Intervention to Educate and Improve Underserved Populations' Uptake and Completion of the HPV Vaccine Series.

Protocol Number: 19-2236

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PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale

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STATEMENT OF COMPLIANCE

This is an investigator-initiated study. The principal investigator (PI), Evelinn Borrayo, PhD, is conducting the study and acting as the sponsor. As the sponsor-investigator, both the legal/ethical obligations of a PI and those of a sponsor will be followed.

The trial will be carried out in accordance with Good Clinical Practice (GCP) as required by applicable United States (US) laws and applications, including but not limited to United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46).

The PI will assure that no changes to the protocol will take place without documented approval from the Institutional Review Board (IRB). All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Sponsor-Principal Investigator: Evelinn Borrayo, PhD
Print/Type Name

Signature: _____ **Date:** _____

Site Principal Investigator: Mona Krull, MD
Print/Type Name

Signature: _____ **Date:** _____

LIST OF ABBREVIATIONS

CHE	COMMUNITY HEALTH EDUCATOR
PN	PATIENT NAVIGATOR
DENVER HEALTH & HOSPITAL AUTHORITY	DHHA
HPV	HUMAN PAPILLOMA VIRUS
UNIVERSITY OF COLORADO CANCER CENTER	UCCC
ENTERTAINMENT EDUCATION	E-E
ELECTRONIC MEDICAL RECORD	EMR
PERTECTED HEALTH INFORMATION	PHI

PARTICIPATING SITES

Denver Health and Hospital Authority (DHHA)
University of Colorado Cancer Center (UCCC)

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Protocol Title: ***Intervention to Educate and Improve Underserved Populations' Participation in Clinical Trials and the Uptake and Completion of the HPV Vaccine Series***

Objectives:

- ***Primary Objective:***

  1) *Educate parents (and young adults) via CHEs about the HPV vaccine, in order improve knowledge and intentions to increase uptake of the vaccine for individuals aged 9-26.*
  2) *We will collect socio-demographic data to explore its association with knowledge, intentions, & vaccine uptake.*

- ***Secondary Objectives:***

  1) *Increase completion of the HPV vaccine via PN to promote uptake of one, two, or three vaccine doses among adolescents and young adults (9-26 years old).*

  2) *Assess intervention delivery and patient-, clinic-, and system-level impact of the PN intervention to increase vaccine completion among adolescents and young adults.*

Endpoint:

- ***Primary Endpoint:***

  1) *Knowledge and intentions to initiate or complete the HPV vaccine series among project participants.*

  2) *Association of sociodemographic variables (e.g., age, gender, ethnicity, health insurance, income, zip code) to knowledge, intentions, and uptake of the HPV vaccine among participants*

- ***Secondary Endpoints:***

1) *Uptake of one, two, or three HPV vaccine doses among adolescents (9 to 17 years of age)*
2) *Uptake of one, two, or three HPV vaccine doses among young adults (18-26 years of age).*

- ***Tertiary/ exploratory:***

1) *To assess PN impact we will record the number of participants to whom the PN scheduled to, a) receive a recommended 1st dose, 2nd dose, or 3rd dose of the HPV vaccine; b) connect to care services such as health insurance, discount or no-cost HPV vaccine programs, and c) facilitate other services such as language translation, appointment scheduling assistance, transportation services, and childcare.*

2) *To assess patient-level impact, we will track for each participant their (a) baseline HPV vaccine doses, and (b) the number of those they obtained in total, and quarterly (c) the number of patients who received a 1st dose, 2nd dose, or 3rd dose of the HPV vaccine.*

3) *To assess clinic-level impact, we will obtain clinic vaccination reports track the number of patients at each clinic who received: (a) 1st dose, 2nd dose, or 3rd dose of the HPV vaccine at baseline; and record quarterly: (b) 1st dose, 2nd dose, or 3rd dose of the vaccine broken by age for adolescents (9 to 17 years old) and young adults (18-26 years old).*

Population:

- ***Sample size***
  - *Maximum number of participants that can be enrolled is 1000*
  - *Minimum number of participants to be enrolled 400 (number of participants needed for analyses)*

