Feasibility of Using Maternal Cancer Screening Visits to Identify Adolescent Girls Eligible for Human Papillomavirus Vaccination

Ruth C. Carlos, M.D., M.S.,¹ Amanda F. Dempsey, M.D., Ph.D., M.P.H.,² Ken Resnicow, Ph.D.,³ Mack T. Ruffin, IV, M.D., M.P.H.,⁴ Divya A. Patel, M.P.H., Ph.D.,⁵ Christopher M. Straus, M.D.,⁶ Andrew Kure,¹ and Vanessa K. Dalton, M.P.H., M.D.⁵

Abstract

Purpose: Breast or cervical cancer screening visits may present an opportunity to motivate mothers to have their daughters vaccinated against human papillomavirus (HPV). In preparation for a future intervention study, we sought to establish the feasibility of using these visits to identify women with at least one daughter in the appropriate age range for adolescent HPV vaccination.

Methods: We conducted a cross-sectional mailed survey of women who had received breast or cervical cancer screening within the 6–18 months before the survey. The study was conducted at two diverse institutions: one serving a mostly black (54.1%) urban inner-city population and another serving a mostly white (87.5%) suburban population.

Results: Our overall response rate was 28% ($n = 556$) in the urban site and 38% ($n = 381$) in the suburban site. In the urban site, the proportions of mothers completing mammography or Pap smear visits with HPV vaccine-eligible daughters were 23% and 24%, respectively. In the suburban site, the proportions of mothers completing mammography or Pap smear with at least one vaccine-eligible daughter were 41% and 26%, respectively.

Conclusions: Women who undergo breast or cervical cancer screening in the two different demographic groups evaluated have at least one adolescent daughter at the appropriate age for HPV vaccination. An important implication of this finding in adolescent daughters of urban mothers is the potential use of maternal breast or cervical cancer screening encounters to target a potentially undervaccinated group.

Introduction

Cervical cancer control through screening

CERVICAL CANCER, the second most common malignancy in women worldwide, remains a leading cause of female cancer-related death. The lack of organized Papanicolaou (Pap) smear screening programs primarily accounts for the disproportionate number of cervical cancer patients and incident cervical cancers in the developing world.^{1,2} The widespread use of Pap smear screening for cervical cancer has led to a marked reduction in incident cervical cancer cases and deaths attributable to cervical cancer in the United States.

Despite the success of Pap smear screening in the prevention of cervical cancer, nearly 10,000 incident cervical cancer cases and 4,000 deaths still occur annually in the United States.³ In addition, over 1 million low-grade and high-grade squamous intraepithelial lesions of the cervix are detected

each year, leading to multiple follow-up visits and invasive procedures to monitor and treat these precancerous cervical changes.⁴ These cervical cancers and precancers are directly attributable to human papillomavirus (HPV) infection.

Cervical cancer prevention through HPV vaccination

The U.S. Centers for Disease Control and Prevention (CDC) currently recommends a quadrivalent HPV vaccine (Gardasil®, Merck) for females aged 9–26 for prevention of cervical, vulvar, and vaginal cancers; precancerous cervicogenital lesions; and genital warts caused by the four HPV types targeted by the vaccine. A second, bivalent vaccine (Cervarix®, GlaxoSmithKline) that prevents cervical precancers associated with oncogenic HPV types 16 and 18⁵ was approved in October 2009 for females aged 10–25 in the United States but is not readily available. Nationally, one fourth of all teens aged

Departments of ¹Radiology, ²Pediatrics, ⁴Family Medicine, and ⁵Obstetrics and Gynecology, University of Michigan Medical Center, Ann Arbor, Michigan.

³School of Public Health, University of Michigan Medical Center, Ann Arbor, Michigan.

⁶Department of Radiology, University of Chicago, Chicago, Illinois.

14–19 are infected with HPV, of which more than half have a high-risk, or oncogenic, HPV type.⁶ Therefore, it is imperative to identify ways to increase HPV vaccine use in the adolescent population in order to protect against cervical cancer.

