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Trends in Influenza Vaccination Coverage among Adolescents in the United States, 2008-2012

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Bachelor of Science

Binghamton University

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Abstract

Trends in Influenza Vaccination Coverage among Adolescents in the United States, 2008-2012

By Mark I. Rosenthal

Background

The Advisory Committee on Immunization Practices first included adolescents up to 18 years old in its influenza vaccination recommendations in 2008 to lower the burden of influenza among this group and increase vaccine coverage. Detailed evaluations of adolescent influenza immunization patterns over time are currently lacking.

Methods

We conducted a serial cross-sectional analysis of combined data from the 2008-2012 National Immunization Survey - Teen surveys to evaluate the progression of influenza vaccination coverage among adolescents in the United States across relevant sociodemographic factors. Unadjusted coverage estimates were computed for the full period and each annual survey. Adjusted annual coverage estimates and adjusted average change per year were calculated. Adjusted odds ratios were calculated to compare vaccination coverage among levels of each covariate.

Results

Between 2008 and 2012, overall adolescent influenza vaccine coverage estimates in the US increased from 9.6% to 19.1%. The average annual change, adjusted for sociodemographic and socio-economic characteristics, was 20% (OR 1.20, 95% CI 1.17-1.24). Younger adolescents were more likely to have received influenza vaccine (18% coverage among 13 year olds) compared to older adolescents (12% coverage among 17 year olds). Adolescents who received an 11-12 year old check-up were 1.46 times (95% CI 1.24-1.72) more likely to be up-to-date for influenza vaccination than those who did not. Adolescents who are covered by any form of insurance were UTD for influenza vaccination 1.58 (95% CI 1.21-2.06) times more often than those who were not covered.

Conclusions

These findings highlight the need to encourage influenza vaccination as part of routine adolescent health care. Regular contact with healthcare providers is essential to improving influenza vaccine coverage. Because influenza vaccinations need to be performed annually, it is critical that healthcare providers take every opportunity to promote vaccination and increase awareness of its importance among adolescents and their parents.

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Chapter 1. Literature Review and Background

Influenza Virus

Influenza viruses are single stranded RNA viruses that infect a wide range of species. Humans are affected by two major subtypes, A and B. The A type viruses are further categorized by their surface antigens, hemagglutinin (H) and neuraminidase (N), which are responsible for interacting with human cells [1]. Major strains are differentiated by their combinations of the H and N proteins (e.g., H1N1; H3N2). Because of the wide genetic variation, an infection with one influenza strain does not protect against other strains [1]. Influenza season is defined as the period between October and May when circulation of the virus in the U.S. is highest. The majority of influenza seasons peak in January or February, though activity may not peak until later [2]. Influenza circulates below an epidemic level year round, and can also be harbored in other susceptible species like pigs and certain birds [3].

Influenza is spread between people by respiratory droplets. Transmission usually requires close physical contact or contact with contaminated surfaces. Asymptomatic individuals may also be able to spread influenza [4]. Symptoms include fever, sore throat, coughing, and headaches [2], which usually resolve after a week. These symptoms are easily confused with those of other viral infections that are common during the influenza season, such as rhinovirus, respiratory syncytial virus, and others, which can complicate diagnosis, and lead to inaccurate estimation of influenza incidence [5]. Influenza can be

distinguished from other infections by the sudden onset of symptoms. In severe cases, influenza can cause pneumonia, or lead to secondary bacterial infections that cause pneumonia or sinus infections. The infectious period can both precede and continue after the symptomatic period [5].

Every year, influenza epidemics cause thousands of deaths and hospitalizations in the United States [2]. Surveillance records estimate the range of annual hospitalizations from 55,000 to 431,000, and a range of deaths from 3,000 to 49,000 [6, 7]. It is difficult to accurately estimate the number of cases of influenza each year for a number of reasons. One is that many people will not experience symptoms severe enough to cause them to visit a healthcare provider, and therefore the cases never reported. While overall mortality is low except in certain groups, morbidity from influenza is very common and is associated with significant healthcare spending and economic costs. Influenza of the H3 strain is associated with higher mortality than H1 strains [8]. In 2003, annual medical costs for influenza were over $10 billion and the total economic impact was over $80 billion [9].

Influenza rates vary widely in different groups. Children are the most frequently infected; children less than one year old have higher rates of hospitalization due to influenza than older children. Those 65 years old and older experience a higher rate of complications and hospitalizations [2]. Based on data from the Influenza Hospitalization Surveillance Network, the overall rate of hospitalizations due to laboratory confirmed influenza was 61.1 per 100,000 people during the 2014-2015 influenza season. In children up to four years old, this rate was 53.2 per 100,000, and for adults older than 65, the rate was 301.8 per 100,000 [10]. Adults older than 65 have had the highest rates of

influenza associated hospitalizations since the 2010-2011 influenza season. The lowest rate of hospitalizations in the 2014-2015 season was 15.5 per 100,000 among 5-17 year olds [10]. This group usually has the lowest rates of influenza related hospitalizations.

The greatest challenge in combating influenza is the constant genetic changes. Antigenic drift, a collection of small mutations, occurs all the time as the virus makes random errors when replicating. These changes accumulate until the virus is different enough to avoid the body's immune response again, and is why a new vaccine is required every year [1]. A greater threat is antigenic shift. The influenza genome is made up of eight segments of RNA, which allows the virus to exchange chunks of its genome with other influenza viruses [1]. Antigenic shift occurs when a virus exchanges all or part of a segment with a different strain of influenza, resulting in a radically new virus, often a new subtype. This process can occur between viruses with different hosts when they mix in a shared host, such as pigs [1]. Antigenic shifts often precede larger outbreaks or pandemics as immunity to the new strain is very low. The high variability in the virus, combined with the fact that there are several strains in circulation, make it difficult to develop effective vaccines every year.

Influenza Vaccine

Influenza vaccination is the most effective way to limit the burden of influenza. Vaccination has prevented over 40,000 deaths from influenza in the period from 2005 to 2014 [11]. Because of the virus's high genetic variability and differences in circulating strains from year to year, the vaccine must be reformulated every year to match the strains that are expected to be most common during the next influenza season. The effectiveness of the vaccine is highly dependent on how well it matches the strains in

circulation each influenza season. Decisions about the formulation of the vaccine are made near the end of an influenza season, based on surveillance indicating which strains are most prevalent at the time [12]. The lead time, approximately 6 months, is necessary to allow manufacturers to produce enough vaccine so that it is available for distribution during the next influenza season. In the 2014-2015 influenza season, there was unexpected genetic drift in the most prevalent circulating strain, influenza A (H3N2). Only 48% of the circulating viruses matched the vaccine strain [13]. This lowered the efficacy of the vaccine, as it was only partially effective against the drifted strains [14].

