPV23 vaccines?

These vaccines were selected as prototypes for both routine and specially-indicated vaccines for adolescents with chronic medical conditions. We anticipate that our findings may be highly generalizeable and the intervention easily adapted to other needed vaccines (e.g., influenza, meningococcal). HPV vaccination of these adolescents is crucial since evidence suggests they are just as likely as healthy adolescents to engage in high-risk sexual behavior,[38-40] yet may be at increased risk of adverse sequellae due to their underlying condition.[3-6] Moreover, many fail to receive appropriate sexual health screening and counseling from their providers, perhaps due to misconceptions of risk.[39, 41] In addition, modeling studies suggest that HPV vaccination must be broadly implemented in order to have a large public health impact.[42] Thus, strategies to increase awareness and improve HPV vaccination coverage in this growing population of vulnerable adolescents are needed. Of note, given the grant duration, we will focus specifically on HPV1; however, this approach could be used for HPV2 and HPV3 vaccines as well. Emphasis on PPV23 vaccination is particularly important given the markedly low coverage levels and life-threatening consequences of pneumococcal infection in these high-risk patients.[6]

Why is the intervention based in the primary care clinics?

Although adolescents with chronic medical conditions are more likely than others to have and access a medical home,[43] many still fail to receive necessary preventive health services,[8, 9, 19, 41] as evidenced by the low HPV and PPV23 vaccination coverage of those seen in our primary pediatric clinics. In addition, adolescents seen in our primary pediatric clinics are predominantly minority and publicly insured, which place them at greater risk of adverse outcomes related to their underlying medical conditions.[2] Therefore, an intervention focusing on these adolescents is an important first step towards improving vaccine outcomes in this population of high-risk adolescents. Furthermore, provider alert and text message reminder interventions have been conducted successfully in our primary pediatric clinics, making these sites an ideal setting for implementing this project.[15-18] Since some adolescents with chronic medical conditions identify their subspecialist as their main physician[41, 44, 45] or have no usual source of primary care,[46] future interventions may adapt the proposed health technology infrastructure to target such adolescents in the subspecialty care setting, likely with additional aims of facilitating establishment of and care coordination with a primary medical home.

What if missed opportunities for HPV1 and PPV23 vaccine differ by clinic site or time of year?

The clinics have similar patient populations and are staffed by one pediatric group practice. We have also selected 4-month periods that include both high and low patient volume periods. Thus, we don't anticipate clinic or temporal variability in missed opportunities. However, if Objective 1 analyses reveal such differences, we will consider instead a randomized cluster crossover study design such that there will be on and off periods during each 4-month interval (i.e., PA only, PA+TM) and their timing will differ by site.

Will we be able to assess the impact of a text message reminder on vaccination outcomes?

We are most interested in assessing whether the text message reminder augments the impact of the provider alert on missed opportunities for vaccination. While our primary analysis includes an ITT comparison of missed opportunities in PA+TM *vs.* PA only groups, we may consider additional strategies to examine the potential impact of the text message reminder.

For example, we could conduct a sub-analysis using a per-protocol approach, i.e., those who received no text message reminder (i.e., walk-in visit, no cell phone, undeliverable message) would be analyzed in the PA only group. We may also compare missed opportunities within the PA+TM group based on text message receipt, adjusting for potential confounders. Given the study design, we will not be able to assess the independent effect of the reminder message.

May factors other than those targeted through the intervention impact vaccination outcomes?
HPV and PPV23 vaccination could be impacted by multiple factors. We will be able to assess many patient (e.g., demographic, diagnostic characteristics) and clinic (e.g., site) level variables. However, certain provider level characteristics may be unavailable.

