Examples of Funded Grants in Implementation Science

Overview
The National Cancer Institute (NCI) frequently receives requests for examples of funded grant applications. Several investigators and their organizations agreed to let Implementation Science (IS) post excerpts of their dissemination and implementation (D&I) grant applications online.

About
We are grateful to the investigators and their institutions for allowing us to provide this important resource to the community. To maintain confidentiality, we have redacted some information from these documents (e.g., budgets, social security numbers, home addresses, introduction to revised application), where applicable. In addition, we only include a copy of SF 424 R&R Face Page, Project Summary/Abstract (Description), Project Narrative, Specific Aims, and Research Strategy; we do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., performance sites, key personnel, biographical sketches).

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424 R&R and PHS-398 Specific

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SF 424 R&R Face Page

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Grant Number: 1 R21 CA231180-01A1

Title: Improving HPV Vaccination using Implementation Strategies in Community Pharmacies

FOA: PAR18-017 Clinical Trial:Optional

FOA Title: Dissemination and Implementation Research in Health (R21 Clinical Trial Optional)

Organization: UNIV OF ARKANSAS FOR MED SCIS

Department: Pharmacy Practice

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Organization: University of Arkansas for Medical Sciences

Role Category: PD/PI

Project Summary/Abstract

Human Papillomavirus (HPV) is the most common sexually transmitted infection currently affecting nearly 80 million people in the United States. Southern states have disproportionately high incidence rates of HPV-related cancers; Arkansas has the highest incidence rate (14.4 per 100,000) in the US. Vaccines exist to protect against the cancer-causing strains of HPV and are recommended for all children beginning at age 11, but vaccination rates remain low. Vaccines For Children (VFC) is a program administered by the Centers for Disease Control and Prevention (CDC) that provides free vaccines to providers for administration to children at no charge. All children under age 18 and enrolled in Medicaid or uninsured are eligible. Despite the strong reach potential afforded by access to free vaccines, participation in the South is low; only 4% of Arkansas physicians are VFC providers and local health departments are the sole resource of VFC vaccines for 20 of 75 Arkansas counties. To improve the reach potential of the VFC program (and thereby HPV vaccination) in the Southern US, this application will explore the use of community pharmacies as HPV vaccination sites.

Community pharmacies are highly accessible when compared to “traditional” vaccination sites due to their extended hours in evening and on weekends, no copays for visits, and no requirement to schedule an appointment to speak with a pharmacist. Pharmacists can administer vaccines to children aged 7 and older as long as certain requirements are met, all of which include physician oversight. This application proposes a variety of potential “collaboration models” which can be utilized by pharmacists and physicians interested in providing more HPV vaccines. One example is a “shared responsibility model” in which the first dose of the vaccine is administered in the physician’s office while the second dose is administered in the pharmacy. This study will use implementation science to determine and pilot-test a promising vaccine-delivery partnership model between pharmacists and physicians and an array of supportive implementation strategies to support uptake and sustainability of HPV vaccine provision in the community pharmacy setting. The following specific aims are proposed: Aim 1) Identify barriers and facilitators to community pharmacies’ provision of HPV vaccine through a mixed methods design with pharmacy staff members and local physicians; Aim 2) Select a pharmacist-physician collaborative model and identify implementation strategies through an Evidence Based Quality Improvement (EBQI) process with key stakeholders; and Aim 3) Pilot the selected pharmacist-physician collaborative model and implementation strategies in two pharmacies (1 rural, 1 urban) and evaluate on relevant implementation outcomes. The long term goal of this project is to improve HPV vaccination rates among adolescents in the US, especially in rural and underserved areas. Results from this study will provide the foundation for a large cluster-randomized implementation trial that will include multiple community pharmacy contexts - large and small, urban and rural, and chain- and independently-operated.

Project Narrative

This pilot study aims to utilize implementation science methods to: 1) conduct a developmental formative evaluation of potential barriers and facilitators associated with increasing HPV vaccinations in community pharmacies, 2) design a partnership model between physicians and pharmacists and determine implementation strategies through a collaborative process known as Evidence Based Quality Improvement, and 3) evaluate the model and strategies by measuring relevant implementation outcomes. The pilot of the partnership model and implementation strategies will take place over a period of one year with an opportunity to adapt and modify after 6 months. The ultimate goal of this application is develop care coordination between physicians and pharmacists to improve HPV vaccination rates among adolescents - especially those who live in rural, underserved areas where immunization providers are scarce.