There are two kinds of influenza vaccine: inactivated influenza vaccines (IIVs) and live-attenuated influenza vaccines (LAIVs). The IIV contains only inactivated viruses or viral particles, and is administered via injection. The LAIV, given as a nasal spray, contains live viruses that have been rendered non-pathogenic [2]. Both vaccines contain multiple strains that are expected to be circulating in a given year. Trivalent vaccines include three strains of influenza expected to be in circulation, often two influenza A strains and an one of the influenza B strains [2]. Quadrivalent vaccines contain an additional influenza B strain. Clinical trials in children have shown that both vaccines are effective at protecting against influenza in most populations. Several studies have found evidence that the LAIV is more effective than the IIV in children [2, 15]. The results of vaccine efficacy studies can be influenced by the specific outcome measured, complicating their interpretation.

Both IIV and LAIV provide effective protection against influenza, either by preventing infection or reducing the severity of illness. Influenza vaccination effectiveness varies depending on the population, with a high level of variability across

age groups. As a result, observational and randomized studies are not necessarily applicable to the general population. Young children may need two doses to reach the same level of protection, especially if they have never received the vaccine before [16]. Up to 95% of vaccinated children develop protective antibodies against the vaccine strain of influenza [2]. Many studies on the effectiveness of the vaccine have been done. A study by Belshe et al. in 2007, found attack rates of all types of influenza to be 10% for children receiving the IIV and 5% for children receiving the IIV. The study also found that the LAIV was more protective when the match to the circulating viruses was weak [15]. Other studies have demonstrated the LAIV is protective in adults as well [17]. However, other studies during different influenza seasons have found that the IIV has better efficacy than the LAIV [18].

IIV have been shown to be safe in multiple studies [19-21]. In children, the most commonly reported post-vaccination symptoms were fever or non-specific pain, most commonly in very young children with no exposure to influenza vaccine or virus [2]. In adults, the most common side effect of vaccination is temporary soreness at the injection site. The IIV is also safe for pregnant women and immunocompromised people [2].

The LAIV has been shown to be safe in multiple studies [15, 17, 22]. LAIV has been associated with increased risk of minor respiratory symptoms after vaccination in adults [22]. Because the LAIV contains live virus, people who are vaccinated with the LAIV are theoretically able to transmit the virus to someone who has not been vaccinated. People are most likely to shed the vaccine strain virus within two days of vaccination [2]. There is evidence that people can be infected by the attenuated vaccine strain, but the illness is mild compared to un-attenuated influenza [23]. There is also

evidence that the vaccine strain virus does not mutate in the vaccine recipient, and stays attenuated after it is shed. Not as much is known about whether the LAIV is safe for use people who may experience complications, such as the elderly and immunocompromised people [2].

History of Influenza Vaccine Recommendations

The Advisory Committee on Immunization Practices (ACIP) is an advisory group that provides expert advice regarding immunization policy in the United States. The group is made up of experts from the public and private sectors who are involved in vaccine production, licensing, and other related fields. The ACIP is responsible for making recommendations regarding the childhood vaccination schedule based on a risk/benefit analysis [24]. Vaccination schedules are determined based on the age that the vaccines will be most effective and streamlined to make it more likely that parents and doctors will be able to follow the schedules. The recommendations are published by the CDC and are generally adopted by the healthcare system [24]. The ACIP has changed its recommendations regarding which age groups should receive the influenza vaccine several times over the past decade, as more evidence has accumulated that the vaccine is safe and effective in all age groups.

Influenza vaccination was first recommended by the Surgeon General in the early 1960s. It was first recommended only for pregnant women, the elderly, and anyone suffering from a condition that put them at increased risk of severe complications [25]. The ACIP issued its first recommendation for use of the influenza vaccine for children in 2004 [26]. The initial recommendation was only for children aged 6-23 months. This was expanded to include children up to 59 months in 2006 [27]. In 2008, the ACIP further

expanded the recommendations to cover all children up to 18 years of age, covering older children for the first time [5]. In 2010, the vaccine was recommended to all people older than 6 months without contraindications to vaccination [28].

The aforementioned changes in 2008 that included all children ages 6 months to 18 years, substantially increased the population base for whom influenza vaccine is recommended. The changes in the recommendations were made because the vaccine was determined to be safe for use among school age children, and that influenza was causing "substantial adverse impacts" in this age group [5]. Because children are frequently spreaders of influenza [29], improving vaccination in this group would benefit the entire population, especially since the vaccine is generally more effective in children than adults. Additionally, by simplifying the recommendations to cover all children, the ACIP hoped to increase vaccine coverage [5].

Current Knowledge about Influenza Vaccine Use

Influenza vaccine coverage is reported through a variety of mechanisms. While the CDC routinely summarizes vaccine coverage for children (19-35 months) and adolescents (13-17 years), influenza vaccine coverage is not contained in these reports [30]. CDC publishes a separate annual report on influenza trends and coverage rates as reported by the NIS surveys on its influenza page [31]. The National Immunization Survey – Flu and Behavioral Risk Factor Surveillance System address influenza vaccine coverage in the general population and among high-risk groups, including infants, pregnant women, healthcare workers, and the elderly. These groups are either especially susceptible to harmful effects of infection, or have the potential to act as major spreaders of the disease.

Pregnant women have been the focus of many studies on the safety and potential benefits of the influenza vaccine, which has been shown to be safe for use in pregnant women [32]. Studies have shown that influenza infection during pregnancy can lead to premature births and lower birth weights, especially when severe complications like pneumonia occur [33]. A study by Omer et al. in 2011 showed that women who received the influenza vaccine during their pregnancy had a 70% lower odds of having a premature birth or a birth that was small for gestational age when the birth was during a period of increased influenza activity [34]. Influenza vaccination protects pregnant women from complications that could adversely affect the health of their fetus.

Healthcare workers, including anyone on staff in hospitals or clinics and in long-term care facilities, have also been the focus of many studies due to their potential to act as spreaders of influenza among vulnerable populations. Nosocomial transmission of influenza is a major problem in hospitals and nursing homes, and unvaccinated healthcare workers are responsible for the majority of its spread [35]. Closed hospital environments are a recognized risk, and influenza vaccine has been promoted strongly among healthcare workers since the vaccine was first widely available. Many studies have looked at acceptance of the vaccine among healthcare workers to improve efforts to increase uptake [36, 37]. Coverage among healthcare workers suffers from the same issues as in the general population, such as lack of concern about influenza or the perception that the vaccine does not work [36]. Promoting better coverage among healthcare workers is important for reducing transmission to vulnerable patients and for reducing sick time among the workers themselves [35]. The National Vaccine Advisory

Committee recommends that healthcare employers make influenza vaccination part of their standard infection control programs in order to achieve these objectives [38].

Another population that has been the focus of previous research is children. Improving influenza vaccine coverage in children, particularly very young children, has long been a focus of the ACIP and professional organizations, such as the American Academy of Pediatrics. Many studies have focused on vaccine uptake and its benefits in children. Children are known to have the highest rates of influenza compared to other age groups. They are also more efficient spreaders of influenza. For this reason, emphasizing childhood influenza vaccinations can be more effective in reducing influenza rates overall than by vaccinating other groups [29]. Vaccinating children is also an effective way of reducing indirect costs, such as hospitalizations and lost work time, regardless of the child's risk-level [39].

