Relational Agents in Cervical Cancer Education (RACE): Phase II

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B. **TITLE:** Relational agents in cervical cancer education: Phase II

C. OBJECTIVE:

Primary objective: To determine the feasibility of a relational agent based interactive intervention in educating cervical cancer patients about HPV and HPV vaccine implementation in their families and communities by measures of rate of participation and rate of completion of survey.

Secondary objective: To examine pre and post test measures separately by arm in exploratory analysis of:

- Intention to discuss HPV vaccination with families
- Health literacy
- Behavior control, Social norms
- Stigma

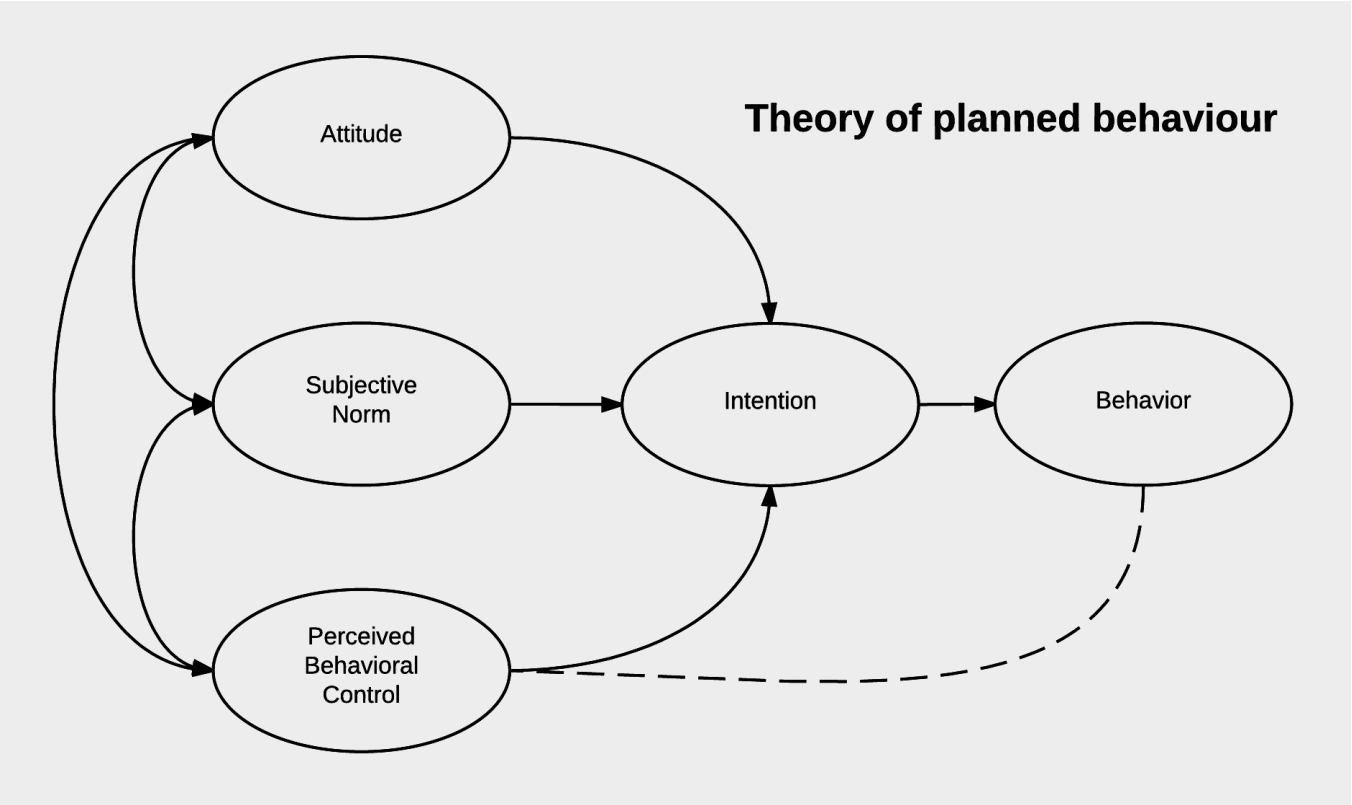
D. BACKGROUND AND SIGNIFICANCE:

According to the Centers for Disease Control and Prevention (CDC) in the United States, high-risk human papilloma virus (HPV) accounts for about 43,000 HPV-related cancers each year (CDC). HPV is the etiologic agent for 91% of all cervical, 70% of all oropharyngeal, 91% of anal cancers [1]. Black and Hispanic women have higher rates of HPV associated cervical cancers than women of other races. While the rates of cervical cancer have continued to decrease by 1.6% per/year between 1999-2015, the rates of oropharyngeal cancers have increased by 2.8% per year among men and 0.6% per year among women. This increase is largely due to the increase in HPV related oro-pharyngeal cancers [2]. The CDC estimates that 92 percent of all HPV associated cancers are attributable to the HPV types that are included in the HPV vaccine and could be prevented if HPV vaccine recommendations were followed. HPV vaccination is recommended in all adolescents starting at age 9-26. Since Oct 2018 the CDC has extended the recommended age for vaccination to age 45. We are far short of the Healthy People Goal of 80% vaccination, with recent data reporting vaccination completion rates of 49% amongst adolescents between 13-17 years of age [3].

