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**Spatio-temporal patterns in individual and concomitant adolescent vaccine uptake in the
State of Georgia, 2006-2017**

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Health
2023

Abstract

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By Alessia Kettlitz

Objective: The objective of this study was to examine spatio-temporal patterns in adolescent tetanus, diphtheria, and acellular pertussis (Tdap), quadrivalent meningococcal conjugate (MCV4), and human papillomavirus (HPV) vaccination coverage, for individual vaccines as well as receipt of multiple vaccines, in Georgia between the years of 2006-2017.

Methods: We conducted a secondary retrospective quantitative data analysis of state immunization records and census data sets. The population of interest was adolescents born between the years 1995-2008 and living in the state of Georgia between the years 2006-2017. We identified vaccine doses administered using data from Georgia state's immunization information system. We used Census data to estimate the denominator to estimate population-level proportion estimates of vaccine coverage, by sex and health district, over time.

Results: In 2017, among adolescents born between 1995-2008, Tdap and MCV4 vaccination rates were similar, while HPV vaccine coverage lagged by 20-30 percentage points in comparison. While 36.5% had received all adolescent vaccines, 24.6% only received the Tdap and MCV4 vaccines, potentially indicating HPV vaccine hesitance. More recent birth cohorts had higher vaccine coverage than older birth cohorts (e.g., 41.3% Tdap/MCV4/HPV for those born in 1997/1998 compared to 54.5% Tdap/MCV4/HPV for those born in 2002/2003). There was geographic variation in complete vaccination, with some Health Districts exhibiting high uptake of Tdap/MCV4/HPV, suggesting high vaccine delivery overall, while others had high uptake of Tdap/MCV4 without HPV, indicating high vaccine delivery but potential HPV vaccine hesitance, while others exhibited low uptake of all adolescent vaccines, suggesting overall vaccine delivery issues.

Conclusions: These results indicate a need for studies with improved methods to evaluate adolescent vaccination in Georgia, as well as further research into identifying why some populations have different patterns of vaccine uptake. Future evaluations, with more recent data, can help monitor these trends while also accounting for the impact of the COVID-19 pandemic on adolescent vaccine uptake in Georgia.

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Acknowledgments

I want to thank my thesis chair, Dr. Robert Bednarczyk, for his immense guidance during this thesis process. I am very thankful for the knowledge, expertise, and support!

I would also like to thank Allie Busbee, a recent graduate of HDGH, for her help with this project! Her past work was foundational for this thesis, and I appreciated her help with SAS programming and HPV-specific knowledge!

Finally, I am grateful to my friends and family for their support, understanding, and patience as I completed my MPH and this thesis.

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Chapter 1: Introduction

Introduction

Adolescent vaccination is a crucial public health intervention and plays a principal role in maintaining the health of youth and the general population. Few other interventions can rival the impact and cost-effectiveness of vaccines in reducing the burden of infectious diseases ¹. The Advisory Committee on Immunization Practices (ACIP) has recommended three adolescent vaccines for routine use in the United States. These vaccines include the tetanus, diphtheria, and acellular pertussis vaccine (Tdap), recommended in 2005, the quadrivalent MCV4 conjugate vaccine (MCV4), recommended in 2006, and the human papillomavirus vaccine (HPV), first recommended in 2007 ²⁻⁵. While vaccination rates have increased among adolescents over time, vaccine hesitancy in the general public and unequal coverage by vaccine, region, and sociodemographic factors warrants further analyses into adolescent trends ⁶⁻¹⁴.

Background & Ramifications

The Tdap vaccine protects against tetanus, diphtheria, and pertussis. Without vaccination, these diseases can often lead to long-term disability or death ¹⁵. Concerningly, pertussis rates have increased in Georgia since 2010, particularly among adolescents ¹⁶. Further, the addition of this recommendation for Tdap vaccination of adolescents was estimated to reduce outpatient visits by 5% and reduce hospitalization by 7% among 16-year-olds in 2016 ¹⁷. Additionally, the adolescent dose of Tdap was estimated to cost \$156,890 per quality-adjusted life year (QALY), highlighting the high cost-effectiveness of the Tdap vaccine ¹⁷. While control of tetanus and diphtheria has been well-documented, continued pertussis infections bear a high cost, with pertussis disease associated with \$500 million of direct medical and productivity losses in 2018, over 30 years ¹⁸.

Similarly, the meningococcal conjugate vaccine (MCV4) prevents meningococcal disease caused by the *Neisseria meningitidis* bacteria, which can lead to severe disease and death without vaccination or treatment ¹⁹. While generally, incidence rates of meningococcal disease are low in Georgia, ranging between 10-25 cases per year, some serogroups of the *Neisseria meningitidis* bacteria have been increasing in incidence since 2014 ²⁰. The ACIP in 2010 estimated that a single dose of MCV4 among adolescents aged 11 years old could save 736 QALYs per year, with a cost per QALY saved of \$256,000 ⁴. Invasive meningococcal disease, a severe form of meningococcal disease, was estimated to cost \$76 million in hospital care in 2016 in the U.S. ²¹. The slight uptick in cases in Georgia and the high cost of treatment highlights the burden of meningococcal disease and the costs avoided through the high uptake of MCV4 vaccination.

Finally, HPV vaccines protect against HPV infection and several cancers (cervical, vaginal, vulvar, penile, anal, and oropharyngeal cancers) and genital warts caused by HPV infection ²². According to the CDC, HPV vaccination has led to a significantly reduced prevalence of HPV infection, and early evidence shows a reduced incidence of cervical cancers ^{23,24}. However, as HPV has a long incubation time for causing HPV-attributed cancers, cases have continued to rise in Georgia since 2011 ^{22,25}. The continued increase in cases due to the long incubation period for HPV indicates a need to vaccinate in the present to achieve the long-term impacts of reduced HPV-attributed cancer cases. HPV vaccination has an estimated cost-effectiveness ratio of \$43,000 per QALY gained, the highest ratio of adolescent vaccines ²⁶. In addition, in 2018, the estimated lifetime medical costs attributed to HPV were \$774 million among people aged 15-59 in the U.S. ²⁷. This significantly high medical cost, paired with the cost-effectiveness of the HPV, accentuates the economic implications of suboptimal HPV vaccine coverage. Thus, all three vaccines play a vital role in maintaining the health and well-

being of the U.S. population by limiting the spread of severe infectious diseases and having significant economic implications associated with suboptimal coverage.

The southeast region of the United States, consisting of Health and Human Services (HHS) regions 4 and 6, have reported lower adolescent vaccination rates compared to national estimates ¹¹. In addition, this region and Georgia have reported high rates of vaccine hesitancy and higher rates of adolescent vaccine-preventable diseases ^{28,25,11,29,30,12}. Thus, due to this region's recorded low vaccination rates, Georgia was chosen as the geography of interest.

Despite the noted importance of these adolescent vaccines, there are often differing levels of confidence, access, and coverage, particularly in Georgia. Further, limited studies examine adolescent vaccination coverage and even less explicitly focus on concomitant vaccine uptake in Georgia. Those that do exist tend to use poor data collection methods, leading to imprecise results exacerbated when stratified by key demographics or location. With the increased incidence rates of related diseases and vaccine hesitancy, **there is a need to identify individual and concomitant vaccination trends of Tdap, MCV4, and HPV among adolescents in Georgia to identify coverage gaps with improved data collection methods.**

Purpose Statement & Research Questions

Therefore, this study aims to assess spatio-temporal patterns of individual and concomitant Tdap, MCV4, and HPV vaccination coverage among adolescents born between 1995-2008 in Georgia between 2006 and 2017. Three key research questions were considered:

1. What is the individual and concomitant vaccine coverage for Tdap, MCV4, and HPV among adolescents in 2017?
2. What differences arise between Tdap, MCV4, and HPV vaccination among adolescents in Georgia, both in individual vaccine coverage and concomitant vaccination over time?

3. How does individual and concomitant vaccination over time differ by sex and geography in Georgia among adolescents?

Significance Statement

Understanding current vaccination coverage for adolescent vaccines in Georgia, especially where gaps in coverage appear, is extremely important due to the health, social and economic impacts of suboptimal coverage. Identifying the current status of these vaccines, their differences, and how demographics impact coverage is needed to inform future programming and policy and limit the spread of severe but preventable infectious diseases in Georgia.

Chapter 2: Literature Review

Overview

Vaccines are a critical medical intervention in global health and are linked to significant improvements in well-being worldwide. Few other interventions can rival the impact and cost-effectiveness of vaccines in reducing the burden of disease ¹. With the ongoing COVID-19 pandemic, the importance of vaccination has been re-emphasized due to the impact the COVID-19 vaccines have had on controlling the pandemic ³¹. Vaccinations during adolescence are of particular importance as these vaccines enhance protection from childhood vaccinations and provide vaccination before exposure to a contagion to reduce the risk of poor health outcomes ¹.

The ACIP has recommended three adolescent vaccines: the tetanus, diphtheria, and acellular pertussis vaccine (Tdap), recommended in 2005, the quadrivalent meningococcal conjugate vaccine (MCV4), recommended in 2006, and the human papillomavirus (HPV) vaccine, first recommended in 2007 ²⁻⁵. The Tdap vaccine protects against three diseases: tetanus, diphtheria, and pertussis, and is the subsequent dose of protection against these diseases after the DTaP vaccine is administered in childhood. The Tdap vaccination in adolescence is necessary to ensure that immune protections developed in childhood from the DTaP vaccine last and do not wane in the long term ¹⁵.

Tetanus is an infection caused by *Clostridium tetani*, and exposure occurs from broken skin coming into contact with spores in the environment ³². The Tetanus infection requires immediate medical intervention and can cause severe complications such as pulmonary embolism. In addition, the case fatality rate is 2 in 10, indicating a high mortality rate ³².

Diphtheria is, similarly, caused by exposure to a bacterium called *Corynebacterium diphtheriae* ³³. Unlike tetanus, however, diphtheria can be spread from person-to-person contact.

In addition, most cases result in respiratory illness, and diphtheria has a case fatality rate of 1 in 10, which increases among cases with young children ³⁴.

