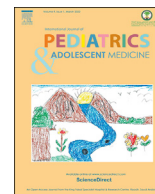


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Original article

Influence of measles-mumps-rubella vaccine series initiation and completion on influenza vaccination among adolescents

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ABSTRACT

Background: Influenza vaccine participation in adolescents is low. Barriers to the influenza vaccine may be shared with the measles-mumps-rubella (MMR) vaccine.

Methods: We studied adolescents aged 13–17 years who participated in the National Immunization Survey-Teen between 2011 and 2017 (N = 129,200). Data were analyzed to determine whether MMR vaccination status was associated with being up-to-date on the influenza vaccination.

Results: A total of 49% adolescents received at least one dose of the influenza vaccine within the past 3 years, and 92% completed the MMR series. In multivariable analysis, not initiating or not completing the MMR series was associated with lower odds of being up-to-date on influenza vaccination.

Conclusions: Adolescents who do not initiate or complete the MMR vaccine series have lower odds of being up-to-date on their influenza vaccination. Lower influenza vaccine participation is associated with lower socioeconomic status, lack of insurance, increased time since last child visit, and higher maternal education.

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1. Introduction

Prior to the development of their respective vaccines in the 1960s and 1970s, measles, mumps, and rubella each had annual incidence rates in millions [1]. Following the 1989 recommendation of 2 doses of the measles-mumps-rubella vaccine (MMR), coupled with a successful federally funded vaccination program in 1993, measles and rubella were declared to be eradicated in the US in 2000 and 2004, respectively, while mumps cases fell below 300 annually from 2001 to 2004 [1–3]. Recently, despite the Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC) recommendations [4], cases of measles are on the rise, and outbreaks of mumps have become increasingly common. There were 372 confirmed cases of measles in 2018, and as of June 2019, there have been over 1044 confirmed cases in 2019 [5]. In 2016, the vaccination rate with MMR was 91.1%,

which was comparable to rates ranging from 89.1 to 91.8 since 2008, but these rates remain consistently below the CDC target goal of 95% [6,7]. The cause for this consistent under-vaccination appears multifactorial, with both socioeconomic characteristics and personal choice playing a role. A review in 2016 showed that specific populations are at an increased risk of MMR under-vaccination, including non-Hispanic Black children, children living below the poverty level, and children with Medicaid as their primary insurance [6].

Similar to the MMR vaccine, influenza vaccination rates remain well below the target goal of 70% for most population groups, with a national average of only 45.4% in adults and 59.9% in children in 2016–17 [8]. Influenza vaccination rates in teens remain some of the lowest in the nation, with rates falling from 48.8% to 47.4% from 2017 to 2018 [8,9]. While adolescents are traditionally not considered to be a high-risk population, this age group made up 25% of the influenza-related deaths in 2014–16 [10]. One potential explanation for low vaccination rates in this age group is the low rate of well-visit attendance among adolescents aged 12–17: only 48% in this age group had a well-visit with a medical provider in 2012–14, limiting the opportunity to receive vaccinations. Another potential reason for influenza under-vaccination may be increasing vaccine

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skepticism due to either the purported yet fraudulent link between the MMR vaccine and autism or skepticism of vaccines in general. A survey of young adults in 2017–18 showed that common reasons for not receiving the flu shot included distrust of the vaccine as well as prior history of not getting vaccinated, fear of developing flu from the vaccine, dislike of shots, inconvenience, expense, and a belief that the flu is not dangerous and they are not at risk [11].

Anti-vaccination movements have garnered increased support over the past several years [12], promoting beliefs that vaccines, particularly the MMR vaccine, are a cause of autism or contain potentially harmful components such as aluminum or mercury, despite significant evidence establishing the safety of the vaccine [13]. Similarly, misinformation regarding the influenza vaccine, such as the vaccine can cause the influenza or influenza is not a serious risk for adolescents, influences many people's decision not to receive the vaccine annually [14]. Given this hesitancy regarding the influenza vaccine, completion of the MMR vaccine series may be a relevant indicator of general trust in vaccination that would increase adolescents' likelihood of receiving the seasonal influenza vaccine. Therefore, we aimed to analyze the relationship between MMR vaccine completion and the rate of influenza vaccination using the National Immunization Survey-Teen (NIS-Teen). As arguments against both vaccines share common themes including distrust of the vaccine and a belief that the diseases they prevent are not dangerous, we hypothesized that adolescents who had completed the MMR vaccine series will have a higher likelihood of influenza vaccine completion in a given year.