Phase: *N/A*

Participating Sites: Denver Health and Hospital Authority

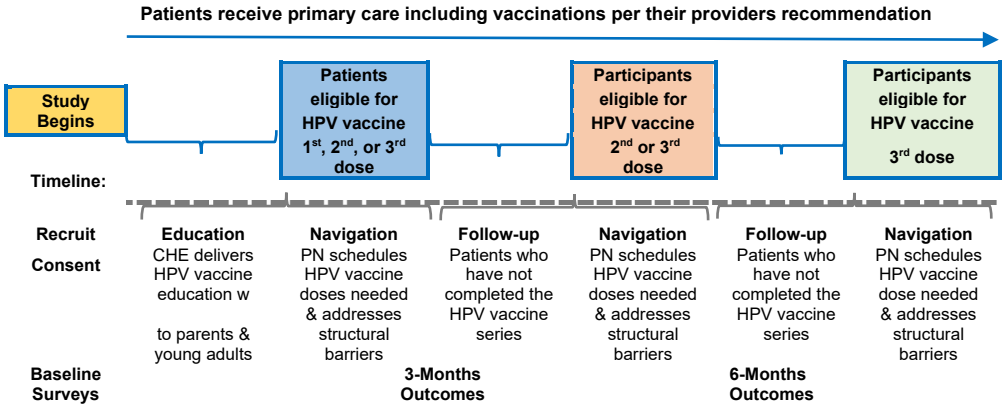
Description of Study Intervention: Education and Patient Navigation

Study Duration: *36 months*

Participant Duration: *Duration will vary for each participant and will be determined by vaccination status. Participants will be contacted to complete a post-education at baseline using the NCI survey. We will only administer the survey pages 1-3.*

1.3 STUDY SCHEMA

Figure 1. Delivery Schema for Subjects Recruited to Participate in the CHE and PN Intervention



Note: CHE=Community Health Educator; PN=Patient Navigator; HPV=Human Papillomavirus; Participants will receive only the intervention strategies they need at strategic points. Timeline of the intervention delivery not drawn to scale.

2. INTRODUCTION

2.1 STUDY RATIONALE

The Cancer Prevention and Control Program within UCCC works to develop, evaluate, and disseminate evidence-based interventions for primary, secondary, and tertiary prevention, and to improve health services delivery for patients. Efforts to meet the Cancer Center's priorities include promoting awareness to increase vaccinations against HPV as part of its goal to eliminate HPV-related cancers in Colorado; giving priority to underserved Hispanic, residents in outlying rural areas, and residents living in areas of high poverty. This proposal leverages several ongoing community outreach efforts to improve HPV vaccine uptake, by educating and navigating patients where HPV vaccine rates are low and where HPV-related cancers are most prevalent.

2.2 BACKGROUND

Dr. Borrayo leads a supplemental award to the University of Colorado Cancer Center (UCCC; 3P30CA046934-31S4) by the National Cancer Institute (NCI) to enhance its community outreach and engagement to underserved populations (i.e., ethnic minority, low-income, uninsured, or underinsured) disproportionately affected by cancer incidence, mortality, and morbidity. More specifically, this project seeks to implement interventions to improve these

populations' knowledge, uptake, and completion of the human papilloma virus (HPV) vaccine to prevent HPV-related cancers. We will partner with Denver Health and Hospital Authority (DHHA) which serves communities with populations where HPV-related cancers' incidence, mortality, and burden are high. Denver Health mostly serves medically underserved patients with a significant percentage of patients covered by Medicaid (62%) and of patients without health insurance (14%). The Denver County population served by Denver Health is at high risk for cancer-related health inequities. The age-adjusted annual incidence of cervical cancer (cases per 100,000), using 2010-2014 county data, [35] is higher for Denver County (6.6) than for the state of Colorado (5.9). Cervical cancer and oropharyngeal cancers are the most common HPV-related cancers in women and men respectively, impacting more than 29,000 individuals in the US each year[8]. One model predicts that HPV infection can be eliminated with global 80% vaccination coverage, but even with more modest rates of vaccine uptake there can still be significant reductions in HPV-related malignancies. Statewide in Colorado in 2016 only 48% of adolescents had completed the HPV series[13]Our intervention will focus on providing education delivered by Community Health Educators (CHEs) and on referring participants to Patient Navigators (PNs) who will facilitate their access to the HPV vaccine.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Loss of confidentiality for patients in the educational intervention delivered by the CHE.

