PROTOCOL

Strengthening Physician Communication About Adolescent Vaccines

COMIRB # 13-2785,

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A. Background:

Adolescent-targeted vaccines, particularly the human papillomavirus (HPV) vaccine, are under-utilized in the U.S. Healthy People 2020 states a goal coverage level of 80% for all vaccines routinely recommended for adolescents. The “adolescent platform” of vaccines includes the tetanus-diphtheria-pertussis (Tdap), meningococcal (MCV4), HPV and influenza (Flu) vaccines. Although coverage rates for all these vaccines have been rising steadily, only Tdap and MCV coverage levels are within reach of the national goals at 78.2% and 70.5%, respectively, as of 2011. Of great concern is the fact that HPV vaccination levels are increasing at a substantially slower pace than the other adolescent-targeted vaccines.

As of 2011, more than 6 years after its licensure for females, and 2 years after licensure for males, only 34.8% and 1.3% of female and male adolescents, respectively, had completed the 3-dose HPV vaccination series. HPV vaccines are preferentially recommended for 11-12 year olds so as to provide the vaccine well before exposure to HPV infection, which typically occurs shortly after sexual debut. Unfortunately in the U.S., 11-12 year olds have the lowest levels of HPV vaccine utilization compared to all other adolescent age categories. Thus, there is an urgent need to find mechanisms to increase levels of HPV vaccination among adolescents, particularly those 11-12 years old. In addition, given the continued, and in some cases increasing, outbreaks of other vaccine preventable diseases among adolescents, there is also a need to strengthen utilization of the “adolescent platform” more broadly.

Lack of a strong provider recommendation appears to be a significant driver of low HPV vaccination levels among adolescents. Prior research demonstrates that 70-90% of adolescents visit their primary care provider at least once a year, thereby providing ample opportunity for vaccines to be administered. Despite this, HPV vaccination coverage lags significantly behind that of Tdap and MCV vaccines. Many reasons underlie this disparity in vaccine utilization, including parental concerns about the safety, necessity and “moral” implications of the HPV vaccine specifically, the fact that 3 doses are needed to complete the HPV series, and the high cost of HPV vaccines compared to other vaccines. What has become clear, however, is that a strong recommendation for the HPV vaccine from the medical provider is one of the most consistently influential factors associated with adolescent HPV vaccine use. Strong provider recommendation has been shown in some studies to be associated with a nearly 20 fold increased odds of receiving the HPV vaccine. Despite this, a national study of parents demonstrated that among those whose adolescent had not yet received any HPV vaccine doses, nearly 15% reported that the main reason for this was because a provider had not recommend it. Given that provider recommendation is recognized as a significant predictor of HPV vaccine receipt across geographic regions and diverse patient populations, increasing the frequency that providers strongly recommend the HPV vaccine is a key target for our proposed intervention.

HPV vaccines are recommended for all adolescent boys and girls, and are considered the standard of care. Despite this, provider recommendation of this vaccine is suboptimal, as has been demonstrated by many previous studies. Provider-levels barriers to implementing strong recommendations for adolescent HPV vaccination are multifactorial and include the limited time available during clinical visits, provider attitudes and beliefs about the HPV vaccine and their patient population’s risk for HPV infection, and low provider self-efficacy for being able to convince HPV-vaccine hesitant parents to accept the vaccine for their adolescent. We address these diverse barriers by proposing to test in a randomized controlled trial where randomization occurs at the practice level, the effectiveness of a multicomponent toolkit that providers can implement in their offices to improve HPV vaccination rates among adolescents. Thus, providers and their offices are the main target for our intervention trial and as such, the research component of this application focuses primarily on comparing the activities of providers in offices who do or do not receive the toolkit.
An important downstream outcome that we will measure in this project is HPV vaccination rates among adolescent patients attending both the control and intervention practices. Thus adolescents will also be a research subject since it is their vaccination data that will be reviewed to assess the overall impact of the provider intervention. However, implementation of the toolkit at the practice level will be variable as providers are not required to adhere to a specific protocol for using the toolkit. Rather, practices will be able to customize both the materials and their implementation to suit their preferences. Given this expected variability among practices in utilization of the toolkit, combined with the fact that adolescent HPV vaccination was recently targeted as an important measure of quality of care, the implementation of the toolkit within the practices is more in keeping with a quality improvement project. Figure 1 below demonstrates the various study activities and how they align more closely with research vs. quality improvement (QI). Further details on these activities are provided in the Methods section below.

