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Text message reminders to promote human papillomavirus vaccination

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ABSTRACT

Objective: To implement and evaluate text message reminders for the second (HPV2) and third (HPV3) vaccine doses.
Design: Site-based intervention.
Setting: Nine pediatric sites (5 academic and 4 private) located in New York City.
Participants: Parents of adolescents 9–20 years who received HPV1 or HPV2 during the intervention period, January–June 2009.
Intervention: Parents who enrolled received up to three weekly text message reminders that their daughter was due for her next vaccine dose.
Outcome measure: On-time receipt of the next vaccine dose, within one month of its due date.
Results: During the intervention period, of 765 eligible HPV vaccine events, 434 enrollment instructions were distributed to parents (56.7% of doses). Parents of 124 adolescent girls (28.6% of those handed instructions) activated text message reminders. Comparing children of parents who enrolled versus those who did not, on-time receipt of next HPV vaccine dose occurred among 51.6% (95% CI 42.8–60.4%) versus 35.0% (95% CI 29.6–40.2%) of adolescents ($p = .001$). Similarly, among a historical cohort of adolescents, receiving HPV1 or HPV2 in the six months prior to the intervention period, on-time receipt of next vaccine dose was noted for 38.1% (95% CI 35.2–41.0%) ($p = .003$). Increases in receipt of next vaccine dose among intervention subjects were sustained at 4 months following the vaccine due date. Using a logistic regression model, after controlling for insurance and site of care, intervention subjects were significantly more likely than either control population to receive their next HPV vaccine dose on-time.
Conclusion: Among those choosing to enroll, text message reminders were an effective intervention to increase on-time receipt of HPV2 or HPV3.

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1. Introduction

The human papillomavirus (HPV) vaccine has the potential to greatly improve the health of women by preventing cervical cancer and precancerous dysplastic lesions [1]. It may also reduce the risk for oropharyngeal and anal cancers in both men and women [2]. In 2006, the Advisory Committee for Immunization Practices recommended the quadrivalent HPV vaccine to be included in the routine immunization schedule for adolescent girls in the United States [3]. More recently, a permissive recommendation to immunize adolescent males was added [4]. The quadrivalent HPV vaccine is administered as a 3-dose series; timing for the second (HPV2) and third (HPV3) doses is two and six months after the initial (HPV1) dose, respectively.

A large body of literature has examined barriers to HPV vaccine initiation, including parental [5–8] and provider beliefs [9–11], financial constraints [12], and failure of adolescents to present for medical care [13,14]. Fewer studies have specifically addressed vaccine adherence. Due to their developmental stage, busy lives with competing priorities [15], and dependence on parents to access immunizations [12], adolescents may find adherence with the three-dose HPV vaccine regimen to be particularly challenging. In an observational study by Neubrand et al., only 58% of adoles-

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CIR, (New York City's) Citywide Immunization Registry; HPV, Human papillomavirus; HPV1, 1st dose of HPV vaccine; HPV2, 2nd dose of HPV vaccine; HPV3, 3rd dose of HPV vaccine; NIS-Teen, National Immunization Survey-Teen; PIN, Personal Identification Number.

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cent girls who received HPV1 completed the 3-dose series over a 17-month period [16]. In the 2009 National Immunization Survey-Teen, among a cross-sectional sample of 13–17 year old females, 44% of girls had started the vaccine series while only 27% had received all three doses [17].

Immunization reminder-recalls are widely recommended and may effectively increase completion rates for the HPV vaccine series [18]. By notifying families when the next HPV vaccine dose is due, reminder-recalls may provide a cue to action, motivating teens and their parents to seek medical care. Unfortunately, traditional mail or phone reminders have had limited impact in adolescent populations [19]. An increasing number of US adults now own mobile phones and many homes are now exclusively wireless [20]. In previous work by our group, urban parents of adolescents reported they would welcome receiving text messages from their child's medical provider and that they would be likely to act based on the content of the messages [15]. In the current study, we implemented and evaluated a text messaging service to remind parents when their daughters were due for their next HPV vaccine dose.