Influenza Vaccination in Adolescents

In spite of all the research about influenza vaccination coverage, studies focusing specifically on influenza vaccination of adolescents are currently lacking. Because a detailed analysis of this group has not been performed, little is known about patterns of influenza vaccine uptake among adolescents, particularly since they were first included in the expanded ACIP recommendations in 2008. Due to better overall health and lower rates of complications due to infection with influenza, there has been less research focusing on adolescents.

An important benefit to vaccinating children is the herd immunity effect gained when vaccinating a large percentage of an at risk group, which affords protection to others in whom the vaccine is less effective [29]. Studies of the effect of the introduction

of the pneumococcal conjugate vaccine (PCV7) for infants provide an example of this indirect protective effect. Introduction of the PCV7 vaccine not only reduces the risk of pneumococcal disease in infants, it also leads to a reduction in pneumonia rates among the entire population [40]. The PCV7 vaccine has also been shown to reduce rates of influenza-associated pneumonia. It is possible that a higher rate of influenza vaccination coverage in adolescents could have similar benefits in terms of protecting the entire population seen when vaccinating younger children.

While infants and the elderly are the populations that frequently have the highest morbidity and mortality due to influenza, in the case of the 2009 influenza A (H1N1) pandemic, adolescents and young adults were heavily affected [41-43]. Cases were most common in those in their teens and early 20s, and severe cases were notably clustered in those younger than 65 [44]. Many older adults were found to have some immunity to the 2009 strain, suggesting previous exposure to a very similar virus. In one study, 33% of adults over 60 displayed reactivity on antibody tests without having received the vaccine [45]. This is a potential explanation for the inversion of the normal pattern of disease burden. The effect of the higher attack rate of H1N1 in adolescents was not necessarily higher mortality, but resulted in high morbidity. Fear that the virus was particularly severe for young adults led to school closures [44]. The 2009 pandemic highlighted the fact that influenza is not solely an issue for the very young and very old, but that it can affect all age ranges. Therefore, knowledge of vaccine uptake among all groups is important for minimizing the effects of influenza epidemics.

While many studies have been done as the higher risk groups mentioned above, adolescents as a group have not been the focus of many studies. The CDC maintains a

website that provides information about influenza and reports on trends in vaccination [31]. Each year, coverage rates for different groups are reported. Statistics are presented by age, race/ethnicity, and other factors. However, these reports do not cover each group in detail. Other research has focused on many of these groups, and looked at the interaction between certain factors, but not for adolescents.

Background on the National Immunization Survey

This study uses data from the National Immunization Survey – Teen (NIS-Teen). The National Immunization Survey was started in 1995 to provide data to support the Child Immunization Initiative's goal of improving vaccination coverage for infants [46]. The NIS-Teen survey is an offshoot of the National Immunization Survey that was started in 2008 to measure progress towards the Healthy People 2010 goals and to improve the information available about vaccination coverage in adolescents [46].

The NIS-Teen is an annual random digit dialing survey of the entire United States to calculate vaccination coverage in the country. The survey contacts people in all 50 states and the District of Columbia. Starting in 2009 the survey also included the U.S. Virgin Islands. Surveys since 2011 have included both landline samples and cellphone samples for all surveyed states, except the U.S. Virgin Islands which only has a landline sample. Households are randomly selected and asked about the vaccination status of their children. In addition to the household survey, the NIS-Teen requests permission to contact the adolescents' healthcare providers. Vaccination records from the providers are used to confirm the household reports and ensure accuracy. Contact with the providers is done through a mail survey [46]. For each year of the NIS-Teen, about 85% of the homes contacted completed the screening interview, about 8% had an adolescent in the home,

and about 80% of eligible homes completed the full interview. Consent for both the screener and full interviews were lower for the cell phone surveys done in 2011 and 2012 (70% and 66%, respectively). Of those interviewed, 67% - 77% gave consent to contact the adolescent's healthcare providers. Approximately 95% of providers supplied the vaccination records, though not all of these were complete [47].

The NIS-Teen survey collects a broad range of demographic variables and vaccination records. The household portion of the survey collects information on vaccine statuses as reported by the adolescent's parent or guardian. If the respondent has a written record of the adolescent's vaccinations, this is used to verify the information. The survey also gathers demographic information such as the adolescent's age, sex, race/ethnicity, and state of residence. It records financial information on the adolescent's family, including total annual income and whether they are in poverty. Other sections of the household survey cover healthcare utilization and access to care. This includes the number and type of healthcare providers the adolescent sees each year, and whether they had an 11-12 year old wellness checkup, which is indicative of healthcare utilization. The last module of the survey covers insurance. Respondents are asked if they have certain types of insurance, including Medicaid and S-CHIP, which are indicators of lower incomes. The 2009-2011 surveys recorded whether the adolescent was eligible for the Vaccines for Children Program (VFC) [47].

The provider survey collects information from the adolescent's healthcare providers about their vaccination history. These records are provided in more detail than the household information. The dataset includes the number and types of all influenza vaccinations in the past three years, and whether the adolescent was up-to-date for

influenza vaccination for three years. This survey also records age at the time they received an influenza vaccination in days, months, and years. It also records the year and month of each vaccination, as well as the type of vaccine used. This information is recorded for up to nine vaccinations. Starting in 2010, the survey also recorded whether the adolescent received H1N1-specific vaccinations with the same age and vaccine type information as the seasonal vaccine [46].

Reason for Study

The purpose of this study is to fill in the gap in knowledge around trends in influenza vaccination rates among adolescents from 2008-2012. As previously mentioned, many studies have looked at influenza vaccination in infants and specific populations of adults like pregnant women or healthcare workers. Better understanding of coverage among the adolescent population could lead to increased improved efforts to increase vaccine coverage in this group, which remain low despite efforts to improve coverage.

This study will investigate how influenza vaccine coverage has progressed in the United States since the recommendations for flu vaccinations were changed in 2008. Additionally, this study evaluates whether the progression has been consistent across different race/ethnicities, income levels, and other categories, on the theory that vaccine uptake may not be even across the whole study population. Specifically, the association between a set of predictor variables and whether an adolescent is up-to-date for influenza vaccination in a given year will be investigated. The study will look how vaccine coverage has changed over time since 2008 and if the pace of the change varies among different strata of important predictor variables.

Chapter 2. Thesis Manuscript

Introduction

Influenza epidemics sicken five to twenty percent of the population of the United States every year [48]. CDC estimates that in the 2013 – 2014 season, vaccination prevented between 1.1 and 6.6 million cases of influenza [49]. While the Advisory Committee on Immunization Practices (ACIP) issued its first recommendations for influenza vaccination of children in 2004, adolescents up to age 18 were not routinely included in influenza vaccination recommendations until 2008. The changes were made because the vaccine was determined to safe for use among school age children, and that influenza was causing "substantial adverse impacts" in this age group [5]. Because children are frequently spreaders of influenza [29], improving vaccination in this group would benefit the entire population. By simplifying the recommendations, the ACIP hoped to increase vaccine coverage [5].