Challenges to adolescent vaccine delivery

Immunization delivery in the adolescent group presents unique challenges. Despite endorsement by the American Academy of Pediatrics (AAP) for adolescent wellness visits, adolescents, as a group, make fewer visits to physicians' offices than at any other time in their lives,⁷ with some studies indicating as few as 35% of adolescent females having a preventive care visit in the past 12 months.⁸ Adolescent HPV vaccine delivery is further complicated by the different types of primary care providers who may provide care to adolescents as they age. Family practitioners, pediatricians, and gynecologists all play an active role in adolescent preventive care, and the multiplicity of providers can cause added difficulty in ensuring that the three-dose HPV vaccine series is completed.

Achieving the high rates of HPV vaccine coverage in adolescents recommended by *Healthy People 2010*⁹ will require novel strategies for improving vaccine uptake. There is substantial contrast between the low rate of adolescent preventive services use and the very high use (65%–80%) of cervical and breast cancer screening services among adult women.¹⁰ These breast or cervical cancer screening encounters represent a unique way to reach large numbers of women for dissemination of educational information for other cancer preventive services for themselves and could serve as an educational gateway with which to inform mothers about the importance and availability of adolescent HPV vaccination.¹¹ Before we can evaluate these screening encounters as potential teachable moments, we first need to determine the proportion of women participating in breast or cervical cancer services who have adolescent daughters in the appropriate age range for HPV vaccination. Therefore, our purpose in this study is to determine the proportion of mothers with HPV vaccine-eligible daughters attending cervical and breast cancer screening visits at two racially, economically, and geographically diverse outpatient clinic systems.

Materials and Methods

Study sites

The study was conducted at two geographically, racially, and economically distinct sites.

The University of Chicago Medical Center (hereafter referred to as the urban site) serves an urban inner-city population in the south side of Chicago, Illinois. In 2006, 25,786 mammograms for breast cancer screening and >10,000 cervical cancer screenings were performed. In the same year, by race and ethnicity, 31.9% of patients were white, 54.1% black, 0.1% American Indian, 0.6% Asian, 3.9% Hispanic/Latino, and 9.4% unknown. Insurance coverage by payer source for outpatients was Medicare 27.1%, Medicaid 23.2%, and commercial insurance 49.7%. The 2000 Census information estimates that 30.7% of families lived below the poverty line.

The University of Michigan Health System (hereafter referred to as the suburban site) serves a suburban and exurban population in southeastern Michigan covering five counties. In 2006, there were 14,877 screening mammography visits and

4,395 cervical cancer screening visits in the target maternal age group at these clinics. An analysis of women undergoing breast cancer screening between 1998 and 2002 showed that 71.4% had commercial insurance, 26.7% had Medicare, and 1.5% had Medicaid, with similar insurance coverage in women undergoing cervical cancer screening. Data on ethnicity and income are not collected during care provision, but 2000 Census data estimate race and ethnicity as follows: white 87.5%, black 6.6%, American Indian 0.3%, Asian 2.6%, and Hispanic 2.7%, with 4.6% of families living below the poverty line.

Patient population

Women 25–55 years old who attended a cancer screening visit (breast cancer screening CPT codes 76092, 77057 or G0202 or cervical cancer screening CPT codes Q0091, G0101) at one of the study sites between December 1, 2007, and November 30, 2008, were retrospectively identified. Of an eligible sample of 39,983 women who attended these visits, a convenience sample of 3,000 women was randomly selected to receive a self-administered, mail-based survey 6–18 months after their cancer screening visit. To ensure adequate representation of African Americans, the urban site was oversampled using a 2:1 ratio (2,000 surveys to women from the urban site; 1,000 surveys to women from the suburban site). At the urban site, surveys were sent to 1,000 women receiving breast cancer screening and 1,000 women receiving cervical cancer screening. At the suburban site, 500 surveys were sent to women receiving breast cancer screening and 500 women receiving cervical cancer screening. Each survey was accompanied by a \$1 bill, and each participant who returned a survey received a \$5 gift card. A second mailing with an additional \$1 incentive was sent to nonrespondents 1 month after the first mailing. The study was approved by the University of Michigan and University of Chicago Institutional Review Boards.