2. Methods

2.1. Setting

Nine pediatric clinical sites located in New York City (NYC) participated in this practice-based intervention to improve adherence with HPV vaccination guidelines. Five sites were hospital-affiliated, academic practices, serving primarily publicly insured youth. The remaining four were private practices, serving primarily privately insured children and adolescents. All sites reported immunization data to the Citywide Immunization Registry (CIR), as mandated for all NYC medical providers. At baseline none of the sites utilized reminder-recalls for HPV vaccination; all sites allowed adolescent girls to receive their second and third HPV vaccine doses at "vaccine-only" visits. At two private practices, physicians administered vaccines. At the remaining sites, vaccines were administered by nurses, with a physician's order. This study was approved by the Columbia University Institutional Review Board, with a waiver of informed consent.

2.2. Intervention

Our text message reminder intervention was implemented at all participating clinical sites during a six-month intervention period, January through June 2009. For all adolescent girls 9–20 years who received HPV1 or HPV2 during the intervention period, the nurse or physician administering the HPV vaccine offered parents an enrollment card with instructions on how to sign up for text message reminders for the next vaccine dose. While the intervention was primarily targeted to parents, young women 18–20 years of age who received the vaccine without an adult present may have been offered enrollment cards directly. Parents were instructed to use their cell phone to call a secure phone number and select a language (English or Spanish) for the phone instructions and text messages. They were then instructed to enter a Personal Identification Number (PIN) from their sign-up card and then confirm which HPV vaccine dose was just received to activate a series of text messages. Our interactive voice-response system captured parents' cell phone numbers and placed this number on cue to receive future text message reminders. From the PIN number we were able to identify the clinical site where the adolescent was immunized and the dose received (HPV1 or HPV2). The provider handing out the enrollment card provided the link between the PIN and patient medical record number, to allow our study team to follow rates of return for next vaccine dose. Enrollment cards, telephone instructions, and all text messages were available in English and Spanish. Content of the enrollment card and the text messages were developed with community input [15].

Parents who enrolled received up to three weekly text message reminders that their daughter was due for her next vaccine dose. Reminders were sent starting three weeks prior to the due date for the next vaccine dose. Timing of the reminders was based on input from parents [15] and providers at the participating clinical sites. English and Spanish language text messages were specific to the teen's clinical site and included instructions to cancel future text messages. An example of one of our text message reminders is: "*Your daughter is due for her 3rd HPV shot in 3 wks! Please call your provider at 212-555-5555 if you need an appt. To stop these reminders, text QUIT*"

2.3. Data sources

Potentially eligible subjects receiving HPV1 or HPV2 during the intervention (January–June 2009) or control period (July–December 2008) were identified through two mechanisms. Private practice subjects were identified by an audit of billing records (CPT code 90649). Academic health center subjects were identified through query of the hospital-based immunization registry. For vaccines administered on-site, reporting to the hospital-based registry is known to be 98% (Dr. Melissa Stockwell, personal communication). Medical records for the index visit, when HPV1 or HPV2 was administered, and for all subsequent visits to the same practice site, were reviewed for up to 4 months after the next vaccine dose was due. Thus, receipt of next vaccine dose was determined for a period of up to 6 months following HPV1 and up to 8 months following HPV2 administration. Missed opportunities were defined as any visit to the patient's usual site for care after the minimum dosing interval, (28 days after HPV1 and 84 days after HPV2), when the next vaccine dose was not administered. Demographic data including age, insurance, site of care, and language were also collected via chart review. Charts were reviewed and coded by a single investigator (HWF). Ten percent of charts were also reviewed by a second investigator (EOK).

2.4. Analysis

Our primary outcome was the proportion of adolescent girls who received their next vaccine dose on-time, defined as receipt within one month of its due date (<92 days between HPV1 and HPV2 and <154 days between HPV2 and HPV3). To measure the impact of our text messaging intervention, we compared on-time receipt of next vaccine dose among adolescents whose parents signed up for text message reminders versus two control groups: Control Group 1–*Opt-out*: adolescent girls who received the enrollment card during the intervention period but did not sign up and Control Group 2–*Historical*: adolescent girls who received HPV1 or HPV2 during the control period, prior to the start of our intervention. Two-way comparisons were made: *Intervention* versus *Opt-out Controls* and *Intervention* versus *Historical Controls* using Chi-square testing, with significance set at $p < .05$.

As a secondary outcome, we compared receipt of next vaccine dose within 4 months of its due date among these same three groups (184 days after HPV1 and 244 days after HPV2). Additionally, the proportion of missed opportunities was also compared for those who signed up versus the two control groups. Logistic regression was used to compare on-time vaccination for the intervention and two control groups, while controlling for factors that varied at baseline among the intervention and control groups.