2.3.2 KNOWN POTENTIAL BENEFITS

Improve knowledge about importance of HPV vaccine among parents of adolescents and young adults eligible for the vaccine and uptake of the vaccine among the interventions' participants.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This a minimal risk study that does not place participants in any increased risk of harm. Thus, the benefits to be gained in knowledge far out way the risks.

The risks to participants are reasonable in relation to the anticipated benefits to participants and/or society, and in relation to the importance of the knowledge that may reasonably be expected to result, thereby falling in favor of performing the study:

- To Participant*: Improved knowledge an intention to initiate or complete the HPV vaccine series.*
- To Society: *Increased uptake of the HPV vaccine, could lead to decreased rates of HPV related malignancies in a population that is disproportionally affected by HPV related malignancies.*
- Justify the importance of the knowledge gained: *We will gain understanding on how to implement a combination of a CHE and PN intervention to increase knowledge, intentions, and uptake of the HPV vaccine to prevent HPV-related malignancies in areas of most need. Additionally, we will evaluate the influence NCI designed educational presentations and materials on increasing*

knowledge and intentions about HPV and the HPV vaccine series. Exploring these interventions will shed knowledge on practices to use when addressing some of HPV-related cancers among underserved populations.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary	Parents & young adults' knowledge & intentions to obtain the HPV vaccine	Behavioral factors precede uptake of preventive vaccines
	Sociodemographic data (e.g., age, gender, ethnicity, insurance, income, zip code)	Variables known as associated with vaccine uptake
Secondary		
	Uptake of one, two, or three HPV vaccine doses among adolescents (9 to 17 years old) and young adults (18-26 years old).	Number of vaccine doses are used to assess full protection (3 doses) or partial (≤3 doses)
Tertiary/Exploratory	Intervention's delivery and patient-level & system-level impact.	Interventions that can be delivered to impact patients & clinics are easier to implement

4 STUDY DESIGN

4.1 OVERALL DESIGN

We will use a one-group post-test design to assess the effects of the intervention on the primary outcomes. The educational intervention will be delivered to 400 participants by a trained CHE who will deliver the educational materials to eligible DHHA patients. The CHE will administer the post-education survey at baseline to participants. Additionally, we will use a one-group post-test design to assess the impact of the intervention on the secondary outcomes. At the patient-level, we will track participants that receive (a) 1st dose, 2nd dose, or 3rd dose of the HPV vaccine; and the number of referrals to care by recording the number of patients received (b) referrals to health insurance, discount, or no-cost HPV vaccine programs; or (c) to other services to facilitate HPV vaccine dose completion. To assess clinic-level impact, we will track each clinic's HPV vaccine rates for adolescents (9-17 years old) and young adults (18-26) and compare rates from before we start the intervention and then quarterly there after we have introduced the intervention to each respective Denver Health clinic.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

This is a pragmatic study that seeks to evaluate in real-world practice the use of a CHE and PN intervention to improve the uptake of evidenced-based HPV vaccinations. Thus, it uses a post-design to evaluate participants' changes in knowledge and intentions to vaccinate by comparing

outcomes at baseline to outcomes after exposure to the CHE educational intervention. Similarly, it uses a post-test design to evaluate the uptake of the HPV vaccine after participating in the PN intervention. In real-world practice it is important to measure an intervention's impact not only at the patient-level but also at the clinic- and system-level. Consequently, we will measure post-intervention the rates of the HPV vaccine1st dose, 2nd dose, and/or 3rd dose uptake for each clinic and for the DHHA systems by comparing its rates to state level HPV vaccine rates.

4.3 END OF STUDY DEFINITION

This study will end when the minimum number of participants (400 participants) for analyses is recruited. The protocol will be closed once data analysis and publications have been completed.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Denver Health Patients:

1. Be a Denver Health patient* 18-26 years old, who has not started or completed the HPV vaccine series (Vaccine completion for this age group is 3 doses).
2. Be a parent of a Denver Health adolescent patient* aged 9-17 years old (), who has not started or completed the HPV vaccine series. (Vaccine completion is 2 doses for 9-14-year-old, and 3 doses for 14-17-year-old)
3. English and/or Spanish Speaking
4. Stated willingness to comply with all study procedures and be available for the duration of the study.