While the very young and very old usually have the highest morbidity and mortality due to influenza, the 2009 influenza A(H1N1) pandemic showed that adolescents and young adults can also be at risk of severe influenza [41-43]. Cases were common in those in their teens and early 20s, and severe cases were notably clustered in those younger than 65, highlighting that influenza affects all ages [44]. Therefore, understanding patterns of vaccine uptake among adolescents will help plan for future immunization activities to prevent influenza infection in adolescents. Higher vaccination rates would limit their ability to transmit disease, reducing indirect costs associated with influenza and protecting those who cannot receive the vaccine or whose vaccination did not confer protection from influenza [29, 39].

Detailed evaluations of adolescent influenza immunization are currently lacking. The Centers for Disease Control and Prevention (CDC) collects influenza immunization data on adolescents as part of the National Immunization Survey-Teen (NIS-Teen), but annual adolescent vaccination coverage reports based on the NIS-Teen do not routinely report influenza vaccination coverage. Additionally, adolescent influenza immunization patterns over time have not been evaluated. We evaluated influenza vaccine coverage among adolescents in the United States between 2008 and 2012, using NIS-Teen data. Additionally, we evaluated whether the progression has been consistent across different race/ethnicities, income levels, and other categories.

Methods

Data source

We conducted a serial cross-sectional analysis of data from the NIS-Teen. The purpose and general methodology of the NIS-Teen has been previously described [46]. Datasets from the 2008-2012 NIS-Teen surveys were merged, omitting variables that were not of interest. Combined weights and stratum variables for estimation of multi-year means were created following instructions in the Data User's Guide provided with each year of data [47]. All analyses were conducted in SAS version 9.4 (SAS Institute, Cary, NC), using the complex sample design specific procedures (survey procedures) in SAS to utilize the weights provided in the NIS-Teen dataset.

Study Variables

Adolescents in the combined dataset were classified by up-to-date (UTD) or not up-to-date (not UTD) for influenza vaccination, based on their provider indicated

influenza vaccination status in the middle year of the survey. Each year of the NIS-Teen contains questions on influenza vaccination status for three influenza seasons. For example, the 2009 survey records this information for the 2007-2008, the 2008-2009, and the 2009-2010 flu seasons. Because of the timing of the provider verification portion of the NIS-Teen, the influenza season with the most complete data would be the middle season assessed (e.g., for the 2009 survey, the most complete data would be available for the 2008-20009 season). For this analysis, only one influenza season was included from each survey year to allow for the creation of a single variable to record whether the adolescent was up-to-date using the most complete influenza season data. All analyses were restricted to provider-verified vaccination coverage.

Influenza vaccine coverage was assessed across the following sociodemographic factors that could impact immunization coverage: adolescents' race/ethnicity, family poverty status, mother's education level, age and sex of the adolescent, history of an 11-12 year old wellness check for the adolescent, adolescent eligibility for the Vaccines for Children (VFC) program, insurance coverage (any type), and coverage by a S-CHIP or Medicaid plan. For adjusted analyses (described below), we also considered maternal age group, number of healthcare providers with vaccination records for the adolescent, and type of healthcare provider.

Analysis

We calculated unadjusted weighted percentages and 95% confidence intervals (CI) for adolescents UTD and not UTD using PROC SURVEYMEANS. Estimates were computed for full period and for each annual survey, for each of the primary covariates described above. The differences in UTD status by primary covariates were assessed with

PROC SURVEYREG using least squares means differences. We used PROC SURVEYREG to generate covariate-adjusted coverage estimates for each year. All primary and adjustment variables were initially included, regardless of whether UTD status varied significantly by levels of each variable. A backwards change in estimate elimination process was used to generate several models, which were compared to determine if any variables could be removed from the adjusted model. We used PROC SURVEYLOGISTIC to generate adjusted estimates for the average annual change in immunization coverage from year to year, and adjusted odds ratios comparing immunization coverage across covariate levels. VFC eligibility was not included because only three years of data were available.

This analysis consisted of secondary analysis of publicly available, de-identified datasets. The Emory University Institutional Review Board reviewed this project and determined that the analysis did not constitute human subjects research, and therefore did not require any further review.

Results

Unadjusted Influenza Vaccine Coverage Estimates

Over the five year period, there were 99,921 adolescents with adequate provider data included for analysis. Over this period, 17% of adolescents received an influenza vaccination (Table 1). Older adolescents were less likely to have received influenza vaccine (12% coverage among 17 year olds) compared to younger adolescents (18% coverage among 13 year olds). Adolescents who had an 11-12 year old check-up were more likely to have received influenza vaccine than those who did not (16% versus 10%, respectively). Adolescents who were covered by any kind of insurance plan were

significantly more likely to have received the vaccine than those without any insurance coverage (16% versus 8%, respectively). Adolescents were slightly more likely to have received the vaccine (17% coverage) when their family's income was greater than $75,000 annually compared to lower income levels (14% coverage).

Between 2008 and 2012, annual adolescent influenza vaccine coverage estimates in the US increased from 9.6% to 19.1% (Table 2). For most groups, the increase was steady from 2008 until 2011, but was not as strong in 2012 (Figure 1). While coverage for all ages followed the overall increasing trend, differences in coverage by age persisted over the five year period. Adolescents who received an 11 -12 year old check-up had a significantly greater increase in coverage (10.7% in 2008 to 20.9% in 2012) than for those who did not receive a similar check-up (6.6% in 2008 to 12.5% in 2012). While adolescents covered by an insurance plan followed the overall trend of increasing vaccine coverage, coverage for those who did not have an insurance plan went from 7.0% in 2008 to 9.9% in 2012. No difference was observed in vaccination coverage by race/ethnicity, sex, adolescent VFC eligibility, or whether the adolescent was covered by an S-CHIP or Medicaid plan. Rates of increase for these covariates closely matched the overall change in coverage rates.

Adjusted Influenza Vaccine Coverage Estimates

Adjusted coverage estimates followed the same trend as the unadjusted, increasing from 10.8% in 2008 to 19.9% in 2012 (Table 3). The average annual change, adjusted for socio-demographic variables, was 20% (OR 1.20, 95% CI 1.17-1.24).

Adolescents who had an 11-12 year old check-up were 1.46 times (95% CI 1.24-1.72) more likely to be UTD for influenza vaccination than those who did not (Table 4).

Each one year increase in age corresponded with a 14% decrease in coverage (odds ratio 0.86, 95% CI 0.84-0.89). Adolescents who are covered by any form of insurance were UTD for influenza vaccination 1.58 (95% CI 1.21-2.06) times more often than those who were not covered. S-CHIP or Medicaid coverage was associated with 1.29 (95% CI 1.15-1.45) times higher vaccine coverage than when the adolescent was not covered by one of these plans. Adolescents who receive all of their healthcare at public facilities less likely (OR 0.56, 95% CI 0.49-0.64) times as likely to be UTD for influenza vaccination as those who received health care from a variety of different types of healthcare facilities. Other variables in the model did not show important differences between covariate levels. Number of providers was not significantly associated with an adolescent's vaccination status, and was not included in the model for determining the adjusted coverage estimates.