In a final intention-to-treat analysis, we compared vaccination rates between all girls who received HPV1 or HPV2 during the intervention period versus all girls who received these vaccines during

the historical control period. In these analyses, the intervention group included all girls eligible to sign up for text messages, even if they were not handed a card or did not sign up. The outcomes for the intention to treat analyses were rates of return for next vaccine dose within one and four months of the due date.

During the intervention period, process measures that were compared across all 9 participating sites included: percent of girls eligible for enrollment who were handed a card and the proportion of those handed a card who signed up for text message reminders.

To increase our power to detect a difference between the intervention and control populations, data for HPV1 and HPV2 were grouped together. With 124 adolescents in our intervention group for our primary analyses, 308 in the opt-out control group and 1080 in the historical control group, with α=.05, we had 80% power to detect 15.3% difference in rates of return for next vaccine dose between intervention and opt out control groups and a 13.6% difference in rates of return for next vaccine dose between the intervention and historical control groups.

3. Results

3.1. Intervention population

During the six-month intervention period, across the nine participating clinical sites, 364 adolescent girls received HPV1 and 401 received HPV2 (256 received both HPV1 and HPV2 during the intervention period). Of the 765 eligible HPV vaccine events, 434 sign-up cards were distributed (56.7% of doses), and 128 (29.5% of those handed cards) signed up for the text message reminders. We observed wide site-based variation in our process measures. Across the nine participating sites, the percent of eligible girls who were handed a sign-up card ranged from 21 to 81% while the proportion of girls receiving a card who then signed up for reminders varied from 16 to 60%.

Four parents who signed up for text message reminders were excluded post hoc as we could not link the PIN to an individual patient, making it impossible to evaluate return for next vaccine dose. Thus, the final intervention population was comprised of 124 adolescent girls (28.6% of those handed cards). Sixty-eight signed up for reminders after receiving HPV1 (55%) while 56 signed up after HPV2 (45%). Subjects were primarily publicly insured and their mean age was 14.2 years. Twenty-one (17%) subjects were between the ages of 18 and 20 years. For this subset, we were not able to determine whether the young adult woman or her parent activated the text message reminders. A sizable minority identified as Spanish-speaking (Table 1).

3.2. Control Populations

Control Group 1–*Opt-out*, included the 308 subjects receiving HPV1 or HPV2 during the intervention period who were handed a sign-up card but did not sign up for reminders. This cohort had a mean age of 14.1 years and was primarily publicly insured. The Opt-out control group was more likely than the intervention group to receive care at one of the five clinical sites affiliated with an academic health center (91.6% versus 83.1%) (Table 1).

Control Group 2–*Historical*, was comprised of 1080 subjects who received HPV1 or HPV2 at one of the nine participating sites in the six months prior to the intervention period (July–December 2008). These subjects had a mean age of 14.1 years and were more likely than the intervention subjects to be uninsured (8.2% versus 0%) (Table 1).

Table 1
Demographic data for intervention and control groups.

	Intervention: signed up for text message reminders (n = 124)	Control 1: offered card but did not sign up (n = 308)	Control 2: historic Control (n = 1080)
Age, mean(SD), y	14.2 (0.55)	14.1 (0.32)	14.1 (0.17)
Insurance, No. (%)			
Medicaid/SCHIP	82.8% (82)	89.9% (223)	67.8%* (702)
Private	17.2% (17)	10.1% (25)	24.0% (249)
Uninsured	0% (0)	0% (0)	8.2%* (85)
Site of care, No. (%)			
Academic center	83.1% (103)	91.6%* (283)	80.7% (871)
Private practice	16.9% (21)	8.4%* (26)	19.3% (209)
Language, No. (%)			
English	52.9% (64)	39.4%* (121)	28.5%* (305)
Spanish	41.3% (50)	42.7% (131)	39.0% (418)
Not available	5.8% (7)	17.9%* (55)	32.5%* (348)

* Differences between intervention and control group(s) that were statistically significant (p < .05).

3.3. Process measures

Among the 124 adolescents whose parents signed up for reminders, none opted to cancel the text messages. A total of 493 messages were sent to the 124 intervention subjects. Of these, two messages bounced and 9 were inadvertently sent after the subject had already returned for the next vaccine dose. These subjects were still included in the intervention group.

