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A composite measure and analysis of adolescent HPV, MenACWY, and Tdap vaccine coverage, as recorded by the National Immunization Survey – Teen, United States, 2020

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A composite measure and analysis of adolescent HPV, MenACWY, and Tdap vaccine coverage, as recorded by the National Immunization Survey – Teen, United States, 2020

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An abstract of

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Abstract

A composite measure and analysis of adolescent HPV, MenACWY, and Tdap vaccine coverage, as recorded by the National Immunization Survey – Teen, United States, 2020

By Jessica Kennicker

Background: An analysis of adolescent vaccine uptake, according to the Advisory Committee on Immunization Practices (ACIP) recommendations, is generally a siloed process, with comparisons of uptake for each of the three vaccines -human papillomavirus (HPV), meningococcal meningitis (MenACWY), and tetanus, diphtheria, and acellular pertussis (Tdap) – reported separately. Coverage estimates are not combined to differentiate completely vaccinated adolescents from the un- and undervaccinated.

Methods: This is a secondary analysis of the 2020 NIS-Teen provider data, with the primary outcome being a composite measure of all three adolescent vaccines, and analysis stratified by key socio-demographic characteristics to identify population subgroup-level differences in total adolescent vaccine uptake. All analysis was conducted using appropriate complex survey analysis methods (e.g., SAS PROC SURVEYFREQ), which were weighted, and 95% confidence intervals applied. Then stratified results were reviewed independently and compared to past trends of the same variables by each of the three vaccines.

Results: In 2020, uptake of Tdap (90.1%) and MenACWY (89.7%) vaccines among adolescents reached the Healthy People 2020 targets of 80.0%, but HPV vaccine uptake is still far from that goal (58.6%). When considered across all adolescent vaccines, complete vaccine coverage was only 55.2%. The groups that were the least likely to be fully vaccinated were the most likely to be vaccinated only with Tdap and MenACWY vaccines. For example, Hispanic adolescents were the most likely to be up to date with all vaccines (58.1%), with the lowest completed vaccination among non-Hispanic White adolescents (53.1%); non-Hispanic White adolescents were more likely to have received only Tdap and MenACWY vaccines (33.9% versus 25.5% for Hispanic adolescents). Females were more likely than males to be completely up to date on adolescent vaccines, 57.9% versus 52.6%, respectively.

Discussion: Coverage disparities such as these may not be fully recognized when the data is not evaluated in aggregate. Consideration of gaps that prevent adolescents from being adequately vaccinated can highlight factors contributing to increased vaccine uptake, such as provider recommendations, and apply them in areas with coverage gaps. Populations with incomplete coverage can be identified and vaccine promotion campaigns can be specifically targeted to those groups.

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Table of Contents

Introduction: 1

Literature Review: 4

Manuscripts/Results: 16

Manuscript Title Page: 17

Abstract: 18

Introduction: 20

Methods: 21

Results: 23

Discussion: 25

References: 31

Tables: 39

Implications: 44

Introduction

Vaccine preventable diseases have dramatically decreased over the past century and decades since vaccination was first implemented (38). So much so that the first disease, smallpox, was declared eradicated in 1980, thanks to widespread surveillance and vaccination efforts (38). Today, vaccination is considered a human right which the World Health Organization is campaigning to equitably reach and protect all people (39). Unfortunately, socioeconomic, political, and informational factors prevent vaccines from reaching all individuals. Combinations of those variables create pockets of undervaccinated people, which threaten to undermine the health and safety of everyone (40). To improve vaccine uptake in these populations, they must be identified and the factors associated with incomplete vaccination specified.

There are currently vaccines for over 20 diseases (1), more than 17 of which are recommended for administration from infancy through adolescence in the United States (2). Most frequently analysis of vaccine uptake and hesitancy is focused on a specific vaccine. Of those studies that analyze uptake trends across multiple vaccines, it is often a comparison of individual vaccines against seasonal influenza (23). However, there are overlapping populations that complete some vaccines and not others. While there is measurement of individual and completion of the seven-vaccine series for children, adolescent vaccination measurement is generally limited to individual vaccines or, for the cases of licensure of new vaccines, analysis of immunogenicity of vaccines that may be administered concurrently (8,9).

All states have vaccination requirements for children attending public school prior to pre-kindergarten or kindergarten entry (7). Adolescent vaccination requirements are less consistent. All states have mandates for tetanus, diphtheria, and acellular pertussis vaccine (Tdap) prior to middle school entry. Currently, 35 states have public school requirements for adolescent meningococcal meningitis (MenACWY) vaccination, and only four have school vaccination requirements for human papillomavirus (HPV) vaccines (7) . At the time of the National Immunization Survey-Teen (NIS-Teen) data collection for this analysis, Virginia had not yet implemented MenACWY or HPV vaccine requirements, so only 34 and

three states, respectively, had school requirements for these vaccines (7). For this reason, the adolescent population can be more susceptible to missed doses of vaccines that could protect them through secondary school and into adulthood.

This lack of consistent state-level school entry requirements for adolescent vaccination is a significant gap that needs to be considered and used as a motivating factor for how we measure adolescent vaccine coverage. Highlighting adolescents who are missing one or more vaccines may help to pinpoint gaps in health equity related to medical care or information accessibility or indicate extensive hesitance to specific vaccines. Then the process of clarifying the specific reasons for incomplete coverage can begin, followed by addressing those issues to try to close the gaps in coverage.

There are three routinely recommended vaccinations for adolescents: Tdap, MenACWY, and HPV. As the incidence of pertussis continued to increase in the adolescent population, one dose of the Tdap vaccine was added to the vaccination schedule for 11–12-year-olds in 2005 (7). Studies showed consistent decrease in immunogenicity over the years after the last childhood vaccine which the added adolescent shot was able to boost (4).

Adolescents and young adults living in communal settings are particularly prone to meningitis, a serious disease of high morbidity and mortality. While the number of annual cases gradually decreased since the mid-90's, it was noted that children under 5-years-old and those 14-24 years old were still two common populations to present with meningitis (5, 41). Since adolescents are primary carriers and have one of the highest case fatality rates, in 2005 the Advisory Committee on Vaccination Practices (ACIP) recommended vaccinating adolescents at the 11–12-year-old well child exam (5). Since then, cases have continued to fall and reached a low of 360 cases in 2018, which is approximately 0.11 per 100,000 (41).

HPV is the most common sexually transmitted infection and is a cause of six types of cancer (cervical, vaginal, vulvar, anal, penile, and oropharyngeal) as well as genital warts. It can reside dormant in an infected individual for years, being transmitted to others unknowingly. Over 5% of adolescents have

sexual intercourse in their early adolescent years, which is why, in 2006, the ACIP recommended vaccination with the HPV vaccine prior to the adolescent years of potential sexual activity (6, 11).

As measured in the NIS-Teen in 2021, coverage of each of the three vaccines is approximately 61.7% (CI 60.2-63.2) for HPV, 89.6% (CI 88.6-90.5) for Tdap, and 89.0% (CI 87.9-90.0) for MenACWY (42).

As noted above, childhood vaccination is routinely measured for individual vaccines and the 7-vaccine childhood series. However, there is no similar composite measure for adolescent vaccination to look at receipt of one or more of the routinely recommended adolescent vaccines. In this thesis, we analyze the differences in patterns of receipt of combinations of all adolescent vaccines using data obtained in the 2020 NIS-Teen. These findings may shed light on common demographic factors or recorded beliefs that contribute to missed or incomplete vaccinations. If correlations are found among those with incomplete vaccine records, the information may prove useful in understanding the next steps to take in addressing those challenges.

Literature Review

Adolescent vaccine recommendations in the US

Key Diseases Needing Prevention

Human Papillomavirus

Human papillomavirus (HPV) is the most common sexually transmitted infection and affiliated with the development of 4.5% of all cancers, globally (14). Most notably, HPV causes genital warts and cervical cancers, in addition to anogenital and oropharyngeal cancers. The double stranded DNA virus is an unenveloped icosahedral capsid with an affinity for basal squamous epithelial cells, meaning it can be transferred via skin-to-skin contact, rather than requiring fluid exchange, as is the case in most STIs (11). Upon infection, most people can clear the virus naturally but for some individuals (approximately 10%), the virus may not be cleared, leaving them susceptible to future disease development. Infrequent presentation of clinical symptoms and ease of transmission are two reasons this virus is so contagious. There are over 100 genotypes that have been identified and can cause disease in individuals, and are divided into high and low risk, depending on the affiliated illness – cancer-causing or wart-causing, respectively. HPV types 6 and 11 are responsible for 90% of genital warts and can cause benign tumors in the respiratory tract, qualifying them as low risk (12). HPV types 16 and 18 are high-risk as they are responsible for 70% of cervical cancers, which is the fourth most common cancer in women around the world. Additionally, types 31, 33, 45, 52, 58 are responsible for an additional 20% of cervical cancer cases (11, 12).