2. Methods

NIS-Teen is a nationwide survey on childhood vaccination conducted by the CDC since 2006. Data collection consists of a phone survey of parents or guardians followed by a questionnaire mailed to the adolescent's health care providers [15]. The provider questionnaire includes information regarding where current or previous immunizations were given, date of patient's first and most recent visit, location of 11- and 12-year-old well-child visit and type of facility, and a complete vaccination history. Data from 2011 to 2017 were analyzed in adolescents aged 13–17 years who had initiated or declined the MMR vaccine series. Cases with missing information regarding MMR or influenza vaccine status were excluded, and immunization status was determined from provider responses. In addition to unknown vaccine status, we excluded adolescents with missing data for study covariates, described below.

The primary dependent variable was up-to-date status of seasonal influenza vaccination in the adolescent population. Up-to-date status was defined by the NIS as receiving the vaccine in any of the most recent 3 years at the time of the survey (influenza vaccination status in the current year was not released as part of the public use file). The primary independent variable was MMR vaccination status, sub-divided into never started, partial (one MMR dose), and complete vaccination (two doses of MMR, deemed up-to-date by the provider reporting vaccination history) as of the time of the survey. Covariates included provider facility type, total family income (in relation to the Federal poverty line), current health insurance type, and time since the most recent physician visit. Additional covariates included age, sex, and race/ethnicity, as well as maternal age, education, and marital status.

Continuous variables were summarized using weighted means, while categorical variables were summarized using weighted proportions. Bivariate comparisons of study variables were performed according to MMR vaccination status using Wald tests. Multivariable logistic regression analysis was performed to determine whether MMR vaccination status and other independent variables were associated with being up-to-date on the influenza

vaccination. All analyses accounted for survey sampling weights, and standard errors were adjusted for the complex survey design. Data analysis was performed in Stata/SE 16.0 (College Station, TX: StataCorp, LP), and $P < 0.05$ was considered statistically significant.

3. Results

The 2011–2017 NIS-Teen originally included 276,751 respondents, of whom 145,140 were deemed by NIS staff to have sufficient provider information on vaccination records. After excluding 15,940 cases with missing data, we retained a final sample of 129,200 adolescents for analysis. In the analytic sample, the weighted mean age was 15 years, and weighted sex distribution was 52% male/48% female. Forty-nine percent of adolescents had received at least one dose of the influenza vaccine within the past 3 years. With respect to MMR vaccination, 92% completed the vaccine series, 3% initiated but did not complete the series, and 4% did not initiate the series. Although a minority of adolescents did not complete the MMR series, this group was much less likely to have received a dose of the influenza vaccination. The influenza vaccine uptake rate was 39% (95% confidence interval [CI]: 38%, 41%) among adolescents who did not initiate the MMR series, and 31% among adolescents who initiated but did not complete series (95% CI: 29%, 32%), as compared to 50% among adolescents who completed the MMR series (95% CI: 50%, 50%; $P < .001$).

Additional characteristics associated with MMR vaccination include race and ethnicity, with Hispanic adolescents being over-represented among adolescents who had not initiated the series (21%) and under-represented among those who completed the series (15%; Table 1). Maternal variables such as mother's age, education, and marital status also significantly differed by MMR completion status. Adolescents with mothers aged 45 years or older, those whose mothers were married, and those whose mothers had completed college were most likely to have completed the MMR series. Economic disadvantage also played a major role in MMR vaccination rates: adolescents who completed the MMR series were least likely to live in poverty and most likely to have private insurance coverage.