Finally, pertussis, also known as whooping cough, is a highly contagious respiratory disease caused by the *Bordetella pertussis* bacteria ³⁵. Pertussis can result in severe symptoms, such as violent coughing or breathing difficulties. While symptoms are most severe among infants, serious cases can still occur in unvaccinated adolescents and adults. Mortality rates are much lower in pertussis than in tetanus and diphtheria; however, severe symptoms can still occur and impact daily life ³⁵. Further, vaccination is essential in limiting the spread to vulnerable populations with a much higher risk of severe disease ³⁶.

Current rates of tetanus, diphtheria, and pertussis are low because of widespread immunization in both childhood and adolescence, highlighting the importance of this vaccine in protecting against the spread of infectious diseases ³⁷⁻³⁹.

MCV4 prevents meningococcal disease caused by four strains of the *Neisseria meningitidis* bacteria ¹⁹. Thus, the primary treatment for meningococcal disease is the administration of antibiotics; however, there has been a rise in penicillin-resistant *N. meningitidis* in the United States, emphasizing further the need for preventative measures against meningococcal disease ⁴⁰. Several types of meningococcal disease exist; the two most common are meningococcal meningitis and meningococcal septicemia (meningococcemia)¹⁹. Furthermore, both types can cause severe morbidities, such as loss of limbs, deafness, and brain damage, and 10 in 100 people diagnosed with meningococcal disease die, even with antibiotic treatment. Therefore, MCV4 vaccination is crucial.

Finally, HPV vaccines protect against HPV infection, the most common sexually transmitted infection ^{22,41}. While the initial infection often has mild symptoms, some strains of

HPV in the long term can lead to six severe cancers, including cervical, vaginal, vulvar, penile, anal, and oropharyngeal cancers. In the U.S., HPV causes 3% of all cancers among females and 2% of all cancers in males ⁴². While all of these cancers have high mortality rates, cervical cancer is particularly severe and the fourth deadliest cancer in females ⁴³. However, according to the CDC, HPV vaccination has led to significantly reduced HPV infection and reduced incidence of related cervical cancers ²³. Thus, HPV vaccination can prevent both infections from HPV and many severe cancers caused by HPV, displaying the exceptional importance of HPV vaccination.

All three of these vaccines play a crucial role in maintaining the health and well-being of the U.S. population by limiting the spread of severe infectious diseases. Despite this, these vaccines often have differing confidence, access, and coverage levels, particularly in the geography of interest, Georgia.

This chapter provides an overview of the current literature, including notable frameworks for understanding low vaccine uptake, current resources for estimating adolescent vaccination coverage in the U.S. and Georgia, an overview of vaccination coverage in the U.S. for the vaccines of interest, and a description of vaccine hesitancy. The primary purpose of this review is to determine what evidence presently exists regarding the coverage of these vaccines in the U.S., why differences in coverage may occur across the country and, in particular, in the state of Georgia, and understand the factors which influence low vaccine uptake among adolescents, such as vaccine hesitancy. In addition, this review identified significant gaps in the current literature for estimating vaccine coverage at the state and county level in Georgia due to the methods used to collect data, biased estimates at a more granular level, and limited understanding of how socioeconomic or demographic factors influence vaccination coverage.

Adolescent Vaccination Coverage in the U.S. and Georgia

Routine vaccination of U.S. adolescents with the Tdap, MCV4, and HPV vaccines MCV4 was recommended by the Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Control and Prevention (CDC) between 2005-2007 ²⁻⁵. The ACIP is the advisory committee that makes recommendations on the use of vaccines for the CDC. In addition, in 2016, the nine-valent (9vHPV) human papillomavirus vaccine was also recommended for protection against more strains of HPV ⁴⁴. Over time, since the ACIP made these recommendations, vaccination rates have increased among adolescents in the United States ^{7,11}. However, there are some discrepancies in vaccine uptake between types of vaccinations, regions, and by sociodemographic factors ^{6,14}.

National Immunization Survey-Teen

The principal method for estimating adolescent vaccination coverage in the United States is through the National Immunization Survey-Teen (NIS-Teen). The CDC conducts the NIS-Teen survey annually to monitor adolescent vaccination coverage ⁴⁵. NIS-Teen focuses on routinely recommended adolescent vaccines (Tdap, MCV4, HPV) and other generally recommended vaccines (e.g., influenza; verification of childhood measles, mumps, rubella vaccine status). NIS-Teen data are collected through random-digit-dialing to locate households with adolescents aged 13-17 years old and then surveys parents/guardians to collect information on vaccines received, socioeconomics, and the adolescents' demographics. If the parent/guardian consents, the adolescent's vaccination providers are contacted to retrieve provider-verified vaccination histories. The data collected from this survey is de-identified and made publicly available on the CDC's website through the "TeenVaxView" dashboard ⁴⁶. These findings illustrate a significant gap between Tdap, MCV4, and HPV vaccinations at national and state

levels (Table 1) ¹¹. Further, the gap in HPV vaccine coverage is accentuated between males and females.

Table 1: National and Georgia Vaccine Coverage Estimates for Adolescents Aged 13-17 Years old in 2021 from NIS-Teen

Vaccine Type	National n=18,002 (%) [95% CI]	National By Sex		Georgia n=260 (%) [95% CI]	Georgia By Sex	
		Male n=9,579 (%) [95% CI]	Female n=8,423 (%) [95% CI]		Male n=142 (%) [95% CI]	Female n=118 (%) [95% CI]
Up-to-date Tdap	89.6 [88.6-90.5]	-	-	92.7 [87.1-95.9]	-	-
Up-to-date MCV4	89.0 [87.9-90.0]	-	-	92.5 [86.8-95.9]	-	-
≥ 1 dose of HPV	76.9 [75.6-78.2]	75.4 [73.5-77.2]	78.5 [76.6-80.4]	78.6 [71.6-84.3]	74.9 [63.7-83.6]	82.5 [73.8-88.8]
Up-to-date HPV	61.7 [60.2-63.2]	59.8 [57.6-61.8]	63.8 [61.5-65.9]	60.9 [52.8-68.4]	55.4 [43.9-66.3]	66.6 [55.6-76.0]

While the NIS-Teen and resulting data set help estimate overall vaccination coverage among adolescents in the U.S., it is subject to several weaknesses, particularly at the state and local levels. These limitations are illustrated through the lowered sample size while stratifying by state. While the overall sample size of this survey is considerable due to the aim to represent the entire population of the U.S., the sample size is severely reduced at the state level. For example, while the sample size for the estimation of provider-verified up-to-date HPV vaccination status among males and females in 2021 is 18,002 for the U.S., the sample size for the state of Georgia was only 260 ¹¹. This smaller state-specific sample size reduces the precision of vaccination coverage estimates at the sub-national level, leading to results that do not accurately represent the population of interest (Table 2).

In addition, the NIS-Teen data is also limited in other ways. Data collection is a significant weakness of the study. Although the telephone survey method is a relatively quick method of data collection, it has significant limitations, such as excluding households without telephones, generally lower response rates than other survey methods, and does not identify all

households of interest; therefore, a determination of the actual population size was not found^{45,47,48}. Further, households with adolescents who did not receive vaccination, or households with vaccine or government-hesitant guardians, are less likely to participate in the survey^{47,49}. Finally, as the survey takes time to complete, households with limited resources may be unable to devote time to respond, leaving out a vital portion of the population, especially when considering issues of equity^{47,50}. Finally, random non-sampling errors also limit NIS-Teen data, such as varying interpretations of questions by respondents. Therefore, while the NIS-Teen data provides a high-level overview of vaccine coverage of adolescents in the U.S., its methodology severely limits its estimates, the limited sample size at the state level, and the lack of county-level estimates.

Georgia Adolescent Immunization Survey

At the state level, the Georgia Department of Public Health (GA DPH) conducts a similar survey to estimate adolescent immunization coverage, called Georgia Adolescent Immunization Survey (GAIS). While GA DPH conducts the study annually, the most recent study available to the public is from 2018. The study uses a cross-sectional design to estimate vaccine coverage among seventh-graders in Georgia⁵¹. The GAIS estimates vaccination rates for Tdap, Polio, MMR, MCV4, Hepatitis B, Varicella, and HPV vaccines. Researchers used a cluster-sampling design to select the study participants, where the primary sampling unit was middle schools, and the secondary sampling unit was students. GA DPH sampled students from each school selected. Vaccination records are then pulled from the school's records and compared to the state's immunization records from the Georgia Registry of Immunization Transactions and Services (GRITS), the statewide immunization information system. These findings suggest a significant disparity in HPV vaccine coverage compared to other adolescent vaccinations, as Tdap and MCV4 have 95% coverage, compared to 50.6% and 23.4% coverage for at least one dose and up-to-date HPV, respectively (Table 2). These results also suggest a gap between sexes in HPV

vaccination coverage, as there is a 2-4% difference in at least one dose and up-to-date HPV vaccination between males and females; however, the gap is not as large as estimated in NIS-Teen, where the difference was closer to 10% between male and female adolescents in Georgia.

Table 2: Vaccination Coverage Estimates by Vaccine and by Sex among Seventh-graders in Georgia from Georgia Adolescent Immunization Survey, 2018

Vaccine Type	Un-Stratified n = 7,057 (%)	By Sex	
		Male n = 3,541 (%)	Female n = 3,474 (%)
Up-to-date Tdap	95.7 \pm 0.5	96.1 \pm 0.6	96.2 \pm 0.6
Up-to-date MCV4	95.5 \pm 0.5	95.8 \pm 0.7	96.0 \pm 0.6
\geq 1 dose of HPV Vaccine	50.6 \pm 1.2	48.9 \pm 1.6	52.8 \pm 1.7
Up-to-date HPV Vaccine	23.4 \pm 1.0	22.8 \pm 1.4	24.2 \pm 1.4

This study from the GA DPH helps estimate vaccination trends among seventh-graders in Georgia who are enrolled at schools and have vaccination history recorded by their school. Further, the confidence intervals are much more precise than in the NIS-Teen data, even when stratifying by demographics or at the district level. While the sample size differs across health districts, the average sample size is 390, which is already larger than NIS-Teen's sample size of 260 for the whole state of Georgia ^{11,51}. Despite these strengths, there are significant limitations present.

First, the study only examines seventh-grade students and does not look at overall adolescent vaccination coverage in the state. Related to the study population, data were only obtained for students enrolled in schools registered by the state. Further, the study does not collect longitudinal data but only collects cross-sectional vaccination information for a student. Therefore, this study is limited in scope to seventh-grade students enrolled at a registered school at a specific time.