Outcome measure

The primary outcome measure in this study was the proportion of respondents undergoing breast or cervical cancer screening who had an adolescent daughter aged 9–17 years. This adolescent age group was chosen to mirror the age group for which the CDC recommends vaccination. Acknowledging that once adolescents reach the age of 18 and they are able to self-consent to HPV vaccination, we set the upper limit at age 17 for adolescents in our study.

Survey instrument

The survey assessed sociodemographic variables, including age of the study participant, ages and number of children in the family, age and insurance status of the eldest adolescent daughter, maternal race/ethnicity, education level, annual income, and marital status. Because we did not have the total family size, we defined poverty as those with <\$20,000 in household income, rather than the conventional definition adjusting for the number of household members.

Statistical analysis

Frequency of the primary outcome was calculated with differences between groups assessed using chi-square tests,

with a statistical significance set at $p \leq 0.05$. All statistical analyses were conducted using Stata 10.0. (StataCorp).

Results

Of the 3,000 women who were sent the survey, 937 responded, for an overall response rate of 31% (Fig. 1). Of these, 232 (25%) were mothers or primary caretakers of adolescent females aged 9–17 years. The mean maternal age was 44 years (range 30–55), and the mean daughter age was 13 years (range 9–17). There were significant differences between the recruitment sites with regard to several demographic characteristics of the respondents (Table 1). Compared to those at the suburban site, respondents at the urban site were more frequently black and single and had a family income below the poverty line. There were also significant differences in the proportion of mothers with adolescent daughters based on the type of cancer screening visit and site of visit. Specifically, the proportion of respondents completing breast cancer screening at the suburban site who are mothers (0.41, 95% confidence interval [CI] 0.34–0.49) is significantly greater than those completing cervical cancer screening at the suburban site (0.26, 95% CI 0.20–0.32) or those completing any cancer screening at the urban site. At the urban site, similar proportions of women attending cervical cancer screening (0.24, 95% CI 0.19–0.28) had adolescent daughters compared with those attending breast cancer screening (0.23, 95% CI 0.18–0.29).

Maternal demographic characteristics varied by site, with significantly higher proportion of black mothers represented in the urban population compared to the suburban population (Table 2). Mothers from the urban site were more likely to be single mothers or to have a family income below the poverty line compared to suburban site mothers. No notable differences by site in adolescent demographic or insurance coverage characteristics were identified.

As women may have had the opportunity to attend both breast and cervical cancer screening during the study period, we evaluated the number of unique women who underwent breast or cervical cancer screening who had adolescent daughters. At the urban site, of the 4,744 unique women, our sampling strategy yielded 1,654 unique women who were sent the survey; 525 unique women returned the survey (31.7% response rate). Of the 525 unique women who returned the survey, 113 (21.5%) were mothers of adolescent

TABLE 1. RESPONDENT DEMOGRAPHIC CHARACTERISTICS

Respondent demographics	Site	
	Urban	Suburban
Age (Mean)*	46	41
Ethnicity*		
Asian	3.0	7.5
Black/African American	51.4	6.1
Caucasian	37.3	80.6
Hispanic/Latina	3.6	1.1
Other	1.1	2.1
Multiracial or multiethnic	3.6	2.7
Income*		
<10,000	11.2**	3.3
\$10,000–19,999	7.7**	4.7
\$20,000–29,999	6.7	3.6
\$30,000–39,999	7.5	9.1
\$40,000–49,999	8.7	6.9
\$50,000–59,999	9.6	9.9
\$60,000 or more	48.6	62.6
% Below the poverty line*	18.8**	8.0
Education*		
High school/GED graduate or less	10.9	4.5
Some college	27.6	22.5
College graduate	61.5	73.0
Marital status†		
Married or with partner	53.4	72.6
Divorced/widowed/separated	16.6	13.2
Single	30.0	14.3

*Significantly different between study sites ($p < 0.05$).