The multivariable model of influenza vaccine receipt is shown in Table 2. Not initiating or initiating and not completing the MMR series was associated with lower odds of being up-to-date on influenza vaccination (odds ratio [OR] 0.68, 95% CI 0.64–72; OR 0.46, 95% CI 0.43–50, respectively). Older age, higher maternal education, lower income, lack of insurance, and longer time since last well-child visit were all associated with lower odds of influenza vaccination ($OR < 1$). Hispanic ethnicity (vs non-Hispanic White; OR 1.35, 95% CI 1.30–39), Medicaid insurance (vs private; OR 1.23, 95% CI 1.19–27), and receiving vaccines at hospital, private, or school clinics (vs. public clinics) were associated with higher odds of being up-to-date on the influenza vaccine ($OR > 1$), and those who received vaccines at multiple facility types were most likely to be up to date (OR 1.72, 95% CI 1.66–79).

4. Discussion

Because of similar misinformation propagated about both the MMR and influenza vaccines as well as similar underlying socioeconomic barriers to vaccination, we hypothesized that adolescents who had completed the MMR vaccine series would have higher seasonal influenza vaccination completion rates. We found that adolescents who did not complete the MMR vaccination series were less likely to receive an influenza vaccination than their MMR-complete counterparts, even after adjusting for observed socioeconomic characteristics. Although our results support our hypothesis, the overall relationship between socioeconomic

Table 1
Adolescent characteristics and influenza vaccination according to MMR vaccine series initiation and completion.

Variable	Did not initiate MMR series (N = 5439)		Initiated MMR series, but not up-to-date (N = 4411)		Up-to-date on MMR series (N = 119,350)		P ^a
	Weighted mean or proportion	95% CI	Weighted mean or proportion	95% CI	Weighted mean or proportion	95% CI	
Received influenza vaccine at least once in past 3 years	0.39	0.38, 0.41	0.31	0.29, 0.32	0.50	0.50, 0.50	<.001
Age (yr)	15.1	15.1, 15.2	15.0	14.9, 15.0	14.9	14.9, 14.9	<.001
Sex							.012
Male	0.51	0.50, 0.52	0.54	0.52, 0.55	0.52	0.52, 0.53	
Female	0.49	0.48, 0.50	0.46	0.45, 0.48	0.48	0.47, 0.48	
Race/ethnicity							
Hispanic	0.21	0.20, 0.22	0.19	0.18, 0.20	0.15	0.15, 0.16	<.001
Non-hispanic white	0.58	0.57, 0.60	0.63	0.61, 0.64	0.65	0.65, 0.66	<.001
Non-hispanic black	0.10	0.09, 0.11	0.09	0.08, 0.10	0.09	0.09, 0.09	.219
Other	0.11	0.10, 0.12	0.10	0.09, 0.11	0.10	0.10, 0.10	.111
Mother's age							
≤34 years	0.09	0.09, 0.10	0.10	0.09, 0.10	0.08	0.08, 0.08	<.001
35–44 years	0.44	0.43, 0.46	0.45	0.43, 0.46	0.41	0.40, 0.41	<.001
≥45 years	0.46	0.45, 0.47	0.46	0.44, 0.47	0.52	0.51, 0.52	<.001
Mother's education							
<12 years	0.13	0.13, 0.14	0.12	0.11, 0.13	0.10	0.10, 0.10	<.001
12 years	0.20	0.19, 0.21	0.19	0.18, 0.20	0.17	0.17, 0.17	<.001
>12 years (no college degree)	0.29	0.28, 0.30	0.29	0.28, 0.31	0.27	0.26, 0.27	<.001
College degree	0.38	0.37, 0.39	0.40	0.38, 0.41	0.46	0.46, 0.47	<.001
Mother's marital status							<.001
Married	0.69	0.67, 0.70	0.71	0.69, 0.72	0.73	0.72, 0.73	
Not married	0.31	0.30, 0.33	0.29	0.28, 0.31	0.27	0.27, 0.28	
Annual household income							
Above poverty, >\$75,000	0.40	0.39, 0.41	0.41	0.39, 0.42	0.48	0.47, 0.48	<.001
Above poverty, ≤\$75,000	0.39	0.37, 0.40	0.39	0.38, 0.41	0.35	0.35, 0.36	<.001
Below poverty line	0.21	0.20, 0.23	0.20	0.19, 0.21	0.17	0.17, 0.17	<.001
Health insurance coverage							
Private	0.55	0.53, 0.56	0.54	0.53, 0.55	0.61	0.61, 0.62	<.001
Medicaid	0.33	0.31, 0.34	0.32	0.30, 0.33	0.29	0.28, 0.29	<.001
Other	0.07	0.06, 0.07	0.07	0.06, 0.07	0.05	0.05, 0.06	<.001
None	0.06	0.05, 0.07	0.08	0.07, 0.08	0.04	0.04, 0.05	<.001
Facilities where adolescent received vaccinations							
Public clinics	0.16	0.15, 0.17	0.19	0.18, 0.20	0.14	0.14, 0.14	<.001
Hospital clinics	0.18	0.17, 0.19	0.12	0.11, 0.13	0.10	0.10, 0.10	<.001
Private clinics	0.45	0.44, 0.46	0.47	0.45, 0.48	0.50	0.50, 0.50	<.001
School or other clinics	0.10	0.09, 0.11	0.04	0.04, 0.05	0.03	0.02, 0.03	<.001
Multiple facility types	0.11	0.10, 0.12	0.18	0.17, 0.19	0.23	0.23, 0.23	<.001
Years since last well-child visit	1.0	0.9, 1.0	1.1	1.0, 1.1	0.8	0.8, 0.8	<.001