***vi. Innovation***

This proposed project is novel in its inclusion of a large population of highly vulnerable adolescents with clear vaccination needs who may face unique and complex challenges to vaccine uptake. In addition, drawing on the particular strengths of faculty and infrastructure at Columbia University and NYP, this project is innovative in its use of customized provider alert and text message reminder/recall systems, integrated with a sophisticated immunization registry, to target both providers and parents caring for these adolescents. Ultimately, this study will provide new and important data about adolescents with chronic medical conditions and strategies to improve their vaccination outcomes. The proposed intervention is a promising approach for rapidly and reliably identifying and reaching a large number of patients accessing multiple providers across clinical settings. Our provider alert has been developed within one of the most common commercially available EHR systems, and text message reminders are readily available with many commercial vendors. Thus, if this intervention is found to be successful in improving vaccination outcomes of adolescents with chronic medical conditions, this model for vaccine delivery could be expanded to other important adolescent vaccines, additional high-risk groups, and multiple venues including primary pediatric practices, subspecialty clinics, or more centralized locations such as hospitals or local health departments.

**C3. DETAILED WORKPLAN**

The research team will meet on a weekly basis to discuss all aspects of the project, including design, implementation, and evaluation. They will problem-solve any issues that arise and make any modifications necessary. Please see Deliverables Schedule below for key activities and responsible personnel during each study period.

**Months 1-3 (July-September 2013)**

During this period, we will primarily focus on missed opportunity data collection, cleaning, and analysis (Objective 1). We will also begin preparations for our survey (Objective 2), submitting our IRB protocol and developing and pretesting survey instruments.

**Months 4-9 (October 2013-March 2014)**

During this period, we will primarily focus on Objective 2. We will screen, recruit, and administer parental surveys, which will be linked with adolescent vaccine data obtained through EzVac. We will also conduct our online provider survey, performing site visits to recruit and administer paper surveys to non-respondents as needed. Survey data will be then be entered into a secure database and cleaned. During this period, we will also complete Objective

1, aiming to submit a scientific meeting abstract and manuscript describing missed opportunities in our study population.

**Months 10-12 (April-June 2014)**
During this period, we will begin preparations for our intervention (Objective 3). We will submit an IRB protocol. Our IT team (Camargo/Stockwell/Vawdrey) will adapt the existing provider alert and text message reminder systems for this study. In addition, we will complete Objective 2, performing data analyses and preparing a scientific meeting abstract and manuscript describing our survey findings.

**Months 13-16 (July-October 2014)**
During this period, our IT team will further refine and pretest the provider alert and text message reminder systems and their integration with EzVac. In addition, we will develop and pretest the content of the provider alert and text message reminder. Importantly, this 4-month period will also comprise the "baseline period" (no provider alert or text message reminder) of our intervention.

**Month 17 (November 2014)**
During this period, we will hold five training/educational sessions for staff and providers at the participating clinics. Site-based individual provider training will also be conducted. In addition, we will collect and clean data for eligible adolescents with visits during the baseline period.

**Month 18-21 (December 2014-March 2015)**
This 4-month period will comprise the "provider alert only" period of the intervention during which the provider alert will be activated at participating clinics. We will offer site-based provider alert support during the first week of activation and as needed over the study period. Any technical support required will be made available, and issues will be resolved accordingly.

**Month 22-25 (April-July 2015)**
This 4-month period will comprise the "provider alert plus text message reminder" period, i.e., the final intervention period. During this time, the provider alert will remain active. We will also conduct daily automated queries of scheduled appointments, and text message reminders for appointments scheduled in two days time will be generated and sent to eligible parents. We will monitor log files of sent messages, received replies, and undeliverable messages on the text-messaging platform. In addition, we will collect and clean data for eligible adolescents with visits during the provider alert only period and develop the post-intervention interview guide.

**Month 26-30 (August-December 2015)**
During this period, we will collect and clean data for eligible adolescents with visits during the provider alert plus text message reminder period. We will conduct the post-intervention interviews. We will then perform intervention analyses and submit our findings for presentation at a scientific meeting and publication in a peer-reviewed journal. We will complete the grant period by planning dissemination activities and preparing the final grant report.

