

FINAL REPORT

Project Title: PRISM: Personalized Reminders for Immunization using Short Messaging systems

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ABSTRACT

Purpose: We compare the effectiveness in improving human papilloma virus (HPV) vaccine series completion for minority adolescents who received personalized text message reminders with tailored vaccine-health-literacy-promoting information versus conventional text message reminders. We also assessed population-wide effects.

Scope: Completion rates among adolescents who initiate the HPV series are low. Previous studies have demonstrated the effectiveness of text messaging on vaccination coverage, however more effective interventions are needed.

Methods: Parents of adolescents who received the 1st HPV vaccine dose were randomized to receive either: 1) personalized which targeted the family's stage of vaccine decision-making or (2) conventional text messages. The primary outcome was series completion within 12 months. As a post-hoc analysis, intervention arms were compared to concurrent non-enrollees and historical controls.

Results: Overall, 956 parents of 1264 eligible families enrolled from four academic-affiliated community health clinics in New York City. Both text message arms had similarly high series completion rates: personalized (72.4%) vs. conventional (75.7%). Two-thirds of families who were not in the preparation stage at the first assessment were either in preparation or vaccinated by 42 days after the first dose. In addition, those in any text message arm had significantly higher completion rates than non-enrollees ($n=1503$)(74.1% vs 45.2%; $P<0.0001$). Even after removing those who only needed 2 HPV doses, adolescents receiving text messages of any kind also had higher rates than the historical controls ($n=2823$)(71.1% vs. 34.8%; $p<0.0001$). A population-wide effect was seen in the study from 2014-16, above historical trends.

Key Words: vaccine reminders, text messaging, adolescents, minorities, trans-theoretical model.

PURPOSE To compare the effectiveness in improving HPV vaccine series completion for minority adolescents of personalized text message reminders with tailored vaccine-health-literacy-promoting information vs. conventional text message vaccination reminders.

SCOPE

Vaccination coverage is below Healthy People 2010 and 2020 goals, with substantial disparities for low-income and other disadvantaged populations. Health information technology interventions that link communication technologies, like text messaging, with electronic health record data offer low-cost, scalable opportunities to foster vaccination as well as other preventive care behaviors. Studies have demonstrated the effectiveness of such interventions on vaccination coverage at levels in line with other forms of reminder/recall particularly in low-income populations for whom other forms of reminder-recall have not been successful. However, their effect has not been as robust as needed. More effective messaging interventions are needed.

Adolescents, particularly minority adolescents, are not adequately protected against human papillomavirus (HPV) and its potential sequelae, which include cancer and genital warts. Despite the highly efficacious vaccine being recommended for all adolescents, completion rates among those who initiate the series are low, particularly among minorities. Using a non-randomized design, we had demonstrated the effect of conventional text message vaccine reminders, notifying a parent their child was due for the next dose, in increasing HPV vaccination in primarily, urban Latina adolescents. Although much improved over controls, only 50% received their next dose on time and only 45% completed the series. While these results strongly support the potential effectiveness of this intervention in minority populations for whom traditional forms of vaccination reminders have not worked, still fewer than half completed the vaccine series.

A potential advantage of text message HIT interventions that has not been well investigated is the ability to provide personalized messages. In this study, we compare the use of personalized HPV vaccine text message reminders to conventional text message reminders among minority adolescents in a pragmatic randomized trial. The trans-theoretical model of behavior change guided the tailoring of our text messages.

OVERVIEW

The objective of this study was to compare the effectiveness in improving HPV vaccine series completion for minority adolescents of personalized text message reminders with tailored vaccine-health-literacy-promoting information vs. conventional text message vaccination reminders.

STUDY SITES

This trial was conducted in four community health clinics affiliated with the New York-Presbyterian Hospital (NYP) Ambulatory Care Network (ACN) and Columbia University. These practices provide ~40,000 visits annually to nearly 19,000 unique patients; 87% for publicly insured patients and 84% for Latino families. The Vaccines for Children (VFC) Program provides the vaccines for free for nearly all patient at the study sites. All the study sites allow walk-ins for 2nd and 3rd HPV vaccine doses without an appointment.