Second, cluster sampling could lead to less representative results, as those within clusters tend to have similar characteristics, and thus the within-cluster variance is often low ⁵¹.

Therefore, the method of sampling chosen could have skewed results.

Third, the sample size per district was only 30 schools, regardless of the population size of the health district, with an average sample size per health district of 290. As a result, larger districts may not have a representative sample and, therefore, inaccurate results ⁵¹. However, despite this limitation, this study has a larger sample size than the NIS-Teen for estimating Georgia's adolescent vaccine coverage, where the total sample size for Georgia in the NIS-Teen is 260, and the total sample size for GAIS is 7,057. Thus, despite the populous districts having disproportionately sized samples, the GAIS has a much higher sample size and precision in its estimates for adolescent vaccination in G.A. than NIS-Teen.

Finally, this study was limited by the school's willingness and ability to provide accurate vaccination records for selected students. Record-keeping may differ drastically between schools, particularly within private schools, which may not be subject to the same regulations as public schools. While this was offset by examining results for students from GRITS, there may still be inaccuracies in vaccination records. Therefore, while this study provides a more precise and localized estimate of vaccination coverage, it is limited by its study population, scope, sampling design, and data collection methods.

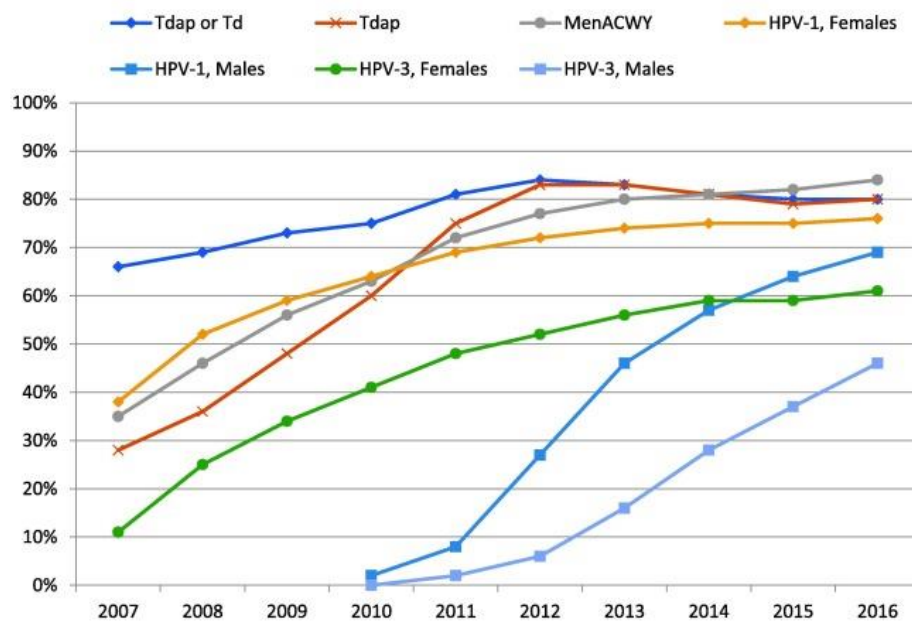
However, as of 2020, the GA DPH no longer conducts this survey. Instead, in recognition of the weaknesses of the GAIS survey, the GA DPH now uses state immunization records to estimate adolescent vaccination coverage ⁵². Vaccination coverage estimates for those aged 13-17 using state immunization records from 2020-2022 are now publicly available as of 2023 on the GA DPH website. This change recognizes the limitations of survey methods for estimating

adolescent vaccine coverage. Despite this, the new reports still lack concomitant analyses of adolescent immunization in GA.

Other Data Sources for Estimating Adolescent Vaccine Coverage

Other methods for estimating vaccine coverage among adolescents include examining insurance or medical records. In 2002, Irving et al. used medical records for an evaluation conducted through the Vaccine Safety Datalink (VSD). The VSD is a database created in collaboration between the CDC and nine managed care organizations⁵³. Irving et al.'s study provides a formidable overview of adolescent vaccination trends across the country, as it examined the change in vaccination rates between the ten years of 2007-2016 (2022). The study was a descriptive, retrospective cohort study. As mentioned, the VSD uses standardized electronic health records while noting insurance enrollment and demographic information data.

Figure 1: Vaccine coverage as of adolescents' 18th birthday – 2007-2016 (Irving et al., 2022)



The study population consisted of adolescents aged 11-18 with more than six months of continuous enrollment at a VSD site during the study period, with a total sample size of 1,025,677 individuals.

Across the years 2007 to 2016, vaccine coverage for MCV4, Tdap, and any form of HPV vaccine increased (Figure 1).

Further, the study found that MCV4 had the highest coverage among 18-year-olds at the end of the study, followed by Tdap, and then farther behind was the receipt of at least one dose of the HPV vaccine. A primary strength of this article is that it provided an estimate of adolescent vaccination coverage over a long-time period using a nationally representative sample. Further, it is one of the few studies examining concomitant adolescent vaccination and holistically investigates the adolescent vaccination platform.

However, this study also has some weaknesses. First, it only features vaccine coverage data and has little demographic data to examine. Therefore, gaps between demographics cannot be identified. Second, the study population may not be generalizable to all adolescent populations in the U.S. as the population consists only of adolescents who were members of VSD sites ⁵⁴. Finally, electronic health records are subject to variability in adherence to the data recording protocol across several sites. Despite these limitations, this study provided a robust overview of the general trends in adolescent vaccination.

These various studies and data collection methods highlight four key considerations: First, overall, adolescent vaccination rates have increased since their recommendations by the ACIP. Second, despite these increases, there is a significant gap in coverage for HPV vaccination compared to Tdap and MCV4. Third, vaccine coverage for HPV has disparities by sex, with males having lower coverage of HPV than females. Fourth, there is a strong need in the U.S. and Georgia for more vigorous studies to estimate adolescent vaccination coverage. Current methods often have significant limitations, whether leaving out key populations and thus having an unrepresentative sample or through poor data collection methods that lead to imprecise results ^{11,47-51}. Further, current data sets have limited information on demographics or other factors influencing vaccine coverage rates ^{11,51,53,54}. Therefore, there is a strong need for studies that

capture fully representative samples and collect data on demographic data to estimate adolescent vaccination rates accurately and identify areas of need to inform future programming and policy.

HPV Vaccination Coverage Among Adolescents

Despite HPV vaccination acting as an effective primary intervention for HPV infection, and resulting cancers, HPV vaccination remains modest in the United States among adolescents⁵⁵. As shown previously, when compared to Tdap and MCV4, HPV generally has lower rates of vaccination at both national and state levels^{11,51}. Socioeconomic factors accentuate these divergences in southern states^{14,55}. While disparities in HPV vaccine coverage exist, little literature has reviewed the HPV vaccine in tandem with the entire adolescent vaccine platform. This analysis is essential to understand how adolescent vaccines compare to each other, and for HPV specifically, understand whether these disparities are due to vaccine delivery issues or HPV-specific vaccine hesitancy. This understanding of the complete adolescent vaccination platform will help better inform policies and programs which ensure the maximal level of protection for adolescents. Therefore, understanding the current literature on HPV-specific disparities is helpful.

Hirth's 2019 study describes the disparities in vaccination rates and HPV prevalence in the United States based on geographic, racial, sex, and ethnic demographics. The study reviewed NIS-Teen data to determine which populations and areas had the lowest HPV vaccination rates. Hirth found that Georgia had a 40.1-55% increase in HPV vaccination between 2009 and 2016. Despite this significant increase in Georgia, southern states generally had lower HPV vaccination rates than other regions of the United States. More generally across the United States, Hirth concluded that vaccination rates for HPV varied significantly based on geography, race, ethnicity, and sex, especially among those that are often already at high risk for other health issues, such as Black and low-income populations in Southern states. Those populations and

areas with lower HPV vaccination rates also had higher cervical cancer mortality rates. Hirth concluded that there was a strong public health need to address the disparity in HPV vaccination to reduce current and future health inequities in the U.S. A significant strength of this study was the unique perspective on HPV vaccination, as many studies do not identify gaps in coverage between different demographics and geographic regions. However, this study did not provide any new data and instead used NIS-Teen's data to conduct its analyses. Therefore, the study has similar weaknesses to the NIS-Teen survey discussed previously. Despite these limitations, this study helps inform stratified analyses and potential areas for policy and programming, as it identifies populations with low vaccination rates for HPV.

Narrowing the focus to the southern United States, Vasudevan et al. conducted a survey to describe current HPV vaccination patterns, compare them to Tdap and MCV4 vaccinations, and suggest predictors for high HPV vaccine initiation and completion (2021). The survey was completed by 1000 English-speaking parents of adolescents aged 9-17 in southern U.S. states, randomly selected via residential addresses. The states included were Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, and Texas. To minimize the sampling bias of the study, Vasudevan et al. provided tablets and internet access to households without internet access. The survey found that HPV vaccination initiation was reported only among 37.3% of adolescents and was highest among adolescents aged 12.

Additionally, cumulative HPV vaccination coverage was highest among adolescents aged 15, with 60% coverage ¹⁴. However, this remained lower than coverage for Tdap (79.3%) and MCV4 (67.3%). Therefore, like other studies, this survey suggests that southern states have lower HPV vaccination rates than national rates ^{11,51,55}. As this survey also collected information

regarding sociodemographic characteristics, access to healthcare, and barriers to HPV vaccine uptake, Vasudevan et al. used weighted multivariate logistic regression models to suggest predictors for HPV vaccination status. The characteristics associated with increased HPV vaccination were provider recommendations, short travel times to a healthcare provider, and co-administration of other adolescent vaccines.

Conversely, home or online schooling and limited healthcare coverage were associated with lower rates of HPV vaccination ¹⁴. A significant strength of this study was that it included both parents of adolescents who did and did not receive the HPV vaccination, allowing comparison between these two groups. Another strength was the recording of additional sociodemographic characteristics, which allowed for suggestions of why HPV vaccination may be lower compared to other adolescent vaccines. However, the overall sample size is reasonably small compared to the population of the geographic region of interest and may not fully represent the general population of interest. Despite this shortcoming, the study provides an estimate of HPV vaccinations compared to Tdap and MCV4 vaccination while also providing suggestions as to why adolescent vaccinations have different rates in the southern region of the United States.