^a P values comparing weighted means or proportions by Wald test. CI, confidence interval; MMR, measles, mumps, rubella.

Table 2
Multivariable logistic regression of receiving influenza vaccination within past 3 years.

Variable	OR	95% CI	P
MMR vaccine series completion			
Did not initiate series	0.68	0.64, 0.72	<.001
Initiated series but not up-to-date	0.46	0.43, 0.50	<.001
Up-to-date on MMR series	(Ref.)		
Age	0.91	0.90, 0.92	<.001
Female	1.02	1.00, 1.05	.047
Race and ethnicity			
Hispanic	1.35	1.30, 1.39	<.001
Non-hispanic white	(Ref.)		
Non-hispanic black	1.01	0.97, 1.06	.495
Other	1.34	1.29, 1.39	<.001
Mother's age			
≤34 years	(Ref.)		
35–44 years	1.03	0.99, 1.08	.147
≥45 years	1.14	1.09, 1.19	<.001
Mother's education			
<12 years	(Ref.)		
12 years	0.80	0.76, 0.84	<.001
>12 years (no college degree)	0.80	0.76, 0.84	<.001
College degree	1.00	0.96, 1.05	.881
Mother not married	0.97	0.94, 1.00	.027
Annual household income			
Above poverty, >\$75,000	(Ref.)		
Above poverty, ≤\$75,000	0.79	0.77, 0.81	<.001
Below poverty line	0.94	0.90, 0.98	.005
Health insurance coverage			
Private	(Ref.)		
Medicaid	1.23	1.19, 1.27	<.001
Other	0.96	0.91, 1.01	.091
None	0.69	0.65, 0.73	<.001
Facilities where adolescent received vaccinations			
Public clinics	(Ref.)		
Hospital clinics	1.53	1.46, 1.60	<.001
Private clinics	1.34	1.29, 1.39	<.001
School or other clinics	1.39	1.29, 1.49	<.001
Multiple facility types	1.72	1.66, 1.79	<.001
Years since last well-child visit	0.89	0.88, 0.90	<.001

CI, confidence interval; MMR, measles, mumps, rubella; OR, odds ratio.

disadvantage and incomplete MMR vaccination reveals that vaccine skepticism is likely only a partial explanation for low influenza vaccination rates. Influenza vaccinations rates in adolescents are low, even among those who completed the MMR series, with only 49% receiving an influenza vaccination compared to 92% completion of MMR. This disparity between the two vaccines points to additional barriers, hesitancy, or misinformation regarding the influenza vaccine compared to the MMR vaccine.