All vaccinations given at the study sites are documented in the NYP Immunization Registry, EzVac. EzVac extracts information about vaccinations directly from the provider order entry module of the electronic health record (EHR) making data accurate for HPV vaccines administered at the clinical sites. EzVac also synchronizes data with the New York Citywide Immunization Registry (CIR) which is a population-based registry. New York City Public Health Law requires documentation for all vaccinations administered to those ≤ 18 years old be submitted to CIR, which captures more than 85% of vaccines administered in New York City, and 93% of vaccines from the Vaccines for Children Program (VFC).

MESSAGE DESIGN AND PRETESTING

We designed the messages (*personalized* and *conventional*) using information gathered during our previous studies, the relevant literature, and the team's expertise in text messaging, HPV vaccination, adolescent medicine, health literacy and the community. While keeping within the 160-character count, we designed the message in English paying attention to reading level, as assessed by the Flesch–Kincaid readability test. Parents were recruited from the waiting room of participating clinics and underwent informed consent. Parents were shown the messages, and asked to say back in their own words what the message meant to them. They were then asked families about any problems or suggested changes. This process was iterative until no new message changes are made. Messages were pre-tested with five parents from each stage of vaccine decision-making to test the personalized messages, as well as five additional parents to pre-test the conventional messages for a total of 20 parents.

Enrollment

For a parent or legal guardian to be eligible for the study, they must have met the following eligibility criteria: 1) have a child who received their 1st HPV vaccine at study clinics who was aged 9-17 years; 2) own a cellphone with text message capabilities; 3) have English or Spanish literacy; 4) plan to remain in New York City through next 12 months; and 5) have not been previously contacted to enroll with a different child. We included children down to 9 years as the vaccine is licensed down to 9 years of age.

We followed a two-pronged enrollment process. First, nurses at the study sites provided families with a recruitment card and information sheet. Those families who were interested in being contacted could put a cellphone number on the card, which was then left for the research assistants. Those who did not want to be contacted could also indicate as such. In addition, we were permitted to abstract from our immunization registry all adolescents who received their first HPV vaccine dose at one of the study sites in the last week. We then contacted all those for whom a card was not left or for whom the nurse did not have time to give a card out to assess eligibility and interest. This study was approved by the Columbia University Irving Medical Center Institutional Review Board.

RANDOMIZATION

After each enrollment, the project coordinator used an electronic randomization algorithm to randomize all participants with a 1:1 allocation ratio stratified by (1) clinical site; (2) adolescent's gender; (3) adolescent age group (9-14 vs. 15-17); and (4) parental language. The statistician and analyst were kept blinded to group assignments.

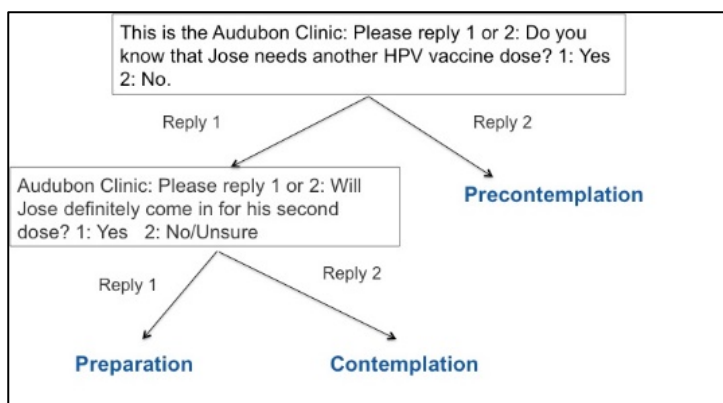
INTERVENTION

Personalized reminders

For families receiving personalized reminders, the customized text messaging application first used a short cascade of questions based on the transtheoretical model to assess in what stage of decision-making regarding vaccination a family was (Figure 1). This was sent on day 21 post-receipt of first HPV vaccine dose. Based on the person's response, the platform automatically then placed them into the correct stage and proceeded to send educational information targeted to that stage of decision-making. Parents who were in the *pre-contemplation* stage were unaware their adolescent needed a vaccination or when it was due.