Both of these studies investigate possible factors that influence HPV vaccination in adolescents in the United States and compare rates to other adolescent vaccines; in particular, both suggest that southern states tend to have lower HPV vaccination rates than the national average ^{14,55}. In addition, both studies also mentioned that adolescents of lower socioeconomic status also tend to have lower HPV vaccination rates, suggesting that these rates may be due to health inequity issues. However, these studies use different data sources. Hirth's study used the NIS-Teen dataset, and Vasudevan et al. collected new data by conducting a large-scale survey. Therefore, while Vasudevan et al. study only had 1000 participants, the confidence intervals

when examining specific groups were larger than with Hirth's use of NIS-teen data. Overall, both studies have their limitations in their datasets because of sampling bias and low sample size, but together suggest that HPV vaccinations are significantly lower than Tdap and MCV4 vaccinations in the southern states due to various socioeconomic or geographic reasons.

These studies highlight the differences in coverage between HPV, Tdap, and MCV4 vaccinations in adolescents across the United States. Further, the results of these studies both suggest that this gap in HPV vaccine coverage may be higher among groups that face significant inequities in medical treatment and public health interventions. Finally, both studies suggest that further studies are needed to compare Tdap, MCV4, and HPV vaccination trends, particularly in areas of the South or among historically-oppressed populations.

This finding of lower rates of HPV vaccination in southern states, in conjunction with the limited research surrounding the HPV vaccine in GA, is why we chose to center this research in this state. A systematic review from 2018 by Dennison et al. identified a key knowledge gap surrounding HPV in GA. In particular, very few studies examined socioeconomic and geographical differences in HPV vaccination in GA. While this study is not HPV-specific, it still gives an insight into how the HPV vaccine compares to other adolescent vaccinations. Thus, this study chose GA as the state of interest to reduce the knowledge gap surrounding HPV vaccination in this geography.

Concomitant Adolescent Vaccination

In the childhood vaccination literature, many studies compare all childhood vaccines concomitantly, and the combined vaccine series metric is considered a standard metric for estimating vaccination coverage^{38,56,57}. For example, the childhood vaccination component of the National Immunization Survey presents data on both individual and concomitant vaccinations³⁸. Further, this metric has been a component of the Health People measures since

2000⁵⁸. In these cases, the combined vaccine series is used to assess the overall state of childhood vaccination and acts as a benchmark to compare individual vaccine coverages³⁸.

Thus, this metric compares vaccine coverages relative to each other to identify gaps per vaccine while also examining the state of the childhood vaccine series as a whole. Therefore, this metric is present in many studies, including the NIS-Child and Healthy People.

Despite the examination of concomitant vaccination being a standard in childhood vaccination, it has not yet become a standard regarding adolescent vaccination¹¹. Currently, NIS-Teen does not examine combination vaccine series, despite the childhood component of the same survey reporting this metric for several years^{11,38,58}. Thus, there is a need for further studies to investigate adolescent vaccination concomitantly, to identify disparities between these vaccines, and identify either vaccine-specific or general vaccine delivery issues.

Determinants of Vaccination Coverage

A prominent framework to describe determinants of vaccination coverage is the 5A framework, detailed by Thomson et al. in 2016. While this framework is not specific to adolescent immunization programs, it still can be used to understand the barriers, facilitators, and contextual factors which may influence vaccine coverage. The various determinations of suboptimal vaccination coverage are grouped into five categories: *Access*, *Affordability*, *Awareness*, *Acceptance*, and *Activation* (Table 3). While this model attempts to capture all influencers on vaccine uptake, it is still an extraordinarily complex issue shaped by multiple contextual factors. Despite this, the framework comprehensively explains the factors influencing suboptimal vaccine coverage. Considering these causes can inform the analysis methods and stratifications, which may be relevant when exploring adolescent vaccination trends.

Table 3: Definitions of Components of 5As Framework (Thomson et al., 2016)

Root Cause	Definition
Access	The ability of individuals to be reached by, or to reach, recommended vaccines
Affordability	The ability of individuals to afford vaccination, both in terms of financial and non-financial costs (e.g., time)
Awareness	The degree to which individuals have knowledge of the need for, and availability of, recommended vaccines and their objective benefits and risks
Acceptance	The degree to which individuals accept, question, or refuse vaccination
Activation	The degree to which individuals are nudged towards vaccination uptake

A similar framework to describe determinants of vaccine coverage is the 5C framework, developed by Betsch et al. in 2018. This framework focuses on the psychological antecedents of vaccination, differing from other frameworks that focus on confidence in vaccines and vaccine delivery systems. They grouped psychological antecedents into five categories: *Confidence*, *Constraints*, *Complacency*, *Calculation*, and *Collective Responsibility* (Table 4). This framework aimed to expand the current understanding of determinants of vaccine coverage while also moving past the focus on vaccine hesitancy as the primary cause of suboptimal vaccine coverage. Thus, examining vaccination practices while considering both the “5A” and “5C” frameworks in conjunction can provide a more robust understanding of reasons for suboptimal vaccine coverage^{59,60}.

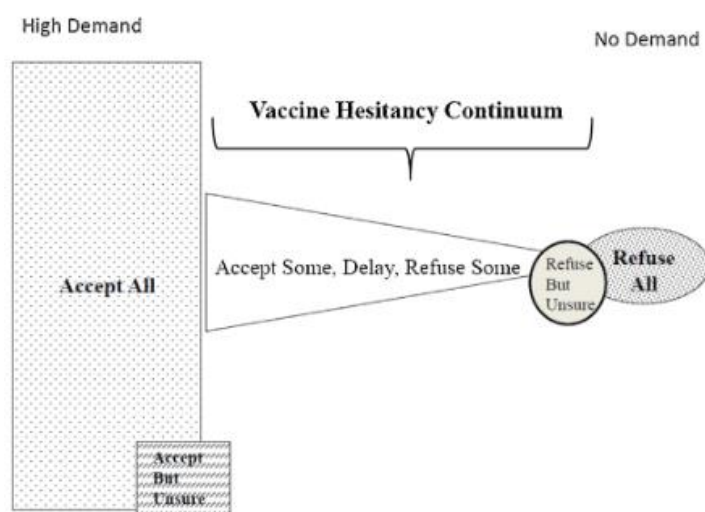
Table 4: The Definitions of the “5Cs” (Betsch et al., 2018)

Psychological Antecedents	Definition
Confidence	Trust in the safety and effectiveness of the vaccine and the vaccine delivery system
Complacency	Individuals’ perceived risk of vaccine-preventable diseases
Constraints	The barriers and facilitators of access to vaccines, including physical availability, affordability, language and health literacy, and appeal of vaccine service, affect uptake
Calculation	Individuals’ ability to infer the risk of infectious diseases and, similarly, their ability to seek out information regarding vaccines
Collective Responsibility	Willingness to protect the general community through vaccination and resulting herd immunity

Adolescent Vaccine Hesitancy in the United States

Increased vaccine hesitancy and misinformation in the United States have impacted adolescent vaccination rates of all recommended vaccines ⁶¹. The WHO SAGE Working Group

Figure 2: Vaccine Hesitancy Continuum (WHO SAGE Working Group, 2014)



created the Vaccine Hesitancy Scale (VHS) in 2014 to define vaccine hesitancy in several contexts. They define vaccine hesitancy as a spectrum from those that fully accept all vaccines to those that outright refuse all vaccines, shown in Figure 2.

However, the VHS does not apply to areas where vaccine uptake is low due

to other factors, such as poor access to healthcare services. As a result, when using the VHS for a specific population, it is essential to identify whether the low vaccine rates are due to vaccine hesitancy or other factors. Thus, the WHO SAGE Working Group defines a vaccine-hesitant community as one with lower-than-expected vaccine coverage and adequate access to healthcare services and vaccines. This definition differs from the previously mentioned “5As” and “5Cs” frameworks, as it does not include *access* as a component of vaccine hesitancy. Instead, this definition of vaccine hesitancy distinguishes between confidence and access. This consideration is critical when examining gaps in coverage, as the differing needs will significantly change the policy or programming best suited.

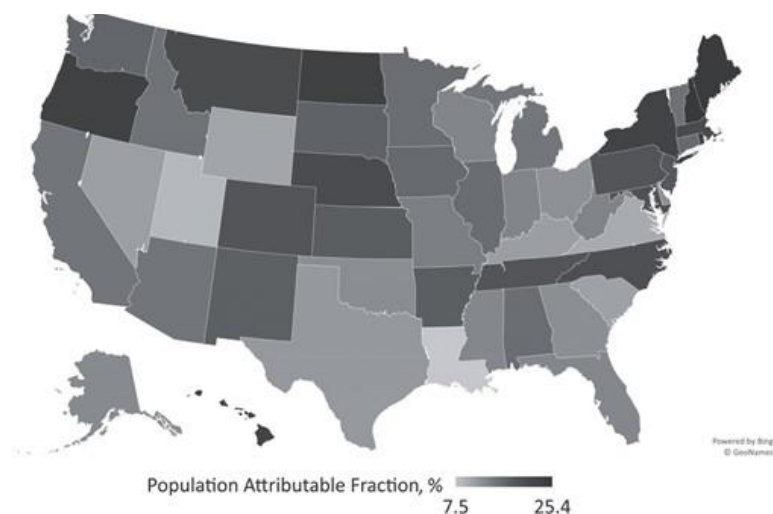
Vaccine hesitancy has increased in the United States in scope and scale and has been amplified by the COVID-19 pandemic and the spread of misinformation on social media

platforms ⁶¹. While vaccine hesitancy is often related to a specific vaccine, for example, the belief that the MMR vaccine could cause autism, it is also often tied to or can spread to vaccines in general ⁶¹. Further, while vaccine hesitancy is challenging to measure, vaccine exemptions, a proxy indicator for vaccine hesitancy, among children and adolescents have increased yearly across the U.S. ⁶². A more recent study from the CDC found that coverage for state-required vaccines among kindergarteners decreased from 95% to 94% nationally between 2021 and 2022 ¹³. This study also highlighted the continued increase in exemption rates across the U.S. Further, vaccination records for specific diseases have decreased in specific areas, such as the MMR vaccine continuing to see lowered coverage rates among children. Vaccine hesitancy and suboptimal vaccine coverage pose risks to individuals and communities and could spread preventable infectious diseases ⁶¹.