Specific Aims

Human Papillomavirus (HPV) is the most common sexually transmitted infection currently affecting nearly 80 million people in the United States.[4,5] Approximately 14 million people become newly infected each year and almost every person will acquire an HPV infection at some time in their life.[4,5] HPV infection causes cervical, vaginal, and vulvar cancers in women; penile cancers in men; and oropharyngeal and anal cancers in both men and women.[6,7] An estimated 19,200 women and 11,600 men are diagnosed with cancer caused by HPV infection each year.[8] The Southern US has a disproportionately high incidence of HPV-related cancers; **Arkansas has the highest incidence rate of cervical cancer for women (11 per 100,000) and the highest incidence rate of HPV-related cancers (14.4 per 100,000)**.[9]

Since 2006, three vaccines (Gardasil, Gardasil-9, and Cervarix) were FDA-licensed and recommended as a three-dose series beginning at age 11. Recently, this recommendation has been changed to a two-dose series for patients who receive their first dose before their 15th birthday and as of May 2017, only Gardasil-9 is available in the US. Although this change has promise to increase vaccine series completion rates, **current rates for adolescents completing the vaccine series fall far short of the Healthy People 2020 goal of 80%**. Current national HPV vaccination rates estimate that 41.9% of females and 28.1% of males complete the series.[10] While national vaccination completion rates are low, they are significantly lower in the American South, particularly in Arkansas (34% for females; 16.4% for males).[10,11]

Vaccines for Children (VFC) is a program administered by the Centers for Disease Control and Prevention (CDC) that provides free vaccines to providers for administration to children at no charge. All children under the age of 18 and enrolled in Medicaid or uninsured are eligible. For providing the vaccine, a provider earns an administration fee from the Centers for Medicare and Medicaid Services (CMS). **Participation in the program is low, especially in southern states; only 4% of the Arkansas' physicians are VFC providers and local health departments are the sole resource of VFC vaccines for 20 of Arkansas' 75 counties**. Additional steps need to be taken to improve access for the more than 304,000 Arkansan children on Medicaid and an additional 35,000 children estimated to be uninsured.

Pharmacists have been able to provide vaccinations since 1996, and a large majority of community pharmacies report administering vaccines in their practices. A 2013 survey found 86% of responding community pharmacies provided immunizations.[12] Most of the focus in community pharmacy has been on influenza vaccine but they also administer pneumococcal (77%), herpes zoster (75%), and tetanus (57%) vaccines.[12-14] A 2018 study estimated that 6.2 million additional influenza immunizations and 3.5 million additional pneumococcal immunizations are attributable to pharmacy-delivered vaccinations, annually.[15] Nevertheless**, HPV vaccine is not one of the vaccines usually kept in stock or offered widely**; only 37% of community pharmacies are estimated to have administered the vaccine (at least once) in the US.[12] Despite overwhelming need in Arkansas, pharmacy participation in the VFC program **is virtually non-existent**. In Arkansas, there are currently zero pharmacies participating in VFC and less than 15 going through the process to become providers. **This is an implementation problem that requires attention**.

We propose to address the problem by initiating a research agenda focusing on how best to utilize community pharmacies as VFC vaccination sites. Community pharmacies are highly accessible when compared to traditional vaccination sites due to extended evening and weekend business hours, no copays for visits, and no appointment required to speak with a pharmacist.[13] This makes community pharmacies potentially attractive for adolescents who do not frequently visit primary care physicians and/or live in rural, underserved areas where immunization providers are scarce. For this research we propose 3 specific aims:

Specific Aim 1: Identify barriers and facilitators to community pharmacies' provision of HPV vaccine through a mixed methods design with pharmacy staff members and local physicians.

Specific Aim 2: Select a pharmacist-physician collaborative model and identify implementation strategies through an Evidence Based Quality Improvement (EBQI) process with key stakeholders.

Specific Aim 3: Pilot the selected pharmacist-physician collaborative model and implementation strategies in two Harps pharmacies (1 rural, 1 urban) on relevant implementation outcomes.

The long term goal of this project is to improve HPV vaccination rates among adolescents, especially in the Southern US. To reach this goal, results from this project will provide the foundation for a large implementation trial to NCI (R01; PAR-18-007). By utilizing community pharmacies as VFC vaccination sites, this project has the potential to expand access to VFC vaccines, develop care coordination between physicians and pharmacists, increase vaccination rates among low income, underserved adolescents, and improve public health.