**Figure 1.** How various study activities are more in line with research vs. QI.

- Practice Data
- Vaccination Rates
- Current Immunization Activities

Study Team Randomizes Practices Using Above Data

**Intervention**
- Practice 1
- Practice 2
- Practice etc.
- Practice 11
- Practice 12
- Practice etc.

**Control**
- Usual Care

**QI**
- Develop Tools*
- Implements Tools*
- Develop Tools*
- Implements Tools*
- Develop Tools*
- Implements Tools*

**Final Vaccination Assessment**
- Final Assessment of Communication Activities
- Feedback to Practices at a Practice-Specific Level

*Tools and implementation of tools is specific to each practice. Strategies and tools developed as collaboration between research team and each practice.

**B. Objective and Aims:**

Our objective is to understand the current practices of primary care physicians regarding how they communicate with parents about adolescent HPV vaccines and to evaluate the impact of a multicomponent intervention for practices on these communication activities, and their downstream impact on adolescent HPV vaccination rates. The Specific Aims of the project are:

1. **To assess baseline adolescent vaccination levels and HPV vaccine communication activities among the study practices.** Baseline vaccination levels and communication activities will be used to...
ensure balance in these outcomes during the randomization of practices into control and intervention arms for Aim 3.

2. To develop in conjunction with provider feedback an adolescent vaccine toolkit and overall study implementation procedures. We will use extensive provider feedback to develop an HPV vaccine toolkit that will be tailored to each clinical setting to reflect the HPV discussion points that are most relevant to the providers and the patients they serve. Providers will also provide feedback into “how” they want the various toolkit components to be implemented. This “toolkit” includes 1) an informational website about HPV vaccines that will be provided to parents before their adolescent well child check-up, 2) the HPV Fact Sheet, 3) a provider training session on how to use motivational interviewing techniques to improve communication with HPV vaccine-hesitant parents, and 4) a decision aid for parents that are still unsure about getting their adolescent vaccinated against HPV.

3. To implement and assess the impact of the toolkit intervention on adolescent vaccine utilization, and provider communication. We will use a cluster-randomized trial design, with randomization occurring at the practice level, to assess the impact of our intervention on adolescent HPV vaccine utilization. We will also assess if the intervention creates any “spill over” effects on the utilization of Tdap and MCV vaccines, and whether it impacts clinical practice and parent perceptions about provider adolescent vaccine communication.

C. Study Activities Overview:

Table 1 below describes an overview study activities, which are conceptually divided into six phases:

<table>
<thead>
<tr>
<th>Phase</th>
<th>General Methods</th>
<th>Participants</th>
<th>Main Data Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Assessment of Current Vaccination Levels</td>
<td>Retrospective analysis of administrative, EMR, and immunization registry vaccination data</td>
<td>All adolescent patients age 9-17 that have visited participating practices in the prior 2 years</td>
<td>Baseline assessment of HPV, MCV4, Flu and Tdap levels among adolescents in the participating practices. Secondary analyses will examine clinical and patient factors associated with vaccine receipt.</td>
</tr>
<tr>
<td>II: Assessment of Current Vaccine Communication Activities</td>
<td>Key informant interviews (KII)</td>
<td>60 KII’s of providers from the clinical sites for the study</td>
<td>In-depth understanding of parent and provider perspectives on the vaccine communication strategies currently being used in the practices.</td>
</tr>
<tr>
<td></td>
<td>Parent survey</td>
<td>40 KII’s from parents of adolescents attending the clinical sites.</td>
<td>Formative information on how to best implement the planned intervention activities.</td>
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<tr>
<td></td>
<td></td>
<td>1000 mail/email surveys to parents of adolescents</td>
<td>Confirm assessments from formative work among a larger sample of parents from the practices.</td>
</tr>
<tr>
<td>III: Intervention Development</td>
<td>Development of materials by study team with feedback from participating providers</td>
<td>Study team</td>
<td>Finalized intervention materials and implementation plan that are individualized to each practice’s preferences.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Providers from intervention sites</td>
<td></td>
</tr>
<tr>
<td>IV: Intervention</td>
<td>Randomized Controlled Trial</td>
<td>Providers at all participating clinical sites and the patients they choose to use intervention with</td>
<td>Demographics of those who access VaxFacts-HPV website (anonymous and no PHI collected) VaxFacts-HPV paradata (anonymous and no PHI collected) General report of number of parents given HPV Fact Sheets General report of number of parents given HPV Decision Aid</td>
</tr>
<tr>
<td></td>
<td>Randomization at clinic level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V: Final Assessment of Vaccination Levels</td>
<td>Retrospective analysis of administrative, EMR, and immunization registry vaccination data that spans the period from study beginning to end.</td>
<td>All adolescent patients age 9-17 that have visited participating practices during the study years.</td>
<td>Final assessment of HPV, MCV4, Flu and Tdap levels among adolescents in the participating practices. Primary assessment will compare HPV vaccination levels between control and intervention practices.</td>
</tr>
<tr>
<td>VI: Assessment</td>
<td>Key informant interviews</td>
<td>60 KII’s of providers from the assessment</td>
<td>In-depth understanding of parent and provider perspectives on the vaccine communication strategies currently being used in the practices.</td>
</tr>
</tbody>
</table>
of Toolkit Utilization and Impact | (KIs) | clinical sites for the study | perspectives on how vaccine communication strategies have evolved over time and how they may be affected by implementation of the toolkit. | Confirm assessments from qualitative work among a larger sample of parents from the practices.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Practice Type</th>
<th>Practice Name*</th>
<th>Estimated # of Adolescents 9-17 years*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric</td>
<td>Private</td>
<td>The Youth Clinic</td>
<td>10,707</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pediatrics 5280</td>
<td>5,500</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cherry Creek Pediatrics</td>
<td>15,300</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pediatrics West</td>
<td>4,400</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Focus on Kids</td>
<td>2,778</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Greenwood Pediatrics</td>
<td>6,000</td>
</tr>
<tr>
<td>Family Medicine</td>
<td>Private</td>
<td>Hampden Family Medicine</td>
<td>450</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The Family Clinic of Ft. Collins</td>
<td>500</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Medicine Practice 3</td>
<td>600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Medicine Practice 4</td>
<td>600</td>
</tr>
<tr>
<td>Pediatric</td>
<td>Public</td>
<td>Denver Health - Eastside</td>
<td>3,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denver Health - Westside</td>
<td>3,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denver Health - Webb</td>
<td>3,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMYC - Thornton</td>
<td>2,018</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMYC - Denver</td>
<td>1,187</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMYC - Aurora</td>
<td>1,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Child Health Clinic TCH</td>
<td>9,116</td>
</tr>
<tr>
<td>Family Medicine</td>
<td>Public</td>
<td>Denver Health - La Casa</td>
<td>1,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denver Health - Lowry</td>
<td>1,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denver Health - Montbello</td>
<td>1,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denver Health - Park Hill</td>
<td>1,100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TOTAL</td>
<td>73,856</td>
</tr>
</tbody>
</table>