†Significantly different between mothers and nonmothers at each site.

**Differences between income and % below the poverty line due to rounding error.

daughters aged 9–17. At the suburban site, of the 27,535 unique women, our sampling strategy yielded 996 unique women who were sent the survey; 380 unique women returned the survey (38.2% response rate). Of the 380 unique women who returned the survey, 114 (30%) were mothers.

Discussion

The CDC targets adolescents as the preferred age for HPV vaccination. Our results demonstrate that a substantial proportion (25%) of women undergoing breast or cervical cancer screening have adolescent daughters in the appropriate age range for HPV vaccination. These results are consistent with an analysis of the Behavioral Risk Factor Surveillance System (BRFSS) 2006 data (R.C. Carlos, unpublished results), where frequencies ranged from 23% to 41% depending on the site and type of cancer screening encounter. Given the consistency of these findings, we can now begin to explore the use of maternal breast or cervical cancer screening encounters as educational gateways to improve HPV vaccination in adolescent daughters.

Improving current rates of adolescent HPV vaccination

The *Healthy People 2010* report advocates coverage levels of 90% for any new universally recommended vaccine within 5 years of the recommendation,⁹ yet none of the recommended adolescent vaccines have reached this level of coverage. Despite an energetic public advertisement campaign by HPV

FIG. 1. Recruitment and enrollment: of the respondents, 21.2% were mothers at the Chicago site and 30.0% were mothers at the Michigan site.

TABLE 2. MATERNAL AND ADOLESCENT DEMOGRAPHIC CHARACTERISTICS

Demographics	Site	
	Urban	Suburban
Maternal		
Mean age in years	45.3	42.8
Ethnicity*		
Asian	2.8	7.7
Black/African American	52.5	5.9
Caucasian	36.5	80.8
Hispanic/Latina	3.7	1.1
Other	1.3	2.4
Multiracial or multiethnic	3.3	2.1
Income*		
<\$10,000	11.3	3.2
\$10,000 to <\$20,000	7.7	4.6
\$20,000 to <\$30,000	7.1	3.5
\$30,000 to <\$40,000	7.3	9
\$40,000 to <\$50,000	8.6	6.8
\$50,000 to <\$60,000	9.4	9.8
\$60,000 or more	48.4	62.5
% Below the poverty line*	26.3	10.5
Education		
High school/GED graduate or less	11.5	4.5
Some college/vocational training	27.9	22.9
College degree or more	60.7	72.6
Marital status*		
Married or in nonmarriage partnership	53.4	72.7
Divorced/widowed/separated	16.1	13.1
Single	30.5	14.2
Adolescent ^a		
Mean age in years $\pm$ SD	12.8	13.3
Insurance coverage		
HMO		
PPO	50.0	45.1
Medicaid	14.8	5.4
S-CHIP	0.9	2.7
Other	3.7	3.6
Multiple sources	4.6	6.3
None	1.8	0.9

^aAdolescent demographic characteristics refer to eldest daughter (if the mother has more than one adolescent daughter).

*Significantly different between study sites ($p < 0.05$).

HMO, health maintenance organization; PPO, preferred provider organization; S-CHIP, State Child Health Insurance Plan.

vaccine manufacturers, adolescent HPV vaccine use remains suboptimal, with only 37.2% of eligible females 13–17 years old initiating the vaccine series and 17.9% completing it in 2008.¹² Significant variations in vaccine uptake by state, race, and economic status have been demonstrated both nationally¹² and among the suburban sample in our study.¹³ These disparities call into question the overall impact that HPV vaccines have on cervical cancer rates in the United States, given the current HPV vaccine use patterns among adolescents. It is well recognized that minority women are at higher risk of developing and dying from cervical cancer.¹⁰ From our work and from national studies, it appears that minority adolescents may be less likely to achieve protection against HPV infection via vaccination.