Research Strategy

BACKGROUND AND SIGNIFICANCE

Human Papillomavirus (HPV): Inadequate Immunization: HPV-associated cancers remain a public health problem. An estimated 19,200 women and 11,600 men are diagnosed with HPV-caused cancer each year in the US, with cervical cancer being the most common.[4,8] Disparities for racial, socioeconomic, and geographic subgroups are concerning with incidence and death rates higher among black, low-income, rural women, particularly in the Southern US. Arkansas has the highest incidence rate of cervical cancer for women (11 per 100,000) and the highest incidence rate of HPV-related cancers overall (14.4 per 100,000) in the US.[9]

Since 2006, three vaccines (Gardasil, Gardasil-9, and Cervarix) were FDA-licensed and have been shown to be nearly 100% effective at preventing precancerous genital lesions attributable to the specific HPV types.[16,17] Guidelines recommended that both girls and boys receive one of these vaccines in a three-dose series beginning at age 11.[16,17] This recommendation was recently updated to a two-dose series for patients who receive the first dose before their fifteenth birthday.[18] Although this change could contribute to an increase in vaccine series completion rates, immunization rates for US adolescents getting at least 2 doses of the vaccine fall far below the target rate of 80% identified by Healthy People 2020.[19] The HPV vaccination rate for 13-17 year old females who received at least 1 dose of HPV vaccine is 62.8% while series completion rate is only 41.9%.[10] These rates are even lower among male adolescents (49.8% initial dose; 28.1% completion rate).[10] In Arkansas, estimated vaccination series completion rate is 34% for females and 16.4% for males.[10,11] Recognizing the severity of this problem, several state-wide groups have been created to facilitate increased delivery of HPV vaccines, including the Arkansas Immunization Action Coalition's HPV Work Group and the Arkansas Cancer Coalition's Cervical Cancer Task Force. Leaders from both groups are study partners (see letters from Dr. Dillaha, Chair of the Arkansas Immunization Action Coalition and Cervical Cancer Taskforce and Dr. Vinson, Vice President of Practice Innovation at the Arkansas Pharmacists Association).

Access to Vaccines For Children (VFC) Providers: VFC is a program administered by the Centers for Disease Control and Prevention (CDC) that provides free vaccines, including HPV, to providers for administration to children at no charge. All children under the age of 18 and enrolled in Medicaid or uninsured are eligible. For providing the vaccine, providers earn an administration fee from the Centers for Medicare and Medicaid Services (CMS). Despite the strong reach *potential* afforded by access to free vaccines, participation in the VFC program is low in the South, especially in Arkansas. Only 4% of Arkansas physicians are VFC providers and local health departments are the sole resource of VFC vaccines for 20 of Arkansas' 75 counties. According to the Arkansas Department of Health, wait times to receive a VFC vaccination can be 3 to 4 months.[20] In an attempt to improve the reach of the VFC program (and thereby HPV vaccination) in Arkansas to the 300,000+ eligible children, this project proposes community pharmacies be used as HPV vaccination sites. We expect underserved areas will benefit greatly from this increased access, and for our results to be generalizable to other Southern states where HPV vaccination rates are also low.[21]

Pharmacy Participation in VFC Can Help Increase HPV Immunization Rates: Community pharmacies are highly accessible when compared to "traditional" vaccination sites due to their extended business hours, no copays, and no requirement to schedule an appointment.[22-24] These characteristics make them especially attractive to individuals in underserved areas with few provider options.[23,24] Pharmacists have been able to administer vaccinations since 1996 and have since established their role as providers of various vaccines.[12] The majority of US community pharmacies offer influenza (86%), pneumococcal (77%), herpes zoster (75%), and tetanus (57%) vaccines.[12] To a lesser extent, pharmacies report offering hepatitis B (47%), hepatitis A (43%), meningococcal (43%), and HPV (37%) vaccines, among others.[12] An Alabama study (a state with similar vaccine delivery laws to Arkansas[25]), found only 15.9% offered HPV vaccine; only 4.4% administered at least 1 dose in the past year.[26] Although Arkansas pharmacies can obtain certification to provide VFC vaccines through a generally straight-forward process, very few have opted to participate, possibly due to requirements certain vaccines have (described below) that create a more complex implementation environment.

Pharmacists are allowed to administer vaccines to children age 7 and older under certain requirements in most states. For influenza vaccine, a *generalized immunization protocol* between a physician and a pharmacist is all that is needed. These protocols allow the covered pharmacist to administer influenza vaccine to any child age 7 or older, regardless of the child's primary care physician and without a prescription. In other words, a pharmacist can administer flu vaccine without a prescription to any patient under a generalized immunization protocol signed by *any* physician. Most pharmacies have these protocols in place and are providing influenza vaccinations for children and adults. For other vaccines, including HPV, the process is