**C4. DELIVERABLES SCHEDULE**

| Months | Activities | Personnel | Measures | Deliverables |
|---|---|---|---|---|
| **1-3** (Jul-Sep 2013) | • Missed opportunity data collection (Obj. 1)<br>• Missed opportunity data cleaning (Obj. 1)<br>• Missed opportunity data analysis (Obj. 1)<br>• IRB proposal preparation (Obj. 2)<br>• Survey instrument design (Obj. 2)<br>• Survey instrument/email pretesting (Obj. 2) | Hofstetter<br>Rosenthal<br>Stockwell<br>LaRussa<br>Camargo<br>Williams<br>Ramakrishnan | • % missed opportunities<br>• Missed opportunity predictors<br>• Surveys finalized | • Submitted IRB (Obj. 2) |
| **4-9** (Oct 2013-Mar 2014) | • Abstract preparation (Obj. 1)<br>• Manuscript preparation (Obj. 1)<br>• Parental, provider survey administration (Obj. 2)<br>• Parental survey linkage to vaccine data (Obj. 2)<br>• Survey data entry/cleaning (Obj. 2) | Hofstetter<br>Rosenthal<br>Stockwell<br>Camargo<br>Williams | • Surveys completed | • Submitted Abstract (Obj. 1)<br>• Submitted Manuscript (Obj. 1) |
| **10-12** (Apr-Jun 2014) | • Survey data analysis (Obj. 2)<br>• Abstract preparation (Obj. 2)<br>• Manuscript preparation (Obj. 2)<br>• IRB proposal preparation (Obj. 3)<br>• Provider alert system development (Obj. 3)<br>• Text message reminder system development (Obj. 3) | Hofstetter<br>Rosenthal<br>Stockwell<br>Vawdrey<br>Camargo<br>Ramakrishnan | • Parental, provider factors related to vaccination<br>• Provider alert/TM reminder systems developed | • Submitted Abstract (Obj. 2)<br>• Submitted Manuscript (Obj. 2)<br>• Submitted IRB (Obj. 3) |
| **13-16** (Jul-Oct 2014) | • Intervention baseline period (Obj. 3)<br>• Provider/TM reminder systems modifications (Obj. 3)<br>• Provider alert design (Obj. 3)<br>• Text message reminder design (Obj. 3)<br>• Provider alert/text message pretesting (Obj. 3) | Hofstetter<br>Rosenthal<br>Stockwell<br>Vawdrey<br>LaRussa<br>Camargo<br>Williams | • Provider alert finalized<br>• TM reminder finalized<br>• Pretested provider alert fully functional<br>• Pretested TM reminder sent/received correctly | |
| **17** (Nov 2014) | • Provider and staff training sessions (Obj. 3)<br>• Site visits for individual provider training (Obj. 3)<br>• Data collection for baseline period (Obj. 3) | Hofstetter<br>Williams<br>Camargo | • Training/education completed<br>• # eligible subjects (baseline)<br>• % HPV1 and PPV23 missed opportunities (baseline) | |

| | | | | |
|---|---|---|---|---|
| **18-21** (Dec 2014-Mar 2015) | • Provider alert only period (Obj. 3)<br>• Provider alert activation at study sites (Obj. 3) | Hofstetter<br>Rosenthal<br>Stockwell<br>Vawdrey<br>Camargo<br>Williams | | |
| **22-25** (Apr-July 2015) | • Provider alert plus TM reminder period (Obj. 3)<br>• Provider alert continuation at study sites (Obj. 3)<br>• Send pre-appointment TM reminders (Obj. 3)<br>• Data collection for provider alert only period (Obj. 3)<br>• Design post-intervention interview guide (Obj. 3) | Hofstetter<br>Rosenthal<br>Stockwell<br>Vawdrey<br>Camargo<br>Williams | • # eligible subjects (PA only)<br>• % HPV1 and PPV23 missed opportunities (PA only)<br>• # alerts "fired"<br>• Alert actions described<br>• Interview guide finalized | • Completed Intervention |
| **26-30** (Aug-Dec 2015) | • Data collection for PA+TM reminder period (Obj. 3)<br>• Conduct post-intervention interviews (Obj. 3)<br>• Intervention data analysis (Obj. 3)<br>• Abstract preparation (Obj. 3)<br>• Manuscript preparation (Obj. 3) | Hofstetter<br>Rosenthal<br>Stockwell<br>Vawdrey<br>LaRussa<br>Camargo<br>Williams<br>Ramakrishnan | • # eligible subjects, PA+TM<br>• % HPV1 and PPV23 missed opportunities, PA+TM period<br>• # alerts "fired"<br>• Alert actions described<br>• # TMs undeliverable<br>• # TM replies<br>• Interviews completed<br>• Interview responses described<br>• Missed opportunities compared between groups | • Submitted Abstract (Obj. 3)<br>• Submitted Manuscript (Obj. 3) |
| **End of Each Quarter** | • Quarterly progress report submission | Hofstetter<br>Rosenthal | • Objectives reviewed | • Submitted Quarterly Report |
| **End of Grant Period** | • Plan dissemination activities<br>• Submit final report | Hofstetter<br>Rosenthal | • Objectives achieved<br>• Intervention impact assessed<br>• Dissemination strategies developed | • Submitted Final Report |

