1 Protocol Title

Community Pharmacists Vaccinating Against Cancer (CPVAC): A Pilot Randomized Controlled Trial Aimed at Increasing HPV Vaccine Completion Rates Among Racially/Ethnically Diverse Youth

2 Background and Objectives

The majority of HPV-related cancers and genital warts can be prevented through the timely uptake and completion of the HPV vaccine series.[23,25,26] Human papillomavirus (HPV) is the most common sexually transmitted infection, and persistent infection with oncogenic HPV strains cause cancer.[27] The HPV strains most commonly associated with cancer are HPV 16 and 18. However, strains 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 are also carcinogenic.[28] Commercially available 9-valent HPV vaccines offer the potential of immunity against seven oncogenic strains (Types 16, 18, 31, 33, 45, 52, 58) and the two low-risk strains (Types 6 and 11) that cause over 90% of genital warts.[29] Vaccine completion is critical because it boosts the body's ability to fight off the virus.[3]

In 2016 only 37.5% of HPV vaccine age-eligible males and 49.5% of females completed the HPV vaccine series[7] with racial/ethnic minorities exhibiting lower rates of completion.[8] Specifically, Black and Latino children and young adults have a higher rate of initiation of the vaccine;[9] however, they have a significantly lower likelihood of completing the vaccine series.[9] Further, Latino patients who prefer speaking Spanish as opposed to English have lower HPV vaccine completion rates.[10] It is critical to enhance HPV vaccine series completion among racial/ethnic minority HPV vaccine age-eligible individuals to reduce cancer disparities. Barriers to complete the HPV vaccine have included the following: lack of time to receive the follow-up vaccines,[11] transportation needed to return for follow-up clinical visits,[11], additional office co-pays, [31] lack of awareness to receive additional HPV vaccine doses,[32] and Lack of strong provider recommendation for vaccine initiation/completion[34] particularly for male patients.

Traditionally, primary care providers (PCPs) administer all HPV vaccine doses. After individuals receive the first HPV vaccine dose from their PCP, they must return to their primary care clinic for additional doses. This places a burden on patients and their caregivers to schedule and attend additional, non-routine clinical visits.[11-13] However, PCPs are not the only providers who can administer the HPV vaccine. Pharmacists can administer additional vaccine doses.[14,15] Receiving additional vaccine doses with pharmacists may prove to be a more convenient method of ensuring vaccine adherence due to pharmacies' extended hours (compared to PCP clinics) and lack of required appointment.[16-18] Many have built-in text-message reminder systems, which increase vaccine adherence[19] by prompting patients to return to the pharmacy when medication (vaccine dose) has been filled. Although numerous studies describe the potential for pharmacists to aid in HPV vaccine series completion, few, if any, intervention research studies have actually tested this integrated model of care.[20-24]

Therefore, we propose to pilot and test a theoretically-informed (Diffusion of Innovation) integrated intervention model that we call CPVAC (Community Pharmacists Vaccinating Against Cancer). CPVAC will be a randomized controlled pilot intervention. Caregivers of patients who complete the initial HPV vaccine will be asked to take part in the study. The PI will recruit a stratified sample of patients, oversampling for Latino (English and Spanish speakers) and African American patients. Patients will be randomized to intervention or control group (usual care). After enrolling in the study, primary care providers of patients in the Intervention Group will contact the patients' community pharmacy (e.g. CVS, Walgreens, Fry's) and prescribe the remaining HPV vaccine dose(s). The pharmacy will electronically update patients' files and schedule the HPV vaccine "refill" (additional doses) at the appropriate dosing schedule. The pharmacy will contact patients or (for minors) patients' caregivers when it is time to complete additional HPV vaccine dose(s). Control group participants will receive usual care, returning to their PCPs to complete the additional HPV vaccine series.

3 Data Use

Data will be published in peer-reviewed journals and presented at academic conferences. Results will be released to Adelante Healthcare Mesa, the site for this research study.

4 Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Caregivers of a child between ages 9-18 who has either not received any HPV vaccine doses or has received only initial HPV dose	Caregivers whose child has completed additional HPV vaccine doses
Receives care at Adelante Healthcare Mesa	
Fluent in English and/or Spanish	
Willing to provide informed consent	

5 Number of Participants

90 participants will be enrolled in the study; 45 in the control group / 45 in the intervention group

6 Recruitment Methods

The study research assistants (RA) will work directly with the clinic during the study enrollment period to generate a list of all patients (and their caregivers) who may be eligible to participate in the study. Adelante office staff will search patients' online medical files to determine which individuals are age-eligible for the vaccine who have either 1) not initiated the vaccine series and/or 2) have only completed one of the HPV vaccine doses. They will generate a list of eligible patients with caregiver contact information to the RA.

