

University of Pennsylvania

Annual Progress Report: 2006 Nonformula Grant

Reporting Period

July 1, 2009 – June 30, 2010

Nonformula Grant Overview

The University of Pennsylvania received \$4,206,097 in nonformula funds for the grant award period June 1, 2007 through May 31, 2011. Accomplishments for the reporting period are described below.

Research Project: Project Title and Purpose

HPV Vaccination of Underserved Adolescent and Young Women in Pennsylvania - The research proposed will address critical questions related to the successful delivery of human papilloma virus (HPV) vaccine in underserved adolescents and young women in urban and rural Pennsylvania. We will evaluate knowledge of and attitudes towards HPV and HPV vaccination among adolescents, parents, and health care providers. With the knowledge gained we will compare interventional strategies to increase HPV vaccination rates on individual and community levels.

Anticipated Duration of Project

6/1/2007 - 5/31/2011

Project Overview

The primary objective of this project is to evaluate whether HPV vaccination rates among adolescent girls/young women ages 9-18 in Philadelphia and NE Pennsylvania can be increased by interventions targeting barriers to immunization.

Initially, we will assess knowledge of and attitudes/intentions towards HPV vaccination among consumers and health care providers through elicitation research. The project will continue with an interventional phase. Research communities will be mapped using census data; five communities of similar size, demographics, and income will be constructed in Philadelphia and three in NE Pennsylvania. Two tiers of interventions will be introduced sequentially into these communities using a stepped wedge study design. The first intervention will consist of community education targeting adolescents and their parents designed to improve knowledge and overcome barriers to vaccination. A small group behavioral intervention will be delivered to adolescents and/or their parents/guardians. Pre- and post-intervention questionnaires will measure the impact of the intervention on HPV knowledge and intent to receive vaccination. Responses to follow-up questionnaires will be solicited to determine the durability of the intervention's effect. In Philadelphia, the rate of HPV vaccination will be tracked using the

Philadelphia KIDS Vaccine Registry to determine whether the intervention had an effect on vaccination rates and how receipt of vaccination is related to intent to receive vaccination. Vaccination rates will be compared to those in control communities in which adolescents and parents complete questionnaires to assess HPV vaccination knowledge and intent to receive vaccination, but do not receive the intervention. In NE Pennsylvania, vaccination rates will be verified using the Geisinger Health System electronic medical record among residents who receive care within that network. Following the completion of the small group intervention a community-wide educational initiative will be conducted using street outreach. The effect of this community-wide initiative will be measured by determining vaccination rates at the community level. A second tier intervention will be developed following an assessment of the effect of the small group and street outreach interventions to determine if vaccination rates can be further improved.

Principal Investigator

Ian Frank, MD
Professor of Medicine
Department of Medicine
Division of Infectious Diseases
University of Pennsylvania
502 Johnson Pavilion
3610 Hamilton Walk
Philadelphia, PA 19104-6073
(215) 662-7419

Other Participating Researchers

Kent Bream, MD, Loretta Sweet Jemmott, RN, PhD, Thomas Ten Have, PhD – employed by University of Pennsylvania
Bradley Buchner, PhD, Christopher Barnes, PhD - employed by Cheyney University of Pennsylvania
Nadja Peter, MD - employed by Children’s Hospital of Philadelphia
Claire Newbern, PhD - employed by Philadelphia Department of Public Health
Allan Arbeter, MD - employed by Albert Einstein Medical Center
Linda Hock-Long, PhD – employed by Family Planning Council
Michael Ryan, DO, Sharon Larson, PhD - employed by Geisinger Health System

Expected Research Outcomes and Benefits

Human papillomavirus (HPV) is the cause of almost all cases of cervical cancer. A vaccine has recently been approved by the US Food and Drug Administration that is safe and effective in preventing infection with two HPV types that cause 70% of cases of cervical cancer, and two other types that cause genital warts. The vaccine is approved for use in adolescent and young women ages 9-26.

We propose a project that will study ways to increase the numbers of adolescent women in

Philadelphia and NE Pennsylvania who are vaccinated. The methods that we will follow will reach large communities that include low income families. In this way we anticipate that our research will mean that many more adolescents in the two regions where the research will be performed will receive HPV vaccine. The strategy that we will follow will also improve relationships between adolescents and their families with health care providers, and this should lead to better health care in general. Also, by increasing knowledge of HPV and how it is contacted, we think our research will lead to less risky sexual behavior and this will decrease the numbers of adolescents acquiring other sexually transmitted diseases.

This project will also increase awareness of how effective educational messages can be delivered to urban and rural communities and how health care providers' practices can work more efficiently to increase the delivery of other types of vaccines, not just the HPV vaccine we are studying.