Those in *contemplation* knew their child or adolescent needed a dose, but may still have had

Figure 1: Day 21 message



questions regarding the vaccine such as vaccine efficacy, side effects and safety. Finally, those in *preparation* were planning to have their adolescent continue the vaccination series but may not have known where or when to access care.

Parents in each stage then

received different messages (Figure 2). For example, messages for parents in *pre-*

Figure 2: Personalized Message Examples. Note: Messages were altered based on gender and language

Example of text message for parent in pre-contemplation stage

Lisa needs to receive 3 HPV shots to fully protect her from HPV infection and diseases like cancer and genital warts.

Example of text message for parent in contemplation stage

Lisa needs her 2nd HPV shot in 4 weeks. Reply 1,2,3,or 4 for info about: 1=protecting her; 2=why need 3 doses; 3=side effects; 4=it is safe

For example, if text back “1”, will be sent a message “The HPV vaccine protects against certain types of cancer and genital warts. Most HPV-related cancers could be prevented by getting the 3 vaccine doses.

Example of text message for parent in preparation stage

Remember, Lisa is due for [her/his] 2nd HPV shot in four weeks! Please place the date on your calendar. She needs it to be fully protected.

contemplation first notified them their adolescent was in need of subsequent doses and why those doses were needed, while messages for parents in the *contemplation* stage provided information needed to answer any remaining questions they may have had regarding vaccination. Some messages were interactive, such that parents were able to self-tailor the content by texting back indicators for which items they wanted more information about. For those in the *preparation* stage, the messages provided information regarding where and when to walk-in for vaccination. Parents in the other two information regarding where and when to walk-in for vaccination

Families also had two additional instances, on days 33 and 40, where their current stage was

Figure 3: D33 and D40 message

Audubon Clinic: Please reply 1 or 2: Will Jose definitely come in for his second dose? 1: Yes 2: No/Unsure

assessed--were they not already in the preparation stage (Figure 3). Based on responses

to these messages, families could switch into a different stage-track of messages.

Conventional text message reminders

Parents not randomized to the personalized text-message arm received conventional text reminders notifying them when the next dose was due. These messages did not include vaccine health literacy-promoting information, and were similar to those used in our previous adolescent studies (Figure 4).

Figure 4: Conventional Message Example. Note: Messages were altered based on gender and language

Example of text message for parent in contemplation stage

Broadway clinic: Lisa has gotten her 1st HPV vaccine dose. Her next dose is due in four weeks.

Message Frequency

Informational messages for both arms began on day 28. This was designed so that if a family reacted to the message and came in to be vaccinated, it would not be before the 28 day minimal interval between the first and second dose. Subsequent messages were sent on days 35, 42, 49, and 56 for both study arms. Day 56 marked when the vaccine dose was next due. A series of five messages (day 28, day 35, day 42, day 49, day 56) was selected based on the protocol from our previous RCT in which a median of 5 messages were needed for a family to bring a child in for vaccination and has been well-tolerated by parents with very few stop requests. Booster messages were also sent on days 63, 70, 84, and 98 post-vaccination.

Messages were sent in English or Spanish based on parent preference. Based on our previous studies, which identified parental preferences, messages were designed to include the child's name as well as stating that it was being sent on behalf of the clinic. The recipient of the messages was the parent, rather than the child, based on previous preferences elicited in this population.

Families stopped receiving messages on their original schedule when the second dose was abstracted from the hospital immunization registry, EzVac which includes the synchronized data from the New York Citywide Immunization Registry (CIR), as described above. If the

second dose was received, messages were later restarted at the appropriate interval before the third dose was due.