3.4. Impact of text message reminders

Adolescents whose parents signed up for text message reminders were significantly more likely than the control populations to receive their next HPV vaccine dose on time–within one month of its due date (Fig. 1). Comparing those who signed up versus the Opt-out control population, on-time receipt of next HPV vaccine dose occurred among 51.6% (95% CI 42.8–60.4%) versus 35.0% (95% CI 29.6–40.3%) of adolescents (p = .001). Similarly, among the Historical controls, on-time receipt of next vaccine dose was noted for 38.1% (95% CI 35.2–41.0%) (p = .003).

At four months following the vaccine due date, the intervention population was still significantly more likely than the control populations to have returned for the next vaccine dose. However, the magnitude of the difference between intervention and control groups was slightly less at four months versus one month. Com-

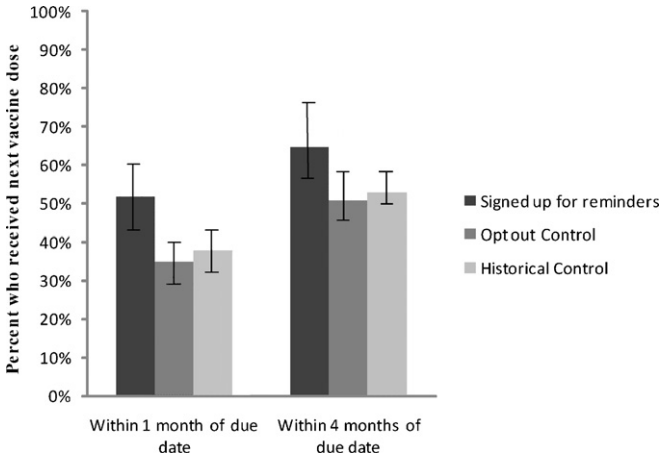

Fig. 1. Impact of text message reminders on receipt of next HPV vaccine dose. p < .05 for two way comparisons (Control group versus those who signed up for reminders). Brackets denote 95% Confidence intervals.

paring those who signed up versus the Opt-out control population, receipt of next HPV vaccine dose within 4 months of its due date occurred among 64.5% (95% CI 56.1–72.9%) versus 51.1% (95% CI 45.6–56.7%) of adolescents ($p = .011$). Similarly, among the Historical controls, receipt of next vaccine dose within 4 months of its due date was noted for 52.9% (95% CI 49.9–55.8%) ($p = .014$).

Missed opportunities occurred among 18.5% of all subjects. Rates of missed opportunities did not differ significantly for intervention versus control populations.

In an intention-to-treat analysis we compared all girls who received HPV1 or HPV2 during the intervention period (regardless of whether they received an enrollment card or signed up for the text message reminders) versus those vaccinated during the historical control period. For the intervention eligible population, 37.8% received their next vaccine dose within one month and 52.9% received their next dose within four months of the due date. These rates are nearly identical to those observed during the historical control period.

3.5. Results of logistic regression

Given the variation noted across clinical sites in rates of handing out cards and differences in insurance coverage between the different cohorts, we conducted multivariable analyses. Using a logistic regression model, after controlling for insurance and site of care, we found that intervention subjects were more likely than either control population (*Historical*: AOR = 1.83, 95% CI 1.23–2.71, $p = .002$; *Opt-out*: AOR = 2.03, 95% CI 1.29–3.22, $p = .003$) to receive their next HPV vaccine dose on-time.

4. Discussion

Despite the potential benefits of the HPV vaccine, to date, vaccine coverage remains sub-optimal. According to the 2009 National Immunization Survey Teen, among a nationally representative sample of 13–17 year old girls, only 27% had completed the three dose series [17]. While educational efforts have targeted vaccine initiation, we are not aware of other studies to demonstrate effective strategies for increasing adherence with the 3-dose HPV vaccine schedule.

In the current study, compared to two different control populations, adolescent girls whose parents signed up for text message reminders had a 13–16% increase in rates of return for their next vaccine dose. This efficacy is similar, if not better than that reported in previous traditional reminder-recall efforts. In a meta-analysis by Jacobson et al., across differing populations and varied practice settings, reminder-recalls were associated with 5–20% increase in immunization coverage [18]. However, in a recent practice-based intervention that specifically targeted adolescents, phone reminder-recalls were only associated with a 4% increase in Hepatitis B vaccine completion [19].