   * Denver Health patients will be identified from one of the following clinics: Denver Health Clinics Eastside Adult Clinic, Eastside Women's Care Clinic, Westside Adult Clinic, Westside Women's Care Clinic, Pavilion C: Women's Care Clinic, La Casa-Quigg Newton Family Health Center, Lowry Family Health Center, Montbello Family Health Center, Westwood Family Health Center, Parkhill Family Health Center, Webb Center For Primary Care, Pena Southwest Clinic

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Individuals who do not meet eligibility criteria, including individuals who do not speak English or Spanish [at the discretion of the CHE or PN upon recruitment]
2. Decisionally-challenged adults with cognitive or personality impairment or due to intoxication (alcohol or drugs) that might interfere with their ability to consent or participate in the study [at the discretion of the CHE or PN upon recruitment]
3. Individuals from vulnerable populations (e.g., inmates, homeless, pregnant women, and those with auditory impairment [at the discretion of the CHE or PN upon recruitment]
4. Individuals under the age of 18 years.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

HPV Educational Intervention: To recruit participants we will distribute flyers regarding our educational events about HPV and the HPV partnering with each outpatient clinics at DHHA.Additionally, The PN and CHE will be fully onboarded at DHHA to access patient records, including upcoming clinic visits to identify potential participants who are eligible for the HPV vaccine. Thus, the PN will be able to call participants that meet the eligibility criteria and will recruit them to participate in the study. All participants will be identified through their own patient record. Young adults (18–26-year-old) will be contacted directly and invited to participate in the study. For individuals under the age of 18 (9–17-year-old), we will use the patient's record to obtain parent contact information and invite the parent to participate in the study. Parents might indicate having additional children that are older than 18 years of age when completing surveys. For those parent participants we will capture vaccinations status on all their children aged 9-26, even if those children are not DH patients. However, the survey will not collect any PHI on children from parent participants, only vaccinations status. To assess uptake of the HPV vaccine from children participants and young adult participants, we will use their DH medical record number to determine vaccination status after the educational and patient navigation intervention has been delivered. Additionally, for parent and adult participants, who volunteer to participate, we will collect name, phone number, mailing address, and email address for follow up at 3- and 6-months intervals if they report not having been vaccinated themselves or their eligible aged children (9-17) at baseline and/or at the 3-month follow up interval.

In order encourage participants to answer our surveys, we will incentivize them by compensating them with a $25 gift for filling the post-education survey at baseline.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

The educational intervention to be delivered by the CHE consists of "toolkit education materials" developed by the National Cancer Institute (NCI) and a small media intervention (i.e., video) that our research team has developed. The NCI-produced toolkit education materials consist of Power Point presentations, flyers, and posters that contain information about HPV, HPV-related cancers, and the importance of the HPV vaccine series for adolescents (9-17 years old) and young adults (18–26-year-old) who are eligible for the vaccine.

6.2 STUDY INTERVENTION COMPLIANCE

Study participants who volunteer to participate in this study will be asked to comply with the following interventions strategies:

1. Watch or participate in approximately a 45-minute educational session conducted by the CHE.
2. Receive a referral to the PN if they and/or their children are eligible for the HPV vaccine but have not completed all the recommended HPV vaccine series doses.
3. Receive navigation for the number of HPV vaccine series doses needed until completion.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION (STUDY STOPPING RULES)

The Sponsor-Investigator has the right to terminate this study at any time. Reasons for terminating the study may include, but are not limited to, the following:

- The incidence or severity of adverse events in this or other studies indicates a potential health hazard to patients.
- Patient enrollment is unsatisfactory.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM STUDY

Participants are free to withdraw from participation in the study at any time upon request.
In addition, the investigator has the right to withdraw a patient from the study at any time. Reasons for withdrawal from the study may include, but are not limited to, the following:

- Patient withdrawal of consent at any time
- Any medical condition that the Sponsor-Investigator determines may jeopardize the patient's safety if he or she continues in the study.
- Sponsor-Investigator determines it is in the best interest of the patient
- Patient non-compliance

Every effort should be made to obtain information on patients who withdraw from the study. The primary reason for withdrawal from the study should be documented on the appropriate eCRF.