Meningococcal Meningitis

Meningococcal meningitis is a life-threatening disease with high morbidity and mortality, caused by the bacterium *Neisseria meningitidis* (15). Of the 13 serogroups identified, three are responsible for 90% of disease (A, B, and C), while W-135 and Y case incidents have increased over the last few decades (15). Epidemiologically, one specific serogroup tends to prevail during certain periods (5). Adolescents and

young adults are the primary carriers of *N. meningitidis*, but infants are susceptible to severe disease, as are those living in close quarters, and people with certain immunocompromising comorbidities. In most instances, fewer than 1% of individuals who encounter *N. meningitidis* develop disease, but the rapid progression and severity of illness in those who do is what makes meningitis so concerning. From colonization in the nasopharynx, bacteria will migrate into the blood stream and develop systemic disease and cross the blood brain/spinal cord barrier, infecting and causing inflammation of the meninges surrounding the primary organs of the central nervous system (CNS) (17). This is known as invasive meningococcal disease (IMD) which is most devastating in 3–12-month-olds, followed by adolescents and young adults (17). The time from disease onset to presentation of deadly symptoms can happen from 15-24 hours, with a 10-15% mortality rate, and CNS related disabilities such as hearing or limb loss, neurologic damage, among other complications in 10-20% of survivors (5, 15, 17).

Meningitis is a reportable disease in the United States, with only two to three cases qualifying as an outbreak. University students and young adults in communal living situations are the most susceptible to outbreaks, but men who have sex with men (MSM) and those with certain medical conditions are other common populations disproportionately impacted by *N. meningitidis* (17). While outbreaks can occur during any time of the year, winter and early spring are the primary times for outbreaks, when people spend more time inside, in closer proximity to one another, making infectious droplet transmission easier and more frequent between individuals (5).

Tetanus

Tetanus is a disease caused by the anaerobic, spore-forming bacterium *Clostridium tetani* exotoxin, tetanospasmin (18). The reservoir for *C. tetani* is in the soil and intestines of several domestic animals, incapable of eradication due to its ubiquitous distribution, globally. The spores are hearty, resistant to heat, common cleaning chemicals, antiseptics, and tolerant of oxygen, unlike the bacterium. It is most frequently acquired via injection of contaminated soil or feces into a wound, where the spores germinate and produce the toxin, which enters the blood stream and migrates throughout the body. In the CNS,

tetanospasmin can block inhibitor signals, resulting in ceaseless neurotransmitter firing, which causes relentless muscle contractions and spasms, and can lead to seizures, among other CNS complications (18). Often, muscle spasms begin in the jaw and descend throughout the body, which is known as generalized tetanus. Less common are: localized tetanus, which presents in the same area as the injury; and cephalic tetanus, which occurs after an injury to the head and involves facial nerves (18). The average incubation period of tetanus is 8 days (ranging from 1-21 days), and if treated in a timely manner, may take months for complete recovery. Mortality increases with the extent of disease onset prior to treatment, recently averaging 11% of cases (18).

Diphtheria

Corynebacterium diphtheriae is the bacilli necessary for diphtheria development. Non-toxic strains can cause mild disease in mucosal membranes, or varying degrees of systemic illness. More extensive morbidity and mortality are from corynebacteriophage viruses that infect *C. diphtheriae*, altering genetic information and causing the bacterium to produce the diphtheria toxin (18). Since the respiratory tract is the primary site of infection, illness is most often spread via respiratory droplets, or from contact with sores of an infected individual as skin infections and ulcer formation are not uncommon (20). Respiratory infections result in a low-grade fever, lymphadenopathy, sore throat, and dyspnea from toxin damage to healthy tissue, promoting development of a tough pseudomembrane forming. This new tissue can obstruct air flow in the respiratory tract, and promote inflammation in the heart, kidneys, or blood vessels. Disease onset ranges from 1-10 days, averaging 2-5 days, with 5-10% mortality in treated individuals and 50% in those untreated (18, 20).

Pertussis

Pertussis, like tetanus and diphtheria, is caused by a toxin-producing bacteria, *Bordetella pertussis*, which creates proteins and enzymes, all of which contribute to respiratory distress in the infected individual (18). Spread from person-to-person via respiratory droplets, the bacteria attach to respiratory cells where

it produces the pertussis toxin that paralyzes cilia, preventing removal of material from the respiratory tract. After a 4–21-day incubation period (averaging 7-10 days), the first of three stages of illness will present, the catarrhal stage. This stage resembles a cold, with runny nose, mild fever and cough that lasts for 1-2 weeks, increasing in severity. As more mucous accumulates and inspiratory volume decreases, the paroxysmal stage presents, with intense periods of coughing followed a distinct high-pitched "whooping" noise, as the infected individual attempts to force high volume air intake. This may result in cyanosis, syncope, vomiting, or exhaustion. Such attacks will happen cyclically throughout a day, most often at night, increasing and decreasing during the one-to-six-week duration of the paroxysmal stage. As the coughing fits regress, the person will enter the third and final, convalescent stage of slow recovery over two to three weeks. Outbursts of coughing and difficulty breathing can still occur for several months after primary disease presentation.

Those most severely impacted by pertussis are infants, under the age of 6 months, and then young children. However, in the early 2000's, incidence of pertussis in adolescents and adults was on the rise, bringing to attention the health implications for those groups as well (25). Concerns in young and the primary cause of pertussis related death is due to pneumonia from secondary bacterial infections, which can occur in over 18% of those under 6 months old. Hypoxia can lead to seizures and encephalopathy, while ear infections, dehydration, and weight loss may occur (18). In the older age groups pneumothorax, rib fracture, urinary incontinence, hernias, and aspiration are common concerns (18, 25).

Vaccines to Prevent these Diseases

The adolescent vaccine schedule is recommended by the ACIP, in agreement with and approved by the American Academies of Pediatrics (AAP) and Family Physicians (AAFP), and the Centers for Disease Control and Prevention (CDC). Due to catchup doses from missed childhood vaccines, the age range is from 7-18 years old (2).

<u>Human Papillomavirus Vaccine</u>

There have been three different HPV vaccine types developed over the past two decades. Initially a quadrivalent (4vHPV) vaccine with virus-like particles for HPV types 6, 11, 16, and 18 was released in the United States in 2006. This was advised for females 11-12 years old, but approved for females ranging from 9-26 years of age (11). In 2009 a bivalent vaccine was released for HPV types 16 and 18. This vaccine included an additional adjuvant believed to induce higher immunogenicity than that of the 4vHPV (12). The nonavalent vaccine induces immunity against HPV types 6, 11, 18, 31, 33, 45, 52, and 58 (12, 14), which are responsible for the majority of genital warts cases and over 90% of cervical cancers, in addition to oropharyngeal cancers around the tongue and tonsils, and anogenital cancers (12). The 9vHPV was first approved by the United States (U.S.) Food and Drug Administration (FDA) in 2014 for 9-26 years old (11). The nonavalent HPV vaccine is recommended to children 11-12 years old as a two-shot series, given 6-12 months apart, but can be administered to those as young as nine years old. For those who start the vaccination series after turning 15-years-old, three doses are recommended to induce the same immunogenic response (10). Titers of adolescents who receive the HPV vaccine when younger, from 9-15 years of age, may remain higher than those of their older counterparts, evidence supporting cause for early administration (11).

Meningitis A,C,W,Y Vaccine

Pathogenic *Neisseria meningitidis* is caused by a gram-negative, polysaccharide encapsulated, diplococcus. The polysaccharide capsule enables cellular invasion, meaning that non-encapsulated *N. meningitidis* is difficult to categorize into subgroup, and not often pathogenic (only opportunistically in certain immunocompromised individuals) (16). Non-pathogenic colonization of meningitis in the nasopharynx, compounded with the low frequency of disease, and rapid onset makes vaccination a preferential prophylaxis to antibiotic use (15). High bacterial prevalence and high susceptibility makes adolescents the primary population for targeting vaccination to prevent spread of *N. meningitidis.* In 2005, the Advisory Committee on Immunization Practices (ACIP) recommended a quadrivalent vaccine composed of polysaccharides from meningococcal subgroups A, C, W, and Y conjugated to a protein

carrier, for 11–12-year-olds, referred to henceforth as MenACWY (5,17). After ongoing research into the effectiveness of MenACWY, it was observed that antibody levels decreased significantly over the subsequent 5 years, such that concern for adequate coverage arose. In 2011, ACIP advised a booster dose of MenACWY for 16-year-olds to provide ongoing protection through additional years of highest susceptibility (5). As previously suggested, vaccination of the adolescent population provides additional protection to infants and other susceptible populations since the vaccine not only protects against disease but also carriage of disease-causing bacteria, decreasing the overall circulation of *Neisseria meningitidis* (15).

