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Staying on track: A cluster randomized controlled trial of automated reminders aimed at increasing human papillomavirus vaccine completion☆

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ABSTRACT

Objectives: To evaluate whether automated reminders increase on-time completion of the three-dose human papillomavirus (HPV) vaccine series.
Methods: Ten reproductive health centers enrolled 365 women aged 19–26 to receive dose one of the HPV vaccine. Health centers were matched and randomized so that participants received either routine follow-up (control) or automated reminder messages for vaccine doses two and three (intervention). Intervention participants selected their preferred method of reminders – text, e-mail, phone, private Facebook message, or standard mail. We compared vaccine completion rates between groups over a period of 32 weeks.
Results: The reminder system did not increase completion rates, which overall were low at 17.2% in the intervention group and 18.9% in the control group ($p = 0.881$). Exploratory analyses revealed that participants who completed the series on-time were more likely to be older (OR = 1.15, 95% CI 1.01–1.31), report having completed a four-year college degree or more (age-adjusted OR = 2.51, 95% CI 1.29–4.90), and report three or more lifetime sexual partners (age-adjusted OR = 3.45, 95% CI 1.20–9.92).
Conclusions: The study intervention did not increase HPV vaccine series completion. Despite great public health interest in HPV vaccine completion and reminder technologies, completion rates remain low.

1. Introduction

The human papillomavirus (HPV) quadrivalent vaccine (Gardasil; Merck & Co) was approved by the U.S. Food and Drug Administration in 2006 for females aged 9–26 and in 2009 for males aged 9–26 [1]. A bivalent HPV vaccine (Cervarix; GlaxoSmithKline) has also been approved for use in females since 2009 [2]. HPV has been linked to genital warts and cervical, vulvar, vaginal, penile, anal, and oropharyngeal cancers [3,4]. In spite of widespread support within the public health community, HPV vaccine initiation and completion rates are persistently low, with disparities in vaccination by age, race, region, and insurance status [5–11].

It is challenging for many patients to return for all three doses of HPV vaccine in accordance with the recommended six-month schedule. In the United States, the national 2012 vaccine series completion rate for girls 13 and younger who had received the first dose was 49.9%, a decrease from the 2011 completion rates of 63.6% for the same age group [12,13]. Vaccine completion is lower among those who present for vaccination after adolescence. In one study of 4,922 women aged 18–26 in a managed care setting, only 47.1% completed the vaccine series [14]. A recent study of eight managed care organizations found that among female initiators 9–26 years old, 42% completed the three dose series within one year [15]. Total rates of completion are even lower in non-managed care settings, with rates ranging from 18.6% for 18–26 year-old initiators at one academic medical center [8] to 35.8% among privately insured women aged 19–26 [16–18].

☆ This study was registered through ClinicalTrials.gov (Registration number: NCT01343485).

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Numerous studies have examined barriers to vaccine series completion and conducted interventions aimed at increasing completion rates among adolescent girls [7–10,14–17]; fewer have examined completion among young adult women. Reminder technologies have been proposed as a method of increasing compliance with various health behaviors, including vaccine series completion [19,20]. Previous studies have documented the efficacy of text message and phone call reminders in a variety of clinical settings, including increased attendance rates for healthcare appointments [21–23], for parents of adolescents for compliance with influenza, HPV, and other vaccines, and improved oral contraceptive adherence in women under age 25 [22,24–28]. Provider reminders have also been explored [29,30]. In a commentary on low rates of HPV vaccine uptake and completion in the United States, the National Cancer Institute cited the infrequent use of reminder and recall systems as one of several contributing factors [20].

Given the promising evidence for the efficacy of automated reminders, the primary aim of this study was to evaluate whether an automated reminder system could increase on-time HPV vaccine series completion. The secondary aim was to conduct exploratory analyses to evaluate whether sociodemographic factors predict vaccine series completion.

2. Materials and methods

This study was a prospective, cluster-randomized study conducted at 10 outpatient reproductive health centers – nine Planned Parenthood health centers located in North Carolina, Utah, Arizona, Washington, Colorado, and California, and one hospital family planning clinic located in Illinois. Intervention sites implemented an automated system to remind participants when their next HPV vaccine dose was due. The study protocol and all study instruments were approved by the Allendale Investigational Review Board and the John H. Stroger, Jr. Hospital Institutional Review Board. The work presented in this article has been carried out ethically, in accordance with human subjects protections.

