PROTOCOL NAME

Impact of Adolescent Vaccine Reminder Notices Sent Via Preferred Method of Communication on HPV Vaccination

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Abbreviation or Term	Definition
CDC	Centers for Disease Control and Prevention
HIPAA	Health Insurance Portability and Accountability Act
HPV	Human papillomavirus
MCHS	Marshfield Clinic Health System
MenACWY	Meningococcal conjugate vaccine
Tdap	Tetanus, diphtheria, and acellular pertussis vaccine

I. PROTOCOL SYNOPSIS

Study Sponsor: Centers for Disease Control and Prevention (CDC)
Title: Impact of Adolescent Vaccine Reminder Notices Sent Via Preferred Method of Communication on HPV Vaccination
Study Short Name: Vaccine Reminders via Preferred Method
Study Rationale: Uptake of adolescent vaccines in the United States is suboptimal in rural areas, especially for HPV vaccine. Furthermore, the proportion of adolescents receiving ≥1 dose of HPV vaccine is low relative to other recommended adolescent vaccines. Patient reminder/recall has been identified as an effective strategy to increase vaccination rates particularly for young children and adolescents.
Study Objective: To assess the impact of vaccine reminder notices sent via the parent's preferred method of communication vs. standard method on HPV vaccine uptake among 12 year-old patients in a regional healthcare system.
Study Design: We will conduct a 1:1 randomized intervention to enhance the current adolescent reminder/recall system by sending vaccine reminders to parents of 12 year-olds using the parent's preferred method of communication. Those randomized to the intervention arm will receive reminders via their preferred method of communication (text, email, letter) while the control arm will receive reminders sent via mailed letters (standard of care). This study will be conducted at a single integrated healthcare system serving patients in central, northern, and western Wisconsin.
Endpoint: The primary endpoint will be receipt of HPV vaccine within 90 days of receipt of the first reminder during the study period.
Analysis: Analyses will compare receipt of HPV vaccine among adolescents assigned to the intervention vs. standard of care (control).

II. BACKGROUND

Uptake of adolescent vaccines in the United States is lower in rural areas, especially for HPV vaccine. There are clear differences in adolescent vaccine coverage between rural and urban populations, but this is not well understood. In 2016 and 2017, the absolute difference in HPV vaccine coverage was 11%-17% lower for adolescents living in rural areas relative to those in urban central cities[1, 2]. MenACWY coverage was also 7%-10% lower in rural versus urban central cities[1-3]. The Midwest (Region V) has one of the highest Tdap and MenACWY coverage rates (91% and 86%), but one of the lowest HPV vaccine coverage.

Centralized reminder and recall systems have been shown to be a cost-effective strategy to increase vaccination rates[4]. Reminder and recall for adolescent vaccinations at Marshfield Clinic Health System (MCHS) are centralized and involve letters to parents of adolescents aged 12 years. Parents who have an adolescent age 12 years who are due for vaccinations receive a reminder letter every other month until the adolescent receives all the recommended vaccinations, turn age 13 years or request to opt out of the reminder notices. Currently, about 3,000 letters are sent out every other month (~18,000 letters/year) to parents of adolescents aged 12 years.

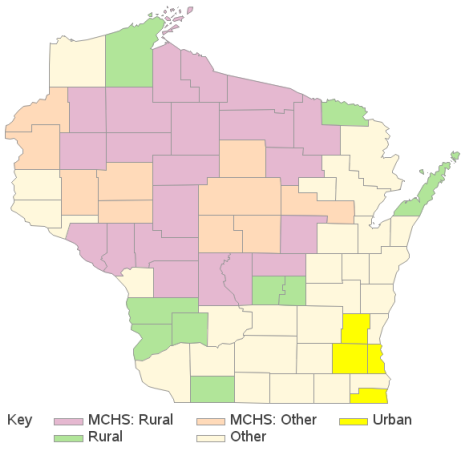
In 2019, MCHS partnered with Odeza, a digital messaging services vendor, to facilitate automated communications with patients regarding appointment and health care updates. We can leverage this process to send vaccine reminder notices using the parent's preferred method of communication. Text messaging has been found to be effective for series completion and is the preferred method for vaccine reminders for 30% of rural Wisconsin parents (unpublished data) [5]. Additionally, text messaging and email are cost effective mechanisms to promote vaccination. Preliminary data suggest about 21% of parents of adolescents aged 11 and 12 years have already opted to receive appointment and health care updates via text and <1% via email. We expect the number opting for text messaging to increase significantly in the coming year.