Discussion

Influenza vaccine uptake among adolescents has increased consistently in most groups since the ACIP recommendations were expanded in 2008; however these increases have generally been modest, with coverage approximately doubling from 9.6% in 2008 to 19.1% in 2012. Our findings highlight the need to encourage influenza vaccination as part of routine adolescent health care, with the routine inclusion of influenza vaccine as part of the recommended adolescent vaccine platform.

Factors related to regular healthcare utilization were most associated with whether an adolescent was vaccinated in any year. Lack of an 11 – 12 year old check-up suggests that the adolescent may be missing out on basic health services, which may prevent their

parents from being made aware of the importance of the influenza vaccine for adolescents. The decline in age-specific vaccine coverage from age 13 to age 17 could be a result of declining contact with a healthcare provider as the adolescent ages out of going to a pediatrician, leaving a gap between pediatric and adult care [50]. Healthcare providers are very important in promoting the vaccine [50], and hearing its importance repeatedly reinforced may increase the chance that parents have their children vaccinated.

In 2008, the National Vaccine Advisory Committee (NVAC) made recommendations regarding the best practices to improve vaccination rates among adolescents, focusing on meningococcal vaccine, human papillomavirus (HPV) vaccine, and Tdap vaccine [51]. They noted that adolescents have reduced contact with all types of healthcare providers, which becomes more pronounced among older adolescents, in agreement with our findings [51]. A primary recommendation for improving adolescent immunization rates was to vaccinate at all opportunities, including at acute care visits, pharmacies, and other visits [51, 52]. Improving communications with the adolescents' parents to remind them when their children are due for vaccinations, and to impress on them the importance of vaccinations would also help improve coverage. Ensuring providers are alerted to an adolescent's vaccination status through the use of electronic medical records or immunization information systems would aid in this effort.

CDC reports using NIS-Teen data from 2013 indicated coverage for Tdap reached 86%, Meningococcal conjugate vaccine reached 77.8%, and three dose coverage for HPV vaccination was 37.6% for females and 13.9% for males [30]. Tdap has exceeded its 80% coverage goal from the Healthy People 2020 objectives [53], and the other vaccines have made substantial progress. Influenza vaccination is lagging considerably, at or below

HPV vaccine series completion, which is often considered to have suboptimal coverage. Influenza vaccination is not generally grouped with the standard panel of adolescent immunizations because it is a seasonal vaccine. While different strategies are required to maintain coverage every year, considering influenza vaccination as one of the standard adolescent vaccines would reinforce its importance and benefit efforts to increase coverage.

Strengths and Limitations

The NIS-Teen is a large national level dataset that provided five years of data at the time of this analysis. Merging data from all five years allows for greater precision in generating coverage estimates. CDC presents influenza vaccination information on their Flutracker website, but this does not address coverage trends over time or adjusted coverage estimates [31].

Because of the way influenza vaccination status was recorded, there were multiple years of coverage history recorded in each year of data. Certain influenza seasons were covered by up to three surveys, while the earliest and latest seasons were only covered in one survey. However, because certain years are over-represented in the merged datasets, variances of the estimates would be uneven, and considerably higher for the earliest and latest years. To fix this, only one year of vaccination information was taken from each survey year, as previously described. This was necessary to calculate coverage rates over the five year period, and to compare coverage rates between years. This leads to the loss of some information, but including all the UTD variables would have led to uneven denominators for each year. We were unable to assess the impact of VFC eligibility, as this was only addressed in three years of NIS-Teen data. Geographic diversity in

adolescent vaccine coverage has been observed for other adolescent vaccines [30]; we did not consider geographic differences in vaccine coverage. Future studies of adolescent influenza vaccination should address geographic differences in influenza vaccine coverage.

There are limitations inherent to using the NIS-Teen data. Despite the use of sample weights, there could still be some bias due to non-response or differences in the land line and cell phone samples. There are no questions that provide information regarding reasons for choosing to vaccinate or not. Although influenza specific questions in the household survey are limited, the provider portion of the survey collects detailed information on when vaccination occurred and the adolescent's age at vaccination. Many of the demographic variables are simplified or imputed. Because coverage did not vary over most of the demographic variables, this is unlikely to have negatively impacted the analysis.

Future Research

Better understanding of coverage in adolescents could help improve the targeting of vaccination campaigns. Adolescents are not often a focus of campaigns to improve influenza vaccination coverage, which usually target groups that are perceived to be at higher risk. Current efforts to improve adolescent vaccination coverage focus on the Tdap, HPV, and meningococcal vaccine [51]. More research on how to promote the influenza vaccine to parents of adolescents could help improve vaccine uptake. Because influenza vaccinations need to be performed annually, it is critical that healthcare providers take every opportunity to promote the vaccine and increase awareness of its importance among adolescents and their parents. Healthcare that is specifically targeted

towards adolescents may lead to more regular doctor visits, which would provide more opportunities to promote vaccination. In the meantime, continuing to promote vaccination every time an adolescent visits a healthcare provider is the best way to maintain and improve coverage levels [50].

Improving coverage among adolescents may also help reduce indirect costs associated with influenza and help protect others who are in close contact with adolescents [29, 39]. This effect was seen with the introduction of the pneumococcal conjugate vaccine for infants, which reduces the risk of pneumococcal disease in infants as well as reducing pneumonia rates among the entire population, including influenza-associated pneumonia [40]. It is possible that a higher rate of influenza vaccination coverage in adolescents could have similar benefits in terms of protecting the entire population as seen when vaccinating younger children.

Improving coverage among adolescents and reinforcing the importance of annual vaccination would be an important step towards meeting public health goals such as Healthy People 2020 [53]. Promoting the vaccine to adolescents is important as health habits picked up as an adolescent could be carried into adulthood, making the increased influenza vaccination coverage long lasting despite the need for yearly vaccination.