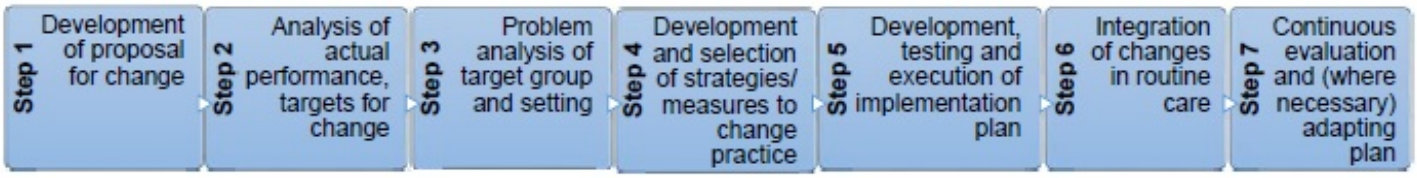
more complicated. Pharmacists can vaccinate children age 9 and older if either of the following conditions are met: 1) the pharmacist receives a patient-specific prescription for the vaccine, or 2) the pharmacist has a *disease state management protocol* with a specific physician that allows administration of the vaccine to any of that physician's patients. In other words, a pharmacist can administer HPV vaccine only if she/he has either a prescription for a specific patient or a signed disease state management protocol with a physician covering any of *her/his specific patients*. **Aim 1 is directed at uncovering potential barriers and facilitators associated with increasing HPV vaccinations in community pharmacies within these legal parameters.**

Within these parameters, a variety of potential "collaboration models" can be utilized. For example, in a "shared responsibility model" an agreement between physicians and pharmacists can be established so that the first dose of HPV vaccine is given in the physician's office while a prescription for the second dose is faxed to the pharmacy for administration there.[27] Another example is a "pharmacy-based model" in which a specific pharmacy and physician sign a disease state management protocol, as noted above, for all of that physician's patients to receive a strong recommendation in the physician's office and all doses of HPV vaccine in the pharmacy.[14] Another example is an "insourced model" in which a physician invites the pharmacy to hold a vaccination clinic in their office (e.g., on specific days/times), facilitated also by a disease state management protocol.[28,29] Regardless of the model chosen, data sharing occurs between pharmacist and physician to track and monitor HPV vaccination doses. Use of the Arkansas immunization registry (WebIZ) and open lines of communication between providers are crucial. It is unknown which collaboration model is most attractive and feasible to which pharmacist-physician dyads/groups; hence, all models will be explored in the Aim 1 formative research. It is vital to understand what models are of interest, what barriers/facilitators are associated with each, and what strategies are needed to support such collaboration. Our deliberative process in Aim 2 will involve the stakeholders *ranking* these possibilities. In Aim 3, we will pilot *one* collaborative model.

Implementation Science: The proposed research falls within the realm of Implementation Science - i.e., the "study of methods to promote the systematic uptake of… evidence-based practices into routine practice".[30] Well-known implementation frameworks and models guide the proposed research as follows:

The *Consolidated Framework for Implementation Research* (CFIR) guides our proposed exploration of barriers/facilitators to uptake of HPV vaccination and development of implementation strategies. This framework borrows constructs from Rogers' Diffusion of Innovations,[31] Greenhalgh and colleagues'[32] review of diffusion of innovations in service organizations, and other sources, to organize a multitude of constructs into 5 domains: 1) intervention characteristics, 2) outer setting, 3) inner setting, 4) characteristics of individuals, and 5) process. This framework will structure our interview guides and data collection for Aim 1 and guide the selection and operationalization of implementation strategies (Aim 2).

Figure 1:Implementation of Change Model



The *Implementation of Change Model* (ICM; Figure 1) guides our stepped approach from identification of barriers/facilitators through pilot testing. The ICM is a process model outlining a recommended order of steps for systematically introducing a novel evidence-based practice into routine practice,[33] and our proposed aims to follow these steps closely. Our pharmacy partners, Harps, have already completed their *development of proposal for change* (step 1). Hence, our Aim 1 efforts will begin with *analysis of actual performance and targets for change* (step 2) and work through the steps in the model until we have iteratively pilot tested and evaluated a pharmacist-physician collaboration model using evidence-based implementation strategies.

The *Evidence Based Quality Improvement* (EBQI) model guides the strategy development process in Aim 2. EBQI is rooted in the principles of participatory research[34] and builds on Continuous Quality Improvement[35] by bringing together clinical and implementation experts with local providers, decision makers, and key stakeholders to adapt evidence-based practices for local context and identify and operationalize accompanying implementation strategies.[36,37] Clinicians and administrators contribute knowledge needed to tailor evidence-based practices and implementation strategies for their own contexts. Implementation experts contribute knowledge on materials, procedures, and tools needed for successful implementation. Clinical experts contribute knowledge on modifiable and non-modifiable elements of the evidence-based practices.