In the late fall 2016, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices recommended a change to 2 doses of the HPV vaccine series (0 and 6 months) for those kids who start the series under 15 years of age. There was no change for those who started the series when they are 15 years of age or older. In response to a discussion with our advisory board and the intervention-site clinician leaders, we made the following changes, which were approved by the IRB. First, any parents of an adolescent less than 15 years when first vaccinated, who was already enrolled, and had not yet received their second dose, got a text message update informing them that their child now only needed two doses six months apart and that we would text them when the second dose was due. Second, these parents then received an updated series of messages to be consistent with the now two-dose recommendation in both phrasing and timing (2nd dose now due 6 months after the first instead of 2 months and is now the last dose). Third, any parents of adolescents who either initiated the series a) at 15 years of age or older or b) at less than 15 years of age but had already received their 2nd dose less than six months after the first, stayed on the original protocol because they were still in need of 3 doses. Fourth, any parents of an already-enrolled adolescent who was less than 15 years when first vaccinated and got their 2nd dose at least 5 months after their first were considered to have completed the series under the new recommendations. These parents got a text message letting them know that because their child's 2nd shot was at least 5 months after the first, they were now done with the series.

STUDY SAMPLE AND ENROLLMENT

Given an estimated 51% in the *conventional* group who were expected to receive 3 doses in 12 months. With the sample size of 956, we were powered to detect a minimum of 9% difference between arms with 80% power, allowing for a type I error of 5% for the primary outcome.

MEASURES

Outcome Measure:

The primary outcome measure was the timely HPV vaccine series completion within 12 months (operationalized as the receipt of 2 or 3 doses, based on age and enrollment date, and accounting for the 2016 CDC guideline change).

DATA ANALYSIS

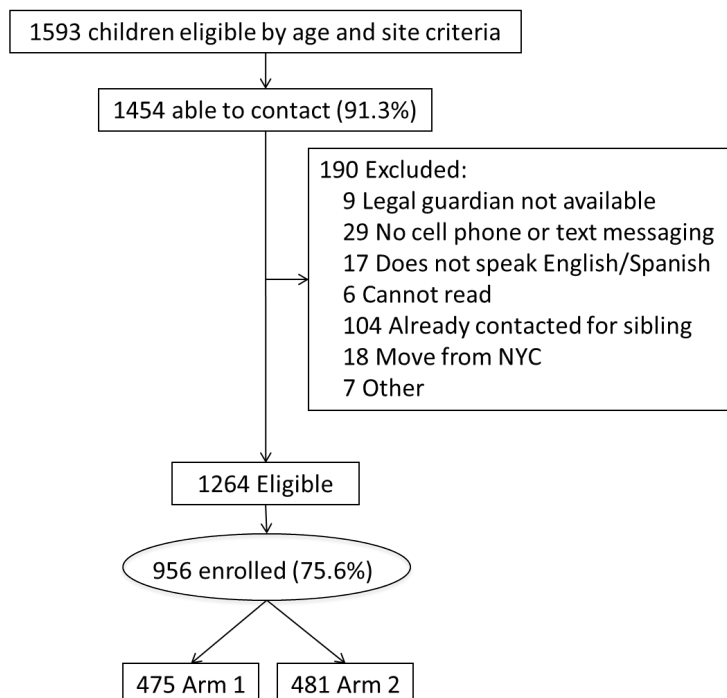
HPV vaccine completion rates were compared for all adolescents of participant parents at the end of a 12-month observation period starting at receipt of their 1st HPV vaccine dose. All primary analyses were done on an intention-to-treat (ITT) basis. Completion rates in the two randomized groups were compared using two-tailed, chi-squared tests at a significance level of $P < 0.05$. We also performed multiple logistic regression analysis to assess any potential differences in receipt among demographic groups.