**REFERENCES:**


1. Perrin JM, Bloom SR, Gortmaker SL. The increase of childhood chronic conditions in the United States. *JAMA*. 2007;297(24):2755-2759.
2. Berry JG, Bloom S, Foley S, Palfrey JS. Health inequity in children and youth with chronic health conditions. *Pediatrics*. 2010;126 Suppl 3:S111-119.
3. Klosky JL, Gamble HL, Spunt SL, Randolph ME, Green DM, Hudson MM. Human papillomavirus vaccination in survivors of childhood cancer. *Cancer*. 2009;115(24):5627-5636.
4. Klumb EM, Pinto AC, Jesus GR, Araujo M, Jr., Jascone L, Gayer CR, et al. Are women with lupus at higher risk of HPV infection? *Lupus*. 2010;19(13):1485-1491.
5. de Araujo MR, Rubira-Bullen IR, Santos CF, Dionisio TJ, Bonfim CM, De Marco L, et al. High prevalence of oral human papillomavirus infection in Fanconi's anemia patients. *Oral Dis*. 2011;17(6):572-576.
6. Centers for Disease Control and Prevention, editor. Epidemiology and Prevention of Vaccine-Preventable Diseases. 12th ed. Washington, D.C.: Public Health Foundation; 2012.
7. Recommended immunization schedules for persons aged 0 through 18 Years - United States, 2012. *MMWR Morb Mortal Wkly Rep*. 2012;61(5):1-4.
8. Nakamura MM, Lee GM. Influenza vaccination in adolescents with high-risk conditions. *Pediatrics*. 2008;122(5):920-928.
9. Lin CJ, Nowalk MP, Zimmerman RK, Ko FS, Zoffel L, Hoberman A, et al. Beliefs and attitudes about influenza immunization among parents of children with chronic medical conditions over a two-year period. *J Urban Health*. 2006;83(5):874-883.
10. Feudtner C, Hays RM, Haynes G, Geyer JR, Neff JM, Koepsell TD. Deaths attributed to pediatric complex chronic conditions: national trends and implications for supportive care services. *Pediatrics*. 2001;107(6):E99.
11. Daley MF, Barrow J, Pearson K, Crane LA, Gao D, Stevenson JM, et al. Identification and recall of children with chronic medical conditions for influenza vaccination. *Pediatrics*. 2004;113(1 Pt 1):e26-33.
12. U.S. Department of Health and Human Services. Healthy People 2020. Objective IID-11: Increase routine vaccination coverage levels for adolescents. http://www.healthypeople.gov. Published 2010.
13. Hofstetter AM, Natarajan K, Martinez RA, Rabinowitz D, Vawdrey DK, Stockwell MS. Influenza vaccination coverage and timeliness among children requiring two doses, 2004-2009. *Prev Med*. 2012;56(3-4):165-170.
14. Hofstetter AM, Natarajan K, Rabinowitz D, Andres-Martinez R, Vawdrey D, Arpadi S, et al. Timeliness of pediatric influenza vaccination compared to seasonal influenza activity in an urban underserved community, 2004-2008. *Am J Public Health*. 2013.
15. Kharbanda EO, Stockwell MS, Fox HW, Andres R, Lara M, Rickert VI. Text message reminders to promote human papillomavirus vaccination. *Vaccine*. 2011;29(14):2537-2541.