We hypothesized that cervical cancer survivors armed with the correct tools could serve as community health educators and advocates for HPV vaccination within their social networks. Our preliminary data in a survey of cervical cancer survivors (unpublished survey data collected from Geisinger Health cervical cancer survivors by Larson et al), 82% reported that they had a conversation with family members about their cancer. Among those responding to the survey, about 66% reported a discussion about the kind of cancer, however only 36% reported having a conversation about the cause of their cancer, and 29% reported discussing an important prevention strategy, HPV vaccination. Among survey respondents who did discuss cancer with their family, 38% reported that they had not had a conversation with their doctor about the connection between HPV and cervical cancer. Moreover, among these same participants, 21% did not know about the Gardasil vaccine. Pt additionally identified embarrassment and fear of judgement (stigma) as reasons for not discussing their diagnosis with family members.

Based on this gap in the data and the potential of therapeutic benefit, the proposed pilot project will explore effective strategies to educate survivors of an HPV related disease (cervical cancer) in a racially diverse urban cancer care setting. One promising strategy is the use of relational agents (RAs). RAs simulate face-to-face counseling sessions with health providers using speech and animated nonverbal behavior such as hand gestures and facial displays. In prior research conducted by Dr. Bickmore's team, the RA has been shown to be an acceptable, user-friendly, highly accessible, and effective patient education and counseling system, especially with older adults, racially diverse populations and patients with limited health literacy.[4-7]

The proposed work is guided by the theory of planned behavior which suggests that one's intention to engage in a behavior (i.e. discussing HPV vaccination) is directly influenced by ones attitude about the behavior (vaccine hesitancy, stigma), perceived subjective norms (what value their physician placed on HPV vaccination), behavioral control (their ability to discuss vaccination) and self-efficacy. These individual domains will be assessed on the HPV pre/post survey.



E. ELIGIBILITY AND RECRUITMENT

Inclusion Criteria:

- Adults age 18 and older
- Patients with an ICD9 diagnosis of cervical/vaginal/vulvar cancer or dysplasia receiving care at Karmanos Cancer Institute or OU Health Stephenson Cancer Center

Exclusion Criteria:

- Patients who are recorded in the EHR as requesting to be removed from research.
- Non-English speakers.
- Any cognitive disability that prevents informed consent
- Any individual recruited in previous phases of the Study will be excluded.

F. METHODS:

Procedures:

Patients who are seeking care at the gynecologic oncology clinic at Karmanos Cancer Institute or the Stephenson Cancer Center with a diagnosis of cervical cancer will be identified. A waiver of consent to pre-screen potential eligible patients will be utilized to better identify these individuals. Research assistants will be trained by investigators to identify and approach potential participants in clinic. Potential participants will be approached by the RA's and asked if they would like to hear more about the study. If the individual expresses interest, the RA will invite her to a private space on site and further describe the study, answer questions or concerns and obtain informed consent. Sixty cervical cancer patients, 30 from each site, will be enrolled into two arms (with-RA arm: 30 patients and without-RA arm: 30 patients). Patients in the RA arm will view a relational agent video on a tablet. The entire video will take approximately 15-20 minutes depending on patient level of engagement. Patients in the control group will receive a standardized handout on HPV and vaccine education which should similarly require 10-15 minutes. All participants (standard and RA group) will complete the HPV Vaccine/Cervical Cancer Knowledge and Attitude Survey (see attachment, HPV Survey1 and 2) pre and post intervention. Surveys have been designed to assess demographics, HPV education, vaccine hesitancy, subjective norms, intention, behavioral control, attitude towards HPV vaccination, health literacy and stigma based on the theory of planned behavior as measures of our secondary objectives. Participants will receive a gift card for $5 for each survey at the end of their completion of both the pre and post surveys. Patients will be asked to allow us to send them a f/u survey (see attachment, HPV follow-up survey) via either a link by email or paper copy (with return envelope and stamp provided) by mail six weeks post-intervention to assess follow through. An additional $5 will be mailed to the participant upon receipt of the survey. After completing the follow-up survey, 20 participants (roughly 10 from each site) will have the potential to complete a final in-depth interview over the phone to provide further feedback. Interviews will be audio recorded for clarity and further analysis. Potential participants will be identified by the study personnel. Upon completion, participants will be mailed final $10 gift card. RA's will be trained to observe and record issues related to feasibility, the informed consent process and clarity of survey which will be discussed by the study team. We anticipate approximately a 50% response to the follow-up survey. The initial survey questions given to the focus group follow a questionnaire previously devised and administered by Dr. Larson for an adolescent HPV vaccination and attitude survey.