D. Subject Population

There are three distinct study populations in our project.

Providers: The main focus of our intervention is on providers. We will work with ~20 primary care (pediatrics and family medicine) offices in the Denver metro area (both UCD-affiliated and non-affiliated sites). Medical providers in the intervention offices will participate in Key informant interviews (baseline and at the end of the study period), motivational interviewing training, and development of final toolkit materials and office implementation procedures. Information gathered during the interviews will help to shape the toolkit materials. Because the intervention occurs at a clinic level, there is no patient recruitment activities in this project. Providers are a subject of the research, but not engage in recruiting or consenting patients for the project. Table 2 below shows the study sites that have preliminarily agreed to participate in the project.

Currently, these practices are being contacted and meetings will be arranged with the PI, representatives from the study team, and representatives from the practices, including any relevant decision makers such as office managers and managing partners. At these meetings, the timeline of the study will be reviewed and questions will be answered. Once the practices confirm participation, Business Associates Agreements (BAA) will be drafted and signed as appropriate. If, during the recruitment phase, one of the practices initially recruited elects not to participate, we will attempt to recruit another, similar practice in the greater Denver metro. However, our study is designed such that even if 20% of the practices drop out during the study period, we will still have an adequate sample size to detect meaningful differences between experimental groups in our primary outcome measures.

Parents: We will perform a baseline and follow up assessment of the clinic’s vaccination communication activities from the parent perspective to determine if there are differences between provider-reported and
parent-reported vaccination communication activities. These assessments will occur among a subgroup of
parents whose adolescents receive care in the participating clinics (control and intervention). These
assessments will include phone interviews with 2-3 parents per clinical site, and a mailed survey of ~50
parents/clinical site.

Adolescents: Adolescents will only be indirectly involved in the research as clinic-level adolescent
vaccination rates will be calculated at the beginning and end of the study period for all adolescents (age 9-
17) who are active patients (seen in the last 2 years) in the participating practices. There are no toolkit
activities that target adolescents specifically. The main focus of the toolkit is on modifying the
parent/provider interaction. Clinic-specific vaccination rates will be provided back to the clinical staff at the
intervention offices at the beginning and end of the project period. Clinic-specific rates will be provided back
to the control offices at the end of the project period.