Regarding adolescent vaccination, vaccine hesitancy is influenced by the adolescent's perception and access and by their guardian's perceptions and access to the vaccines ⁶³. Despite this, there are a limited number of studies measuring how vaccine hesitancy among parents influences adolescent vaccination rates. However, Nguyen et al.'s 2022 study aimed to assess the proportion of non-vaccination for influenza and other childhood vaccines attributed to parental vaccine hesitancy. This study used results from the NIS and had a sample size of 37,405 in 2018 and 41,320 in 2019. The study sample consisted of guardians of children aged 19-35 months or adolescents aged 13-17. Nguyen et al. calculated the population-attributable fraction across sociodemographic characteristics and states. For all vaccines, the proportion of unvaccinated children was higher among hesitant parents than non-hesitant parents, suggesting that parent vaccine hesitancy is associated with lower adolescent vaccination rates.

Further, the population-attributable factor ranged from 15.4% for non-Hispanic White and Black populations to 12.4% for Hispanic populations. Figure 3 displays the population-attributable factor by state, showing that states in the northwest and northeast tend to have the

Figure 3: State-level Population Attributable Factor of Non-Vaccination of Childhood Influenza Vaccine Attributed to Parental Vaccine Hesitancy



highest population-attributable fractions. The study concluded

that the population-attributable factor was highest among high-income, high-education, and urban areas, and thus suggests that in these areas and among these demographics, parental vaccine hesitancy has the most impact on

adolescent vaccination rates. As these populations tend to have higher healthcare access, access is unlikely a primary factor for lowered vaccine rates. This conclusion relates to the differences noted previously between the “5As” and “5Cs” models and the WHO’s SAGE Working Group’s definition of vaccine hesitancy, particularly that lack of access is not necessarily a component of vaccine hesitancy^{59,60,64}. A strength of this study is its discussion of an essential but underrepresented topic: the relationship between parental vaccine hesitancy and adolescent vaccination⁹.

Further, as the study used NIS data, the sample size was large, encompassing a large, diverse population. However, it also is subject to the limitations of the NIS data, as discussed previously, such as smaller sample sizes when stratifying by state or demographic characteristic and recall or social bias due to the self-report of vaccination status and vaccine hesitancy.

Nevertheless, despite these limitations, the study provided a unique insight into how parental vaccine hesitancy influences adolescent vaccination.

The rise of vaccine hesitancy among the general public and specific guardians of adolescents is a prominent cause for concern. A rise in lower vaccination rates for specific and general vaccines could lead to increased spread of preventable infectious diseases, consequently increasing morbidity and mortality. Because of the importance of vaccinations, particularly among minors, more studies are needed to understand the reasons for low vaccine uptake in specific communities. Further, distinguishing between vaccine hesitancy or other factors influencing vaccine uptake as a cause for low vaccine coverage is vital for understanding the specific needs of each population and thus aids with developing future policies and programs to improve vaccination rates.

Conclusion

This investigation into the literature regarding adolescent vaccines in the United States and Georgia has revealed that the quality of data available for estimating adolescent vaccination rates is subpar. Thus, further research that provides accurate and precise coverage estimates through representative and larger sample sizes at local levels is needed. Further, a knowledge gap was identified in understanding the reasons for differences in coverage between Tdap, MCV4, and HPV. While researchers have identified these differences, reasons why these differences exist, such as whether it was due to vaccine hesitancy or differing access, are largely unknown. Finally, more research is needed to identify disparities in vaccine coverage by demographics, location, and socioeconomic status. While some studies have noted these disparities, most studies do not have generalized information on race, ethnicity, income level, education level, or locality, which are needed to identify whether there are disparities in vaccine coverage to these

factors. Thus, there is a comprehensive need for more representative data on vaccine coverage, with further information on vaccine hesitancy and demographics.

Chapter 3: Results

Title Page

Manuscript submission for JAMA Pediatrics

Spatio-temporal patterns in individual and concomitant adolescent vaccine uptake in the State of Georgia, 2006-2017

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Ethical Considerations

This project was approved by the Institutional Review Board of Emory University in the United States (IRB00100271) and the Institutional Review Board of the Georgia Department of Public Health (180401). IRB approval was required as this study included human subjects, personal health information, and access to restricted data.

Manuscript Count: 3000

Key Points

Question: What is the individual and concomitant vaccine coverage for Tdap, MCV4, and HPV among adolescents in the state of Georgia between 2006-2017?

Findings: In this epidemiological observational study, we identified individual coverages of adolescent vaccines with a Tdap coverage of 65%, an MCV4 coverage of 63%, an HPV vaccine series initiation coverage of 39%, and an HPV vaccine series completion coverage of 24%, no statistical analyses. We noted differences across geography, time, and sex when examining concurrent vaccination.

Meaning: In Georgia, there is suboptimal coverage of adolescent vaccination, with a marked reduction in HPV coverage; differences arose across geography, time, and sex.

Abstract

Importance: There is limited research explicitly investigating adolescent vaccination coverage in Georgia, despite this state exhibiting vaccine disparities compared to national averages, both individual and concomitantly, using reliable data methods.

Objective: The objective of this study was to examine spatio-temporal patterns in adolescent tetanus, diphtheria, and acellular pertussis (Tdap), quadrivalent meningococcal conjugate (MCV4), and human papillomavirus (HPV) vaccination coverage, for individual vaccines as well as receipt of multiple vaccines, in the state of Georgia between the years of 2006-2017.

Design, Setting, and Participants: We conducted an epidemiologic observational study of state immunization records and census data sets. The population of interest was adolescents born between 1995-2008 and living in Georgia between 2006-2017.

Main Outcome and Measures: The main outcome of interest was receiving at least one dose of either Tdap, MCV4, or HPV vaccine. We measured vaccine doses administered using data from Georgia state's immunization information system. We used Census data to estimate the denominator to estimate population-level proportion estimates of vaccine coverage, by sex and health district, over time.

Results: In 2017, among adolescents born between 1995-2008, Tdap and MCV4 vaccination rates were similar, while HPV vaccine coverage lagged by 20-30 percentage points in comparison. While 36.5% had received all adolescent vaccines, 24.6% only received the Tdap and MCV4 vaccines, potentially indicating HPV vaccine hesitance. More recent birth cohorts had higher vaccine coverage than older birth cohorts (e.g., 41.3% Tdap/MCV4/HPV for those born in 1997/1998 compared to 54.5% Tdap/MCV4/HPV for those born in 2002/2003). There was geographic variation in complete vaccination, with some Health Districts exhibiting high

uptake of Tdap/MCV4/HPV, suggesting high vaccine delivery overall. In contrast, others had high uptake of Tdap/MCV4 without HPV, indicating high vaccine delivery but potential HPV vaccine hesitance, while others exhibited low uptake of all adolescent vaccines, suggesting overall vaccine delivery issues.

Conclusions and Relevance: These results indicate a need for studies with improved methods to evaluate adolescent vaccination in Georgia, as well as further research into identifying why some populations have different patterns of vaccine uptake. Future evaluations, with more recent data, can help monitor these trends while also accounting for the impact of the COVID-19 pandemic on adolescent vaccine uptake in Georgia.

Introduction

Adolescent vaccination is a critical public health intervention and plays a principal role in maintaining the health of adolescents and the general population ¹. In the United States, three adolescent vaccines – tetanus, diphtheria, and acellular pertussis (Tdap) vaccine, quadrivalent meningococcal conjugate vaccine (MCV4), and human papillomavirus (HPV) vaccine – were recommended for routine use by the Advisory Committee on Immunization Practices (ACIP) between 2005-7 ²⁻⁵. While adolescent vaccination rates have increased over time, vaccine hesitancy and unequal coverage by vaccine, region, and sociodemographic factors warrant further analyses into adolescent trends ⁶⁻¹⁴.

National Immunization Survey-Teen, an annual survey conducted by the Centers for Disease Control and Prevention (CDC) to monitor adolescent vaccination coverage, is the primary data source for estimating adolescent vaccination coverage in the U.S. ^{11,45}. While these data help provide a high-level overview of adolescent vaccination coverage, the data is limited by methodological weaknesses and large confidence intervals ¹¹. These limitations have prevented detailed state- and sub-state-level analysis of vaccine uptake.

The southeast region of the United States has reported lower adolescent vaccination rates compared to national estimates ¹¹. In addition, this region and Georgia have reported high rates of vaccine hesitancy and higher rates of adolescent vaccine-preventable diseases ^{11,12,28-30,51}.

Further, there is a low level of HPV vaccine-specific research in GA, indicating a need for further research regarding this vaccine ²⁸. Thus, we chose Georgia as the geography of interest because of these identified needs.

Further, there is a need for additional research investigating concomitant vaccination of adolescent vaccines, as while concomitant vaccination is a standard metric for investigating the childhood vaccine platform, it is not yet standard for adolescent vaccination ^{38,58}.

This study aims to examine adolescent vaccination coverage for Tdap, MCV4, and HPV in Georgia among adolescents in the years 2006-2017, using immunization data from the statewide immunization information system. In this study, we examine both individual vaccine receipt and composite measures of receipt of all possible combinations of the three routinely recommended adolescent vaccines for the state of Georgia and individual Health Districts.

Methodology

Overview

We conducted an epidemiological observational study of Georgia's spatial-temporal adolescent vaccination patterns using immunization records from the Georgia Registry of Immunization Transactions and Services (GRITS), the statewide immunization information system. This analysis covers records of vaccinations received between 2006-17 among those aged 9 to 17 at any time during that window. Because GRITS data is "numerator only" data, to measure the proportion of the population that received the vaccines of interest, we linked the vaccine data to U.S. Census Bureau population data, stratified by age, sex, and county, to estimate the proportion of the population vaccinated ⁶⁵. Data analysis was primarily conducted through the creation of visualizations and comparisons between age groups, by time, and through stratifications by sex and health districts.

Data Sources & Instruments

The primary data set was obtained from GRITS and provided by Georgia's Department of Public Health (GA DPH). GRITS collected vaccination records, and all vaccinators must report vaccinations ⁶⁶.