Tetanus, Diphtheria, Acellular Pertussis Vaccine

Diphtheria, tetanus, and acellular pertussis (DTaP) vaccination is recommended as part of the childhood vaccination schedule for infants 2, 4, 6, and 15-18 months old then again as boosters for children 4-6 years old (2). The Tdap vaccine is also a combination vaccine of tetanus, diphtheria, and pertussis toxoids but in reduced toxoid volumes, compared to DTaP, to decrease the risk of reactogenicity while effectively boosting the immune response (4). Toxoid vaccines are composed of inactivated toxins produced by the bacterium. These proteins may be bound to an adjuvant to increase immunogenicity against the disease-causing toxins rather than immunity against the bacteria that produce them (19, 27). However, toxoids are not as effective as bacterial cells at inducing a long-term immune response which is why increasing incidence of adolescent pertussis around the turn of the century resulted in the ACIP recommending a Tdap booster for 11-12-year-old children (4,18,21,25,27). Not only would this address the issue of waning immunity in adolescents, but it would also decrease the number of carriers able to transmit the highly contagious disease to the more vulnerable infant population (25).

Assessment of adolescent vaccine coverage with NIS-Teen

Adolescent vaccine coverage

Adolescent vaccine coverage has been gradually increasing over the last decade. The CDC releases an annual article in the Morbidity and Mortality Weekly Report (MMWR) each August of the year following the most recent year's iteration of the NIS-Teen. Vaccination coverage is assessed overall, compared to the prior year's vaccine coverage estimate, and select stratifying variables (age, sex, geography, race, ethnicity) are used to provide context to the estimates.

Looking back over the five years prior to the NIS-Teen 2020 records, trends that had been clearly established included a gradual plateauing of Tdap vaccine uptake and a period of exceptionally rapid increase in adolescent male coverage of the HPV vaccine, among others (29-32). Unfortunately, all adolescent vaccines are viewed in silos of their own coverage, only compared to one another when trends are similar. At no point to-date do the MMWR publications provide a complete evaluation of all vaccines, together. However, completion of the seven-vaccine series for children is addressed in the MMWR NIS-Child article summary annually (27). This deficit in evaluation of adolescent vaccination leaves gaps in understandings that may highlight common denominators between those who are up to date on their vaccine series versus those who are missing one or more of the advised vaccines.

HPV Vaccine Coverage

The HPV vaccine consistently has the lowest coverage, in all categories, for all ages, which decreases further with each of the three dose requirements. One reason for the lower vaccination rate with HPV is because it is the most recent addition to the adolescent schedule, and has receive the most updates since the original quadrivalent version was released in 2006, initially only recommended for females (11).

In 2009, ACIP advised males 9-26 years old receive the vaccine to prevent genital warts, but it was not added to the routine adolescent schedule until after updated recommendations in 2011 (11). This gave adolescent females a head start on vaccine uptake and contributes to the significantly lower coverage among males. During the five years prior to the 2020 NIS-Teen the nonavalent HPV vaccine was released, in 2015 (11,30). ACIP recommendations were updated in December 2016 to the current

schedule of two doses for immunocompetent adolescents initiated prior to their 15th birthday, and three doses for immunocompromised or anyone who began the series after their 15th birthday (30). Additionally, some states have started to implement HPV vaccine mandates for adolescents, which contributes to their higher coverage. Rhode Island and the D.C. consistently have the highest HPV vaccine rates, but they are two of four areas that implemented school mandates (34).

Noteworthy factors include the higher vaccination uptake in adolescents of households that are below the national poverty level (≥1 dose 70.2%) compared to 57.3% of adolescents at or above the poverty level (30). It is theorized that this improved uptake is due to the Vaccines for Children (VFC) program, for which children who are underinsured or on Medicaid qualify to receive free vaccines. Providers through such programs may be more persistent encouraging parents to agree to HPV vaccines for their children (28). The impact of provider recommendation on vaccine uptake is well documented. An expressed concern, in the face of reversed or little improvement in vaccine uptake, is that providers are not taking time to discuss vaccines with patients (28, 36).

The 2016 MMWR observed that states which implemented vaccination programs that increased information for both providers and community partners had increases in their vaccine uptake, further supporting this theory (30). 2016 was also the first year that HPV vaccination split recommendation for two or three doses based around initiation prior to the 15th birthday. From that year on, rather than identifying those who had 1, 2, or 3 HPV vaccines, it was split between those who had received only one or more doses of HPV or those who were up to date (UTD), according to their age and vaccination status (30). In 2016, 43.4% of adolescents were UTD with the HPV vaccine, 48.6% in 2017, 51.5% in 2018, 53.7% in 2019 (30-32). This increase was quite slow, and oddly, attributed more to male coverage than females. In 2018 male adolescents UTD on their HPV vaccine increased by 4.4% while females only increased 0.6% (32). This emphasizes the exponential uptake in males compared to females. While females consistently have higher coverage than males, the annual increase in uptake has been more gradual among females, while males have a shaper curve (28-32). A few theories for this are presented in

the literature. One is provider recommendation bias favoring females either because the vaccine was first advertised for females or because of perception HPV presenting higher risks in females (49). A second bias may be that adolescent parents/guardians, particularly those of females, may not believe they are yet nor likely to soon become sexually active. They believe it is unnecessary or too soon for the vaccine (49, 35). This disproportionate resistance to females would slow their uptake relative to males.

MenACWY Coverage

Vaccination coverage for meningococcal meningitis can be broken into two factors for adolescents since two doses must be taken into account when considering NIS-Teen. Children from ages 11 through 15 should have received one dose of MenACWY, which consistently has a higher uptake rate than the second dose. From 2015 through 2019 81.3%-88.9% of adolescents had received at least one dose of the meningitis vaccine, while the second dose was only given to 33.3%-53.7% of the population by age 17 (28-32).

A few factors that may contribute to this deficit between the two doses of MenACWY include the age limitation, since NIS-Teen only inquires about adolescents through the age of 17, those who receive the booster dose after turning 18 are missed (29). Another consideration is that only 17 states required a booster for adolescents in secondary school at the start of the 2020 school year while 34 states required the first dose (34).

It was also noted in 2015 that the first dose of MenACWY had higher coverage in Hispanic adolescents than those who identified as non-Hispanic, White (29). However, in 2016 Black only, non-Hispanic adolescents had the best coverage (up to 85.5% from 81.7%) with the first dose of MenACWY and Hispanic adolescents actually decreased from 85.0% to 83.8% (29, 30). While both Black and Hispanic MenACWY uptake increased the following year, Asian adolescents had the greatest coverage of the racial/ethnicity identifiers with 91.0% (31). In 2018 three race/ethnicity groups were incredibly similar in their uptake, 87.6% and 87.1%, Hispanic and Black only, non-Hispanic which was the same as

multiracial, non-Hispanic, respectively (32). In 2019 uptake for one dose of MenACWY was as follows: Asian, non-Hispanic (93.3%); multiracial, non-Hispanic (90.0%); Black only, non-Hispanic (89.4%); Hispanic (89.3%); White only, non-Hispanic (88.4%); and American Indian/Alaska Native only, non-Hispanic (85.3%) (32). American Indian/Alaskan Native only, non-Hispanic frequently has the lowest representation in MenACWY uptake, for both one and two doses. So much so, that some years there is no data available for record of the second dose (30-32). Alaska does not have a MenACWY requirement for public schools, but a more detailed explanation for why uptake is so low in Native communities may be due to lack of access to medical facilities or providers.

Vaccination differences between insurance were noted in the 2017 MMWR which highlighted that, while those with private insurance only had the highest vaccine coverage with one dose of MenACWY (85.7%), those with Medicaid were close (85.1%), and higher than both other forms of insurance or the uninsured, 83.9% and 80.7%, respectively (31). This is similar to the information in the 2018 MMWR, which may mean that parents may not be aware of the Vaccines for Children program which ensures that all underinsured minors are qualified to receive free vaccines (32).