The RA will use a vacant office space for all recruitment and enrollment activities. To initiate contact with potential participants, she will send a letter to caregivers of children eligible for HPV vaccine, inviting them to take part in a study about HPV vaccine intentions. The letter will contain study-specific phone number that will reach RA's office directly. RA will screen caregivers for eligibility and notify clinic staff of all patients/ caregivers eligible for study. Caregivers will work with clinic staff to schedule an office visit. When the clinic staff schedules the patient's visit, they will ask caregivers to stay an addition 15-20 minutes after their scheduled appointment to complete the study informed consent and baseline surveys.

7 Study Timelines

We anticipate participants being a part of the study for up to 8 months. We expect that individuals will spend up to 2 hours (1 hour on 2 days) on completing study surveys, one on the first day of the study and another after six months. They will also spend time taking their child to receive the additional HPV vaccine doses.

8 Procedures Involved

The project utilizes a software (REDCap) which randomizes individuals into intervention and control groups, using permuted block randomization. As participants enroll in the study, they will be given a study identification number (e.g. 1,2,3). Both the intervention and control groups will complete baseline surveys.

Control group participants will receive standard care and will be expected to return to Adelante Healthcare Mesa to receive the additional HPV vaccine booster doses. Intervention group participants will be referred to receive the additional HPV vaccine doses at their community pharmacy. At post-intervention, intervention participants will be asked if their children completed the HPV vaccine series.

Primary behavioral outcome: At the end of the 16-month intervention, PI will ask clinic staff to report HPV vaccination dose completion (for vaccine doses 1,2,3) for all study participants.

Follow-up Survey Data Collection: RA will call all participants and administer follow-up survey to measure potential changes in DOI theoretical constructs (see baseline survey).

Qualitative telephone in-depth interviews: To qualitatively explore intervention feasibility and acceptability, PI will conduct telephone interviews with patients, patients' caregivers, clinic primary care providers, and clinic pharmacists.

- In-depth interview with Caregivers and/or Young Adult Patients: PI will conduct telephone interviews with caregivers from the control group (standard care) and from the intervention group (pharmacist-administered HPV vaccination) related to their experiences taking part in the study.
- In-Depth interviews with Providers and Pharmacists: Researchers will conduct telephone interviews with all the clinic's participating primary health care providers and office manager (n= 4) and local pharmacists who work at pharmacies where patients were referred to receive the HPV vaccine (n=4) to explore their acceptability and perceived feasibility of the intervention. They will be asked how the intervention impacted the quality of patient care, ways in which the intervention impacted patient flow within the clinic, how satisfied they were with the intervention, and perceived fit of the intervention within their workplace.

Participant Incentives: Research participants will receive e-gift card incentives (of their choosing from Tango Card, Inc) for completing study surveys ($20 dollars per survey completed) and for participating in telephone interviews ($30).

9 Withdrawal of Participants

There are no anticipated circumstances under which participants will be withdrawn from the research study without their consent.
If participants choose to no longer take part in this study, they are asked to contact the PI (Alexis Koskan, 602-827-2792) to notify her that they will no longer be involved in the study. The PI will remove and destroy all participant data from the study.

10 Risks to Participants

There are no foreseeable risks to research participants. Risks of the HPV vaccine (a non-virus vaccine –which utilizes a protein which looks similar to HPV) include a fever, pain at injection site, and a headache. A much less common side effect of the vaccine is fainting within 15 minutes of injection. For this reason /risk, patients are told to remain at the clinic/pharmacy for an additional 15 minutes after they receive the vaccine to ensure that they are safe to leave.

11 Potential Benefits to Participants

HPV vaccine age-eligible children will complete the HPV vaccine series, thus preventing the risk of HPV-related cancers. Also, intervention participants will learn more about the role of the community pharmacist in administering vaccines and vaccine booster doses. This may help aid in the completion of vaccine series without having to schedule and revisit primary care providers' offices.

12 Setting

This study will be conducted at Adelante Healthcare Mesa, a local federally qualified health center. Intervention participants will be referred to receive additional HPV vaccine booster shots with their community pharmacists. Pharmacists are currently licensed to administer the HPV vaccine.