As a post-hoc analysis, chi-square analyses were conducted to compare intervention arms to concurrent non-enrollees ($n=1503$) who received their first vaccine dose during the study period as well as to historical controls ($n=2823$) (1st dose administered 2011-2013). Intervention-arm adolescents who received 2 doses were removed for comparability for this final analysis.

RESULTS

In total, we screened 1593 adolescents who received their first HPV vaccine dose at the study sites. We were able to contact the majority (91.3%) of them. Of those who we were able to contact, only 2.0% did not have a cell phone with text messaging and 11.1% were excluded based on other exclusion criteria. Of the 1264 eligible families, most ($n=956$; 75.6%) enrolled. This exceeded the minimal percent of eligible families needed to enroll of 61.1%. (Figure 4)

Figure 4: Study Enrollment



The arms were well-balanced. Most adolescents of families that have been enrolled were 14 years old or younger (92.0%). Half (50.0) were female, and most (94.5%) were publicly-insured. Two-thirds (64.2%) of parents/caregivers were primarily Spanish speaking, 60.0% had a high school education or less (Table 1).

Table 1: Characteristics of Study Population

	Total, %(n)	Arm 1, %(n)	Arm 2, %(n)	P
Age				
<14	92.0 (880)	92.0 (437)	92.1 (443)	.95
15-17	8.0 (76)	8.0 (38)	7.9 (38)	
Gender				
Female	50.0 (478)	51.0 (242)	49.1 (236)	.56
Language				
Spanish	64.2 (614)	64.0 (304)	64.5 (310)	.88
Site				
Clinic 1	24.9 (238)	25.5 (121)	24.3 (117)	.90
Clinic 2	25.0 (239)	24.0 (114)	26.0 (125)	
Clinic 3	31.0 (296)	30.9 (147)	31.0 (149)	
Clinic 4	19.1 (183)	19.6 (93)	18.7 (90)	
Insurance				
Public	94.5 (903)	93.7 (445)	95.2 (458)	.30
Parental Education				
<High school	22.9 (219)	24.0 (114)	21.9 (105)	.64
Finished HS	37.1 (354)	35.8 (170)	38.3 (184)	
>High school	40.0 (382)	40.2 (191)	39.8 (191)	

Movement through Stages

Overall, 12,000 messages were sent. One family got their second dose early and therefore did not receive second dose messages; a second family requested to stop the program before the messages started. This left 473 families eligible for the second dose intervention. Most families (90.5%, n=428) in the personalized reminder arm received the day 21 message; there were technical issues for 45 families (9.5%). Of those who received the message, two-thirds (67.3%, n= 288) of families responded to stage-assessment messages: 52.6% (n=225) began in preparation, 10.3% (n=44) contemplation, 4.4% (n=19) pre-contemplation. The remaining families including the 140 (32.7%) that did not respond and the 45 (9.5%) remained in pre-contemplation.

At day 33, there were 214 families randomized to the personalized arm and were either not in preparation or had not yet been vaccinated. Of those, 49.1% (n=105) responded; 98 (45.8%) were automatically switched to preparation, 1.9% (n=4) remained in contemplation, and

1.4% (n=3) moved into contemplation. The remaining stayed in the stage since baseline. At day 40, there were 108 families randomized to the personalized arm and were either not in preparation or had not yet been vaccinated. Of those, 27.8% (n=30) responded; 21 (19.4%) were automatically switched to preparation, 1.9% (n=2) remained in pre-contemplation, and 6.5% (n=7) moved into contemplation. The remaining stayed in stage.