Table 3 below provides an overview of the consent and authorization procedures for the various study
activities that are proposed.
<table>
<thead>
<tr>
<th>Phase</th>
<th>Study Element</th>
<th>Population</th>
<th>Subject Consent</th>
<th>Assent</th>
<th>Rationale for Consent/Assent</th>
<th>Authorizaton for accessing PHI</th>
<th>PHI Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>I &amp; V</td>
<td>Assessment of Vaccination Status</td>
<td>Patients 9-17 seen in previous 2 years (baseline) or during study period (follow up)</td>
<td>Full Waiver</td>
<td>Full Waiver</td>
<td>QI project, &gt;20,000 records to be reviewed, baseline and f/u vaccination rates to be provided back to practices as part of QI process</td>
<td>Business Associate Agreement/ HIPAA waiver</td>
<td>QI project</td>
</tr>
<tr>
<td>II &amp; VI</td>
<td>Key informant interviews</td>
<td>Providers, staff at participating offices</td>
<td>Waiver of documentation of consent; invitation to participate</td>
<td>Not Applicable</td>
<td>Part of QI project – data collected will be used to develop vaccination improvement tools. Participation is optional and self-directed. Interviews will not be face to face, but will instead take place over the phone. Verbal consent will be obtained. Written invitation to participate will have consent components</td>
<td>Not Applicable</td>
<td>No PHI collected</td>
</tr>
<tr>
<td>II &amp; VI</td>
<td>Key informant interviews</td>
<td>Parents of patients 9-17 years of age</td>
<td>Waiver of documentation of consent; invitation to participate</td>
<td>Not Applicable</td>
<td>Data to be used to develop vaccination improvement tools and processes. Participation is optional. Interviews will not be face to face, but will instead take place over the phone. Verbal consent will be obtained. Written invitation to participate will have consent components</td>
<td>Not Applicable</td>
<td>Study participants will be recruited via advertisement through participating offices. Interested parents will provide research staff with their contact information or contact research staff directly. No PHI will be asked during interview.</td>
</tr>
<tr>
<td>II &amp; VI</td>
<td>Parent Surveys</td>
<td>Parents of patients 9-17 years of age</td>
<td>Waiver of documentation of consent; invitation to participate</td>
<td>Not Applicable</td>
<td>Data to be used to develop vaccination improvement tools. Participation is optional. Written invitation to participate will have consent components. Returning survey implies consent.</td>
<td>Business Associate Agreement HIPAA Waiver</td>
<td>Patient EMR data will be reviewed in order to oversample parents of patients with well-child visit in last year. No PHI will be asked during the survey.</td>
</tr>
<tr>
<td>III</td>
<td>Intervention development</td>
<td>Providers</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>IV</td>
<td>Intervention pre-visit</td>
<td>Parents</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>Parent use of website will be anonymous. No personal identifying info will be collected. Participation is optional and self-directed. Parents are accessing common information that is easily available to them by other means</td>
<td>Business Associate Agreement HIPAA Waiver</td>
<td>Research team may notify parents of patients about pre-visit intervention opportunity on behalf of practice. No PHI will be collected when using the website.</td>
</tr>
<tr>
<td>IV</td>
<td>Intervention, during visit</td>
<td>Parents/Adolescent</td>
<td>Not applicable</td>
<td>Not Applicable</td>
<td>Physicians conveying standard of care information using tools at their own discretion</td>
<td>Not Applicable</td>
<td>Study team has no interaction with parent/patient during the encounter</td>
</tr>
</tbody>
</table>
E. Scientific Design:

E.1. Phase I: Assessment of Current Vaccination Levels

Data Source: To capture the most accurate and comprehensive immunization utilization for patients, vaccine administration data will be combined from the Colorado Immunization Information System (CIIS) registry (described below), and clinic-specific administrative/claims and electronic medical record (EMR) databases. The CIIS includes all public health and community health offices, and the majority of private pediatric and family medicine offices, respectively, in the state. Over 85% of children in the state of Colorado have at least 2 immunizations recorded in the CIIS. All study sites recruited to the project participate in CIIS already. The CIIS combines the immunization information from multiple sources into a consolidated and valid record of immunizations for most children and adolescents in the cohort. Data quality assessments are done frequently. Offices are required to have <5% error rate in the registry, making the CIIS a highly accurate data source for assessing vaccine utilization.

Design and Methods: A retrospective analysis of vaccination uptake for HPV, Tdap, MCV4 and flu vaccines among all adolescents in the participating practices will be performed. Data collected for this specific aim will include: patient-level immunization data, including the number, type and date of specific vaccines received; patient-level demographic data, including age, gender, and race/ethnicity when available; and patient-level administrative/claims data, including ICD-9/10 and CPT codes to enable identification of vaccines delivered, and visit types.122,129

Analytic Plan: For each potential predictor and outcome variable, estimates of means and proportions with 95% CI will be obtained. Immunization up-to-date proportions will be calculated for the percentage of active adolescent patients receiving: 1) ≥ 1 HPV vaccine; 2) ≥ 3 HPV vaccines; 3) ≥ 1 MCV vaccine; 4) ≥ 1 Tdap vaccine; and 5) ≥ 1 influenza vaccine in the prior influenza season. Chi-squares and one way ANOVA will be used to determine whether there are differences in the outcomes assessed between practices. Because patient demographics could impact the efficacy of our intervention that will be assessed in Aim 3, we will assess at baseline whether there are differences among patients within each practice related to demographic and practice characteristics (i.e. payer mix, patient socio-demographics, and number of providers, practice type, medical specialty, visit types). Multivariable regression models will be used to determine independent predictors of the various vaccination outcomes and will include all predictor variables identified in bivariate analyses as potentially significant (p<0.1).