Tables and Figures

Table 1. Unadjusted Influenza Vaccine Coverage Estimates among Adolescents (13- 17 Year Olds) by Covariate, United States, NIS-Teen, 2008-2012

	UTD for IFV[1]		Not UTD for IFV[1]	
	Unweighted N	**% Up To Date (95% CI)**	**Unweighted N**	**% Up To Date (95% CI)**
Overall	17,145	15.1 (14.7, 15.5)	82,776	84.9 (84.5, 85.3)
Race/Ethnicity				
Hispanic	2,169	15.1 (14.0, 16.3)	10,582	84.9 (83.7, 86.0)
Non-Hispanic White	11,665	15.0 (14.5, 15.4)	57,193	85.1 (84.7, 85.6)
Non-Hispanic Black	1,577	14.0 (12.9, 15.2)	8,722	86.0 (84.8, 87.1)
Other or Multi-Racial	1,734	18.4 (16.9, 20.0)	6,279	81.6 (80.0, 83.1)
Poverty Status				
Above Poverty > $75K	8,051	16.8 (16.2, 17.4)	34,647	83.2 (82.6, 83.8)
Above Poverty <= $75K	6,073	13.9 (13.3, 14.6)	33,364	86.1 (85.4, 86.7)
Below Poverty	2,327	14.4 (13.4, 15.4)	11,658	85.6 (84.6, 86.6)
Missing	3,801	--	--	--
Age				
13	4,198	18.3 (17.4, 19.3)	15,786	81.7 (80.7, 82.6)
14	3,781	15.9 (15.0, 16.8)	16,784	84.1 (83.2, 85.0)
15	3,483	15.4 (14.5, 16.3)	16,929	84.6 (83.7, 85.5)
16	3,127	13.7 (12.9, 14.6)	17,246	86.3 (85.4, 87.1)
17	2,556	12.3 (11.4, 13.1)	16,031	87.7 (86.9, 88.6)
Sex				
Female	8,388	15.5 (14.9, 16.1)	39,354	84.5 (83.9, 85.1)
Male	8,757	14.8 (14.2, 15.3)	43,422	85.2 (84.7, 85.8)
11-12 yo check up				
yes	13,519	16.5 (16.0, 17.0)	59,848	83.5 (83.0, 84.0)
No	825	10.0 (8.7, 11.3)	6,234	90.0 (88.7, 91.3)
Missing	19,495	--	--	--
VFC eligibility				
yes	3,204	15.0 (14.1, 15.9)	15,042	85.0 (84.1, 85.9)
No	7,899	16.1 (15.5, 16.7)	36,602	83.9 (83.3, 84.5)
Missing	37,174	--	--	--
Mother's Education Level				
Less Than 12 Years	1,514	13.8 (12.6, 15.1)	7,894	86.2 (84.9, 87.4)
12 Years	3,020	13.6 (12.8, 14.4)	16,953	86.4 (85.6, 87.2)
>12 Years, Non-College Grad	4,454	14.3 (13.6, 15.1)	24,202	85.7 (84.9, 86.4)
College Graduate	8,157	17.5 (16.9, 18.2)	33,727	82.5 (81.8, 83.1)
Any Insurance Coverage				
Yes	16,551	15.7 (15.3, 16.1)	77,501	84.3 (83.9, 84.7)
No	503	7.7 (6.4, 9.0)	4,778	92.3 (91.0, 93.6)

Missing	588	--	--	--
S-CHIP/Medicaid Coverage				
Yes	4,461	16.5 (15.7, 17.4)	19,495	83.5 (82.6, 84.3)
No	12,540	14.5 (14.1, 15.0)	62,554	85.5 (85.0, 85.9)
Missing	871	--	--	--

1. Influenza Vaccine

Table 2. Unadjusted Influenza Vaccine Coverage Estimates by Year for Adolescents (13-17 Year Olds) by Covariate, United States, NIS-Teen, 2008-2012

	2008	2009	2010	2011	2012
	% Up To Date (95% CI)	% Up To Date (95% CI)	% Up To Date (95% CI)	% Up To Date (95% CI)	% Up To Date (95% CI)
Overall	9.6 (8.7, 10.4)	12.3 (11.5, 13.1)	16.4 (15.5, 17.3)	18.4 (17.5, 19.4)	19.1 (18.2, 20.1)
Race/Ethnicity					
Hispanic	9.7 (7.1, 12.2)	11.5 (9.3, 13.8)	15.0 (12.6, 17.4)	19.6 (16.8, 22.3)	19.0 (16.4, 21.7)
Non-Hispanic White	9.2 (8.2, 10.1)	12.6 (11.7, 13.5)	17.2 (16.2, 18.3)	17.7 (16.8, 18.7)	18.8 (17.8, 19.9)
Non-Hispanic Black	9.6 (7.0, 12.2)	11.0 (8.9, 13.0)	13.9 (11.4, 16.3)	17.6 (14.9, 20.2)	18.5 (15.7, 21.3)
Other or Multi-Racial	12.6 (9.3, 16.0)	14.8 (11.5, 18.0)	18.2 (15.1, 21.4)	22.2 (18.4, 25.9)	22.2 (18.8, 25.7)
Poverty Status					
Above Poverty > $75K	11.0 (9.7, 12.3)	14.2 (12.9, 15.5)	18.8 (17.3, 20.3)	20.3 (19.0, 21.6)	20.6 (19.1, 22.1)
Above Poverty <= $75K	9.3 (7.8, 10.8)	11.1 (9.9, 12.3)	14.5 (13.2, 15.7)	16.3 (14.9, 17.7)	19.2 (17.6, 20.8)
Below Poverty	7.9 (6.0, 9.7)	9.7 (7.8, 11.5)	14.5 (12.3, 16.8)	19.2 (16.9, 21.6)	17.6 (15.5, 19.7)
Age					
Age 13	10.6 (8.5, 12.7)	14.6 (12.8, 16.3)	21.0 (18.7, 23.4)	23.4 (21.3, 25.4)	21.9 (19.8, 23.9)
Age 14	10.0 (8.3, 11.7)	12.5 (10.8, 14.1)	18.3 (16.1, 20.4)	18.9 (16.9, 20.8)	20.1 (17.9, 22.3)
Age 15	10.0 (7.9, 12.1)	13.0 (11.2, 14.8)	15.7 (13.8, 17.5)	19.0 (16.7, 21.4)	19.6 (17.4, 21.9)
Age 16	8.7 (6.8, 10.6)	11.8 (9.9, 13.6)	14.5 (12.6, 16.3)	16.3 (14.3, 18.2)	17.7 (15.7, 19.6)
Age 17	8.5 (6.7, 10.3)	9.6 (7.9, 11.3)	12.5 (10.8, 14.2)	14.6 (12.7, 16.5)	16.3 (13.9, 18.6)
Sex					
Female	9.7 (8.6, 10.8)	12.7 (11.5, 13.8)	16.7 (15.4, 18.0)	19.2 (17.8, 20.6)	19.5 (18.1, 20.8)
Male	9.4 (8.1, 10.8)	12.0 (10.9, 13.0)	16.1 (14.9, 17.2)	17.7 (16.5, 18.9)	18.8 (17.5, 20.2)
11-12 yo check up					
Yes	10.7 (9.7, 11.8)	13.6 (12.7, 14.6)	17.3 (16.3, 18.3)	19.6 (18.5, 20.7)	20.9 (19.7, 22.0)
No	6.6 (4.2, 9.1)	9.0 (6.0, 12.0)	11.2 (8.3, 14.0)	12.0 (8.8, 15.2)	12.5 (9.2, 15.9)
VFC eligibility					
Yes	--	10.6 (9.2, 12.0)	15.1 (13.5, 16.6)	18.6 (16.9, 20.2)	--
No	--	13.1 (12.2, 14.1)	17.1 (16.0, 18.2)	18.4 (17.3, 19.5)	--
Mother's Education Level					
Less Than 12 Years	9.1 (6.2, 12.1)	9.6 (7.5, 11.7)	14.0 (11.2, 16.9)	17.9 (15.3, 20.5)	18.7 (15.7, 21.7)