Given this, an important finding from our study was the high proportion of mothers with diverse racial backgrounds

undergoing cancer screening visits at our study sites who had daughters in the age range for HPV vaccination. Maternal cancer screening visits may represent a unique teachable moment (TM) to educate mothers about the importance of adolescent HPV vaccination, subsequently resulting in improved adolescent HPV vaccination rates. A paucity of data exists on the use of parental cancer screening visits as TMs to improve their child's cancer preventive care, although use of child office visits has been demonstrated as an effective TM for parental smoking cessation.¹⁴ Previous work has discussed the efficacy of using targeted educational materials to address the specific concerns mothers may have about HPV vaccination.^{15–19} Using cancer screening visits as the educational gateway through which to provide these materials may be a cost-effective and efficient way to increase mothers' motivation for having their daughters vaccinated.

Study implications

In our current study, we have shown that we are able to recruit study participants representing the racial/ethnic and socioeconomic distribution of the underlying population at two geographically and economically diverse sites. The prevalence of adolescent daughters in these populations surveyed by mail establishes the lower limit of the potential population from which we will recruit for a future intervention study that evaluates the use of targeted educational material to improve adolescent HPV vaccine uptake.

We found that in the suburban population, more women completing breast cancer screening were mothers of adolescent daughters, consistent with national demographic trends of later childbearing in women with higher education or socioeconomic status.²⁰ This suggests that targeting of maternal educational materials may need to account for differences in socioeconomic and educational status of the underlying population. To date, there have been no trials in the literature evaluating the impact of maternal education on actual adolescent HPV vaccination practices, with limited evaluation of maternal educational interventions to improve maternal intention to have their daughters vaccinated.²¹ We are actively developing interventions targeted to maternal factors that Brewer and Fazekas¹⁵ have shown to be associated with HPV vaccination.

The most significant limitation of our study is the 31% response rate. Despite inviting 3,000 women to participate and offering incentives for both reading and completing the survey, our response rate remained low, which has implications for the generalizability of our results to the wider population the study clinics serve. In the absence of data on total family size to inform our definition of poverty, we likely underestimated the number of households below the poverty line.

Conclusions

Primary prevention of cervical and other HPV-associated cancers via vaccination is an important breakthrough in women's health. Over the long term, widespread vaccination against HPV will mean fewer cases of cervical cancer. In the short term, it will mean fewer cases of genital warts and less need for procedures used to diagnose and treat precancerous changes in the cervix. The success of HPV vaccination, however, will depend largely on acceptance of the vaccine by those at risk of infection and its clinical consequences. Beyond

the United States, other countries have implemented successful HPV vaccination programs. For example, Australia has established the National Human Papilloma (HPV) Vaccination Program providing free vaccines for 12–18-year-olds as well as the National HPV Vaccination Program Register to monitor and evaluate HPV vaccination. The system of medical care and reimbursement in the United States differs sufficiently from that in Australia and requires alternative strategies to improve HPV vaccination.

In the United States, implementing programs to reach adolescents is challenging because of relatively limited preventive healthcare encounters in this age group. Mothers' cancer screening encounters may represent a unique opportunity to encourage vaccine use among their adolescent daughters. The differences between adolescent and maternal preventive service use and the central role mothers play in their adolescent's receipt of health services provide compelling evidence for the use of maternal cancer preventive services as a TM to improve HPV vaccination in their adolescent daughters.

Acknowledgments

This work was funded in part by NIH/NCI K07 CA108664 and R21 CA 133333 (R.C.C.), Michigan BIRCWH K12 HD001438. (A.F.D.), NIH/NCI CA120040 (D.A.P.), and AHRQ K08 (V.K.D.).

Disclosure Statement

The authors have no conflicts of interest to report.