Tdap Vaccine Coverage

The Tdap vaccine consistently has the highest vaccine uptake from 86.4% in 2015 increasing annually to 90.2% in 2019 (28, 32). Noteworthy information about this vaccine is that, where MenACWY and HPV have statistically significant differences across variables, Tdap remains relatively consistent regardless of race, income, age, or gender (28-32). There are variations in vaccine uptake across states, which is not surprising as states have different requirements for school attendance. Currently, all states have Tdap requirements that generally require Tdap vaccination by a certain grade year in school (34). However, those mandates were still being implemented in some states during the five years leading up to the NIS-Teen 2020. In some instances, those states that did not have Tdap requirements for adolescents attending public schools were on the lower end of coverage, such as South Dakota in 2015 with 72.4% ($\pm$5.8) (29). However, after implementation of the vaccine mandate for children entering grade six at South Dakota

public schools during the 2016-2017 school year, the number of adolescents that were UTD with their Tdap vaccines increased to 79.5% (CI 73.6-84.4) in 2017 (31, 34). This follows a previously established trend in the benefits of state mandates for vaccines, which generally results in an increase in coverage of the vaccine in question (23).

Vaccine Series

Assessment of the completed adolescent vaccine series is not prioritized, or easy information to find. The data must be independently compiled from NIS-Teen records, as was done for this thesis. Studies that do reference cross-comparison of different vaccines are most often focused on whether immunogenicity of one specific vaccine changed during concomitant or sequential administration with others that are recommended for the same age group (5, 22). The other category of comparison that is not uncommon is uptake of a specific vaccine as a predictor of influenza vaccine uptake (23, 24).

A common theme with all three vaccines under review is that coverage increases with age, a feature which has been consistent throughout the years (23-32).

Disparities

Vaccine disparities have been attributed to lack of access and/or education. Lack of access could be physical access, such as living too far from a provider, too few providers in an area, inability to attend appointments, or lack of financial or insurance support to afford seeing a provider. An overall shortage of healthcare providers in rural areas would make access to one more challenging which can decrease the opportunity for coverage (30). Underinsured adolescents qualify for VFC, but not all parents may be aware of this option or take advantage of it, which is why adolescents that are uninsured are more likely to be undervaccinated (29). The COVID-19 pandemic created a unique access deficit in that fewer well child visits and medical appointments were made (48). Well child exams are important checkpoints for children and adolescents so providers can ensure they are meeting developmental milestones and offer a chance for early disease detection (33). They are also often opportunities for age-appropriate vaccination

(2, 47, 33). This is reflected in NIS-Teen data and the significant decrease in vaccine dose requests from VFC providers (48).

The impact of provider recommendations on vaccine uptake is mentioned in almost every resource that addresses disparities (48). Willingness to vaccinate has been reported to increase approximately 25% after educational information has been shared with parents/guardians (6, 48). People in non-urban areas receive fewer provider recommendations for HPV vaccines and it is theorized that they may even be less aware of HPV (30). Further, the lower number of pediatric providers in rural areas could mean that even adolescents who do have access to medical care, could see someone who is less familiar with the age-appropriate vaccine schedule and overlook the opportunity to advise vaccination (29). Areas that have emphasized vaccine education for providers and general vaccine advocacy campaigns have shown greater increase in uptake compared to years without increased vaccine emphasis (29). This highlights the importance of both recommendation conversations from provider to patient but conversations with providers from continuing education events or public health experts working on vaccine campaigns (29). Providers can reassure and debunk myths for those who are hesitant due to misinformation (35).

Manuscript/Results

Title: A composite measure and analysis of adolescent HPV, MenACWY, and Tdap vaccine coverage, as recorded by the National Immunization Survey – Teen, United States, 2020

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Abstract

Background: An analysis of adolescent vaccine uptake according to the Advisory Committee on Immunization Practices (ACIP) recommendations is generally a siloed process, with comparisons of uptake for each of the three vaccines -human papillomavirus (HPV), meningococcal meningitis (MenACWY), and tetanus, diphtheria, and acellular pertussis (Tdap) – reported separately. Coverage estimates are not combined to differentiate completely vaccinated adolescents from the un- and undervaccinated.

Methods: This is a secondary analysis of the 2020 NIS-Teen provider data, with the primary outcome being a composite measure of all three adolescent vaccines, and analysis stratified by key socio-demographic characteristics to identify population subgroup-level differences in total adolescent vaccine uptake. All analysis was conducted using appropriate complex survey analysis methods (e.g., SAS PROC SURVEYFREQ), which were weighted, and 95% confidence intervals applied. Then stratified results were reviewed independently and compared to past trends of the same variables by each of the three vaccines.

Results: In 2020, uptake of Tdap (90.1%) and MenACWY (89.7%) vaccines among adolescents reached the Healthy People 2020 targets of 80.0%, but HPV vaccine uptake is still far from that goal (58.6%). When considered across all adolescent vaccines, complete vaccine coverage was only 55.2%. The groups that were the least likely to be fully vaccinated were the most likely to be vaccinated only with Tdap and MenACWY vaccines. For example, Hispanic adolescents were the most likely to be up to date with all vaccines (58.1%), with the lowest completed vaccination among non-Hispanic White adolescents (53.1%); non-Hispanic White adolescents were more likely to have received only Tdap and MenACWY vaccines (33.9% versus 25.5% for Hispanic adolescents). Females were more likely than males to be completely up to date on adolescent vaccines, 57.9% versus 52.6%, respectively.

Discussion: Coverage disparities such as these may not be fully recognized when the data is not evaluated in aggregate. Consideration of gaps that prevent adolescents from being adequately vaccinated can highlight factors contributing to increased vaccine uptake, such as provider recommendations, and apply them in areas with coverage gaps. Populations with incomplete coverage can be identified and vaccine promotion campaigns can be specifically targeted to those groups.

Introduction

Vaccination continues to prove to be one of the most effective means of disease control, elimination, and eradication (39). New and improved vaccines continue to be developed to protect humans and animals from infectious diseases however, subpopulations of vaccine hesitant people present themselves with every advancement in the field. Publications analyzing vaccine uptake trends often focus on one vaccine or measure safety and immunogenicity of concurrently administered vaccines (8, 9). Trends in completion of vaccine series are not often measured, particularly among the adolescent population. The National Immunization Survey (NIS) annually collects childhood and adolescent vaccine data, the latter of which is referred to as "NIS-Teen". Publication of this extensive information accumulation provides valuable insight into the patterns of vaccine series participation and will share a composite measure of children who completed the seven-vaccine series advised in the United States, but does not include the same information for the three vaccine-series for adolescents.

These three vaccines are tetanus, diphtheria, and acellular pertussis (Tdap) recommended for 11–12-year-olds since 2005 in response to rising pertussis cases in the adolescent population as immunity wanned over the years after childhood vaccination (6, 7). Also in 2005, a meningococcal meningitis vaccine (MenACWY) was recommended for adolescents at their 11-12-year-old well child exam to address the most susceptible population and common carriers of the bacteria (5). In 2006 the Advisory Committee for Immunization Practices (ACIP) added the human papilloma virus (HPV) vaccine to the adolescent vaccine schedule. This vaccine protects against the most common sexually transmitted infection, HPV, which is capable of causing six types of cancer (cervical, vaginal, vulvar, anal, penile, and oropharyngeal) as well as genital warts. Receipt of this vaccine prior to sexual activity increases the chances of effectiveness (6, 11).

State mandates help to increase coverage with these vaccines, but the number of states with laws requiring adolescent vaccination decrease with each adolescent vaccine. The most common requirement is for Tdap (all states), then MenACWY (35 states), and finally HPV for which only four states have

some type of mandate in place (7). Evaluating uptake of these vaccines can help to differentiate patterns between adolescents who are fully and incompletely vaccinated. The NIS-Teen from 2020 can a useful resource for a composite measure analysis of demographics, which could help direct steps to take in addressing the issues preventing complete vaccine coverage.

Methods

This analysis was conducted using the publicly available, deidentified dataset for the 2020 NIS-Teen (42). Briefly, the Centers for Disease Control and Prevention (CDC) conducts an annual survey of heads of households with adolescents ages 13-17 years to measure vaccine uptake and socio-demographic characteristics. This survey is conducted with a random digit dialing (RDD) telephone that contacts cellular phone numbers at which a surveyor can inquire about households with adolescents 13-17 years of age. For eligible households, one adolescent fitting the age requirement is selected as the focus of the survey, with questions asked of the available or most informed adult in the household. At the conclusion of the survey interview, the parent/guardian of the adolescent is then asked for consent from the surveyor to request vaccination information from the adolescent's medical provider. Identified healthcare providers are then contacted to obtain information about vaccines delivered to the adolescent. In total, 45,626 household interviews of qualifying adolescents were conducted (46). Territories Puerto Rico and Guam were excluded, so the final number of adolescents with adequate provider verified data available was 20,163. This analysis exclusively uses provider-verified information as it is considered more accurate than that shared by parents/guardians (44).