7.3 LOST TO FOLLOW-UP

The evaluation of the educational intervention occurs at baseline during the post education survey. Our sample size of 200 will achieve 80% power the moment the 200th participant completes the post survey at baseline. Thus, lost to follow-up is not a concern in our study. Follow-up is only to capture vaccination status, as well as to facilitate patient navigation if it applies. Furthermore, follow-up will only occur for some participants. Only those that indicate at baseline not being vaccinated themselves or indicate being parents of children that have not been vaccinated will be contacted at 3 months post baseline. Similarly, only those that indicate not being vaccinated themselves or indicate having children not being vaccinated at 3 months post baseline will be contacted at 6 months post baseline. For those that are contacted at 3 months and 6 months, we will make a maximum of 6 contacts (e.g., phone calls, texts, or letters) to each consented participant. After 6 unsuccessful contact attempts, we will consider participant as "lost to follow up" and no longer make attempts to contact them.

8 STUDY PROCEDURES

8.1 STUDY PROCEDURES/EVALUATIONS

The CHE's will deliver evidence-based educational material (i.e., toolkits) via one-on-one sessions to a total sample of 400 participants. Participants will be given the option to have the education presented over the phone or via zoom. The CHE will use educational materials on HPV, HPV-related cancers, and the HPV vaccine and to motivate participants to initiate and complete the HPV vaccine. The CHE will administer post education surveys to participants. Educational material will be presented separately in English or in Spanish. Participants will be invited to participate in their preferred language. Name, telephone number, address will also be collected in order to administer the follow-up calls. Participants will be given a $25.00 gift card for completing the post education survey.
Those that choose to participate in the evaluation process of the education materials will complete the informed consent process and complete the immediate post education survey. Those that indicate not being vaccinated on the immediate post education survey will be contacted to participate in the 3-month follow up survey. If participants missed a scheduled vaccine dose or indicate they have not been vaccinated at 3 months, they will be contacted again at 6 months for follow up.

Additionally, the PN will refer those that are interested in receiving the HPV vaccine to the PN. During the delivery of the PN intervention, the PN will track participants that a) receive a 1st dose, 2nd dose, or 3rd dose of the HPV vaccine; and connections to care by recording the number of services provided including (b) patients connected to health insurance, discount or no-cost HPV vaccine programs; or (c) other services to facilitate HPV vaccine dose completion (e.g., language translation, appointment scheduling assistance, transportation services, childcare).

We will track HPV vaccine doses at the patient-level and rates at DHHA clinics to the access the system-level impact of the interventions on increases overall HPV vaccination rates for adolescents (9-1\7 years old) and young adults (18-26) in the respective DHHA clinics. Our goal is to conduct the educational sessions and the post education survey in person. However, current circumstances as a result of the COVID-19 outbreak require we execute our educational sessions remotely. We will send educational material to be watched via REDCap links or present the materials over Zoom or over the phone. Secured REDCap links will be used to obtain the post education survey. We will also use REDCap to obtain any PHI needed to for follow up.

Post education surveys will be physically mailed, without any PHI, to the NCI after we have uploaded and stored the surveys in REDCap.

8.2 STUDY SCHEDULE

8.2.2 ENROLLMENT/BASELINE

Enrollment will occur at the educational sessions s to be hosted by CHE's to eligible DHHA patients.

8.2.3 INTERVENTION VISITS

Participants who indicate that either their adolescent children or they have not completed the HPV vaccine series at baseline, they will be refer to the PN intervention to schedule the needed HPV vaccine dose. Participants whose children or them missed the HPV vaccine dose appointment will receive a recall text or phone call to reschedule another vaccine appointment.

8.2.4 FOLLOW-UP VISITS

If participants indicate that their children or they have not completed the HPV vaccine series at 3-months and 6-months, they will be schedule for the HPV vaccine dose needed, and if they missed receiving it, they will be followed through a recall text or call to reschedule to receive the missed dose.