E.2. Phase II: Assessment of Current Vaccine Communication Activities

This phase has two sub-components: KIIs of parents and providers, and a parents survey.

E.2.1. KIIs of parents and providers

Data Sources: The study population will consist of 1) up to 4 providers or other medical providers at each participating practice; and 2) up to 3 parents of adolescent patients at each of the practices. Interviews will be conducted over the phone. Detailed interviewer notes and the transcripts of audiotaped interviews will be generated.

Design and Methods: We will conduct key informant interviews with providers at study practices in order to inform our intervention materials that will be implemented in Aim 3. Key informants are often conceptualized as being the key decision-makers within an organization. However, because one of the over-arching goals of this project is to develop a sustainable program, we will seek input not only from the decision-makers within study practices but also from other medical providers involved in immunization programs at the clinical sites. Therefore, all types of medical providers (including nurses and medical/physicians assistants, if applicable) in participating practices will be invited to participate. Potential provider informants will be identified by participating practice contacts and will be invited to participate via email or phone call made to the practice by research staff. Practice contact information is available through practice websites or public directories. Interviews with provider key informants will focus on the following content: provider perceptions of barriers to administering HPV vaccines to adolescents; overview of current vaccine communication
strategies used by the providers and/or by the practice as a whole; discussion of most salient facts about
HPV that would facilitate further discussions about the HPV vaccine with hesitant parents; acceptability of
the three components proposed for the intervention; assessment of the advantages and disadvantages of
various implementation options for each of the three intervention components; exploration of the resources
and planning needed to implement the three intervention components; and finally, an assessment of
provider and staff commitment to the various intervention strategies. See attached "Provider KII document"
for details about the interview contents.

Prior research demonstrates that there is often a “disconnect” between what providers perceive they are
doing during clinical encounters versus what patients recall. In addition, preferred vaccine
communication strategies may be different for patients versus providers. To ensure that our intervention
materials are developed so as to be acceptable to both providers and patients, it is critical to capture both
perspectives. Thus, in addition to provider interviews, we will also conduct a series of interviews among
parents of adolescent patients attending the practices. Interviews with parent informants will focus on the
following content: parent perceptions of barriers to administering HPV vaccines to adolescents; parents’
assessment of current vaccine communication strategies used by the providers and/or by the practice as a
whole; discussion of most salient facts about HPV that would facilitate further discussions about the HPV
vaccine with providers; acceptability of the components proposed for the intervention; and finally, an
assessment of the advantages and disadvantages of various implementation options for each of the three
intervention components. See attached “Parent KII document” for details about the interview contents.

Parent recruitment will occur in the following ways: 1) self-referral to the study based on advertisements
placed in the clinics’ waiting and exam rooms and 2) by advertisements provided directly to parents of
adolescent patients by office or research staff. Office staff may elect to provide interview recruitment
materials to parents of adolescents who come to the clinic for a well-child exam, or via a general mailing.
Research staff will provide interview recruitment material to the office to be handed out to such parents.
Research staff may also present at participating offices to distribute recruitment advertisements and talk
with such parents directly if the clinic prefers this approach. Study advertisements placed in the office
waiting room, exam rooms and handed out to parents will describe the research (see "Clinic Advertisement"
Document). Potential participants will be instructed to contact research staff with any questions or interest
they have regarding the research opportunity. Parents contacting the study team about participation will be
asked a series of eligibility questions to ensure heterogeneity with regard to age, race, insurance and views
on HPV vaccination. Eligibility criteria, which will be included on the advertisement, will include: being the
parent of a 9-17 year old that attends one of the study practices, able to converse in English, and the
adolescent has not yet completed the HPV vaccine series.

All interviews (parent and provider) will be conducted by a trained interviewer using established qualitative
research methods. These interviews will be in-depth and semi-structured, utilizing a combination of
broad, open-ended questions and more specific probes. The interviewer will take detailed notes during the
session, and each interview will also be audiotaped. An invitation to participate with consent components
will be used with both parent and provider interviews. Parents will be provided with a $30 incentive for
participation. Providers will be given a $50 incentive for participation in the interviews.