For this analysis, we considered uptake of three vaccines: human papillomavirus (HPV), quadrivalent meningococcal vaccine (MenACWY), and tetanus, diphtheria, and acellular pertussis combination vaccine (Tdap). These three vaccines have comprised the primary adolescent vaccination platform since 2006 (13).

NIS-Teen data, SAS codes, and applicable documentation were downloaded from the CDC website, and all analysis was conducted in SAS (v9.4, The SAS Institute, Cary NC) (42-46). Analysis was conducted using PROC FREQ weighted to the national adolescent population, in accordance with standard practices and weighting procedures documented for the NIS-Teen (46). Our primary outcome was the combination of adolescent vaccines received, defined as an eight-level outcome variable: Tdap/MenACWY/HPV, Tdap/MenACWY, Tdap/HPV, MenACWY/HPV, Tdap alone, MenACWY alone, HPV alone, and no adolescent vaccines received. Each of the three vaccines was evaluated as up to date (UTD) according to the following specifications: HPV vaccination was considered UTD based on the number of doses received, age at first dose, and assessment of intervals between vaccine doses, per the NIS-Teen definitions used during data processing; UTD meningitis vaccine is qualified as one or more meningococcal serogroup ACWY shot(s); and Tdap is qualified as UTD if one or more Tdap-only shot has been administered since 10 years old. For all three vaccines, any shots after the provider interview date are excluded (43, 46). Given this set of definitions, adolescents who initiated the HPV vaccine series but have not completed it are not considered UTD. For example, an adolescent who received one dose each of Tdap, MenACWY, and HPV vaccines would be categorized in the Tdap/MenACWY group, whereas an adolescent who received one does each of Tdap and MenACWY vaccines and is fully vaccinated against HPV would be categorized in the Tdap/MenACWY/HPV group.

We estimated vaccine uptake for the eight combinations of adolescent vaccination at the national level, stratified by key socio-demographic characteristics that have been associated with vaccine uptake (42-46). Selection of the independent variables used was based on literature reviews of previous NIS-Teen annual MMWR reports, for trend comparison. The twelve variables selected were: age, sex, insurance status, family income, attendance of 11–12-year-old well child visit, maternal age, maternal years of education, facility type, number of providers, Hispanic/Latino or not, and race/ethnicity. PROC SURVEYFREQ was used to stratify the eight vaccine combinations and each socio-demographic characteristic using SAS

v9.4, at the alpha = 0.05 level. For income-to-poverty status, we collapsed NIS-Teen data to at or above poverty and below poverty.

All analysis was conducted using appropriate complex survey analysis methods (e.g., SAS PROC SURVEYFREQ) in accordance with the NIS-Teen data users guide (46).

Results

In 2020, 58.6% of adolescents were UTD on the HPV vaccine, 89.7% were UTD on their MenACWY vaccine, and 90.1% were UTD on the Tdap vaccine (Table 2). However, only 55.2% of adolescents were UTD with all three recommended vaccines, driven primarily by low uptake of HPV vaccine (Table 2). Additionally, 33.6% of the population received only two adolescent vaccines (30.5% received Tdap/MenACWY; 0.9%received Tdap/HPV, 2.2% received MenACWY/HPV). A small percentage (5.7%) received only one of the three vaccines (3.5% Tdap only; 1.8% MenACWY only; 0.4% HPV only), and 5.5% were completely unvaccinated for the three adolescent vaccines.

Receipt of the complete adolescent vaccine series increased with age ranging from 43.5% in 13-year-olds to 60.8% in 17-year-olds. Females were 5.3 percent points more likely to be UTD than males (57.9% versus 52.6%, respectively).

Uninsured adolescents were the least likely to be UTD for all vaccines and the most likely to have received none of the three vaccines (39.6% and 8.9%, respectively). Interestingly, uninsured adolescents had a higher percentage of Tdap and MenACWY coverage than UTD with all three, 41.9%. Specific insurance coverage was associated with differences in vaccine uptake. While those who were privately insured were least likely to have received none of the adolescent vaccines (5.0%) they were not more likely to have received all routine adolescent vaccines (55.9%, compared to 56.5% of children insured through Medicaid). When insurance status and the 11–12-year-old well child visit (WCV) are stratified (Table 3) those registered for Medicaid have the highest attendance for the well child exam and those who

received the WCV had a 24.4 percent point higher chance of being UTD on their vaccines than those who did not attend a WCV (61.9% versus 37.5%, respectively). Those who attend their WCV are most likely to receive their Tdap booster and first MenACWY dose and start the HPV series (if not yet done), as per schedule.

Adolescents from families below the poverty line were 3.4 percent points more likely to be UTD on all vaccines compared to those from families at or above the poverty line (58.1% versus 54.7%, respectively). Adolescents of older mothers (over or equal to 45 years old) were most likely to be UTD on vaccinations while those with younger mothers (under or equal to 34 years old) were least likely to be UTD (57.3% and 51.3%, respectively). These two groups were opposite in almost every single of the eight possible combinations of the adolescent vaccine series (Table 1). Coverage stratified by the education level of the mother showed that adolescents with mothers who had 12 years of education were the least likely to be UTD (50.1%), but those who had mothers who received less than 12 years of education were both the most likely to be UTD and the most likely to have received zero adolescent vaccines (61.4% UTD and 7.8% with none of the three).

Hispanic adolescents had the highest coverage with all vaccines at 58.1%, which was 5.0 points higher than non-Hispanic white adolescents and 3.9 points higher than all non-Hispanic or Latino identifying adolescents. The variable category of "Non-Hispanic Other + Multiple Race" closely followed as second most UTD (57.8%). The patterns recorded among different racial/ethnic groups followed previously mentioned trends (Table 1).

Coverage stratified by the type of facility in which adolescents received vaccines indicated the lowest uptake of all adolescent vaccines among those exclusively attending STD/school/teen clinics (36.4%); these adolescents were most likely to be completely unvaccinated (20.8%). Uptake of all adolescent vaccines was similarly high for adolescents who were seen exclusively at hospital facilities (58.2%), and

private medical facilities (58.0%). Those receiving medical care at public facilities were most likely to have both Tdap and MenACWY (32.5%).

Adolescents without a specifically identified provider did not have anyone to provide responses to the NIS-Teen questionnaire, which was representative of approximately 0.2% of the population, so they were identified as completely unvaccinated. Vaccination coverage decreased with increasing number of valid, unique providers. Those with one provider were most likely to be adequately vaccinated (57.0%), similar to those with two providers (55.4%), though there was a large drop in UTD status among those with three or more providers (46.6%).

Discussion

Overall, the composite measure of vaccine uptake for all three routinely recommended adolescent vaccines was low (55.2%) but this was primarily driven by low overall HPV vaccine uptake. Excluding HPV, 85.7% of adolescents were UTD on both MenACWY and Tdap. Additionally, adolescents with the lowest coverage of all three adolescent vaccines often had the highest coverage of both MenACWY and Tdap. This highlights the ongoing gap in HPV vaccination and the fact that hesitancy regarding this vaccine may be operationalized in different ways than for other vaccines. One reason for this significant difference in the uninsured adolescents is likely related to state mandates for school vaccines encouraging Tdap and MenACWY in all and most states, respectively, compared to only three states (at the time) requiring HPV vaccination (7). As previously mentioned, provider recommendations and education may help to decrease these rifts between uptake of HPV and other adolescent vaccines (6, 49, 35). A closer analysis of the differences in vaccine coverage between states with school mandates for each of the vaccines and those without certain requirements could better define the benefits of this avenue in encouraging complete coverage and closing the gap between Tdap/MenACWY and HPV.

Nationally, HPV vaccine uptake increased by 4.4 percent points, which is greater than the difference between 2018 to 2019, but not as great as each proceeding year since 2015. This is similar when considering HPV UTD by sex. Both males and females increased, but by less than previous years. Following the historic trend, a greater number of females were vaccinated overall, but the improved difference is less than that of males.

Vaccination for Tdap was down 0.1% and MenACWY was only up 0.8%, each of which is atypical. Consideration must be given to the limitations created by COVID-19 in 2020. Hospital, clinic, and school restrictions and shutdowns prevented many adolescents who would have otherwise been vaccinated from receiving the boosters necessary to stay UTD for their age group. While vaccines were considered essential healthcare, they and well child visits fell to the wayside for many (47). One consideration to hold while examining these data is that the three vaccines evaluated here are routinely recommended at/around ages 11-12 years, and the NIS-Teen assesses vaccine uptake among 13-17-year-olds, meaning that at the point of evaluation in 2020, many adolescents may have already been vaccinated before the onset of the COVID-19 pandemic, highlighting the need for continued monitoring as we move forward in time.