EBQI has produced successful adapted practices[38] and implementation strategies[39] while promoting buy-in from implementing organizations and fostering beneficial researcher/clinician partnerships.[40,41] EBQI is a flexible process conducted across a series of meetings with topic driven agendas (see details of the proposed EBQI process below).

The *Taxonomy of Implementation Outcomes* of Proctor et al.[42] guides our selection of outcome measures. It describes eight conceptually distinct implementation outcomes demonstrated in the literature as important in determining the success/failure of implementation.[42] In our proposed pilot (Aim 3), we include the following measures: *feasibility*, *acceptability*, *appropriateness*, *adoption*, and *cost*.

Summary of Significance: Arkansas has the highest incidence rate of HPV related cancers in the US. Community pharmacies provide a unique opportunity to increase HPV vaccination rates, especially in underserved areas. This study will use implementation science to determine and pilot test a promising vaccine-delivery partnership model between pharmacists and physicians and an array of implementation strategies to support uptake and sustainability of HPV vaccine administration in the community pharmacy setting.

INNOVATION

This application is innovative in that it:

1. *Utilizes community pharmacies as HPV vaccination sites.* Community pharmacies are established vaccination providers yet very few provide VFC and HPV vaccines. Guidelines for implementation of VFC and/or HPV vaccines in pharmacies have not yet been established which distinguishes our application from other NIH research attempting to address low HPV vaccination rates. *2. Explores pharmacist-physician collaboration models.* Pharmacists are certified to provide vaccines with appropriate agreements in place with physicians. However, little research has investigated the multitude of options available to establish effective collaborations or which are favored by participating parties. This research will advance such collaborations and facilitate beneficial communication between providers, especially in rural, underserved areas. *3. Incorporates key stakeholders to develop implementation strategies.* Pharmacists, physicians, patients, and leaders from HPV-focused community workgroups will provide feedback on proposed implementation strategies to select and develop novel ways to implement HPV and VFC vaccines in community pharmacies. We know very little about how to best support implementation in community pharmacies. Research incorporating key stakeholder perspectives is an important contribution to implementation research in pharmacy.

APPROACH

Specific Aim 1: Identify barriers and facilitators to community pharmacies' provision of HPV vaccine through a mixed methods design with pharmacy staff members and local physicians.

Design and Sample: As we know little about barriers/facilitators to HPV vaccination in community pharmacies, our mixed methods design is primarily qualitative with a quantitative assessment for concurrent triangulation.[43,44] Consistent with our previous work,[39,41,45-47] we will conduct a Developmental Formative Evaluation[48] using semi-structured interviews. Key informants (pharmacists, pharmacy managers, technicians) from 5 Harps pharmacies selected by Dr. Duane Jones, Harps Pharmacy District Manager, will be interviewed. We selected Harps as our partner because they are the only pharmacy group in Arkansas working to provide VFC vaccines. Harps has 10 stores obtaining VFC certification this year. These locations received basic training in storing and reporting VFC supplied vaccines and have purchased the necessary storage equipment. Harps is focusing their initial VFC efforts on flu vaccine only; our project *will serve as* their development and planning process to pilot test HPV vaccine provision. Through this partnership, we have the unique opportunity to capitalize on Harps' institutional decision to explore VFC adoption and to work within an organization that has already addressed some early implementation barriers– a leadership decision to support adoption and dedication of resources to support initial implementation. Thus, we will be able to *document strategies already in use* to get this far in the decision-making and pre-implementation phases (during Aim 1), while *focusing on development of novel pharmacist-physician collaboration models and implementation strategies* to enhance the active implementation and sustainability phases of the process (Aim 2). We have previously collaborated with Harps[49] and are confident our partnership will be successful (see Jones' support letter).

We will interview at least 15 pharmacy staff (minimum of 1 pharmacist, 1 pharmacy manager, 1 technician per pharmacy). It is important to include individuals in different roles within the organization to consider all points of view, especially when implementation strategies will likely target multiple roles within the pharmacies. Each participant will also complete the Organizational Readiness to Change Assessment