References

- Parkin DM. Cancer in developing countries. *Cancer Surv* 1994;19–20:519–561.
- Womack SD, Chirenje ZM, Blumenthal PD, et al. Evaluation of a human papillomavirus assay in cervical screening in Zimbabwe. *Br J Obstet Gynaecol* 2000;107:33–38.
- Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2006. *CA Cancer J Clin* 2006;56:106–130.
- Insinga RP, Dasbach EJ, Elbasha EH. Assessing the annual economic burden of preventing and treating anogenital human papillomavirus-related disease in the U.S.: Analytic framework and review of the literature. *Pharmacoeconomics* 2005;23:1107–1122.
- U.S. Food and Drug Administration. FDA approves new vaccine for prevention of cervical cancer, 2009. Available at www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2009/ucm187048.htm
- Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV infection among females in the United States. *JAMA* 2007;297:813–819.
- Albertin CS, Rand CM, Fryer GE, Shone LP, Schaffer SJ, Szilagyi PG. Adolescent healthcare utilization across the U.S.: Who may be reached for immunization? *Pediatric Academic Societies*, 2006 Available at www.abstracts2view.com/pasall/view.php?nu=PAS6LI_2171
- McInerney TK, Cull WL, Yudkowsky BK. Physician reimbursement levels and adherence to American Academy of Pediatrics well-visit and immunization recommendations. *Pediatrics* 2005;115:833–838.
- Healthy People 2010: Understanding and Improving Health. Immunization and Infectious Diseases. Available at <http://www.healthypeople.gov/Document/HTML/Volume1/14immunization.htm>
- American Cancer Society. Cancer prevention & early detection facts & figures. Atlanta, GA: American Cancer Society, 2009.
- Carlos RC, Patel DA, Dalton VK. Cervical cancer prevention through HPV vaccination: Using the “teachable moment” as a delivery setting for educational interventions. *Obstet Gynecol* 2010;115:834–838.
- National, State, and Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years, United States, 2008. *MMWR* 2009;58:997–1001. www.cdc.gov/mmwr/preview/mmwrhtml/mm5836a2.htm#tab3 Vol. 2010.
- Dempsey A, Cohn L, Dalton V, Ruffin M. Patient and clinic factors associated with adolescent human papillomavirus vaccine utilization within a university-based health system. *Vaccine* 2010;28:989–995.
- McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: The case of smoking cessation. *Health Educ Res* 2003;18:156–170.
- Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: A theory-informed, systematic review. *Prev Med* 2007;45:107–114.
- Dempsey AF, Zimet GD, Davis RL, Koutsky L. Factors that are associated with parental acceptance of human papillomavirus vaccines: A randomized intervention study of written information about HPV. *Pediatrics* 2006;117:1486–1493.
- Constantine NA, Jerman P. Acceptance of human papillomavirus vaccination among Californian parents of daughters: A representative statewide analysis. *J Adolesc Health* 2007;40:108–115.
- Davis K, Dickman ED, Ferris D, Dias JK. Human papillomavirus vaccine acceptability among parents of 10- to 15-year-old adolescents. *J Low Genital Tract Dis* 2004;8:188–194.
- Slomovitz BM, Sun CC, Frumovitz M, et al. Are women ready for the HPV vaccine? *Gynecol Oncol* 2006;103:151–154.
- Rindfuss RR, Morgan SP, Offutt K. Education and the changing age pattern of American fertility: 1963–1989. *Demography* 1996;33:277–290.
- Cox DS, Cox AD, Sturm L, Zimet G. Behavioral interventions to increase HPV vaccination acceptability among mothers of young girls. *Health Psychol* 2010;29:29–39.

Address correspondence to:

Ruth C. Carlos, M.D., M.S.

Associate Professor

Department of Radiology

University of Michigan Medical Center

1500 E. Medical Center Drive, UH B2A209

Ann Arbor, MI 48109-0030

E-mail: rcarlos@umich.edu