These differences between those below the poverty level and those who are uninsured on opposing sides of vaccine uptake follows precedent (27-31). It has previously been assumed that those who are below the poverty line and meet the adolescent vaccine schedule requirements on time do so because they likely qualify for the VFC program and registered providers vaccinating through that program are both well informed of the adolescent vaccine schedule, and take time to recommend it to parents. Where a disconnect lies is in the uninsured adolescents who would certainly qualify for the VFC program but are not enrolled and, as indicated by undervaccination, are not receiving all of the advised medical care. However, the higher coverage of MenACWY and Tdap vaccines compared to those with all three suggests that vaccine access may not be the primary or only contributing factor to incomplete uptake. State mandates help ensure many or most adolescents have certain degrees of vaccination, which include

Tdap, and often MenACWY (7). While this helps to increase vaccination rates and protection, the limited number of states with HPV vaccine requirements, compared to the other two, further contributes to the disparity gap in uptake.

Attending WCV are preventive measures inversely related to use of other healthcare resources, such as acute or emergency care visits, and are an opportunity for providers to administer and discuss vaccination with parents and adolescents (47, 33). Rates of 2020 and early 2021 WCV for adolescents trended proportionately with vaccination rates during the same time and though there were a few spikes in late 2020, they did not make up for the difference compared to pre-pandemic years (47).

Hispanic adolescents were among the most UTD with the complete adolescent vaccine schedule, while Non-Hispanic White adolescents were least UTD with all three vaccines but most likely to be UTD with both Tdap and MenACWY. This follows historic trends of White adolescents leading in only Tdap vaccination, if at all, and exceptionally so in the case of HPV vaccination. American Indian/Alaska Native and Asians were the two racial identities that were most UTD with HPV vaccines the previous two years of NIS-Teen data collection (27-31). This trend is reflected in the "other + multiple race" variable, which was 0.3 percent points behind completely UTD Hispanic adolescents. As is the case for adolescents in general, there needs to be closer analysis of racial and ethnic disparities to completing the adolescent vaccine schedule. Stratification of race/ethnicity by the other variables evaluated here may help to highlight specific health inequities encountered by different racial/ethnic groups that contribute to incomplete vaccination and require unique program development to adequately address.

Older mothers are both more likely to have their adolescents completely UTD with vaccines and least likely to have adolescents without any vaccines. Adolescents of younger mothers are the exact opposite. Adolescents of younger mothers are also the least likely to be UTD with the HPV vaccine. Their mothers would have been 17-21 years old when they had these adolescents and may have a significantly different perceived susceptibility of vaccine preventable diseases from older mothers. Adolescents of mothers who had less than 12 years of education were 3.0 percent points more likely be completely UTD compared to

adolescents of mothers who were college graduates. While adolescents of mothers who were college graduates were unique in that they were not the highest with both MenACWY and Tdap vaccines (as is the case with most other variables) they were the least likely to be unvaccinated. Those who had mothers with more than 12 years education were the most likely to have both MenACWY and Tdap vaccines. Education level of the adolescent's mother highlights the importance of considering additional factors. For example, mothers who have less than 12 years of education are more likely to have adolescents in households below the poverty line, they are also most likely to have their children on Medicaid which may contribute to their higher observation of vaccine recommendations.

The significant disparity in vaccinations of adolescents who see practitioners exclusively at STD/student/teen clinics suggests that providers at those locations may not be discussing vaccine schedules or options. It is most likely that the primary focus of those visits is sexual health care. Unfortunately, those adolescents are also least likely to be UTD on HPV vaccines exclusively. This leaves room for consideration of targeting vaccination education at providers in these facilities. While this group represents only 2.3% of the population, it has the most significant vaccine disparities. The next closest group, all public facilities, was 13 percent points less likely to be unvaccinated but they are also less than 50% likely to be fully vaccinated (47.5%). Since they are most likely to be UTD on both Tdap and MenACWY, this suggests greater HPV vaccine hesitancy in the group and/or a lack of provider recommendation. Further stratification by other variables could help to determine what may help providers at public facilities to increase vaccine uptake. Adolescents seeing providers at all private or all hospital facilities represented 58.2% of the population[1] and are 10.5% more likely to have complete vaccine coverage. Further research into the differences in these populations and in the vaccine related practices of their providers may shed some light on the vaccine uptake disparities. Interestingly, HPV

[1] These two groups are being referenced in combination as their complete UTD vaccination coverage differed by less than 0.2 percent points.

hesitancy may not be a contributing factor at the public facilities, as they have higher HPV coverage both alone and with MenACWY than either hospital or private clinics.

In instances of multiple primary providers, the vaccine coverage disparity is most likely to be an issue of fragmentation of care. Providers may not take time to advise or discuss specific vaccines, or assume that one of the patient's other providers will broach the subject. This creates the opportunity for gaps in care, as evidenced by the decreasing UTD vaccine status of adolescents who have a greater number of providers. This emphasizes the importance of explicit vaccine campaign signage and educational material in healthcare facilities, to try to help cover informational gaps from providers, since educational reading material has been shown effective at increasing vaccine uptake, particularly in populations hesitant because of lack of information on the subject (6). Further there is value in educating healthcare staff about adolescent vaccines and the value of providing recommendations to any adolescent not completely UTD on the vaccine schedule (23, 48, 49). Primary providers do not have to be the only sources of vaccine promotion. Incorporating the exchange of information about vaccination status and provider advice to complete vaccine series should be incorporated into general intake and assessment information of any appointment (48).

Limitations

This study has some limitations. First, those who consent to survey participation and the responsive providers may differ from those in non-responsive households. Further, lower response rate could create a skewed representation of vaccine coverage. Another limitation that has existed since 2018 is that only cell phone numbers have been used for the random digit dialing system that selects households (30). This creates a bias excluding households without attached cell phone numbers (i.e., they have only a landline or are phoneless). A third limitation is survey brevity. It was intentionally shortened in 2014 to increase response rates (46). Unfortunately, it means fewer data differentiating demographic variables. Migration history and nationality may have cultural implications on one's view of vaccination and is not addressed.

In terms of NIS-Teen data, there is a race/ethnicity difference between what is shared in public data and that reported in the annual MMWR releases. These include American Indian/Native Alaskan and Asian variable considerations within "race/ethnicity", however that information is collapsed into "non-Hispanic other + multiple race" category. This oversimplifies the identity of people from all around the world. Those two race/ethnicities are specifically identified here as they were, each, historically most UTD on adolescent vaccines.

One limitation of the data analysis was consideration of only provider information. This is important for accuracy when considering the quantitative aspects of vaccine coverage, but excludes respondents' qualitative answers that could shed light on vaccine hesitancy. Such examples would include the reasons given for an adolescent not receiving a specific shot. A second data analysis limitation is only stratifying by two variables at a time. Given the large number of outcome levels, the proportion within each group rapidly shrinks with additional stratification. Further breakdown could result in misrepresentation of data appearing statistically significant due to mere population size limitations. Finally, this analysis is a secondary analysis of data collected from the 2020 NIS-Teen. A more thorough exploration of other years, both pre-COVID-19 and since, could be used to examine patterns in complete adolescent vaccination. Changes in these patterns could indicate impacts of past events on vaccination uptake.

Certain results could be expected, such as increased vaccine coverage with age, as each year means additional time for an adolescent to receive doses of whichever vaccine(s) they are missing. This is likely to remain consistent, regardless of interventions. In other cases, quantifying the differences highlighted the extent of vaccine uptake disparities between certain demographics, such as those who are uninsured versus covered by Medicaid or private insurance, especially in the instance of HPV coverage. This provides an argument for the successful impact of state mandates on adolescent vaccine uptakes. Nuanced but significant points become apparent in coverage gaps between the individual vaccines. While HPV is known to lag behind Tdap and MenACWY coverage amongst adolescents, the 21.4% deficit of HPV vaccine uptake from reaching the Healthy People 2030 80.0% goal is only part of the overall coverage

problem. There is a 24.8% deficit between the current (55.2%) extent of complete vaccine coverage for adolescents and the 80.0% goal Healthy People 2030 would mean. Finally, composite analysis of vaccination establishes a point from which trends can be tracked, moving forward, or even considered retrospectively.