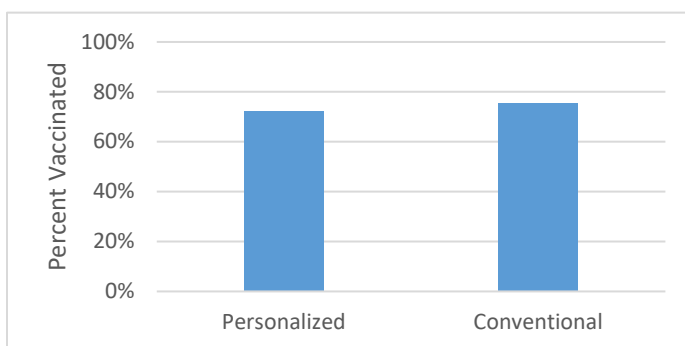
By day 42, there were 344 families (70.6%) in preparation, with 225 (47.6%) being there at day 21 and an additional 119 (25.2%) who moved there through prompts. An additional 34 who had not been in preparation at the beginning of the study had already been vaccinated by day 42, resulting in 79.9% either being in preparation or already vaccinated by day 42. Overall, 64 families, 13.5% never responded to the stage questions.

Movement was similar for 3rd dose. Overall, 336 families randomized to the enhanced message arm needed a third dose of the vaccine which includes those for whom a third dose was needed based on the year of the first dose and their age at first dose. We received replies from approximately half (53.8%, n=181). Based on their replies, 179 families (53.3%) remained in pre-contemplation, including those that did not answer. Twenty nine (8.6%) families were switched to contemplation, and 128 (38.1%) families to preparation. Of the 203 families randomized to the enhanced arm who reached day 33 and were not in preparation, 45.3% responded; 83 (40.8%) were automatically switched to preparation and 120 (59.1%) stayed in stage. Similarly, for the 118 families who reached day 40 and were not in preparation, 24.6% responded with 22 (18.6%) automatically switched to preparation and 96 (81.4%) staying in stage. In total, of those who were not in the preparation stage at day 21 for the 3rd dose vaccine cycle, half were able to be moved into preparation by day 42.

Receipt of HPV vaccination

Both arms had very high timely series completion rate that did not significantly differ, p=

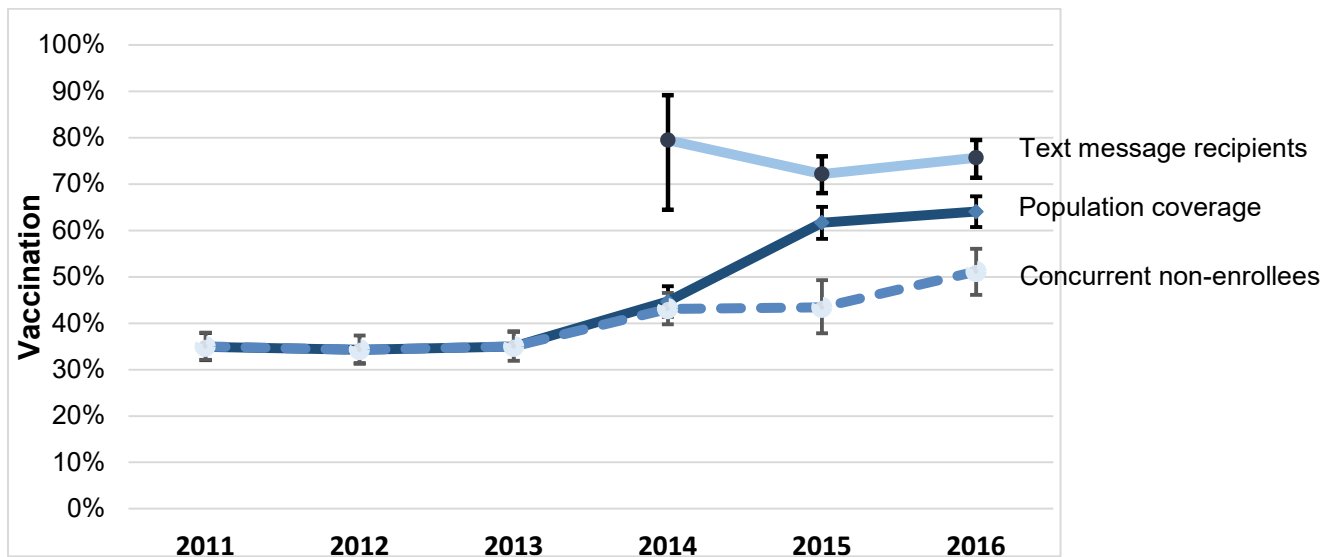
Figure 5: Series Completion Rates by Arm



0.25)(Figure 5). Those with Spanish-speaking parents (aRR 1.17 (1.08-1.27)) had increased rate of timely completion; ≥15 year-olds had decreased rate (aRR 0.95 (0.93-0.98)). No differences existed by sex, education or insurance.