(ORCA)[50] to determine organizational characteristics of Harps pharmacies that may impact implementation. ORCA items are mapped to CFIR items which allows for concurrent triangulation (i.e., use of qualitative and quantitative data and the combination of their strengths to answer research questions).[44,51] This enables us to more fully characterize the Harps organizational context as we have successfully in other contexts.[52] It is also necessary to collect data from physicians who will collaborate with pharmacists. We will interview at least 15 physicians that practice in the same geographical areas, send prescriptions to Harps, and treat a high number of eligible patients. We have identified target physicians/clinics via nominations from Harps pharmacists based on their number of shared patients. We are currently recruiting physicians, reached out to a small number who have agreed to participate (see support letters), and given our strong track record of recruiting physicians in numerous implementation research studies, we are confident we can recruit the full sample. Although our prior clinically-oriented formative evaluations with similar sample sizes achieved saturation of barriers/facilitators and recommendations,[39,41,53] if saturation is not reached, additional interviews will be conducted. Parents of patients will not be interviewed in Aim 1 for the following reasons. Along with our previous qualitative research in Alabama finding strong parental acceptance of HPV vaccinations in community pharmacies, recent publications detail the findings of a quantitative research study of 1504 parents and found 81% of parents endorse pharmacist-provided HPV vaccination if pharmacists receive proper training, report vaccine doses to the adolescent's physician, and refer the adolescent to the physician for other health services (all of which will occur in the proposed study).[1-3,54] Additionally, we have secured local funding to add to the existing body of literature by exploring Arkansas parents' perceptions of pharmacies as HPV vaccination sites.

Data Collection and Measures: Interviews (30-60 minutes) will be conducted at Harps pharmacies and physician offices. Draft interview guides (see Appendix) are informed by CFIR and ICM. Questions for pharmacy staff cover general services offered, current vaccines administered, frequency of vaccine administration, workflows supporting vaccination, and barriers/facilitators to HPV vaccination. Additionally, we will elicit feedback on the 3 proposed collaborative models including barriers/facilitators to each. Questions for physicians will cover current participation in VFC, whether/how they recommend the HPV vaccine, how their patients obtain such vaccines currently (e.g., provide vaccination, refer out, etc.), and barriers/facilitators of the different collaborative models. Interviews will be recorded using a digital recorder and transcribed verbatim.

Data Analysis: A rapid content analysis technique successfully used by Curran et al.[41] and based on methods described by Sobo et al.[55] will be used. No transcription is needed and analysis begins soon after interviews are initiated. This is necessary because interview findings will be used to facilitate the EBQI sessions that will take place immediately following completion of all interviews. To conduct rapid analysis, an interview summary template is used to quickly code information while listening to audio recordings.[56,57] Content analysis is frequently used by health researchers to interpret interview data.[58] It allows us to classify interview passages into categories that represent overarching themes.[59] Because our analysis will be guided by CFIR and ICM, our summary templates will reflect these frameworks (similarly to the interview guides). Coding itself will involve interpreting and assigning interview responses into the coding schema, e.g., "stigma around sexuality" being coded as "inner context barrier." Two researchers will code each recording using the templates and meet to compare results and resolve discrepancies. Two coders are used to enhance rigor in analysis.[60] After all interviews have been completed, a results summary matrix will be created to compile all coding from individual interview templates into one document for presentation during the EBQI process. Interview transcriptions will be completed later to support more detailed analysis and ensure accuracy of verbatim interview excerpts for inclusion in manuscripts and other dissemination products. Analysis of quantitative data collected via the ORCA will consist of item and subscale means guided by the ORCA manual/publication.

Specific Aim 2: Select a pharmacist-physician collaborative model and identify implementation strategies through an Evidence Based Quality Improvement (EBQI) process with key stakeholders.

Design and Sample: EBQI goals for this study are: 1) reach consensus on key barriers/facilitators to providing HPV vaccine in community pharmacies, 2) select a collaborative model to pilot test, and 3) develop implementation strategies to pilot test. The following stakeholders will participate in 5 EBQI sessions: 2 pharmacy managers (Madison and Washington county Harps pharmacies; see Jones' support letter), 2 local physicians (Brimberry and DePriest; see support letters), 2 parents of eligible adolescent patients (identified from our locally-funded interviews), creator of the Arkansas Immunization Action Coalition HPV workgroup (Vinson; see support letter), chair of the Arkansas Cancer Coalition Cervical Cancer Taskforce (Dillaha; see support letter), our pediatric immunization physician champion (Romero; see support letter), Harps Pharmacy

district manager (Jones), and 2 research team implementation experts (Teeter, Curran). Each session will last 2 hours. Scheduling will be flexible and incentives will be offered to ensure participation and retention of stakeholders. The first 4 EBQI sessions will take place over 5 months at the end of year 1. The final EBQI session will occur in the middle of year 2 (detailed in Aim 3). The first session will be conducted in-person to build rapport. Sessions 2-4 will occur via conference call. The final session will occur in-person to serve as closure for participants. In EBQI session 1, the research team will present a summary and check validity of Aim 1 findings, reach consensus on key barriers/facilitators and contextual factors that will drive implementation strategy selection, and prioritize the pharmacist-physician collaborative models. Due to feasibility concerns, only the top prioritized collaborative model will be piloted. In EBQI session 2, the research team will summarize literature on implementation strategies (detailed below), suggest strategies we hypothesize will yield successful results based on the agreed-upon barriers/facilitators and contextual factors, and reach consensus on which strategies to develop and pilot. In EBQI session 3, the group will reflect and reach consensus on design specifications for the selected strategies. After this session, the research team will take 2 months to develop and draft the strategies/tools selected by the group. In EBQI session 4, the research team will present the draft strategies/tools, revise as recommended, and receive final approval.