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Tables

Table 1: Composite Measure of Adolescent HPV, Tdap, and MenACWY Vaccine Coverage by Sociodemographic Variables from the National Immunization Survey – Teen, United States, 2020

	Distribution	HPV/Tdap/ MenACWY	Tdap/MenACWY	Tdap	MenACWY	HPV	HPV/Tdap	HPV/MenACWY	None
	%	% (95% Confidence Interval)							
Age									
13	20.2	43.5 (40.5,46.4)	40.7 (37.8,43.6)	4.0 (2.5,5.5)	2.4 (1.3,3.4)	0.0 (0,0.1)	0.6 (0.4,1.1)	1.4 (0.8,1.9)	7.3 (5.9,8.8)
14	20.1	53.4 (50.5,56.4)	31.4 (28.7,34)	4.0 (2.5,5.6)	1.5 (0.9,2)	0.2 (0,0.4)	0.5 (0,1)	1.8 (1.1,2.5)	7.2 (5.2,9.1)
15	20.2	57.9 (55,60.9)	28.6 (26,31.2)	3.2 (2.1,4.4)	1.6 (0.8,2.3)	0.1 (0,0.2)	1.0 (0.6,1.4)	2.8 (1.5,4.2)	4.8 (3.6,6)
16	20.6	60.6 (57.6,63.5)	25.0 (22.3,27.6)	3.5 (2.3,4.8)	1.3 (0.8,1.8)	0.9 (-0.3,2)	1.3 (0.6,2)	2.7 (1.6,3.8)	4.8 (3.8,5.7)
17	18.9	60.9 (57.8,64)	26.7 (24,29.3)	2.9 (1.9,3.9)	2.5 (1.4,3.6)	0.6 (-0.1,1.3)	0.6 (0.3,0.9)	2.4 (1.3,3.6)	3.4 (2.1,4.8)
Mother's Age									
≤ 34 Years	7.3	51.3 (46,56.5)	32.5 (27.8,37.3)	2.1 (1.1,3)	2.0 (0.3,3.7)	0.0 (0,0)	1.5 (0.5,2.5)	1.5 (0.2,2.7)	9.1 (6.6,11.7)
35-44 Years	43.7	53.5 (51.5,55.6)	31.1 (29.3,32.9)	3.8 (2.9,4.7)	2.5 (1.7,3.2)	0.1 (0,0.2)	0.9 (0.5,1.3)	2.3 (1.6,2.9)	5.8 (4.9,6.8)
≥ 45 Years	49.0	57.3 (55.3,59.2)	29.7 (27.9,31.4)	3.5 (2.6,4.4)	1.2 (0.9,1.6)	0.6 (0.1,1.2)	0.7 (0.5,0.9)	2.3 (1.6,3)	4.7 (3.8,5.6)
Census Region									
Northeast	15.8	63.9 (61.4,66.3)	27.9 (25.6,30.2)	1.2 (0.7,1.8)	1.3 (0.7,1.8)	0.2 (0,0.5)	0.9 (0.4,1.4)	2.2 (1.4,3)	2.3 (1.6,3.1)
Midwest	21.1	57.0 (54.8,59.2)	32.5 (30.4,34.6)	1.6 (1.2,2.1)	1.3 (0.8,1.7)	0.2 (0.1,0.4)	0.4 (0.2,0.6)	1.8 (1.2,2.4)	5.3 (4.4,6.2)
South	39.0	50.2 (48.1,52.3)	32.7 (30.7,34.6)	4.4 (3.6,5.3)	2.6 (1.8,3.4)	0.4 (0,0.7)	1.1 (0.7,1.4)	2.6 (1.8,3.4)	6.1 (5.1,7.1)
West	24.1	56.0 (52.4,59.7)	27.0 (23.8,30)	5.3 (3.4,7.3)	1.4 (0.8,2.1)	0.7 (-0.4,1.5)	0.9 (0.3,1.5)	2.0 (0.9,3.1)	7.0 (5,8.8)
Maternal Education									
<12 Years	12.4	61.4 (56.7,66.2)	24.0 (19.9,28)	2.6 (0.9,4.2)	1.6 (0.4,2.9)	0.1 (0,0.3)	0.9 (0.3,1.5)	1.6 (0.8,2.5)	7.8 (5,10.5)
12 Years	21.3	50.1 (46.8,53.3)	32.3 (29.3,35.2)	4.4 (2.7,6.2)	2.1 (1.1,3)	0.7 (-0.4,1.8)	1.1 (0.5,1.6)	3.2 (1.9,4.5)	6.2 (4.6,7.8)
>12 Years, Non-College Graduate	24.0	51.0 (48.3,53.6)	32.7 (30.3,35.1)	5.7 (4.2,7.1)	1.9 (1.2,2.6)	0.4 (0,0.9)	0.7 (0.3,1.1)	2.0 (1,3)	5.7 (4.3,7)

College Graduate	42.3	58.4 (56.6,60.1)	30.3 (28.7,31.9)	2.2 (1.7,2.6)	1.7 (1.2,2.2)	0.2 (0,0.5)	0.8 (0.5,1.1)	2.0 (1.4,2.6)	4.4 (3.8,5)
Hispanic Or Latino									
Yes	25.0	58.1 (54.6,61.6)	25.5 (22.6,28.4)	3.3 (1.6,4.9)	2.7 (1.5,3.9)	0.8 (-10,11.6)	0.7 (0.2,1.2)	3.1 (1.9,4.3)	5.7 (4.1,7.4)
No	75.0	54.2 (52.8,55.6)	32.2 (30.9,33.4)	3.6 (3.1,4.2)	1.5 (1.2,1.8)	0.2 (0.1,0.3)	0.9 (0.6,1.2)	1.9 (1.5,2.4)	5.4 (4.8,6.1)
Race Or Ethnicity									
Hispanic	25.0	58.1 (54.6,61.6)	25.5 (22.7,28.4)	3.3 (1.6,4.9)	2.7 (1.5,3.9)	0.8 (-0.2,1.9)	0.7 (0.2,1.2)	3.1 (1.9,4.3)	5.7 (4.1,7.4)
Non-Hispanic White Only	50.0	53.1 (51.5,54.6)	33.9 (32.5,35.4)	3.7 (3,4.4)	1.4 (1.1,1.7)	0.1 (0,0.2)	0.8 (0.6,1.1)	1.4 (1,1.8)	5.6 (4.8,6.4)
Non-Hispanic Black Only	13.1	55.5 (51.6,59.3)	29.1 (25.5,32.6)	3.1 (1.8,4.5)	1.8 (0.8,2.8)	0.3 (0,0.7)	1.3 (0.4,2.2)	3.6 (1.7,5.4)	5.3 (3.9,6.7)
Non-Hispanic Other + Multiple Race	11.9	57.8 (54,61.6)	28.1 (24.6,31.5)	3.9 (2.4,5.4)	1.9 (1.1,2.8)	0.5 (-0.3,1.2)	0.7 (0.2,1.1)	2.3 (1.3,3.4)	4.8 (3.5,6.2)
Sex									
Male	51.0	52.6 (50.7,54.5)	32.8 (31.1,34.5)	3.8 (2.9,4.8)	1.8 (1.3,2.3)	0.5 (0,1)	0.6 (0.4,0.9)	2.3 (1.6,3)	5.6 (4.7,6.4)
Female	49.0	57.9 (56,59.8)	28.1 (26.4,29.8)	3.2 (2.5,4)	1.86 (1.3,2.4)	0.3 (0.1,0.5)	1.1 (0.7,1.4)	2.1 (1.6,2.7)	5.5 (4.5,6.4)
Insurance									
Private Insurance Only	53.0	55.9 (54.3,57.6)	31.5 (30,33)	3.3 (2.5,4)	1.6 (1.2,2)	0.3 (0.1,0.5)	0.9 (0.5,1.2)	1.6 (1.2,2)	5.0 (4.1,5.8)
Any Medicaid	36.1	56.5 (54,59)	27.3 (25.1,29.4)	3.7 (2.7,4.8)	2.1 (1.3,2.9)	0.5 (-0.1,1.2)	0.9 (0.5,1.3)	3.1 (2.1,4.2)	5.8 (4.7,6.9)
Other Insurance	6.7	52.2 (47.4,57)	33.0 (28.5,37.4)	4.1 (2.2,5.9)	2.0 (0.8,3.1)	0.1 (0,0.2)	0.6 (0.1,1.1)	2.1 (1,3.2)	5.9 (4.3,7.6)
Uninsured	4.2	39.6 (32.3,46.9)	41.9 (34.7,49.2)	4.5 (2.4,6.5)	2.3 (0.4,4.3)	0.2 (-0.2,0.5)	0.4 (0,0.7)	2.3 (-0.8,5.3)	8.9 (5.2,12.6)
Number Of Providers									
Zero	0.2	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	100 (100,100)
One	61.7	56.9697 (55.2,58.7)	30.145 (28.6,31.7)	3.2085 (2.5,3.9)	1.4936 (1.1,1.9)	0.349 (0,0.7)	0.991 (0.7,1.3)	2.5203 (1.9,3.2)	4.3229 (3.6,5.1)
Two	26.0	55.4303 (52.9,58)	29.2749 (27,31.5)	4.421 (3.1,5.7)	2.2718 (1.4,3.2)	0.241 (-0.1,0.6)	0.6886 (0.3,1)	1.7345 (1.2,2.2)	5.9378 (4.8,7.1)