Risks and Benefits: Risks include potential emotional distress or discomfort from discussion of personal information, heath issues and cancer care. Research assistants will remind participants of the voluntary nature of the research and that participants have the right to not answer specific questions and may withdraw from the study at any time and for any reason.

Measures (see Qualtrics survey block questions):

- Demographics: age, race/ethnicity, income, family members, religious affiliation, education.
- Social norms will be assessed with 4 items assessing cervical cancer related injunctive norms and descriptive norms.
- Behavioral control- level of control and ease or difficulty in receiving HPV vaccine (vaccine hesitancy)
- HPV knowledge
- Health literacy
- Stigma

G. DATA MANAGEMENT AND CONFIDENTIALITY

The current study will provide the same level of confidentiality as is standard with medical information. All participants will be assigned a numeric code so they cannot be identified in publications and presentations. While the specific participant will not be identified, pre, post and follow-up surveys from the same patient will be compared before and after the intervention. Patient permission will be requested to mail out surveys at 6 weeks to assess follow through with HPV vaccination discussion. Research records (electronic survey data) will be kept on a secure shared drive and be encrypted and password protected. Only the PI and the study team will have access to these records. The PI will secure an encrypted, password protected electronic cross-referenced file that will link numeric codes with participants consent forms. No investigational drugs will be administered, and no investigational devices will be used.

H. STATISTICAL CONSIDERATION

Objectives

The primary objective is to determine the feasibility of a relational agent based interactive intervention in educating cervical cancer patients about HPV and HPV vaccine implementation in their families and communities by measures of rate of participation and rate of completion of survey.

The secondary objectives are to examine the change from pre to post/follow-up intervention survey as exploratory analysis separately by arm:

1. To examine the change in intention measures in pre and post intervention surveys and between pre and follow-up surveys separately by arm.
2. To examine the health literacy of women with cervical/ vaginal cancer in regards to their knowledge of the HPV virus and prevention in pre and post intervention and follow-up surveys separately by arm.
3. To examine the change in social norms and behavioral control measures in pre and post intervention surveys separately by arm.
4. To examine change in stigma measures in pre and post intervention surveys separately by arm.

Measurable variables

The primary measurable variables of interest are the rate of participants and that of survey completion, which will be defined as the ratio of the number of participants to the number of patients who were asked to join the study and the ratio of the number of patients who complete the survey to the number of participants, respectively. The secondary measurable variables are changes from pre to post/follow-up intervention survey for (i) intention to discuss HPV vaccination with families, (ii) health literacy (such as HPV knowledge), (iii) behavior control and social norms, and (iv) stigma. The other measurable variables of interest are patient demographics (age, race, income, etc.).

Sample size and power justification

The study has two parallel arms: with-RA arm and without-RA arm and the patients will be recruited for each arm simultaneously and using randomization. The without-RA arm is needed to estimate an effect size for the future main trial. The sample size was not formally justified and but decided based on several factors: resources and pilot two-arm study. In particular, we desire to have a medium effect size (0.5) for the future main trial with 90% power at a 2-sided 5% level. Thus, according to Whitehead et al. (Statistical Methods in Medical Research, 2016; 25(3): 1057-1073), we plan to have 15 patients per arm, yielding a total of 30 patients who will enter the study. The required number of eligible patients to be asked is estimated according to the expected rates of participants in order to accrual 30 patients (= 15 patients x 2 arms) in Fig. 2. For example, if the expected participation rate is 0.5, 60 eligible patients should be asked to join the study in order to enroll 30 patients.

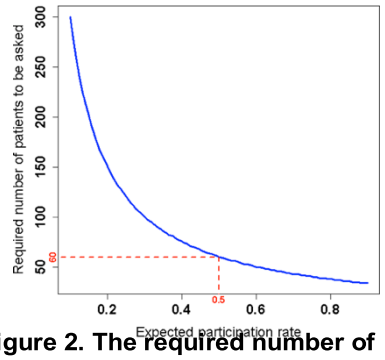


Figure 2. The required number of eligible patients to be asked by the expected participation rate.