16. Stockwell MS, Kharbanda EO, Andres R, Lara M, Vawdrey D, Natarajan K, et al. Text4Health: Text Message Reminder-Recalls to Improve Pediatric and Adolescent Immunizations. *Am J Public Health*. 2012;102(2):e15-21.
17. Stockwell MS, Kharbanda EO, Martinez RA, Vargas CY, Vawdrey DK, Camargo S. Effect of a text messaging intervention on influenza vaccination in an urban, low-income pediatric and adolescent population: a randomized controlled trial. *JAMA*. 2012;307(16):1702-1708.
18. Stockwell MS, Catalozzi M, Camargo S, Findley S, Kukafka R, Ramakrishnan S, et al. FluAlert: using tailored, influenza vaccine alerts in the electronic health record to decrease missed opportunities for vaccination in a low-income pediatric population. In: Pediatric Academic Societies Annual Meeting; 2013; Washington, D.C.; 2013.
19. Daley MF, Beaty BL, Barrow J, Pearson K, Crane LA, Berman S, et al. Missed opportunities for influenza vaccination in children with chronic medical conditions. *Arch Pediatr Adolesc Med*. 2005;159(10):986-991.
20. Seale H, Trung L, Mackie FE, Kennedy SE, Boros C, Marshall H, et al. A qualitative study investigating knowledge and attitudes regarding human papillomavirus (HPV) and the HPV vaccine among parents of immunosuppressed children. *Vaccine*. 2012.
21. Szilagyi PG, Rand CM, McLaurin J, Tan L, Britto M, Francis A, et al. Delivering adolescent vaccinations in the medical home: a new era? *Pediatrics*. 2008;121 Suppl 1:S15-24.
22. Boyce T, Holmes A. Addressing health inequalities in the delivery of the human papillomavirus vaccination programme: examining the role of the school nurse. *PLoS One*. 2012;7(9):e43416.
23. Daley MF, Crane LA, Markowitz LE, Black SR, Beaty BL, Barrow J, et al. Human papillomavirus vaccination practices: a survey of US physicians 18 months after licensure. *Pediatrics*. 2010;126(3):425-433.
24. Vadaparampil ST, Kahn JA, Salmon D, Lee JH, Quinn GP, Roetzheim R, et al. Missed clinical opportunities: provider recommendations for HPV vaccination for 11-12 year old girls are limited. *Vaccine*. 2011;29(47):8634-8641.
25. Britto MT. Improving outcomes for youth with chronic conditions: it's time for increased collaboration. *J Adolesc Health*. 2006;39(1):1-2.
26. Birmingham E, Catallozzi M, Findley SE, Vawdrey DK, Kukafka R, Stockwell MS. FluAlert: a qualitative evaluation of providers' desired characteristics and concerns regarding computerized influenza vaccination alerts. *Prev Med*. 2011;52(3-4):274-277.
27. Hofstetter AM, Vargas CY, Kennedy A, Kitayama K, Stockwell MS. Parental and provider preferences and concerns regarding text message reminder/recall for early childhood vaccinations. *Prev Med*. 2013.
28. Fiks AG, Hunter KF, Localio AR, Grundmeier RW, Bryant-Stephens T, Luberti AA, et al. Impact of electronic health record-based alerts on influenza vaccination for children with asthma. *Pediatrics*. 2009;124(1):159-169.
29. Verani JR, Irigoyen M, Chen S, Chimkin F. Influenza vaccine coverage and missed opportunities among inner-city children aged 6 to 23 months: 2000-2005. *Pediatrics*. 2007;119(3):e580-586.
30. Metroka AE, Hansen MA, Papadouka V, Zucker JR. Using an immunization information system to improve accountability for vaccines distributed through the Vaccines for