Three +	12.1	46.5528 (42.8,50.3)	35.3189 (31.7,38.9)	3.4316 (2.1,4.8)	2.5624 (1.3,3.8)	0.6838 (-0.2,1.6)	0.4532 (0.1,0.8)	1.8144 (0.6,3)	9.1829 (6.7,11.7)
Facility Types [2]									
All Public Facilities	12.0	47.5 (43.3,51.6)	32.5 (28.9,36.1)	5.6 (3.7,7.5)	2.5 (1.4,3.5)	0.6 (-0.2,1.4)	0.9 (0.4,1.4)	2.7 (1.4,4)	7.7 (5.2,10.3)
All Hospital Facilities	10.7	58.2 (54.8,61.5)	29.4 (26.2,32.5)	2.9 (1.3,4.3)	1.5 (0.8,2.2)	0.2 (0,0.3)	0.4 (0.2,0.6)	2.4 (1.4,3.4)	5.1 (3.6,6.7)
All Private Facilities	47.6	58.0 (56.1,59.9)	30.6 (28.8,32.3)	2.0 (1.6,2.5)	1.9 (1.3,2.4)	0.1 (0,0.2)	1.0 (0.6,1.4)	2.3 (1.7,2.9)	4.2 (3.3,5.1)
All Other[3] Facilities	2.3	36.4 (29,43.8)	29.6 (22.7,36.5)	6.0 (1.6,10.3)	1.1 (0.2,2)	0.1 (0,0.1)	1.6 (-0.3,3.4)	4.6 (0.5,8.7)	20.8 (13.4,28.2)
Mixed	14.4	56.7 (53.5,59.9)	32.2 (29.2,35.2)	4.3 (2.9,5.7)	1.7 (0.7,2.7)	0.5 (-0.3,1.2)	0.7 (0.2,1.1)	1.3 (0.8,1.7)	2.7 (1.9,3.6)
Unknown	13.2	52.7 (47.9,57.4)	28.4 (24.3,32.5)	6.6 (3.5,9.7)	1.6 (0.3,3)	1.1 (-0.7,2.8)	0.8 (0.3,1.3)	2.1 (0.1,4)	6.7 (5,8.4)
11-12 Year Old Well Child Visit									
Yes	48.9	61.9 (60.1,63.8)	31.1 (29.3,32.8)	1.9 (1.3,2.5)	1.4 (0.9,1.9)	0.0 (0,0.1)	0.8 (0.5,1.2)	2.3 (1.7,2.9)	0.6 (0.4,0.8)
No	8.4	37.5 (32.8,42.2)	36.7 (32.4,41)	5.4 (3.8,6.9)	3.0 (1.7,4.4)	0.2 (0,0.4)	0.6 (0.1,1.1)	3.7 (1.9,5.5)	12.9 (9.4,16.3)
Don't Know	42.8	51.0 (48.9,53.1)	28.6 (26.8,30.5)	5.1 (3.9,6.2)	2.1 (1.4,2.7)	0.8 (0.1,1.4)	0.9 (0.6,1.2)	1.9 (1.2,2.6)	9.7 (8.4,10.9)
Family Income									
Below Poverty	19.6	58.1 (54.6,61.6)	26.8 (23.7,29.8)	3.8 (2.4,5.2)	1.4 (0.6,2.1)	0.4 (-0.1,0.9)	1.2 (0.5,1.9)	3.4 (2,4.9)	5.0 (3.8,6.1)
Above Poverty	80.4	54.7 (53.2,56.1)	31.4 (30.1,32.7)	3.4 (2.8,4)	1.8 (1.4,2.2)	0.4 (0,0.7)	0.8 (0.5,1)	2.0 (1.5,2.4)	5.6 (4.9,6.4)

[2] CHIP, HIS, Military or other, alone or in combination with private insurance

[3] STD/School/Teen clinics or other facilities

Table 2: Individual and Composite Measure of Vaccine Coverage of All Adolescents from the National Immunization Survey – Teen, United States, 2020	
Individual	**Percent (95% CI)**
HPV	58.6 (57.3-60.0)
MenACWY	89.7 (88.9-90.6)
Tdap	90.1 (89.2-91.0)
Composite	
HPV/Tdap/MenACWY	55.2 (53.9-56.5)
Tdap/MenACWY	30.5 (29.3-31.7)
Tdap	3.5 (3.0-4.1)
MenACWY	1.8 (1.4-2.2)
HPV	0.4 (0.1-0.6)
HPV/Tdap	0.9 (0.6-1.1)
HPV/MenACWY	2.2 (1.8-2.7)
None	5.5 (4.9-6.1)

Table 3: Insurance Coverage By Well Child Visit Status					
%	**Private Insurance Only**	**Any Medicaid**	**Other Insurance**	**Uninsured**	**Total**
Yes	28.4	16.0	3.0	1.5	48.8
No	3.4	3.6	0.6	0.8	8.4
Don't Know	21.2	16.5	3.1	2.0	42.8
Distribution*	53.0	36.1	6.7	4.2	100.0

*Missing 0.6 from Distribution Total percent is due to rounding error.

Public Health Implications and Conclusions

This composite measure and analysis of adolescent vaccination emphasizes the need for further research into finer details of vaccine disparities. Stratification by extent of vaccine uptake and individual demographic variables shows areas that require additional research into tertiary factors or beyond that will point to the specific hurdles preventing vaccination. This may be education, insurance, income, accessibility to providers, religious, or cultural. The complex interplay of variables makes it difficult and unadvisable to draw blanket conclusions about any specific group within each variable. More extensive evaluation of individual variables is necessary to better understand the specific reason(s) behind incomplete vaccination for groups and individuals. Stratification of variables across combined vaccine uptake, such as was done in this study, should be paired with comparative evaluation of other, related variables. Ideally, each variable could be analyzed with each other variable, to find overlapping themes. For example: stratification of maternal age by insurance coverage, education, income, etc. each. Then analyze which factors overlap with vaccine uptake and undervaccination. From there, education and advocacy can be more precisely targeted.

The annual MMWR summary of main findings of the NIS-Teen from the previous year is a principle resource for researchers working in any area of adolescent vaccination in the U.S. This is indicated in the reference section of most sources cited in this thesis. If such a prominent publication was to start concatenating the three standard adolescent vaccines and comparing their combined uptake alongside the other standard demographic variables, other scholars would likely start taking such a viewpoint into consideration during their analyses.

This may have a cascade of benefits on adolescent healthcare. Expectations for complete vaccine coverage would likely increase. This could mean increased provider visitations, which could help mitigate use of other health programs, similar to a benefit of WCV. Additionally, it could help to increase HPV vaccine uptake faster, so that it reaches the Healthy People 2030 target sooner.

Analysis of state vaccine records can help shed light on some of the gaps in the NIS-Teen data collection. One of these benefits would be the specificity of information for each state, which could be evaluated independently for unique vaccine coverage disparities to be addressed by public health workers in the state in question. Additionally, the state data could be compiled with regional and national data to build on information gathered from NIS-Teen.

HPV vaccination is the limiting factor in attainment of completing target coverage for adolescent vaccines. Composite expectations for adolescent vaccine coverage are so uncommon that Healthy People 2030 does not list a target for such an achievement. However, Healthy People 2020 aimed for MenACWY and Tdap to each reach 80.0%, which they accomplished as of 2015. (28, 33). The target of Healthy People 2030 for HPV vaccination is now 80.0%. This would unofficially create a target of 80.0% for complete vaccine coverage among adolescents. Achieving this will require more extensive examination of HPV vaccine hesitancy to identify the specific issues hindering delivery.

Advocacy for both ManACWY and Tdap should continue, though coverage of each has already reached the Healthy People decade targets. COVID delt a blow to vaccine progress, the implications of which we are likely still uncovering. We must resume striving to increase vaccine uptake in all populations to avoid losing any more progress. Provider recommendations are an important part of making that possible.

Moving forward, secondary analysis of the NIS-Teen, including a composite measure of adolescent vaccine coverage could provide increased depth in understanding vaccine hesitancy and present, small, better defined, subgroups of undervaccinated adolescents. One-by-one the specific barriers to access and information concerns can be identified and addressed.