Analytic Plan: We will utilize a qualitative, iterative approach to analyzing data from small group and
individual key informant interviews of providers and separately, from parents. The principal investigator and
a qualitative methods expert (Dr. Albright) will review interviewer notes and transcribed audiotapes in order
to develop working themes and hypotheses to be tested and revised in subsequent interviews. In addition,
interview transcripts will be entered into Atlas Ti qualitative data analysis software (Scientific Software
Development, 1999), and data will be analyzed using the “editing” approach suggested by Crabtree and
colleagues. This particular analytic method encourages interpretation of the data using a team approach.
Two investigators will independently read through the interview transcripts, highlighting particular issues or
elements that appear to significantly impact the perceived desirability and feasibility of the provider
communication intervention components. The investigators will then meet to discuss interpretation of the
data, and transcripts will be re-reviewed to confirm or disconfirm initial and ongoing themes and codes.

These themes will then be organized into an overall framework to describe the desirability, feasibility,
perceived effectiveness, and potential for sustainability of various strategies to implement the provider communication intervention.

E2.2 Parent Survey

To augment data about current provider vaccine communication activities, and also to ensure that our planned interventions are as patient-centered as possible, we will conduct a parent survey regarding provider communication about adolescent vaccines.

Data Source: Surveys will be provided by email and/or postal mail depending on the participating practices electronic record capabilities and preferences. The study population will consist of up to 50 parents of adolescents attending each of the practices, for a total of up to 1000 parents, divided evenly between the 20 participating clinical sites.

Design and Methods: Using data from provider and parent interviews described above, the research team will draft a short survey to assess among a larger sample of parents their understanding and perceptions of current vaccine-related communication activities being performed by the providers and/or practices, and of the acceptability of the proposed intervention components. The content of the survey will focus on the following: parent and child demographics (age, gender, race, insurance); recollection of whether they or their adolescent experienced any of provider/clinic vaccine communication strategies identified in the interviews described above; attitudes and beliefs about HPV and other adolescent vaccines; and acceptability and implementation preferences for the three components of the provider communication intervention. Based on previous immunization studies we have performed, we estimate that the parent survey will take between 4-7 minutes to complete. A first draft of this survey is included with this submission (See "Parent survey" document). Mail-based survey data will be double-entered into an Access database by research staff. Up to three contact attempts will be made for parents who either do not return the completed survey or do not opt out of the study.

As part of the data pull for Phase I above (under a BAA), contact information for all active adolescent patients at the participating practices will be provided to the research team. The research team will randomly select 50 adolescents age 9-17 years old, divided evenly between male and female patients and by year of age. Adolescents who have had a well-child appointment in the last 12 months will be oversampled, since this is the visit type where vaccines are most likely to have been discussed. A survey packet will be sent to the parent/guardian of the adolescents in the sample that will contain an invitation to participate in the survey, the survey (which will include a response option to opt-out of participation), a pre-paid return envelope addressed to the university, and a $5.00 incentive. Parents interested in the study would return the survey completed using the postage-paid envelope. The survey will also be available online. For clinics with email addresses as part of their contact information, the research staff will send the study information packet to parents via email. For parents who answer survey questions on-line the email-based survey data will be housed on Research Electronic Data Capture (REDCap), a secure site for online data collection that is HIPAA compliant. These parents will also receive a $5.00 incentive after taking the survey. Up to three contact attempts will be made for parents who either do not complete survey or do not opt out of the study via email.

Analytic Approaches: For each potential predictor and outcome variable, estimates of means and proportions with 95% CI will be obtained. These will then be compared among different subgroups using Chi-square tests for binary outcomes or one-way ANOVA for continuous outcomes. Planned subgroup analyses include examining outcomes by clinical type (public/private), medical specialty (family medicine/pediatrics), gender of parent, gender of child, age of child, race, insurance and number of providers in the clinic. Linear and logistic multivariable regression models will be used to determine independent predictors of linear and categorical outcomes, respectively. Multivariable models will include all predictor variables identified in bivariate analyses as potentially significant (p<0.1).
E.3. Phase III – Intervention Development

This phase of the project does not fall under human subject's regulation as no human subjects data will be collected. Rather we will work with office staff at each of the intervention practices to finalize the toolkit materials and plans for implementation.

E.4. Phase IV – Intervention Evaluation

E.4.1. Overview of Toolkit Intervention Components

The Toolkit to be used by intervention clinics specifically is comprised of 4 components: 1) a pre-visit website; 2) motivational interviewing training to be used as needed during the clinical encounter; 3) an HPV fact sheet to be used as needed during the clinical encounter; and 4) an HPV vaccine decision aid to be provided as needed at the end of the clinical encounter. Each of these components, and how they may be implemented, are described in detail below.