13 Multi-Site Research

NA

14 Resources Available

This clinically based study will take place at Adelante Healthcare Mesa, a Federally Qualified Health Center (FQHC) which predominantly serves ethnic/racial minority, low-income populations.

15 Prior Approvals

We have received prior approval and secured an MOU with Adelante Healthcare Mesa to conduct this study.

16 Data Management and Confidentiality

Data Analysis:

Aim 1 Data Analysis: Assessing Preliminary Efficacy.

The specific aim of the proposed project is to investigate the effect of CPVAC on HPV vaccination completion rate compared with primary care provider (Aim 1).

Patient-related outcomes: Two proportion Z tests will be used to examine the proportion differences in HPV vaccination completion between CPVAC and primary care provider (PCP) groups. We will also compare which medical professionals completed the vaccine doses. We will create codes for various health care professionals (e.g. nurse, nurse practitioner, physician, pharmacist, etc.) to differentiate who administered the vaccine. The HPV completion status will be classified as dichotomous variable (0 = no; 1 = yes). Independent variables will be classified as either categorical or continuous scale: age, gender, race; location, HPV vaccine dose (1, 2, 3, etc); provider types (PCP vs pharmacist); facility type/place of service (health clinic vs. pharmacy). Multiple logistic regression with stepwise selection procedures will be used to identify whether these independent variables are associated with HPV completion status.

Psychosocial Constructs Data Analysis: Baseline characteristics of the study participants will be summarized using descriptive statistics. Multiple logistic regression will be used to investigate whether psychosocial factors (e.g. intention, norms, efficacy) relate to HPV vaccine completion (yes/no). General linear models or Mann-Whitney U tests will be used to test mean or median differences for self-efficacy and response-efficacy to complete the vaccine series between CPVAC and PCP groups.

Missing Data: We will conduct sensitivity analyses including imputation methods and completer-only analyses. All statistical procedures and analyses will be performed in SPSS software.

Aim 2 Data Analysis: Qualitatively exploring feasibility and acceptability of CPVAC
PI will submit the interview audio-recordings to an ASU-approved transcription company. Using the interview guide to determine a priori themes, PI will create a coding book for the interview data. Reading through all interview transcripts, PI will add emerging themes to expand the coding guide. PI will train the RA in descriptive content analysis. They will review and code one transcript together, code an additional three transcripts separately, meet to discuss coding choices, and reach an agreement on data interpretations and analysis before they split the remaining interview transcripts for review. PI and RA will upload all transcripts and codes into ATLAS.ti software. PI will take the outcomes from the analyses from ATLAS.ti and begin to summarize findings for each in-depth interview question with the RA to ensure interpretation consensus and create a comprehensive summary of the findings related to intervention acceptability and feasibility.

Data Storage:
Patients' information will be de-identified and given a unique Participant Study Number for data analysis by an Adelante Healthcare Mesa healthcare practitioner. All signed informed consent documents will remain with the PI. She will secure them in a locked drawer of a locked office. These forms will be kept up to two years and will be destroyed at the end of those two years.

17 Safety Monitoring

Koskan (PI) and the research assistants will meet on a monthly basis to evaluate the data collected for the study. They will review completeness of patient surveys and informed consent and updates related to HPV vaccine series completion.

18 Consent Process

The clinic will notify the RAs when potential participants have scheduled office visits. After the office visit, a nurse or office staff member will walk the patient to the RA's research office. The RA will briefly explain that this study is about HPV vaccine intentions and vaccine completion and invite caregivers to sign up for the study. If patients decide not to sign up that day, they will be given a study information sheet and a phone number to call should they decide to participate later. RA will also write down their contact information to follow up on study enrollment. For caregivers interested in signing up for the study, the RA will administer the informed consent and baseline surveys.

The project biostatistician will have already generated a randomization table for the intervention and control groups, using permuted block randomization. As participants enroll in the study, they will be given a study identification number (e.g. 1,2,3). Based on their study number and the randomization table, they will be assigned to either intervention or control group.

For the in-depth interviews with caregivers (at post-intervention), the RA will contact participants via phone. The RA will administer informed consent via the phone and verbally consent participants prior to conducting the phone interviews.

19 Investigational New Drug or Devices

NA

20 CITI

Provide the date that the members of the research team have taken the CITI training for human participants. This training must be taken within the last 4 years. Additional information can be found at: http://researchintegrity.asu.edu/training/humans

CITI certification for Koskan and Lee can be found at ASU's IRB.
Dr. Karuppana completed CITI certification. Documentation is soon to come.