The data set for analysis contains information on individuals' birth dates, sex, race, ethnicity, type of vaccine received, the date the vaccine was received, the administering organization for the vaccine, and the zip code of the individual's residence at the time of receiving the

vaccination. The vaccination-specific information was available for each instance of vaccination, including when excess vaccination was received (for example, receiving multiple Tdap vaccinations or more than the recommended number of HPV vaccine doses).

The secondary data sets were the Bridged-Race Population Estimates from 2000-2020, retrieved from the CDC's website ⁶⁵. These data sets contain population estimates stratified by state, county, age, ethnicity, race, and bridged-race and sex.

Population and Sample

The population for this analysis was adolescents born between 1995-2008 and living in the state of Georgia between the years 2006-2017. The U.S. Census Bureau reported sample size for this population was 2,012,115 adolescents in 2017. Within the GRITS data set, we identified a sample size of 1,387,616 adolescents with at least one dose of either Tdap, MCV4, or HPV vaccine administered during this period between the ages of 9-17 in Georgia.

We conducted analyses for separate birth cohorts. However, the sample size of individuals with vaccines in GRITS for the more recent birth cohorts was smaller relative to older birth cohorts, as they were less likely to have received a vaccination between 2006-2017 due to less time elapsing between them becoming eligible for these vaccines and the timing of the data extract.

Procedures

Data management, cleaning, analysis, and geospatial mapping were conducted using SAS® software, with Microsoft Excel used for graphical or tabular visualizations ^{67,68}. Because individuals may have moved between vaccine doses, the ZIP code of residence was assessed as the ZIP code associated with the last vaccine administered; ZIP codes were then linked to county, and counties were grouped in the GA DPH Health Districts ⁶⁹. To link Census population data with GRITS' immunization data, we extracted Georgia-specific Census data and stratified the data by Census fiscal year, which begins on July 1st. As the Census data was stratified by

age, sex, and county, we merged Census and GRITS vaccination data by these factors, accounting for temporal changes in children's age to link to the corresponding age group in the Census data.

For each birth cohort, we assessed vaccine uptake by identifying the year an adolescent received a particular vaccine and considered them vaccinated from that point forward. For Tdap and MCV4, complete vaccination occurred when the first dose was recorded. Because the HPV vaccine requires multiple doses (either two or three doses, depending on age and calendar year relative to changing vaccination recommendations), we focused on the initiation of the HPV vaccine as of when the first dose was recorded as received. Concomitant vaccination was measured by assessing receipt of Tdap, MCV4, and HPV vaccines. There were eight combinations, ranging from receipt of all three vaccines to no record of receipt of any adolescent vaccine. Over time, individuals could shift from one group to another, for example, shifting from the Tdap and MCV4 group to the Tdap, MCV4, and HPV vaccine group in the next year. Once the counts of individuals with vaccines according to these combinations were computed by age and year, these non-stratified counts were merged with Census population estimates. Once merged, the "No record of adolescent vaccine receipt" category was computed based on the difference between the total count and population estimates. Finally, the proportion of the population vaccinated with each combination was calculated and exported for data visualization in Excel. We repeated this process for stratifications based on sex and health district. In addition, for context to the analysis of vaccine combinations, we conducted an analysis not stratified by age for each vaccine individually to examine overall vaccine coverage for Tdap, MCV4, and HPV (both initialized and up-to-date) for each year. Concomitant vaccination over time was then stratified by sex, and health district, as well.

Data Analysis

This study was an epidemiologic observational study of Georgia's spatio-temporal distribution of vaccine uptake. We analyzed data by visualizing and comparing graphs, tables, and maps; thus, no statistical or hypothesis testing occurred.

Results

Individual Vaccine Coverages

In 2017, for all adolescents aged 9-22 in Georgia, uptake of Tdap and MCV4 was similar, and both were higher than that of HPV vaccine series initiation or completion (Table 5). Because HPV vaccine recommendations initially differed by sex, we computed sex-specific vaccine coverage estimates. Tdap and MCV4 had similar rates, even when stratified by sex, but the disparity in HPV vaccine uptake, for both initiation and completion, was still seen, with male adolescents having approximately 7-9% lower coverage than females. However, the difference in proportions between those who initiated but did not complete the series was similar for male and female adolescents.

Overall Vaccine Coverages by Health District

We noted geographical differences across all adolescent vaccines, where urban areas, such as those encompassing Atlanta, Columbus, and Savannah, had the highest coverage rates, and districts in rural areas had the lowest coverage rates for all individual vaccines (Figure 4). When stratifying by health district, the gap in HPV vaccine coverage was still present compared to Tdap and MCV4, and some districts also had larger or smaller disparities. For example, significant disparities appeared in districts 5-1 (Dublin) and 5-2 (Macon), with high Tdap and MCV4 coverage but inadequate coverage of HPV vaccine initiation and completion.

Concomitant Vaccination Over Time

To examine concomitant vaccination changes over time, all time graphs presented in this manuscript will illustrate just those aged 18 years old by July 1st, 2017, as the timing of receiving a vaccine is highly dependent on age. We chose this age group as the entire eligible vaccination period of 9-18 was available, and the vaccination pattern is similar across all age groups. Graphs of the other age groups are available in the Appendix.

Tdap and MCV4 are generally received much earlier than HPV vaccination in adolescence, despite similar recommended ages (Figure 5). For instance, joint Tdap and MCV4 vaccination mainly occurred between the ages of 10-12, while HPV vaccine initiation was common between the ages of 13-15. These findings again suggest a discrepancy between HPV, Tdap, and MCV4 acceptance and uptake. These patterns remain relatively consistent across age groups. However, one notable difference is the increase in HPV vaccine coverage among younger age groups and lower HPV vaccine coverage among older age groups. Individuals can move between groups as they receive more vaccinations over time. For example, the dip in the Tdap/MCV4 as the Tdap/MCV4/HPV line increased in 2013 suggests many individuals received the HPV vaccine.

Concomitant Vaccination Over Time Stratified by Sex

Similar to before, there were minor differences in Tdap and MCV4 joint vaccination timing when compared by sex (Figure 6). However, these results show that, compared to females, males had lower coverage rates of all three adolescent vaccines concurrently and instead had higher coverage rates of just Tdap and MCV4. Further, if HPV vaccine initiation did occur, it occurred later in males than in females. However, when examining younger age cohorts, this difference in the occurrence of concurrent vaccination is less pronounced, with a smaller gap in HPV vaccine coverage between males and females.

Concomitant Vaccination Stratified by Health District

These results reveal three patterns of concomitant vaccination in Georgia by health district:

Health districts with high Tdap, MCV4, and HPV vaccination, health districts with high Tdap and MCV4 coverage but low HPV vaccine coverage and low no vaccine coverage, and health districts with low vaccine coverage for all three vaccines (Figure 7). The complete concomitant vaccination is concentrated in urban health districts, particularly those around Atlanta. The health districts with high Tdap and MCV4 concurrent vaccinations range in regions and do not necessarily follow the rural-urban divide as the individual vaccination coverages did. This pattern occurs in certain health districts, such as 5-1 (Dublin), 7 (Columbus), and 9-1 (Savannah). Finally, health districts with the lowest vaccine coverage tended to occur in rural areas, such as health districts 8-2 (Albany) and 9-2 (Waycross).

Discussion

When comparing Tdap, MCV4, and the HPV vaccine individually and concurrently, we found a disparity in HPV vaccination among adolescents. For example, when comparing individual vaccine coverage estimates, HPV vaccine initiation and completion were much lower than Tdap and MCV4 coverage, with an approximate 20% and 40% reduction for initiated and completed HPV, respectively. Further, when examining concurrent vaccination over time, Tdap and MCV4 were often received earlier in age than HPV vaccination. These earlier vaccinations of Tdap and MCV4 align with the timing necessary for school-required vaccination, whereas HPV vaccination often occurs later than ACIP recommendations ^{70,71}. However, the reduction in this timing gap among younger birth cohorts and between sexes suggests an improvement in encouraging HPV vaccination among all adolescents regardless of sex. The timing differences also suggest a critical difference between Tdap, MCV4, and HPV vaccination among adolescents and also align with other studies examining concurrent vaccination ⁵⁴. These findings also

suggest that encouraging simultaneous vaccination for all adolescents' vaccinations could improve coverage of HPV immunization, as Tdap and MCV4 have higher and earlier vaccination rates, aligning with Irving et al.'s study (2022).

Another key finding identifying specific HPV vaccine hesitancy issues was identifying three geospatial patterns across health districts in GA: health districts with high overall vaccine coverage, health districts with high Tdap and MCV4 vaccine coverage but low HPV vaccine coverage, and health districts with low overall vaccine coverage. Districts with high overall vaccine coverage suggest robust vaccine delivery methods, and low vaccine hesitancy in these districts, whereas districts with low overall vaccine coverage suggest either a poor vaccine delivery method or high vaccine hesitancy. In contrast, districts with high Tdap and MCV4 vaccine coverage, but suboptimal HPV vaccine coverage, likely have specific HPV vaccine hesitancy issues rather than vaccine delivery issues.

Thus, these findings suggest a vaccine hesitancy issue related to HPV, particularly among males and rural health districts in G.A., as similar adolescent vaccinations have much higher coverage rates. These findings are consistent with the current literature^{11,28,51,72}. Similar studies have found clustering of high vaccine coverage in urban regions and lower rates of HPV vaccine coverage in males, both in other states and in Georgia^{72,73}. Similar studies have also found high vaccine hesitancy for HPV vaccination among rural districts in the United States and the misconception that HPV immunization is only for females^{9,74}. The geospatial distribution of HPV-related cancers in Georgia similarly follows the urban/rural divide^{29,75}. Thus, in context with these studies, the findings from this study suggest low confidence in HPV vaccination among rural areas and males in Georgia as well. Further investigation into these disparities by

geography and sex is needed to examine the reasons for low coverage and confidence in the HPV vaccine.

This study is consistent with the current literature; however, all vaccine coverage estimates are about 10% lower than what is reported for Georgia by NIS-Teen with corresponding age groups, the current principal method for estimating adolescent vaccine coverage ^{11,51}. This difference between NIS-Teen and our results could indicate that survey methods may overreport the coverage of adolescent vaccines, particularly at the state level. Similar studies conducted in other states have also noted inflated results from NIS-Teen compared to state immunization records ^{76–78}. Further, a direct comparison between NIS-Teen and our results is impossible as NIS-Teen does not report on combinations of adolescent vaccines. These findings suggest a need for more robust data collection and study methodologies, particularly at more granular levels.