E.4.1.a. Pre-Visit Website – Vax-Facts-HPV, a Tailored Message Educational Tool

Data shows that many parents are unaware of the need for HPV vaccination prior to encounters with their adolescent's medical provider. However, when parents do become aware of the need for the HPV vaccine (either at the time of the visit or before), this knowledge often raises questions and concerns. The complexity of these concerns can make it exceedingly difficult for providers to adequately address them during the 10-20 minutes typically allotted for a clinical encounter. Therefore, to raise parental awareness about HPV vaccination and provide a "first pass" at addressing concerns about HPV vaccines, parents in intervention clinics will be provided with VaxFacts-HPV prior to their adolescent's scheduled clinical encounter. This should minimize the amount of provider time needed to address parental HPV vaccination concerns.

VaxFacts-HPV is a web-based intervention that informs parents about the need for HPV vaccination. Upon entering the website an anonymous baseline survey (no PHI or personal identifying information is collected) assesses demographic characteristics and attitudes about HPV vaccines. VaxFacts-HPV then uses a "tailoring engine" to adapt this information in real time into a series of educational pages that reflect that each parent's unique and specific vaccination barriers, demographics, and HPV-related experiences. (See attached "VaxFacts-HPV Baseline Survey," "VaxFacts-HPV Message Library" and "VaxFacts-HPV Screen Shots" documents for more detail).

Practices will provide feedback about which type of clinical visit(s) they would like to target for implementation of VaxFacts-HPV and how to best deliver the website information to parents. Several possibilities exist, and may be chosen by practices individually or in combination. Examples include:

- Providing a web link to the intervention via emailed appointment reminders that parents access from their home or work computer.
- Providing the web address for the intervention via mailed appointment reminders that parents type in to access the intervention from their home or work computer.
- Having a kiosk or roving iPad in the clinic to be used just prior to the clinical visit.

When practices elect to provide VaxFacts-HPV information to parents by email, mail or text, research staff will work with intervention offices to develop a system to notify parents of adolescent patients with upcoming scheduled visits about the possibility of accessing VaxFacts-HPV. Once parents receive the notification they will self-direct to the website. As responses will be anonymous there will be no person-specific log in needed for accessing the site, nor will an individual account need to be established. Since responses are anonymous, consent will not be obtained.
The VaxFacts-HPV server and data will be maintained by the Center for Health Communications & Research (CHCR) group at the University of Michigan. Data that will be captured include 1) responses to baseline survey questions, and 2) paradata on the length of time participants spent on each page of the website. To ensure that the data are protected, CHCR uses virtualized servers provided by the University of Michigan Information Technology Services group. The virtualized servers are housed at two redundant datacenters. These datacenters provide protection from lengthy outages, 24/7 staffing, restricted physical access and disaster recovery. Virtual servers are backed up automatically onto encrypted tape for recovery and security. The datacenters also reduce the use of physical resources such as electricity and air conditioning. The data that will be maintained on these servers includes all data entered by parents (login information, survey questions, consent) and a record of the webpages that were viewed (paradata).

All servers and the back end databases are password protected. The server runs the Ubuntu Linux Server Edition operating system and security patches and updates are downloaded and installed automatically. Each server is also protected by firewalls to restrict network access to the server. More details are available at vaas.umich.edu. When a participant accesses the study website, content is transmitted securely using secure socket layer (SSL) protocol, the same protocol used to protect financial and other personal information when transmitted from a web site to a user's browser. This prevents anyone else on the network from intercepting and viewing the content that is being provided to the participant.

E.4.1.b. Motivational Interviewing Training for Providers

Providers at each intervention site will receive a 60-90 minute educational session to enhance their communication skills. The first 15 minutes of the education session will highlight key facts about HPV infection and vaccination in male and female adolescents. Piggy-backing on these data, the remainder of the educational session will be comprised of personalized training on how to use Motivational Interviewing (MI) techniques to identify, explore and resolve parental indecision about the vaccine. Training sessions will be led by Ms. Kathleen Garrett from the UCD who has extensive prior experience in teaching providers MI techniques in relation to a wide variety of clinical issues. Ms. Garrett is a MI Lead Facilitator with experience in advanced clinical MI and "train the trainer" education. She is also certified in Motivational Interviewing Treatment Integrity and has been a member of the International Motivational Interviewing Network of Trainers since 2004.

E.4.1.c. HPV Fact Sheet

We will develop the HPV Fact Sheet in conjunction with significant provider feedback over a series of 3 meetings. The goal of the Fact Sheet is to present highly influential printed "stat bites" about HPV infection and vaccination. Providers from the intervention clinics will be given an HPV Fact Sheet template (see "HPV Fact Sheet Template" document) and a "menu" of HPV-related informational points, facts, graphs, pictures, and charts that they might find compelling. Providers then will be asked to choose those components they find personally the most persuasive, while also considering which information would resonate most with their patients (for example - cervical cancer rates among African Americans in a clinic with a high proportion of African American patients). Providers will also have the ability to add their own graphics, logos and text. Suggested changes will be incorporated by the research team into an updated version of the Fact Sheet which will be presented to providers at subsequent meetings until a final version is agreed upon. While the overall structure of the Fact Sheet will be the same across intervention practices (1 side of a single 8x11 page), the content of the Fact Sheet is likely to vary by clinical site.