The vaccine reminder notices can also be used as an opportunity to educate parents, providing them with additional information about vaccines (or links to the information), and to let them know that MCHS recommends vaccination before vaccinations are due. The intervention will leverage the existing MCHS's centralized reminder/recall system and process for enrolling patients for text and email communication regarding appointments and healthcare updates. The proposed study is one component of a larger project funded by the Centers for Disease Control and Prevention (CDC) to understand the determinants of rural-urban differences in vaccine uptake among adolescents in the upper Midwest. The project protocol has been reviewed and approved by the Institutional Review Board at the Marshfield Clinic Research Institute.

A. Marshfield Clinic Health System

Marshfield Clinic Health System is a large integrated regional healthcare system that serves a predominantly rural population. MCHS has over 10,000 employees working at 55 clinical locations throughout central, western, and northern Wisconsin, serving ~24,000 adolescents aged 11-17 years. The MCHS primary service area covers 32 Wisconsin counties, including 70% of rural counties in Wisconsin (**Figure 1**).

Figure 1. Marshfield Clinic Health System Service Area and Rural/Urban Classification of Counties based on Urban Influence Codes
USDA ERS - Urban Influence Codes



III. STUDY OBJECTIVE

To assess the impact of vaccine reminder notices sent via the parent's preferred method of communication vs. standard method on HPV vaccine uptake among 12 year-old patients in a regional healthcare system.

IV. STUDY POPULATION

The target population is parents of MCHS adolescent patients aged 12 years who are due for Tdap, MenACWY, and/or HPV vaccine. Queries will be developed to identify eligible 12 year-old patients using electronic data. Inclusion and exclusion criteria are outlined below.

A. Inclusion Criteria

- MCHS patient aged 12 years with at least one preventive visit or two evaluation & management visits with a MCHS provider in the last 36 months
- Due for at least one adolescent vaccine (HPV, MenACWY, Tdap)

B. Exclusion Criteria

- Primary care provider is not affiliated with MCHS
- Opted out of MCHS vaccine reminder notifications
- Missing or invalid contact information
- Deceased

V. INTERVENTION PERIOD

The intervention period will begin in August 2021 and continue for approximately 9 months.

VI. INTERVENTION

This is a 1:1 randomized intervention in which adolescents who are due for Tdap, MenACWY, or HPV vaccine will be randomly assigned to receive the intervention or control (standard of care). Parents of adolescents who are due for adolescent vaccinations will receive a reminder every other month until the adolescent receives all recommended vaccines, opts out of reminders, or turns 13. The difference between intervention and control is how the reminders will be sent to parents.

Intervention arm: Parents of adolescents who are randomly assigned to receive the intervention and have chosen letter, text or email as their preferred method of communication will receive a letter, text or email reminding them that their child is due for vaccination, with a link to MCHS's vaccine webpage for more information. The default preferred communication method is letter. We attempted to keep messages consistent across methods of communication (letter, text, email), but messages vary given different restrictions on privacy and length across communication methods **(APPENDIX).**

Control arm: Parents of adolescents who are randomized to the control arm will receive the standard of care. Current standard of care at MCHS includes receipt of a mailed vaccine reminder letter.

A. Randomization

Eligible adolescents will be stratified based on communication method and rurality (using home address). Each patient who becomes eligible during the study period will be assigned a random number, which will be used to facilitate stratified random sampling. Within each strata, the random number will be used to assign patients to intervention (vaccine reminder letter, text or email) or standard of care (vaccine reminder letter) arm in a 1:1 ratio. The adolescent will remain in the assigned arm for the duration of their eligibility.

VII. OUTCOME MEASURES

A. Primary Endpoint

The primary endpoint will be receipt of first or second dose of HPV vaccine within 90 days of receipt of the first reminder during the study period.

HPV vaccine was selected as the primary endpoint because vaccine coverage is the lowest for this vaccine and the gap between adolescents living rural and urban areas were the largest. Receipt of HPV vaccine within 90 days of receipt of reminder will be assessed using data available from the MCHS electronic health data, including immunizations administered outside of MCHS through data exchanges with the Wisconsin Immunization Registry.