12 Years	8.1 (6.6, 9.7)	10.5 (9.0, 12.0)	14.6 (12.9, 16.3)	17.9 (15.8, 20.1)	17.7 (15.7, 19.8)
>12 Years, Non-College Grad	9.7 (8.0, 11.3)	11.5 (10.0, 13.0)	15.9 (14.2, 17.6)	16.8 (15.2, 18.4)	17.6 (15.7, 19.4)
College Graduate	11.0 (9.6, 12.3)	15.5 (14.1, 16.9)	19.0 (17.5, 20.5)	20.3 (18.9, 21.8)	21.5 (20.1, 23.0)
Any Insurance Coverage					
Yes	9.8 (8.9, 10.6)	12.8 (12.0, 13.6)	17.0 (16.1, 17.9)	19.2 (18.2, 20.2)	19.9 (18.8, 20.9)
No	7.0 (3.1, 10.8)	5.4 (2.9, 8.0)	8.5 (5.9, 11.2)	7.6 (5.2, 10.1)	9.9 (7.1, 12.7)
S-CHIP/Medicaid Coverage					
Yes	10.6 (8.7, 12.5)	11.9 (10.3, 13.6)	16.1 (14.3, 17.8)	20.4 (18.6, 22.3)	20.8 (18.9, 22.8)
No	9.2 (8.2, 10.1)	12.4 (11.5, 13.3)	16.5 (15.5, 17.6)	17.4 (16.4, 18.4)	18.2 (17.1, 19.2)

Table 3. Adjusted Yearly Influenza Vaccine Coverage Estimates for All Adolescents (13-17 Year Olds), United States, NIS-Teen, 2008- 2012

Year	% Up To Date (95% CI)
2008	10.8 (9.6, 12.0)
2009	13.1 (11.9, 14.2)
2010	16.5 (15.2, 17.7)
2011	18.9 (17.6, 20.2)
2012	19.9 (18.6, 21.2)

Table 4. Adjusted Odds Ratios Comparing Influenza Vaccine Coverage Estimates for Adolescents (13-17 Year Olds) by Covariate, United States, NIS-Teen, 2008- 2012

Variable	OR (95% CI)
Year	1.20 (1.17, 1.24)
Age	0.86 (0.84, 0.89)
Maternal Age Group	1.08 (1.01, 1.16)
Race/Ethnicity	
Hispanic	1.17 (1.04, 1.33)
Non-Hispanic Black	0.94 (0.83, 1.06)
Other/multiple Race	1.24 (1.08, 1.42)
Non-Hispanic White	ref
Sex	
Female	1.02 (0.95, 1.10)
Male	ref
Education Level	
Less than 12 Years	0.85 (0.72, 1.00)
12 Years	0.82 (0.74, 0.92)
12+ years, Non-College Graduate	0.87 (0.79, 0.96)

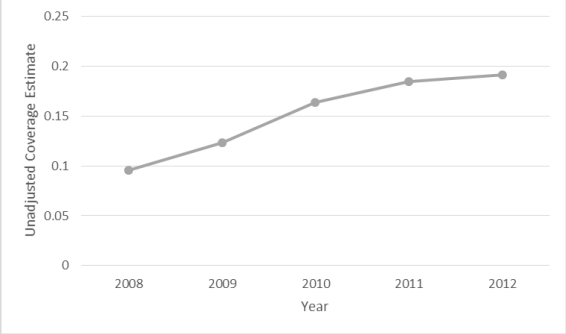
College Graduate	ref
Poverty	
Above Poverty, <= $75K	0.88 (0.81, 0.97)
Below Poverty	0.83 (0.71, 0.97)
Above Poverty, > $75K	ref
Facility Type	
All Public	0.56 (0.49, 0.64)
All Hospital	1.12 (0.96, 1.30)
All Private	0.93 (0.85, 1.03)
All STD/School/Teen Clinics or Other	0.87 (0.68, 1.12)
Mixed	ref
11-12 year old check-up	
Yes	1.46 (1.24, 1.72)
No	ref
Any Insurance coverage	
Yes	1.58 (1.21, 2.06)
No	ref
S-CHIP/Medicaid coverage	
Yes	1.29 (1.15, 1.45)
No	ref

Figures

Trends in Unadjusted Influenza Vaccine Coverage Estimates for 13-17 Year Olds in the United States from 2008-2012 by Covariates, NIS-Teen

A. All Adolescents. **B.** Race/Ethnicity of the adolescent. **C.** Income level and poverty status of the adolescent's family. **D.** Age. **E.** Sex. **F.** Whether the adolescent received and 11-12 year old check-up. **G.** Whether the adolescent was eligible for the VFC program. **H.** Maternal Education Level. **I.** Whether the adolescent was covered by any type of health insurance. **J.** Whether the adolescent was covered by and S-CHIP or Medicaid insurance plan.

A.



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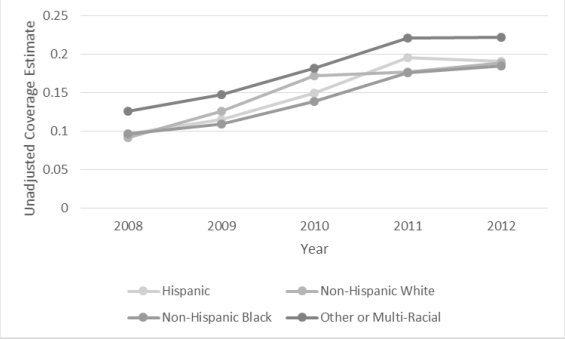

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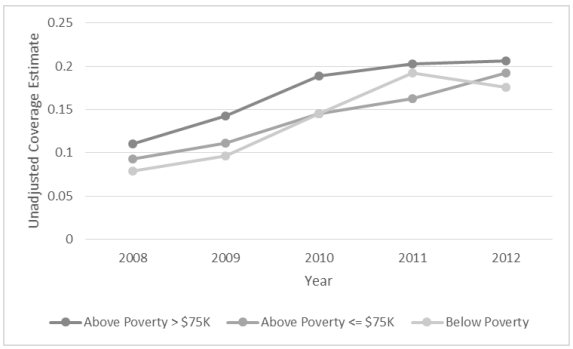
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0.15
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2008
2009
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Year
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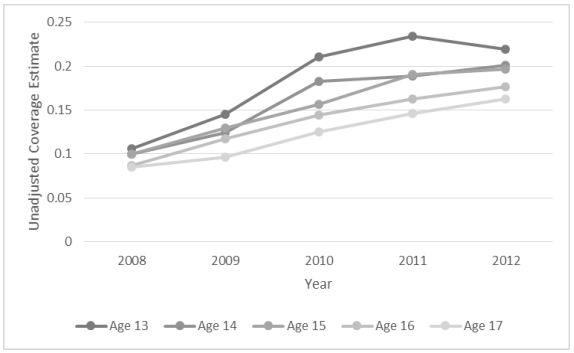
Above Poverty <= $75K
Below Poverty