Though a significant difference between the two arms was not found, those in any text message arm had significantly higher completion rates than non-enrollees (74.1% vs 45.2%; $p < 0.0001$). In addition, even after removing those who only needed 2 doses to complete the series, they had higher rates than the historical controls ($n = 2823$)(71.1% vs. 34.8%; $p < 0.0001$). Finally, a population-wide effect was seen during the years of the study 2014-16, above historical trends (Figure 6).

Figure 6: HPV Vaccine series completion within 12 months of initiation by year of initiation



LIMITATIONS

This study was conducted in primarily Latino, urban population which may be particularly sensitive to text message interventions. Additionally, the majority of study population received first dose prior to new CDC guidelines implementation.

DISCUSSION

In this study, text message reminders led to timely series completion in a low-income, urban, minority population with relatively few differences among groups. This led to population-level effects, illustrating the potential impact of such reminders should they be implemented. Levels of completion also far exceeded historical trends.

Among this study population, education information in the text messages did not provide added benefit over conventional text messages without educational information. It is possible that in a different population additional educational information could be important. We had

previously found that for reminders for second dose of influenza vaccine for families of children in need of two doses in a season, adding educational information did have a significant impact.

In this study, we also demonstrated the ability to use text messages to both assess a family's stage of vaccine decision-making as well as move them along the stages of the transtheoretical model. The majority of families (86.5%) responded to at least one message prompt and two-thirds of families who were not in preparation at the first assessment were either in preparation or vaccinated by 42 days after the first dose. Similarly, half of families of adolescents who needed three doses who were not in preparation at the first assessment were either in preparation or vaccinated by 42 days after the second dose. While ultimately such an in-depth intervention may not have been needed for this population, it does lay the foundation for using text messaging both to assess a person's stage of decision-making as well as to intervene to move them through to a possible behavior change.

Finally, during this study, the CDC changed their recommendations for the number of doses of vaccine needed by adolescents who initiate the series before 14 years of age. Text messages facilitated the rapid communication with families to inform them of the CDC schedule changes. Such ability extends the possibilities for health care providers to notify families when they need them to either take or not take a certain action. If sites had had to call families to tell them not to come in, it would have led to the use of extensive personnel time. Conversely, it would have been frustrating to families if they had not been notified and had showed up too early.

In conclusion, text message reminders led to timely HPV series completion in a low income, urban, minority study population, which additionally led to population-wide effects. We also demonstrated the feasibility of using text messages to both identify a family's stage of vaccine decision-making as well as move them further down the pathway to behavior change. However, ultimately education information did not provide added benefit in this very responsive population.

AHRQ priority populations

This study is taking place in four urban, academically-affiliated community clinics that serve a primarily low-income, Latino population.

LIST OF PUBLICATIONS AND PRODUCTS:

Stockwell MS, Kolff C, Catalozzi M, Alba L, Holleran S, Meyer D, Ramakrishnan R. Impact of Text Message Reminders On HPV Vaccine Series Completion, *Poster symposium* 2019 Pediatric Academic Societies Annual Meeting (Baltimore, MD)

Kolff C, Catalozzi M, Barrett A, Camargo S, Fernandez N, Alba L, Holleran S, Meyer D, Ramakrishnan R, Stockwell MS. Comparison of Text Message Reminders Types On HPV Vaccine Series Completion, *Poster presentation* 2018 Pediatric Academic Societies Annual Meeting (Toronto, ON)