VIII. PLANNED ANALYSIS

Data will be analyzed using the data analysis software, SAS. We will build a logistic regression model with receipt (yes or no) of HPV vaccine within 90 days after exposure to the intervention or control as the outcome/dependent variable.

A. Sample Size and Power

Based on current estimates of the potentially eligible population for an intervention that is 9 months in duration and vaccine coverage of 50%-70%, we will have sufficient power to detect a difference >10% points between the intervention group (letter + text + email) vs. standard of care (control) for the overall population and rural population (**Table 1**). However, power is limited to detect a difference >5% between the intervention and standard of care groups.

Table 1. Estimated Sample Size (Number of Unique Patients) and Power

	Rural	**Not Rural**	**Total**
***Letter**	444	249	693
***Text**	352	198	550
***Email**	4	3	7
Standard of care	800	450	1250
Vaccine coverage in reference population (standard of care group)	50% - 70%		
Overall: Power to detect >5% difference	71% - 80%		
Overall: Power to detect >10% difference	> 99%		
Rural population: Power to detect >5% difference	52% - 61%		

Rural Population: Power to detect >10% difference	98% - > 99%

*Intervention group

IX. HUMAN SUBJECTS CONSIDERATIONS

This is a quality improvement initiative aimed at measuring the impact of a focused intervention to improve adolescent vaccination rates. Potential risks are limited to the possibility that participants' identifying information would be inadvertently disclosed. We do not anticipate any major risk to participants hence, a waiver of informed consent and HIPAA authorization have been requested and approved by the MCHS Institutional Review Board.

X. REFERENCES

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XI. APPENDIX

Intervention letter/email

Make sure your child is protected.

Dear Parent or Guardian:

Our records show that <<child's name>> is due for the following vaccines:

<<Meningococcal vaccine	Protects against a type of bacteria that can cause serious illnesses. The two most common types of illnesses are meningitis and bloodstream infections. >>
<<HPV vaccine	Protects both girls and boys from future infections that can lead to certain types of cancer. The HPV vaccine works better if given sooner rather than later. Younger adolescents need 2 doses, but older teens need 3 doses to get the same protection. >>
<<HPV vaccine – 2nd dose	Protects both girls and boys from future infections that can lead to certain types of cancer. Two doses are necessary for full protection. >>
<<Tdap vaccine	Protects against three serious diseases: tetanus, diphtheria, and pertussis (whooping cough). >>
<<COVID-19 vaccine	Helps protect against COVID-19. Preteens can get very sick from COVID-19 and spread it to others. Preteens who are up to date with their COVID-19 vaccinations and symptom free do not have to miss school or other activities because of quarantine after close contact.>>
[September-March]<<Influenza vaccine	Helps protect against seasonal influenza. Even healthy preteens can get very sick from influenza and spread it to others. Influenza vaccination is beneficial as long as influenza viruses are circulating.

Vaccines work best when they are given on time. These vaccines can be given during a yearly wellness visit, sports physical, or a vaccination only visit. We recommend <<child's name>> get vaccinated as soon as possible to protect against serious diseases. Please contact Marshfield Children's at XXX-XXX-XXXX to schedule an appointment today. <<Child's name>>'s doctor will be happy to tell you more about these vaccines and answer your questions. You can also visit https://www.marshfieldclinic.org/vaccine for more information.

If <<child's name>> received these or other vaccines from another provider, please let us know so we can update our records. If you need help paying for vaccinations or well child visits, our Patient Assistance Center can help. Please call them at 1-800-782-8581, extension 94475.

Thank you for allowing us to care for <<child's name>>.

<<MCHS Center>> Providers

Intervention text message

[April – August] From Marshfield Children's: <<child's name>> is due for 1 or more of the 4 vaccines recommended for all preteens. Vaccines work best when they are given on time.

Please call xxx-xxx-xxxx to schedule today. Visit https://www.marshfieldclinic.org/vaccine for more info. Please do not reply.

[September – March] From Marshfield Children's: <<child's name>> is due for 1 or more of the 5 vaccines recommended for all preteens. Vaccines work best when they are given on time. Please call xxx-xxx-xxxx to schedule today. Visit https://www.marshfieldclinic.org/vaccine for more info. Please do not reply.