8.2.5 EARLY TERMINATION VISIT

If participants who receive the CHE education intervention indicate that their children or they have completed all the HPV vaccine doses recommended for them, they be terminated from receiving the PN intervention. Participants who are referred to the PN intervention to receive a needed HPV vaccine dose, will be terminated for further PN intervention if they complete the HPV vaccine series at the 3-month or 6-month follow-up period.

8.2.6 SCHEDULE OF EVENTS TABLE

HPV Educational Intervention and Data Collection	Baseline/ Intervention			Recall upon missed dose	Quarterly
Informed Consent	X				
Post-education (baseline survey)	X				
Gift card compensation	X				
PN vaccine referral/navigation	X			X	
PN vaccine follow-up/navigation				X	X
Clinic Assessment of HPV vaccination rates EMR system					X

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8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

NA

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

NA

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

NA

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

NA8.3.3.3 EXPECTEDNESS

NA

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

NA

8.3.6 SERIOUS ADVERSE EVENT REPORTING

NA

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UAP)

NA

8.4.2 REPORTING OF UNANTICIPATED PROBLEMS

NA

9 STATISTICAL CONSIDERATIONS

9.2 SAMPLE SIZE DETERMINATION

A sample size of 200 participants achieves 80.0% power to reject the null hypothesis of zero effect size (i.e., improvement in, HPV and HPV vaccine knowledge, and HPV vaccine intentions' scores) when the Cohen's effect size is 0.20 (small effect size)[34] and the significance level is 0.050 using a two-sided one sample paired t-test.

9.3 POPULATION FOR ANALYSES

The population for analyses will constitute all patients at DHHA who are parents of adolescents aged 9 to 17 years old who are eligible for the HPV vaccine series, as well as young adults ages 18 to 26 years old who are also eligible for the HPV vaccine series.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The effects of the education intervention on the primary outcomes measured by the continuous scales regarding, HPV and HPV vaccine knowledge, and HPV vaccine intentions, will be assessed using two-sided one-sample paired t-test for the null hypothesis that the paired difference is 0 against the alternative hypothesis that the paired difference is not 0. Appropriate transformation and/or the non-parametric Wilcoxon test will be performed if the data suggests severe non-normality. The significant level is 0.05.

Exploratory analysis of the characteristics that influence participants' adherence (0=non-adherent; 1=adherent) to the recommended HPV vaccine dosage will be conducted use logistic regression analysis. Our analyses will adjust for co-variates that likely influence the primary outcomes and exploratory outcomes, which include prior HPV vaccine dosage. We will also adjust for other potential co-variates if our descriptive analysis suggests this may be needed. Summary descriptive statistics will be calculated and presented for all primary, exploratory outcomes for all participants, and for subgroups defined by participants predisposing (e.g., gender, age), enabling (e.g., insurance, barriers), and need (e.g., cancer risks) characteristics. The demographic characteristics of the participants will be presented with descriptive statistics also. The means, medians and the 95% confidence intervals will be calculated for continuous variables; the frequencies, estimated rates, and the exact 95% confidence intervals will be calculated for the binary and categorical variables.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent form describing in detail the study procedures, and risks are provided to the participant. Completion of the informed consent process is required prior to starting intervention/ administering study product.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent process will be initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families.

Consent forms will be IRB-approved, and the participant will be asked to read and review the document. The consent process will occur over the phone. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Consent will be reviewed prior to participants receiving in any of the educational materials and before completing the surveys. The consent form will be read, and clarification will be confirmed, and questions will be addressed as needed. Participants will have time to review the consent prior to deciding if they would like to participate and will verbally acknowledge understanding and willingness to participate in the study prior to any procedure being done specifically for the study. We are unable to hold in person meetings due to COVID-19 restrictions. At this point in time those restrictions will remain indefinitely. Hosting virtual education sessions requires a high level of computer and technological literacy that has become a barrier to enrollment. Similarity, asking patients to complete a consent form that requires a digital e-signature and join a zoom call is too cumbersome and creates a barrier to enrollment. Thus, we will use a postcard consent that will be sent via text or email or will otherwise be made available to the subject in advance of the informed consent discussion. The participants may withdraw consent at any time throughout the course of the trial. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

The study allows the inclusion of non-English speaking and non-reading participants. Witnesses to these consent processes will be individuals not associated with the trial and will not have a conflict of interest.