Summary of Research Completed

Overview of Progress

The work performed during this period has been focused in two areas: i) recruitment into the small group behavioral intervention in Philadelphia; ii) development and implementation of the educational intervention in NE Pennsylvania. Progress made in each of these areas is outlined below.

Small Group Behavioral Intervention in Philadelphia

Objective. The primary objective is to evaluate the impact of a small group behavioral intervention on the initiation of HPV vaccination among adolescents ages 11-18.

Methods. A two-hour educational curriculum based upon the principles of the Theory of Planned Behavior is delivered to adolescents or to parents/guardians of adolescents residing within selected neighborhoods of Philadelphia based upon the demography of predominant African American households with incomes below poverty level. Eligible participants are adolescent girls ages 13-18 or parent/guardians of adolescent girls ages 9-18 who have not received any HPV immunization. [The difference in ages is due to the fact that adolescents ages 13-18 may make the decision to receive HPV vaccination in the absence of specific parental consent, while younger adolescents require parental consent.] Pre- and post-intervention questionnaires are administered to measure intent to receive vaccination, as are follow-up questionnaires at 3- and 6-month post intervention. In two control neighborhoods participants complete questionnaires but do not receive the intervention. Street-level recruitment strategies are used to identify eligible participants.

Enrollment. Table 1 describes the number of participants in the intervention and control groups within the five designated neighborhoods of Philadelphia. Through June 30, 2010, 805 individuals participated in the study, 508 in the intervention group (243 parents and 265 adolescents) and 297 in the control group (133 parents and 164 adolescents). Enrollment was brisk during the summer months and early fall. In the winter months recruitment slowed and has increased somewhat in June. Enrollment has neared targeted goals in Neighborhoods 3, 4 and 5,

and primarily lags in Neighborhood 1. Figure 1 outlines the number of adolescents and parents/guardians who were screened to yield the 508 participants in the intervention groups. Of 2914 adolescents screened, 265 (9.1%) enrolled; of 1297 parents/guardians screened, 243 (18.7%) enrolled. Thus, extensive resources have been required for recruitment. Recruitment strategies, including blanket posting of flyers in neighborhoods, advertising in local media, and peer recruitment near schools, churches, recreation centers, pools, health fairs, sporting events, and other venues have been described in our Year 2 report. The primary reasons individuals were not eligible to participate were because they did not reside within a study neighborhood or they or their daughter had already started the HPV vaccination series. Eligible participants were often reluctant to schedule interventions, and many individuals who agreed to participate and were scheduled for an intervention session failed to show up.

Obstacles to Enrollment and Strategies to Enhance Enrollment. Recruitment of subjects and completion of the intervention is strongly influenced by weather. During inclement weather individuals often are not willing to stop to discuss the study with recruiters, and individuals who have been scheduled to participate in sessions may not wish to venture outside. Individuals who miss sessions are contacted and provided other opportunities to participate. We have used a mobile van for recruitment to offer additional shelter. Over time a greater number of adolescents were not eligible because of increased rates of HPV vaccination within the community. Feedback during the early recruitment period suggested that our incentive was not sufficient for parents who may have needed to arrange for child care or purchase of meals in order to participate in an evening or weekend session. We increased incentives for parents to participate. Throughout the study we have continued to develop our recruitment strategy and have solicited participation at neighborhood recreations centers, churches, community organizations, health fairs, neighborhood sporting events, local businesses, and other venues. Intervention and control sessions are held in neighborhood locations that are convenient for participants.

Implications of less than total recruitment on power to detect stipulated effect size. With 1200 participants as originally planned, the study had 80% power to detect at least a 17% difference in vaccination rates with a binary outcome (vaccination or not) between the intervention and control groups. We need 800 intervention participants and 400 control participants without a history of HPV vaccination. The sample size computations assumed a logistic regression analysis with a binary outcome (vaccine or not) and intervention neighborhood and neighborhood-level and child-level covariate predictors. If we have only 800 evaluable subjects (550 intervention participants / 250 control participants) there is 80% power to detect a difference of 21%. With 900 evaluable subjects, (600 intervention / 300 control) there is 80% power to detect a 20% difference. With 1000 evaluable subjects (650/350) there is 80% power to detect a difference of 19%. We will continue to conduct small group interventions through October 2010 and anticipate enrolling 900-1000 participants. Our shortfall from our original recruitment targets will have only a small impact on our ability to evaluate the effect of the intervention, because the range of above treatment differences fall within the range of "small" Cohen's Effect Sizes (Helena Chmura Kraemer, David J. Kupfer. Size of Treatment Effects and Their Importance to Clinical Research and Practice Biological Psychiatry 59; 2006: 990-996.)