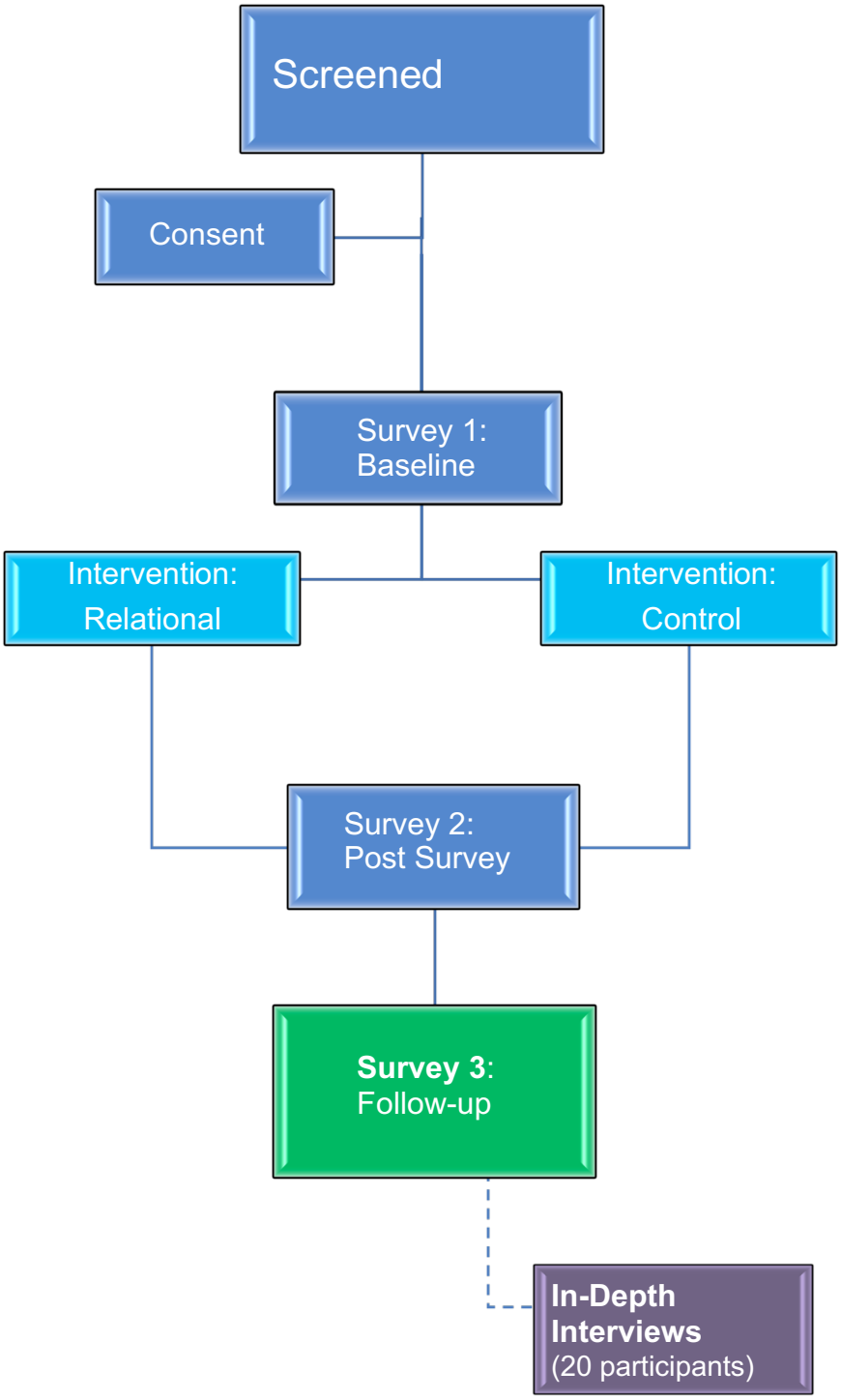
Analysis

Patient baseline characteristics will be summarized by count and percentage for categorical variables and median and range for continuous variables, separately by groups. The numbers of participants and survey completion will be summarized descriptively with count, percentage, and confidence interval, separately by arm (only for survey completion). The change of each of secondary endpoints will be summarized with mean, median, standard deviation, and confidence interval after, if needed, data transformation, separately by arm. In particular, the rate of survey completion will be calculated for each survey separately by arm.

Expected accrual and study duration

During a two-year period (across from 2015 to 2017), ~300 eligible patients were seen at Karmanos Cancer Institute (KCI) with either cervical dysplasia or cervical cancer (i.e., ~150 eligible patients per year with 4 gyn-oncologists). We conservatively estimate the accrual rate at KCI with 20% variation, yielding an expected number of at least 120 eligible patients per year (= ~150 patients per year x 80%). We also anticipate that the participation rate will be at least 50%, thus requiring 60 eligible patients to be asked for the study population of 30 patients. The expected accrual duration is therefore 8 months (= 60 eligible patients x 12 months / 120 patients). Considering additional 6 months for IRB approval and data analysis, the expected study duration is 14 months.

STUDY SCHEMA:



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