Providers in the intervention clinics will be encouraged to use the Fact Sheet as part of their overall discussion about HPV vaccines, particularly with parents that seem reluctant for the vaccine. However, use of the fact sheet is entirely up to the provider's discretion. We collect data on the fact sheet utilization by periodically checking in with the practices to see how often they use it.

E.4.1.d. Post-Visit Intervention – The Decision Aid for HPV Vaccines

The before- and in-clinic tools are designed to help parents understand the need for HPV vaccination and allay their concerns. However, some parents will remain unconvinced about HPV vaccination even after viewing the intervention materials and talking with the provider. To address these parents concerns, they
will be provided with the Decision Aid for HPV Vaccines that was developed by the research team previously (See "Decision Aid" document).

As with the HPV Fact Sheet, the Decision Aid for HPV Vaccines will be available for providers in the intervention clinics in paper format. Use of the fact sheet is entirely up to the provider’s discretion. We collect data on the fact sheet utilization by periodically checking in with the practices to see how often they use it.

**E.4.2. Comparison of Vaccine Communication and Uptake Between Control and Intervention Practices**

The interventions conducted as part of this specific aim will be practice-based, and will thus involve all providers at a given site. Thus, our study will be conducted as a group-randomized trial, also known as a cluster-randomized trial.

A key issue in cluster randomized trials is the possibility of covariate imbalance in practices assigned to different treatment arms. Because intervention effects and potential sources of confounding are likely to vary by type of practice (pediatric versus family medicine, private versus public), randomization will be performed in a stratified manner, with 2-4 practices within each type of clinical site randomly designated as intervention practices, and 2-4 practices designated as control practices for a total of 10 intervention and 10 control practices. Additionally, pre-study information will be collected on patient characteristics, practice characteristics, and baseline performance characteristics related to communication, and to immunization that may influence outcome measures (e.g., baseline immunization rates and communication activities, VFC eligible patients, % of providers, total % of patients) will be used to develop and evaluate a balance criterion, defined as the sum of the squared differences between standardized practice means on these variables.

**Intervention Practices:** Although the intervention components and tools will be similar in all intervention practices, the precise intervention strategies and the final look and feel of the tools will be developed collaboratively with the practices, and therefore may have some variability. Using the same methodology and data sources as for the baseline assessment of vaccination status described in Aim 1, vaccination status will again be assessed in Year 3 of the project, after the intervention period is complete.

**Control Practices:** Practices assigned to the control arm will conduct usual care throughout the study period. As in the intervention practices, baseline immunization rates will be determined in Year 1 and vaccination levels will be reassessed using the same methods in Year 3.

**Analytic Plan:** The *primary outcome measures* will be the change from baseline in the % of adolescent patients receiving 1) ≥ 1 HPV vaccine; and 2) ≥ 3 HPV vaccines. The *secondary outcome measures* will be the change from baseline in the % of adolescent patients receiving: 1) ≥ 1 MCV vaccine; 2) ≥ 1 Tdap vaccine; and 3) ≥ 1 influenza vaccine in the prior influenza season.

Initially, descriptive statistics will be computed to describe patient and practice characteristics. Chi-square tests and 1-way ANOVA will determine whether there are differences in the study outcomes and patient populations between the study arms. Any variables that appear unbalanced between study arms will be included as covariates in subsequent analyses if they differ between groups or are associated with the outcome. However, we expect that the randomization approaches described earlier will minimize differences between groups. The main analysis will be a comparison between the two study arms in the change from baseline of HPV vaccine utilization. Secondary analyses will examine differences between study arms in Tdap, Flu and MCV vaccine uptake. We will explore through multivariate analyses whether practice type (public versus private), medical specialty, payer mix, patient socio-demographics, and number of providers impact the effectiveness of the intervention. We will employ intent-to-treat analyses using generalized linear mixed model approaches (random effects, multilevel, hierarchical), which are recommended for the analysis of cluster-randomized trials.
E.5. Phase V - Final Vaccination Assessment

Data sources, design and methods for Phase V will be the same as described in Phase I. The only difference is that for Phase V, the study population will include all adolescents seen at the participating practices during the study period (from the baseline assessment date to intervention close).

E.6. Phase VI - Assessment of Toolkit Utilization and Impact

Data sources, design and methods for Phase VI will be the same as described in Phase II.