Completion of Follow-up Questionnaires. Table 2 provides the number of participants who have completed 3-month post-intervention questionnaires designed to measure a secondary objective

- the persistence of the intervention on knowledge of HPV and the HPV vaccine, intent to receive the vaccine, and experiences of individuals who sought the vaccine (successfully or unsuccessfully). Completion of the 3-month questionnaires was obtained in 58.6% of all participants, 61.7% of parents/guardians and 55.8% of adolescents. Table 3 provides the number of participants who have completed 6-month post-intervention questionnaires. These have been completed by 53.8% of all participants, 56.8% of parents/guardians and 50.9% of adolescents. Power calculations were not performed for this secondary objective. The missing data may introduce a selection bias to the conclusions that we will be able to draw from this eventual analysis. However, these follow-up rates and our experience with large no show rates among adolescents scheduled to participate in the intervention suggests that securing a commitment to study participation is a challenge among the population of inner city adolescents targeted in this study.

Development and Implementation of the Intervention in NE Pennsylvania

Objectives. 1) Evaluate the effect of an educational intervention delivered by a health educator or viewed on DVD on rate of initiation of the HPV vaccine among adolescents in NE Pennsylvania. 2) Evaluate the effect of educational intervention messaging on initiation of the HPV vaccine series by comparing an intervention that describes the HPV vaccine as both a cancer prevention and a method to protect from sexually transmitted infection versus a message that only describes the HPV vaccine as a cancer prevention.

Methods. Eligible adolescents are ages 11-18 who have not received HPV vaccine. Adolescent-parent dyads are randomized to receive one of five interventions: i) long intervention delivered by a health educator; ii) long intervention viewed on DVD at home; iii) short intervention delivered by health educator; iv) short intervention viewed on DVD at home; and v) control - no intervention. Participants complete pre- and post-intervention questionnaires to measure changes in knowledge, attitudes, and intent; and will return to complete 3- and 6-month follow-up questionnaires, similar to the Philadelphia site. The rationale for this approach is as follows. Our earlier elicitation research in NE Pennsylvania revealed that all decisions made related to vaccination were made by parents. Therefore, the intervention is being delivered to adolescent-parent dyads. In addition, previous work revealed parents in NE Pennsylvania are motivated more by the concept of HPV vaccination as a cancer prevention and have neutral to negative feelings about it as a prevention from sexually transmitted infection. On the other hand, adolescents had the opposite view – they were more motivated by the concept of HPV vaccination as prevention from sexually transmitted infection. Therefore, we developed two interventions, a longer intervention which included messages involving the HPV vaccine as both cancer prevention and prevention from sexually transmitted infection, and a shorter version that emphasized cancer prevention. The Geisinger Health System has a tradition of patient education through provider practices. Therefore, we decided to compare the impact of an intervention delivered by a health educator compared to viewing the intervention on DVD, given the popularity of electronic media.

Description of the Intervention. The intervention was developed around several central messages based upon the content created by the Philadelphia group (see Year 2 report), modified to address a more conservative population. A scripted curriculum was developed for delivery by

a health educator. A DVD was created using an avatar to deliver the content. Adolescents and parents are instructed to view the DVD together. Both the daughter and parent will receive \$75 for participation in the study.

Recruitment Plan. Eligible adolescents are identified through the Geisinger Health System electronic medical record, and an invitation to participate in the research project is mailed to the adolescents and her parents. Approximately 200 letters are sent at two-week intervals. The Geisinger calling center is used to contact eligible adolescents and confirm eligibility; this is a service provided by the Health System to reach their patient population for patient scheduling and for broad delivery of health messages and alerts. Calls are made starting 10 days after letters are delivered. Interested dyads are randomized to one of the five groups and are then mailed informed consent documents and the questionnaires and intervention content if randomized to the control or home intervention groups. Parental consent is obtained in all cases. Dyads randomized to the groups who receive the intervention from a health educator are scheduled an appointment at their Geisinger practice location.

Sample size calculations. The sample size for this study is 600, with 120 dyads in each of the five groups. This was derived based upon the goal to have at least 80% power to detect at least a 20% difference for the two primary comparisons involving the 5 groups, the two intervention types and the two delivery methods compared to the control, with two-sided alpha of .025 to control for multiple comparisons.

Enrollment. An initial wave of 91 letters of invitation was sent out on May 5. Through June 21, 991 letters were mailed, the call center attempted to reach 783 families, and 318 eligible dyads were reached. Of these, 116 (36.5%) have been randomized. We estimate that 75% of the dyads who are randomized will complete and return questionnaires or make appointments based upon previous studies that have used this recruitment strategy. The number of mailings is being increased to approximately 800 monthly. Targeted recruitment is 80 dyads monthly.