As noted above, the research team will summarize literature in EBQI session 2 to stimulate discussion. Specifically, we will present findings from an important study of implementation strategies - Expert Recommendations for Implementing Change (ERIC). It refined the breadth of strategy terminology and generated a "dictionary" to encourage consistent language and descriptions of strategies.[61] The study resulted in a list of 73 strategies characterized into 9 purposive categories, or types of strategies.[62] After summarizing the categorized list, researchers will highlight categories and specific strategies expected to address barriers/facilitators and contextual factors identified in Aim 1. For example, we expect to find barriers associated with knowledge, perceptions, and attitudes around providing HPV vaccines, and subsequently we will highlight strategies that fall under the ERIC "Train and Educate Stakeholders" category - e.g., *conduct educational meetings* and *provide ongoing consultation*. Further, we expect to find a lack of available tools to support implementation as a barrier, and therefore we will highlight strategies that fall under the ERIC "Support Clinicians" category - e.g., *remind clinicians* and *develop resource sharing agreements*. Other strategies suggested by EBQI stakeholders will be explored. A guiding principle in selecting strategies will be feasibility. For example, we will look to exploit existing dispensing and medical record systems for deploying clinician reminders, and will not explore developing such tools "from scratch." We understand that a limitation of the proposed study is that we are not able to present *now* the final list of strategies to be tested. However, we are following an evidence-based multi-stakeholder development process we have successfully used before to develop feasible sets of implementation strategies matched to specific contexts. We expect the process to again provide us with a mutually-agreed upon, literature-supported, and feasible set of strategies to be tested.

Data Collection and Analysis: Given that this aim facilitates a deliberative *process*, we are not collecting/analyzing "data" per se. However, an EBQI summary template developed by Curran and colleagues will be used by a trained research associate to document discussions, consensus, and decisions.

Specific Aim 3: Pilot the selected pharmacist-physician collaborative model and implementation strategies in two Harps pharmacies (1 rural, 1 urban) on relevant implementation outcomes.

Design and Sample: A mixed-methods design will evaluate the implementation strategies and relevant outcomes. We will collect quantitative vaccination data to calculate pre- and post-implementation vaccination rates (i.e., level of *adoption*). We will conduct qualitative interviews with participating pharmacists, physicians, pharmacy staff, clinical staff, and parents to explore *feasibility*, *acceptability*, and *appropriateness* of the collaboration model and implementation strategies. While the pilot nature of this study precludes us from doing cost-effectiveness analyses of the strategies, we will document their development and deployment *costs*. We will use results from analysis of an initial post-implementation period (6 months) to revise the implementation strategies based on feedback from a 5th EBQI session. A 2nd post-implementation period of 6 months will be used to evaluate the revised strategies (on adoption measures only). Two Harps pharmacies will participate - Madison county (rural) and Washington county (urban) - each contributing 3 participants for qualitative interviews (pharmacist, manager, and technician). The number of participating physician practices will depend on local availability (e.g., rurality will limit the pool) and willingness to participate. Thus far, we have one volunteer practice per participating pharmacy region (see support letters). We will include up to 3 practices per pharmacy. Each practice will contribute 3 interview participants (physician, nurse, front desk staff).

Data collection, Measures, and Analysis: The primary outcome measure to determine *adoption* will be HPV vaccination rate - i.e., number vaccinated out of the target eligible population - measured at the pharmacy level. Numerator data (patients vaccinated) will be collected from the pharmacy dispensing software and provided by Harps in aggregate, de-identified form. The denominator data will be the total target eligible population and will also be collected from the dispensing software and provided by Harps.