A cluster randomized trial design was used to minimize logistical challenges and to accurately evaluate a site-level intervention [31]. The 10 centers were matched based on monthly overall patient volume, number of HPV vaccine doses administered, and patient demographics (Fig. 1). Online randomization software was used to assign paired units to intervention or control arms using a block randomization technique. Site randomization was conducted prior to participant recruitment and, due to the nature of the intervention, neither participants nor providers were blinded to study arm assignment.

Participant recruitment and enrollment was conducted by trained research staff at each health center. Women aged 19–26 and fluent in English were eligible for screening. Exclusion criteria included previous HPV vaccination, contraindication to HPV vaccine, or lack of access to at least one of the reminder methods (text, phone, e-mail, Facebook message, or mail). Additionally, pregnant women, women who stated that in the next eight months they might want to become pregnant or planned to move from the area, and women who were unwilling to be contacted for follow-up were excluded.

At the enrollment visit, informed consent was obtained and all participants completed a baseline questionnaire. Questions covered demographic characteristics, insurance status, reproductive health history, and knowledge and attitudes regarding HPV. The questionnaire was conducted electronically at intervention sites and on paper at control sites. At this visit, women in both study arms received the first dose of the three-dose quadrivalent HPV vaccine series at no cost. For doses two and three, participants could use insurance, pay for vaccine out-of-pocket, or, with the assistance of health center staff, complete a short application for the financial assistance program maintained by the vaccine manufacturer, which provides same-day approval and reimburses the health center for the vaccine costs for low-income uninsured adults [32].

At the time of the enrollment visit, women in the intervention arm also selected their preferred method for reminders – text message, e-mail, phone call, private Facebook message, or standard mail. The "Staying on Track" software system, designed for this study, recorded subject data and sent the automated reminders. Each intervention participant received four messages (one if she selected standard mail), sent three days apart prior to doses two and three (Fig. 2). The reminder schedule mirrored the recommended dosing schedule. Reminders for dose two were sent six weeks after the initial visit. Timing of reminders for dose three was dependent on when the participant returned for dose two; reminders were sent either 12 weeks after the second dose or 24 weeks after the first dose, whichever was sooner. All messages reminded patients to schedule their next vaccine and provided health center contact information. For example, the text message for participants at Planned Parenthood sites stated: "*Reminder: schedule your next HPV Vaccine if you have not done so. Call 1-800-230-PLAN or go to www.plannedparenthood.org. You will get a total of 4 reminders.*" At nine study sites, patients were able to walk-in to receive same day HPV vaccine, but scheduled appointments were encouraged; at one study site, patients needed to schedule an appointment for vaccination. Each participant had 32 weeks to return for all three doses as part of the study, which allowed for an eight-week "grace period" beyond the recommended 24 week schedule. Women in the control arm received standard care for HPV vaccine follow up from their health center, which was limited to mail reminders at two control sites. None of the control sites provided automated reminders. All participants who failed to return to their initial health center for all three doses by the end of the 32-week study period were contacted via e-mail or phone with five automated survey questions probing reasons for non-completion of the series.

2.1. Statistical methods

Sample size calculation was based on previously published vaccine completion rates, which were estimated at 40% [8,14]. The calculation was adjusted to account for the pair-matched cluster-randomized trial design. Using a coefficient of variation of true proportions between clusters within each group of 0.20, we determined that a total of 10 health centers and 37 participants from each would sufficiently power the study at 90% and account for failure to follow up and for vaccine completion rates that were lower than anticipated [33].

A total of 365 participants ($n = 180$ intervention, $n = 185$ control) were included in analysis at the individual level. The primary outcome measure, proportion of patients completing the vaccine series on time in each group (intervention vs. control), was evaluated using a test for two binomial proportions to account for the cluster design. Categorical variables were compared across groups using one-way, two-way, or multi-level frequency tables and Chi-square tests. Continuous variables were examined for normality and compared across groups using appropriate parametric (t-test, ANOVA) or nonparametric procedures. Multivariable logistic regression was conducted to adjust the treatment effect for baseline differences (race/ethnicity, number of lifetime sex partners, and age) between the two groups. As there was no statistically significant effect of the intervention, the intervention and control arms were pooled together for an exploratory analysis of vaccine completion, and further adjustment for the cluster design was deemed unnecessary. Bivariate logistic regression was used to examine the effects of the baseline covariates on on-time completion of the vaccine series