Children program in New York City, 2005-2008. *J Public Health Manag Pract*. 2009;15(5):E13-21.
31. Hofstetter AM, Natarajan K, Al-Husayni N, Stockwell M, Rosenthal S, Ompad D, et al. HPV vaccination: are we initiating too late? In: Pediatric Academic Societies Annual Meeting; 2013; Washington, D.C.; 2013.
32. Stockwell MS, Brown J, Chen S, Vaughan RD, Irigoyen M. Is underimmunization associated with child maltreatment? *Ambul Pediatr*. 2008;8(3):210-213.
33. Stockwell MS, Martinez RA, Hofstetter A, Natarajan K, Vawdrey DK. Timeliness of 2009 H1N1 vaccine coverage in a low-income pediatric and adolescent population. *Vaccine*. 2011.
34. Uwemedimo OT, Findley SE, Andres R, Irigoyen M, Stockwell MS. Determinants of Influenza Vaccination Among Young Children in an Inner-City Community. *J Community Health*. 2011.
35. Kharbanda EO, Vargas CY, Castano PM, Lara M, Andres R, Stockwell MS. Exploring pregnant women's views on influenza vaccination and educational text messages. *Prev Med*. 2010;52(1):75-77.
36. Ahlers-Schmidt CR, Chesser A, Hara T, Jones J, Williams KS, Wittler R. Assessing physician response rate using a mixed-mode survey. *Kansas Journal of Medicine*. 2010;3(5).
37. Klabunde CN, Willis GB, McLeod CC, Dillman DA, Johnson TP, Greene SM, et al. Improving the Quality of Surveys of Physicians and Medical Groups: A Research Agenda. *Eval Health Prof*. 2012;Epub Ahead of Print.
38. Britto MT, Garrett JM, Dugliss MA, Daeschner CW, Jr., Johnson CA, Leigh MW, et al. Risky behavior in teens with cystic fibrosis or sickle cell disease: a multicenter study. *Pediatrics*. 1998;101(2):250-256.
39. Britto MT, Rosenthal SL, Taylor J, Passo MH. Improving rheumatologists' screening for alcohol use and sexual activity. *Arch Pediatr Adolesc Med*. 2000;154(5):478-483.
40. Suris JC, Michaud PA, Akre C, Sawyer SM. Health risk behaviors in adolescents with chronic conditions. *Pediatrics*. 2008;122(5):e1113-1118.
41. Britto MT, Garrett JM, Dugliss MA, Johnson CA, Majure JM, Leigh MW. Preventive services received by adolescents with cystic fibrosis and sickle cell disease. *Arch Pediatr Adolesc Med*. 1999;153(1):27-32.
42. Garnett GP, Kim JJ, French K, Goldie SJ. Chapter 21: Modelling the impact of HPV vaccines on cervical cancer and screening programmes. *Vaccine*. 2006;24 Suppl 3:S3/178-186.
43. Mulvihill BA, Altarac M, Swaminathan S, Kirby RS, Kulczycki A, Ellis DE. Does access to a medical home differ according to child and family characteristics, including special-health-care-needs status, among children in Alabama? *Pediatrics*. 2007;119 Suppl 1:S107-113.
44. Carroll G, Massarelli E, Opzoomer A, Pekeles G, Pedneault M, Frappier JY, et al. Adolescents with chronic disease. Are they receiving comprehensive health care? *J Adolesc Health Care*. 1983;4(4):261-265.
45. Palfrey JS, Levy JC, Gilbert KL. Use of primary care facilities by patients attending specialty clinics. *Pediatrics*. 1980;65(3):567-572.

46. Bethell CD, Kogan MD, Strickland BB, Schor EL, Robertson J, Newacheck PW. A national and state profile of leading health problems and health care quality for US children: key insurance disparities and across-state variations. *Acad Pediatr*. 2011;11(3 Suppl):S22-33.