Limitations

A limitation of this study was that GRITS data only held records for those who received a vaccination in Georgia while under the age of eighteen. Consequently, these data excluded a key population: unvaccinated adolescents and residents who received vaccinations outside the state. This limitation also meant that younger birth cohorts had a reduced sample size compared to older birth cohorts, as they were less likely to have received a vaccination in the specified time range. To reduce this limitation, Census data was incorporated to provide population estimates. While these estimates helped establish proportions and the proportion of those unvaccinated, they were not entirely accurate, particularly at the county level. When conducting county-level estimates, the vaccinated population in a given county in GRITS sometimes exceeded the population of that county estimated by Census data. Thus, we excluded county-level estimates. A second limitation regarding race and ethnicity data was the differing definitions of race between GRITS and Census data, which did not map directly to each other. Additionally, within

the GRITS data, a high level of race and ethnicity data was missing, with 33% of individuals missing ethnicity data and 10% missing race data. Thus, we could not compute estimates specific to race and ethnicity due to these limitations.

Finally, the GRITS data set is subject to the limitations of its data collection. While recording vaccination records in GRITS is required by law, there are likely instances where vaccination is not recorded in GRITS ⁶⁶. As a result, this sample may not represent the entire population of those who received the vaccines of interest. Further, the quality of the data collection is likely to vary significantly between providers because it is self-reported by vaccine administrators.

Finally, GRITS requires the manual upload of vaccine records to the system, which can lead to errors in data reporting ⁷⁹.

Additionally, while GRITS does offer onboarding training when an organization is first enrolled in the system, there is limited long-term training, which could lead to protocol adherence ⁷⁹.

Similarly, there are no links to vital statistics; thus, we could not track changes in births and deaths over time. Therefore, while the GRITS data set has significant advantages over traditional vaccine coverage measures, there are still data quality issues to consider.

Conclusion

Overall, these results revealed three key findings. First, overall vaccine coverages for adolescent vaccinations in Georgia are suboptimal, and estimates using state immunization records are below the national average estimated by NIS-Teen ¹¹. Second, there is a notable difference between Tdap and MCV4 vaccinations and HPV vaccinations, as Tdap and MCV4 had significantly increased individual and concurrent vaccine coverages over time. Third, there were notable gaps in coverage based on geography and sex, with HPV vaccine disparities accentuated in these stratifications. These results together indicate a need for further research into the

reasoning for why suboptimal vaccine coverage is occurring among adolescents in Georgia, particularly concerning HPV, to inform programs and policies better.

Further research is needed to identify gaps between demographic and socioeconomic factors.

There is also a need to improve accuracy and standardize definitions of race and ethnicity at the federal and state levels to facilitate research investigating gaps by race or ethnicity. Finally, as results differed from NIS-Teen, it indicates a need for improved data collection methods to record adolescent vaccination coverage more accurately. Further evaluations, with more recent data, are needed to monitor these trends while also accounting for the impact of the COVID-19 pandemic on adolescent vaccine uptake in Georgia.

Tables and Figures

Table 5: Adolescent Vaccine Coverage in 2017 for those Born Between 1995-2008, Non-Stratified and Stratified by Sex

	Non-Stratified n = 2,012,115 (%)	Stratified by Sex	
		Male n = 1,024,844 (%)	Female n = 987,271 (%)
Tdap	65.83	65.55	66.11
MCV4	63.24	63.00	63.48
HPV Vaccine Initiated	39.01	34.82	43.36
HPV Vaccine Up-to-date	24.14	20.54	27.88

Figure 4: Individual Adolescent Vaccine Coverage in 2017 by Health District for those Born Between 1995-2008

A: Tdap B: MCV4 C: HPV Vaccination Initiated D: HPV Vaccination Up-to-date

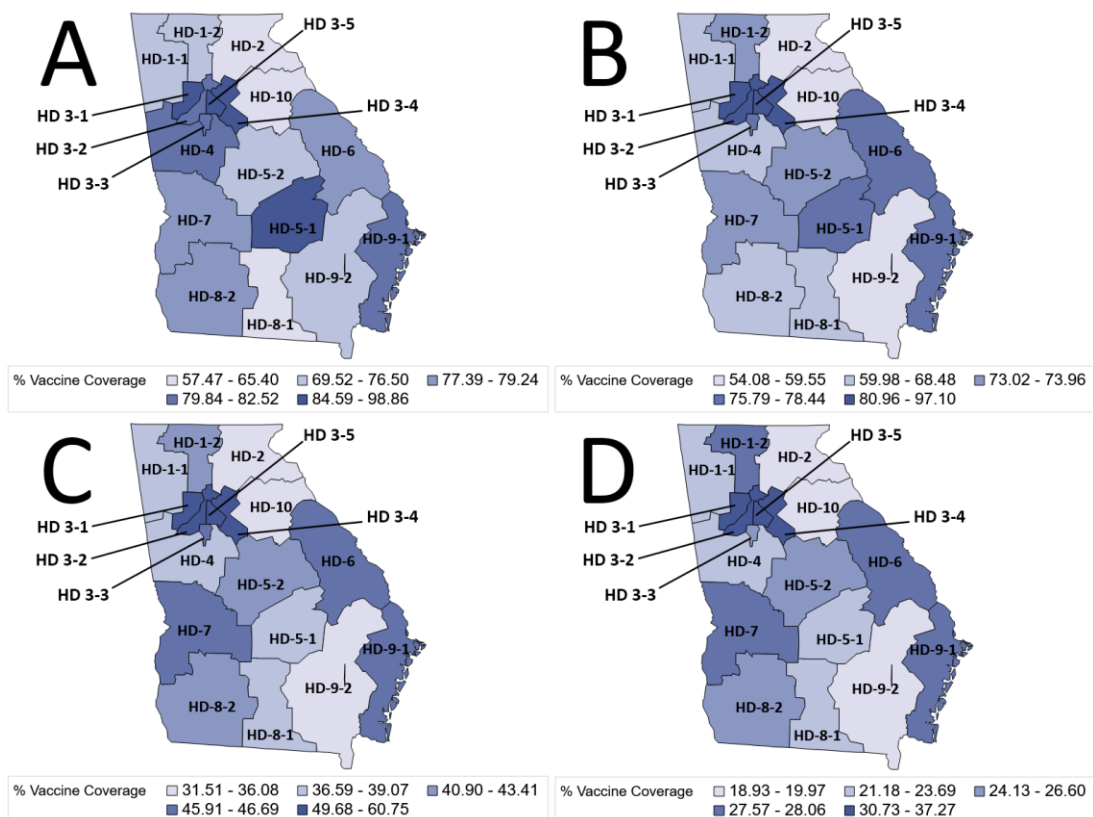


Figure 5: Percent of Those Aged 18 Years Old by July 1st, 2017, per Vaccine Combination by Year in G.A.

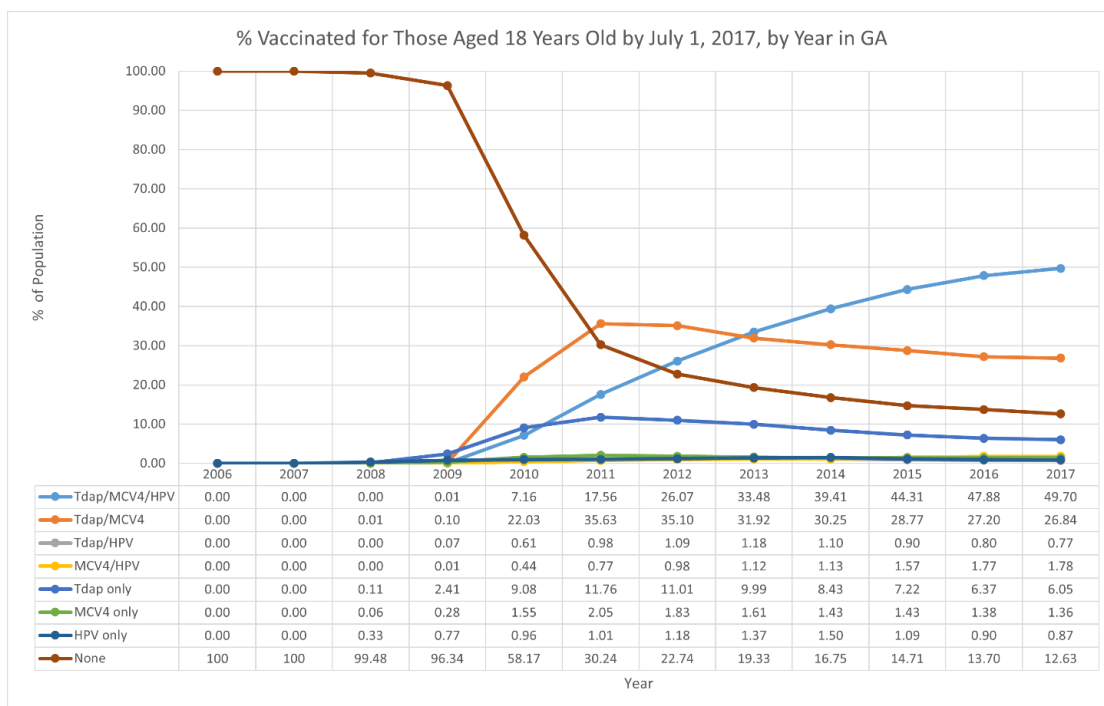


Figure 6: Percent Vaccinated by Vaccine Combinations Among Those Aged 18 Years Old by July 1st, 2017, Stratified by Sex