Figure 1. Subject Recruitment into Intervention Groups (July 1, 2009 – June 30, 2010)

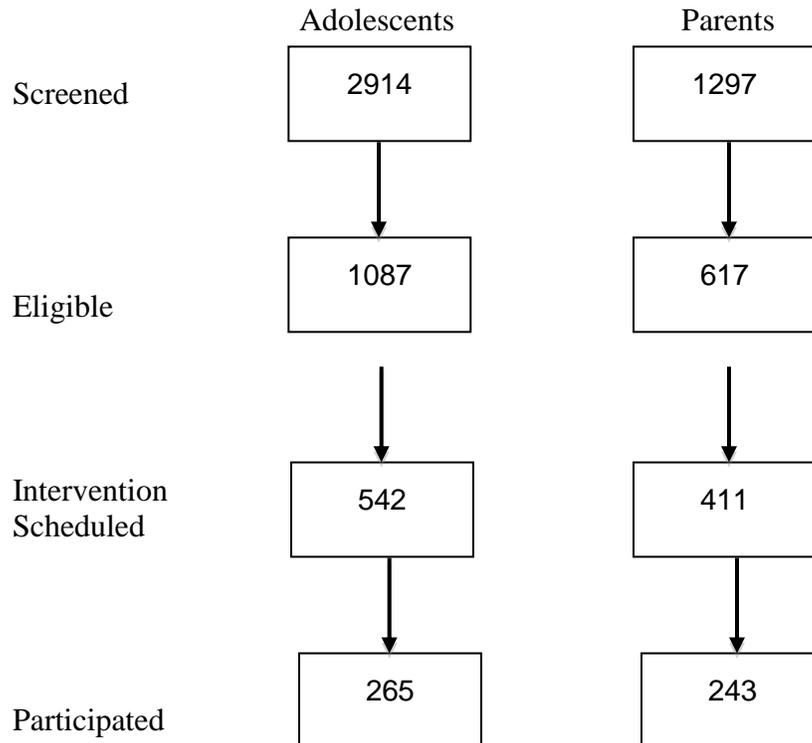


Table 1. Participants in small group interventions in Philadelphia (July 1, 2009 – June 30, 2010)

Neighborhood # Control / Intervention	Targeted Groups Sample Size (n)	June	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	Total To Date
# 1 Intervention	Adolescent (n=200)	2	0	21	8	19	13	4	5	0	0	6	4	0	82
	Parent (n=200)	5	6	4	5	15	3	9	9	0	3	3	0	5	67
# 2 Control	Adolescent (n=100)	1	8	11	5	4	11	10	1	0	5	8	5	2	71
	Parent (n=100)	1	7	6	2	3	6	2	2	0	6	0	5	3	43
# 3 Intervention	Adolescent (n=200)	9	37	24	14	13	24	11	7	2	8	16	5	13	183
# 4 Control	Adolescent (n=100)	16	10	9	13	9	5	9	7	1	1	1	3	9	93
	Parent (n=100)	19	8	9	3	6	17	5	1	0	6	2	2	9	90
# 5 Intervention	Parent (n=200)	18	20	30	35	25	13	11	7	3	6	2	0	6	176
Total		71	96	114	85	94	92	61	39	6	35	38	24	47	805

Table 2. Three-month follow-up visits completed, number of participants missing follow-up, number of participants with window still open (through June 30, 2010).

SA	Cumulative Completion Three-Month Follow-up			Three-Month Window Closed			Three-Month Window Open		
	Total	Parent	Adol	Total	Parent	Adol	Total	Parent	Adol
1	68	27	41	61	25	36	4	0	4
2	53	21	32	33	12	21	5	2	3
3	72	-	72	54	-	54	14	-	14
4	84	42	42	60	23	37	4	1	3
5	100	100	-	58	58	0	7	7	0
Inter.	240	127	113	173	83	90	25	7	18
Con.	137	63	74	93	35	58	9	3	6
Total	377	190	187	266	118	148	34	10	24

Table 3. Six-month follow-up visit completed, number of participants missing follow-up, number of participants with window still open (through June 30, 2010).

SA	Cumulative Completion Six-Month Follow-up			Six-Month Window Closed			Six-Month Window Open		
	Total Enrollees	Parent	Adol	Total Enrollees	Parent	Adol	Total Enrollees	Parent	Adol
1	48	21	27	53	18	35	16	12	4
2	32	11	21	39	15	24	5	1	4
3	65	-	65	40	-	40	8	-	8
4	62	38	24	56	23	33	7	2	5
5	80	80	-	58	58	-	12	12	0
Inter.	193	101	92	151	76	75	36	24	12
Con.	94	49	45	95	38	57	12	3	9
Total	287	150	137	246	114	132	48	27	21