The favorable efficacy of our reminder-recall intervention may, in part, be attributable to our method for contacting parents–text messages. Traditional mail or phone reminders can be costly [21] and in previous studies their impact has been lessened due to changing address or phone numbers [19,22]. As of June 2010, 93% of US adults own a mobile phone and an increasing number of homes are now exclusively wireless [20]. In prior work by our group, parents reported text messages would be more likely than other modes of communication (traditional mail, email or phone) to grab their attention. Thus, text messaging may be a simple and effective strategy to remind teens and their parents of a needed in vaccine. Only one published study from Spain, by Vilella et al., has reported specifically on their use of text message immunization reminders. This study also reported a substantial improvement associated with text message reminders; adult travelers who received text messages had 8–20% increase in their rates of receipt of their next Hepatitis A or Hepatitis B vaccine dose [23].

Along with the demonstrated efficacy, a second strength of our intervention was its simplicity. Providers were required to hand out enrollment cards at the time of vaccination. Parents choosing to enroll needed only to call a secure phone number and follow simple voice prompts. As our intervention did not rely on integration with an electronic medical record or immunization information system, this method could be easily adapted to any clinical site where vaccines are administered. Furthermore, while our intervention was specific to HPV, the intervention could easily be adapted to other multi-dose immunizations.

As expected, our text messaging intervention was efficacious in promoting on-time vaccination, increasing receipt of the next vaccine dose within one month of its due date. We were also pleased to note the intervention effect was sustained at four months following vaccine due date, highlighting the challenges of multi-dose vaccine schedules for adolescents. We anticipated that our intervention would both prompt adolescents and their parents to seek vaccination and also remind families to request the HPV vaccine at other clinical encounters. However, we did not observe a difference in rates of missed opportunities between intervention and control groups.

Several limitations to this research should be noted. First, unlike many prior studies of immunization reminder-recalls, this was not a randomized controlled intervention. Due to the additional costs associated with randomization, all adolescents vaccinated during the intervention period were eligible to participate. A potential bias was that intervention parents had to actively sign up for our reminders; these parents may have differed from Control Group 1 (parents who were offered the enrollment card but did not sign up) in how motivated they were to have their daughters receive their next vaccine dose on-time. For this reason, we also compared intervention subjects to a large historical control group, girls who received HPV1 or HPV2 prior to the intervention period. While neither control group is ideal, the initial and sustained increase in vaccine rates in the intervention group, exceeding both control groups, was reassuring.

Second, our study was limited by varied clinic adherence with handing out enrollment cards and low rates of parents signing up for reminders. This study was conducted in several large, busy, urban practices. As such, integrating additional tasks for nurses or providers to complete at the time of immunization can be a challenge. However, by implementing our intervention clinic-wide and by relying on providers to distribute enrollment cards, the current study may approximate how our system would function in a non-research setting. Our hope is that outside of a research setting both clinic participation and enrollment rates could be improved. One potential barrier for the current study was that teens may have presented for HPV1 or HPV2 without a parent present. While young adults 18–20 were offered enrollment cards directly, younger teens were not. Future interventions should be targeted to both teens and their parents. In addition, with further input from providers and practice managers, and by removing the need to link participants with their medical records, enrollment processes could be further streamlined.

Third, due to timing constraints, we were unable to follow adolescents from their first HPV vaccine dose through completion of the three-dose vaccine series. Furthermore, in order to increase the power of our study, we combined data on rates of return for HPV2 and HPV3. As most other studies of multi-dose vaccines use series completion as their outcome, this limitation makes comparisons more complicated. However, as our text messaging intervention was effective in improving receipt of next vaccine dose on-time, we can presume that a similar strategy would also increase series completion rates.

A final limitation was that our intervention group was relatively small and geographically limited. Barriers to HPV vaccine initiation and completion may reflect local factors, including cost and access to medical services [12]. In the most recent NIS-Teen, wide state and urban area variation in HPV vaccine initiation was observed. Latino and African American females received HPV1 at rates similar to white females but their rates of series completion were lower [17]. As our sign-up rate was <30%, we did not observe an intervention effect for the entire population (all adolescents immunized during the intervention period) versus the historical control period. Nevertheless, the increased rates of return for next vaccine dose among parents who enrolled were substantial; if widely disseminated and with increased rates of enrollment, our intervention could provide important benefits across communities.

In conclusion, our study provides evidence that among parents choosing to enroll, text message reminder-recalls can effectively promote on-time receipt of subsequent HPV vaccine doses. Future studies should explore how to increase parental interest in signing up for such interventions. In addition, similar text messaging interventions should be conducted in larger, more geographically diverse populations.

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