Policy is one likely explanation: the MMR vaccine is required by all 50 states for public school attendance unless an exemption is obtained [17], while currently, only Connecticut requires an influenza vaccine for public school attendance, and it is only required for children under 4 years of age [18]. The influenza vaccine is also an annual vaccine rather than a 2-dose series, which compounds the socioeconomic barriers to remaining up-to-date. These socioeconomic barriers are highlighted by the fact that lower family income and a lack of insurance were associated with lower odds of receiving the influenza vaccination. Receiving an annual vaccine requires time, transportation, and expense that some families may not have. Adolescent compliance with vaccine recommendations is further confounded by the degree of autonomy adolescents have over their health care decisions. The MMR series is typically completed by age 6 when recipients have little input regarding whether they receive the vaccine. Adolescents can refuse the influenza vaccine for a variety of reasons such as fear of needles, cost, time requirement, and belief the influenza is not dangerous, as seen in a 2017–18 survey [11]. Additional encounters with health

care providers may also play a role; as previously noted, only 48% of adolescents in 2012–2014 had a well-child visit, mirroring the 49% influenza completion rate seen in this study. Furthermore, a longer time since last well-child visit was associated with lower odds of receiving an influenza vaccine. Adolescents who received vaccines from multiple facility types or facilities other than public clinics were also more likely to receive the vaccine which may suggest that increased contact with the health care system during influenza season may increase annual vaccine uptake. Subsidized vaccine fees, expansion of insurance coverage for uninsured minors, and school-based vaccine programs may provide means to alleviate these barriers and increase influenza vaccine participation in this population.

In our multivariable analysis, higher maternal education was associated with lower odds of influenza vaccination. Specifically, maternal completion of a high school diploma or some college was associated with lower odds of adolescents' influenza vaccination, compared to adolescents whose mothers did not complete college. However, odds of being up-to-date on influenza vaccination did not differ between the latter group and adolescents whose mothers completed a 4-year college degree. These results may be related to the impact of misinformation regarding vaccines that has been a side effect of the recent anti-vaccine movement surrounding the MMR vaccine. A review in 2016 found that religious reasons were the most common vaccine exemptions, but concerns about vaccine safety were a major motivation for vaccine refusal [19]. One of the primary proposed methods to increase vaccine compliance is increased education regarding vaccines [20], but this may prove difficult if parents feel their opposition to vaccines are well-founded and supported in the literature or media. Efforts to refute vaccine misinformation will likely need to reassure vaccine skeptics that vaccines are both safe and effective.

The findings from our study are limited by available data in the NIS-Teen. A key limitation is that up-to-date status on the influenza vaccination is determined according to whether the vaccine was received at any time in the past 3 years. While this allows us to identify adolescents who are willing and able to receive the influenza vaccine, we cannot be certain that those listed as receiving the vaccine are in fact receiving it annually or in a more sporadic manner. Additionally, the NIS-Teen data are limited by time as the survey itself is relatively new and major changes in the survey's methods occurred in 2010. This allows the NIS to provide current data, but it limits the extent to which we can analyze how these associations may have changed over time given the recent anti-vaccination movement. As the NIS-Teen does not include a survey or analysis of why the adolescents did not receive either the MMR or influenza vaccine, we must rely on reasons found in previous studies or socioeconomic associations seen in the data, further limiting our understanding of direct causes for these associations. Future studies should directly assess reasons for missed or incomplete vaccination. Future studies featuring patient interviews and direct observation in clinics or hospitals would allow us to determine to what extent socioeconomic or personal beliefs regarding vaccines determine vaccine participation.

5. Conclusions

We postulated that the association between the MMR and influenza vaccines would allow providers to more accurately predict which adolescents were at higher risk for not receiving annual influenza vaccines. The results of this study indicate that children who do not complete the MMR vaccine have lower odds of receiving the influenza vaccine as adolescents. Interventions designed to target this at-risk group to increase influenza vaccination participation should be designed to address common

barriers shared by the two vaccines including socioeconomic standing, lack of insurance, and inconsistent well-child visit participation. Based on these barriers, interventions most likely to be successful would be those that make use of the school system to bypass these common barriers and increase adolescent access to vaccines. Interventions in clinics should also stress the importance of the influenza vaccine in the adolescent population and address common concerns such as safety that may cause more educated parents to distrust the vaccine or prevent adolescents from choosing to be immunized annually.

Ethical approval

This study was certified exempt from the East Carolina University Institutional Review Board.

Declaration of competing interest

The authors received no funding for this work and declare no conflicts of interest.

Visual abstract

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