Vaccination rates will be compared across three 6-month time periods: pre-implementation, implementation period 1, and implementation period 2 (post-revision of strategies). Eligible patients for each 6-month period are: 1) age 11-17, 2) on Medicaid or uninsured, 3) in the dispensing software as having received a prescription during the past 6 months, and 4) not vaccinated against HPV. To compare the probability of vaccination across each period, a chi-square test will be used. A power analysis using SAS was conducted to determine the sample size needed using an alpha level of 0.05 and power set at 0.80.[63] Previous research on vaccine uptake interventions in pediatric/primary care settings (mailed reminders, reminder calls, text messages, or combination of these) has demonstrated increases in HPV vaccination rates around 20%.[64-67] Using the estimated proportion of adolescents that have received the vaccine in Arkansas (34.5%) and the effect size of similar vaccine uptake interventions (20%), at least 597 eligible patients are needed in each period. Estimates of the number of eligible patients were derived from Harps pharmacies' annual reports, Arkansas Medicaid annual reports, and county-level census data. In 2013, Madison County, Arkansas, had an estimated 2,320 (60.9%) adolescents on Medicaid and an estimated 206 (5.4%) were uninsured. In Washington County, 28,531 (55.3%) adolescents were on Medicaid and 3,821 (7.4%) were uninsured. A Harps pharmacy sees an average of 1550 - 1750 patients age 11-17 in a 6-month period. Using the lower end of this range, we estimate that 995 adolescents in Madison County and 972 in Washington County are eligible based on Medicaid/uninsured status. When considering Arkansas HPV vaccination completion rates are estimated to be 35.5% (95% CI=27.1-45.0) and 33.6% (95% CI=26.3-41.7) for females and males, respectively, we estimate 642 – 661 VFC HPV eligible adolescents will be seen in the Madison County Harps and 627 – 645 will be seen in the Washington County Harps during the first 6 months of the pilot period. As we do not yet know the complete list of participating physicians/clinics (nor the collaborative model), estimates of the number of shared patients between the participating physicians and the pharmacy (the denominator) are not possible. However, in Madison County, there is only one FQHC that participates in the VFC program and they have agreed to partner with us on this project (see letter of support), so we do not anticipate problems achieving our required minimum sample sizes of shared patients. The numerator will be calculated similarly to the pharmacy vaccination rate. Secondary adoption measures explored will be HPV vaccination rates at the physician/clinic level to explore how differences in their involvement could be reflected in vaccination rates.

Qualitative evaluation of the implementation strategies and collaborative model will begin 3 months post-initial implementation and results will be used to guide revision of the strategies in EBQI Session 5. Interviews will be conducted at both Harps pharmacies and the participating practice locations. Interview guides will be created and tailored to the specific strategies and collaborative model implemented. Questions will focus on feasibility, acceptability, and appropriateness outcomes. For example, to assess feasibility we will ask, "How does the collaboration between you and the pharmacist/physician fit within your workflow?" We will also elicit feedback on the collaborative model and implementation strategies-- what is going well/not, implementation barriers, compatibility, leadership engagement, perceived successes/failures, and recommendations for improvement. We will also interview 10 parents of patients that received the HPV vaccine during the initial implementation period to gain their perspectives on feasibility, acceptability, and recommendations for improvement. All interviews will be analyzed using the rapid analysis technique described in Aim 1. In month 6 of the pilot, EBQI Session 5 will be held. Data from interviews will be discussed and recommendations elicited to improve the implementation strategies. Feasible strategy revisions will be made and re-deployed during the 2nd 6-month implementation period.

ANTICIPATED CHALLENGES AND APPROACHES

The study will only include one small pharmacy chain in one state. Although only Harps Pharmacies in Arkansas will participate, they are similar to other small supermarket chains and independently-owned pharmacies. Arkansas pharmacy laws are similar to other Southern states. Therefore, we believe our results will be generalizable to Southern states and small chain and/or independently-owned pharmacies and can be used to propose a large, multi-state study in multiple pharmacy contexts. The pharmacies already have buy-in. While it is possible to view Harps Pharmacies' interest in the VFC program as a limitation, we feel it is a

strength. We will document and describe the implementation strategies Harps utilized to overcome barriers and get to this point. Therefore, we can suggest potential implementation strategies that may be successful for other pharmacies that are considering participation in VFC as well as develop strategies and collaboration models for those that have made the decision to participate. Difficulty recruiting physicians/clinics. We have recruited 3 physician offices including 2 that have volunteered to take part in the Aim 3 pilot. We have not encountered resistance thus far and will continue to recruit during the submission period.

POTENTIAL AND PLANS FOR FUTURE FUNDING

Improving HPV vaccination rates in the Southern US is an increasingly important area as evidenced by numerous regional and state initiatives. Despite interest in and importance of this topic, immunization rates remain very low. Research is needed to address vaccination rates, especially in low income, underserved, Southern populations. This study will inform the development and submission of a R01 to NCI (PAR-18-007). Building on these findings, the subsequent project will conduct a large cluster-randomized implementation trial to determine the impact of the collaborative model and implementation strategies on vaccination rates in pharmacies. This large implementation trial will include multiple pharmacy contexts - large and small, urban and rural, and chain- and independently-operated.

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