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor-investigator(s) and their agents. This confidentiality is extended to cover the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor, other authorized representatives of the sponsor-investigator, or representatives of the IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the University of Colorado Cancer Center. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by the University of Colorado Cancer Center, research staff will be secured, and password protected. At the end of the study, all study databases will be de-identified and archived at the University of Colorado Cancer Center.

10.1.4 FUTURE USE OF STORED SPECIMENS OR DATA

- **Intended Use:** Data collected under this protocol will only be used to complete the scope of this project.
- **Storage:** Data will be stored using codes assigned by the investigators. Data will be kept in password-protected computers. Only investigators will have access to the samples and data.
- **Tracking:** Data will be tracked using REDCap.
- **Disposition at completion of the study**: No samples will be collected in this study.

10.1.5 SAFETY OVERSIGHT

The principal investigator will be responsible for the conduct of this study, overseeing participant safety, executing the data and safety monitoring (DSM) plan, and complying with all reporting requirements to local and federal authorities. This oversight will be accomplished through additional oversight from the Data and Safety Monitoring Committee (DSMC) at the University of Colorado Cancer Center (CU Cancer Center). The DSMC is responsible for ensuring data quality and study participant safety for all trials at the CU Cancer Center. A summary of the DSMC's relevant activities is as follows:

- Conduct of internal audits
- May submit recommendations for corrective actions to the CU Cancer Center's Executive Committee

Study audits conducted by the DSMC will consist of a review of the regulatory documents, consent forms, and source data verification. Documentation of the audit conducted by the DSMC will then need to be submitted to the IRB of record at the time of the IRB's continuing review of this trial (if applicable).

10.1.6 CLINICAL MONITORING

Risks to patients include the potential loss of confidentiality if identifiable study data are inappropriately disclosed. However, several steps will be taken to prevent this: Patients will be given a coded identifier for research purposes which will be stored with identifier data separate from research data. We will use best practices for IT based security such as utilizing OIT supported hardware and software, the use of VPNs to access research data, the use of REDCap whenever possible, the use of secure data transfer protocols, and access and change logging which will be reviewed monthly for any aberrant activity. We have experience in implementing such enterprise security processes for similar uses; however, we anticipate we will work closely with OIT to ensure that the design and implementation of these systems mitigate the risk of loss of confidentiality.

10.1.7 QUALITY ASSURANCE AND QUALITY CONTROL

Quality Control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/ resolution.

Following written SOPs, the study monitor will verify that the clinical trial is conducted, and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements.

The investigational site will provide direct access to all trial-related sites, source data/ documents, and reports for the purpose of monitoring and auditing by the DSMC audit team, and inspection by local and regulatory authorities.

10.1.8 DATA HANDLING AND RECORD KEEPING

10.1.8.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant's official electronic study record.
Data will be entered into REDCap. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.8.2 STUDY RECORDS RETENTION

There is no plan to destroy study data.

10.1.9 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or SOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly. These practices are consistent with ICH E6, sections:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3.
- 5.1 Quality Assurance and Quality Control, section 5.1.1.
- 5.20 Noncompliance, sections 5.20.1 and 5.20.2.

It is the responsibility of the study team to use continuous vigilance to identify and report deviations. All deviations must be addressed in study source documents, reported to COMIRB. Protocol deviations must be sent to the local IRB per institutional guidelines. The site PI/ study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the -SOP and/or study procedures manual.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will ensure that the public has access to the published results of this research.

10.1.12 CONFLICT OF INTEREST POLICY

Independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed.by the University of Colorado Denver's (UCD) Office of Regulatory Compliance Conflict of Interest and Commitment Management (COIC) program. Persons with a perceived conflict of interest will have such conflicts managed in a way that is appropriate to their participation in the trial. Conflict of Interest management plans are project-specific and are reviewed at least annually. UCD has integrated the institutional conflict of interest management program with its existing program.

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