D.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0.2
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0.1
0.05
0
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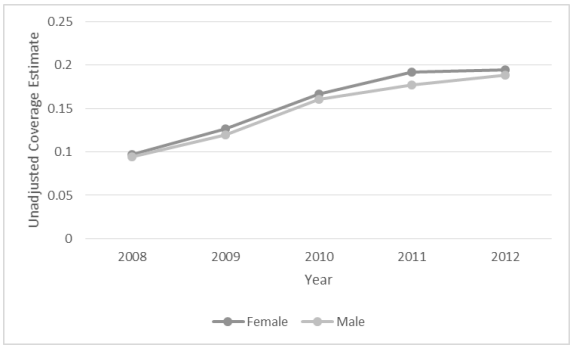
2009
2010
2011
2012
Year
Age 13
Age 14
Age 15
Age 16
Age 17

E.


Unadjusted Coverage Estimate
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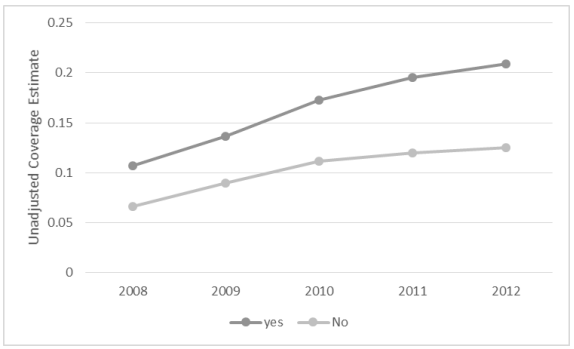
0.2
0.15
0.1
0.05
0
2008
2009
2010
2011
2012
Year
Female
Male

F.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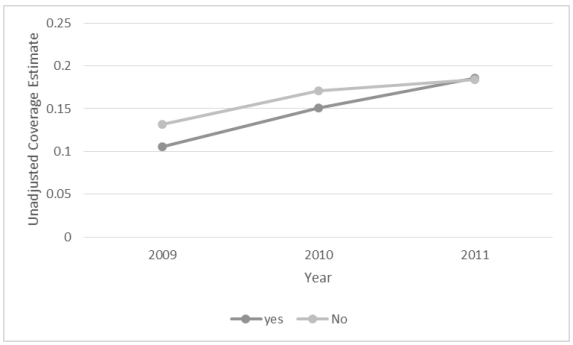
0.15
0.1
0.05
0
2008
2009
2010
2011
2012
Year
yes
No

G.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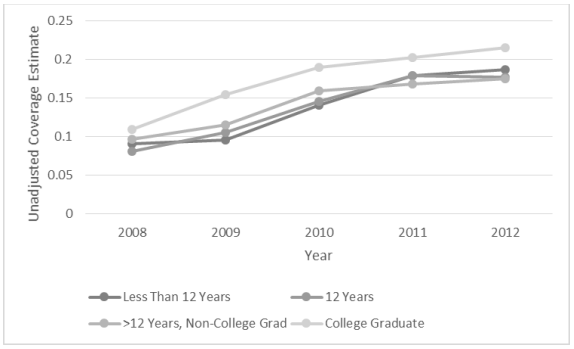
0.2
0.15
0.1
0.05
0
2009
2010
2011
Year
yes
No

H.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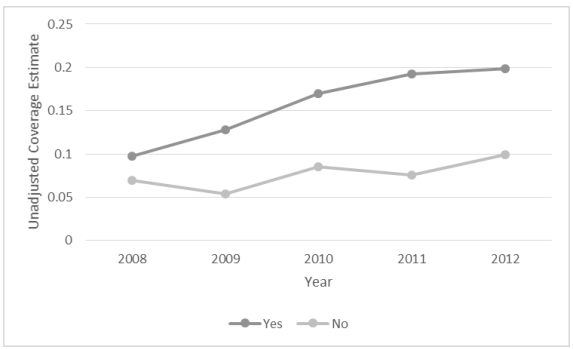
0.15
0.1
0.05
0
2008
2009
2010
2011
2012
Year
Less Than 12 Years
12 Years
>12 Years, Non-College Grad
College Graduate

I.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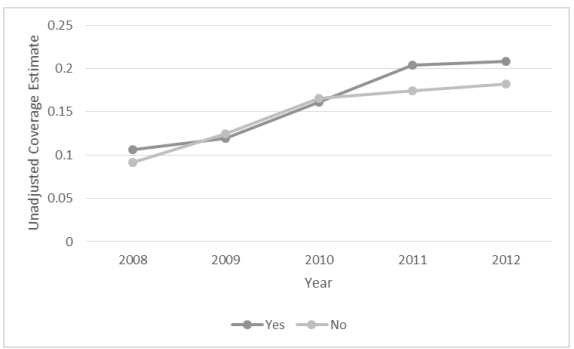
2008
2009
2010
2011
2012
Year
Yes
No

J.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0.25
0.2
0.15
0.1
0.05
0
2008
2009
2010
2011
2012
Year
Yes
No

Chapter 3. Summary – Public Health Implications and Possible Future Directions

Better understanding of coverage in adolescents could help improve the targeting of vaccination campaigns. Adolescents are not often a focus of campaigns to improve influenza vaccination coverage, which usually target groups that are perceived to be at higher risk. Current efforts to improve adolescent vaccination coverage focus on the Tdap, HPV, and meningococcal vaccine [51]. More research on how to promote the influenza vaccine to parents of adolescents could help improve vaccine uptake. Because influenza vaccinations need to be performed annually, it is critical that healthcare providers take every opportunity to promote the vaccine and increase awareness of its importance among adolescents and their parents. Healthcare that is specifically targeted towards adolescents may lead to more regular doctor visits, which would provide more opportunities to promote vaccination. In the meantime, continuing to promote vaccination every time an adolescent visits a healthcare provider is the best way to maintain and improve coverage levels [50].

Improving coverage among adolescents may also help reduce indirect costs associated with influenza and help protect others who are in close contact with adolescents [29, 39]. This effect was seen with the introduction of the pneumococcal conjugate vaccine for infants, which reduces the risk of pneumococcal disease in infants as well as reducing pneumonia rates among the entire population, including influenza-associated pneumonia [40]. It is possible that a higher rate of influenza vaccination coverage in adolescents could have similar benefits in terms of protecting the entire population as seen when vaccinating younger children.

Improving coverage among adolescents and reinforcing the importance of annual vaccination would be an important step towards meeting public health goals such as

Healthy People 2020 [53]. Promoting the vaccine to adolescents is important as health habits picked up as an adolescent could be carried into adulthood, making the increased influenza vaccination coverage long lasting despite the need for yearly vaccination.

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