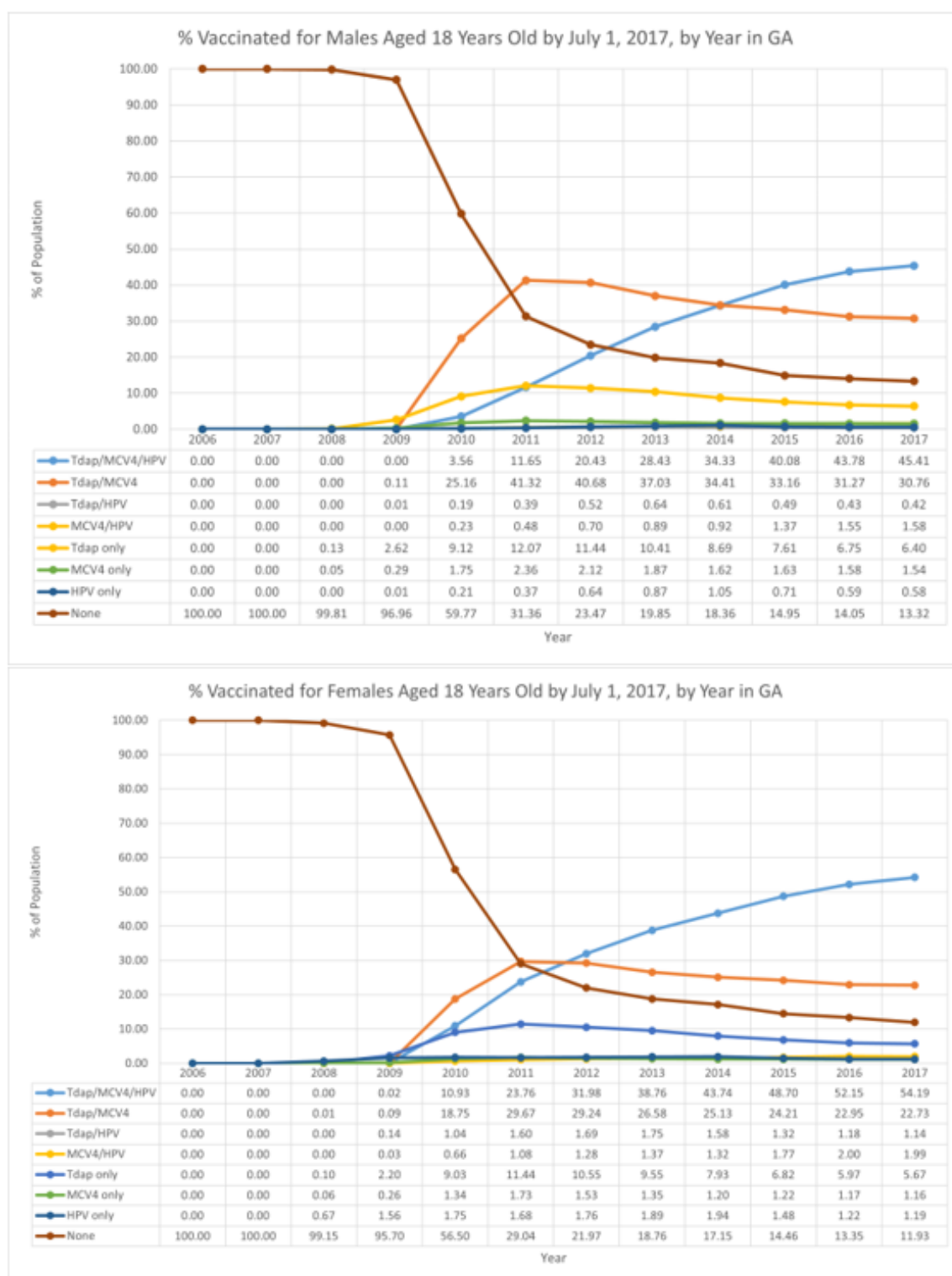
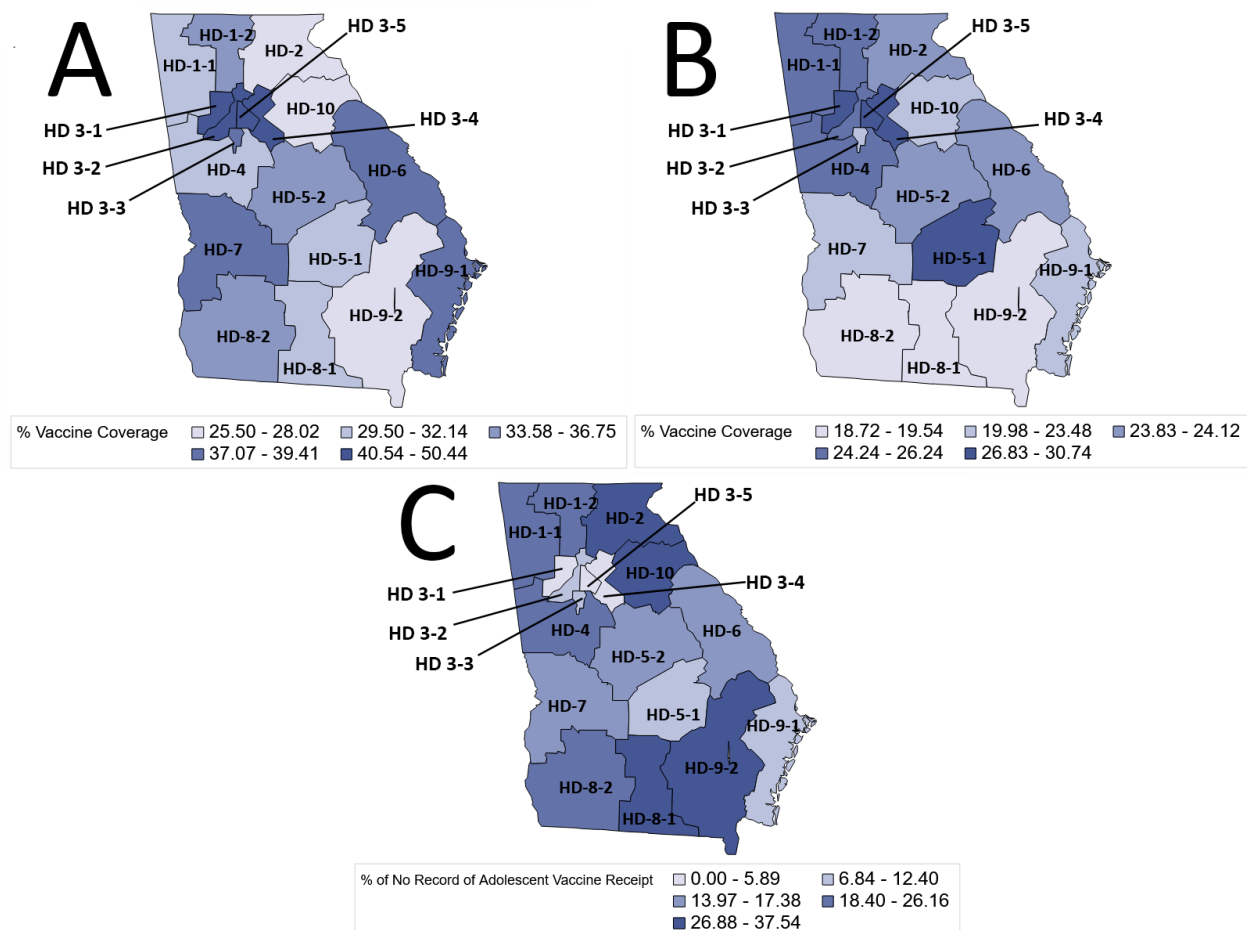


Figure 7: Vaccination Combination Percentages in 2017 by Health District
A: Tdap + MCV4 + HPV Vaccine Initialized B: Tdap + MCV4 C: No Record of Adolescent Vaccine Receipt



Chapter 5: Public Health Implications, Recommendations, and Conclusion

Adolescent vaccination is an effective method of preventing diseases with significant risks of morbidity and mortality. While vaccination coverage has increased over time among adolescents in Georgia, there are critical coverage gaps across sex, geography, and in particular, with the HPV vaccine. These coverage gaps are a cause of concern as they could increase the spread of preventable infectious diseases and HPV-related cancers in the future. These gaps, coupled with increasing rates of vaccine hesitancy among guardians, suggest a strong need for further research to identify and evaluate possible causes for these gaps in vaccine coverage.

In addition, some key recommendations arose for research on adolescent vaccination in the U.S. and Georgia. This analysis revealed a significant discrepancy in estimates for vaccination coverage between survey-based studies and immunization record-based studies. Therefore, there is a need for improved data collection methods in public health when estimating vaccination coverage.

Recommendations

A recommendation for the GA DPH is to improve the data quality of GRITS, improve data collection methods, and conduct more comprehensive vaccine coverage estimate studies in the state. This recommendation is essential due to the recent shift by the GA DPH to use GRITS data to estimate vaccination coverage across the state⁵². During this analysis, we noted issues in the recording of race and ethnicity in GRITS data, and the high percentage of missing data for these variables prevented reasonable race and ethnicity stratification. However, public health experts have noted health inequities tied to race and ethnicity and vaccination coverage^{81,82}. Therefore, there is a need for improved data quality in GRITS of the recording of race and

ethnicity. A specific improvement could be mandatory race or ethnicity input and re-training for healthcare providers in entering data in GRITS.

Finally, a recommendation for the CDC is to change the data collection methods for the National Immunization Survey. These results indicate a significant difference between NIS-Teen estimates of Georgia and are inherent in the use of telephone-based survey methodology and its many limitations. Further, the imprecision of the estimates at state levels makes this data source less trustworthy at more granular levels. Finally, these analyses have noted significant gaps in coverage at the health district level, which researchers have not previously seen when estimating at the state level. Other studies with similar methods have also identified these weaknesses in the NIS in other states, highlighting that these weak data collection methods result in widespread issues⁷⁶⁻⁷⁸. Our results further suggest the need for more localized vaccination coverage estimates. Thus, as other researchers have, we recommend that the NIS use state immunization records to estimate vaccination coverage in localized geographic areas.

Conclusion

The results of this thesis provided four key findings. First, overall adolescent vaccination coverage in Georgia is lower than NIS-Teen and GA DPH estimated initially. Instead, our findings have estimated that around 65% of adolescents in GA had received Tdap, and 63% had received the MCV4 in 2017. Second, there is a notable difference between Tdap and MCV4 vaccinations and HPV vaccinations, as Tdap and MCV4 had significantly increased individual and concurrent vaccine coverages over time. Third, we identified coverage gaps by sex and geography in Georgia, and the gap in HPV vaccine coverage was accentuated at these levels. Thus, these results suggest a strong need to further investigate the coverage of HPV immunization in Georgia, particularly by different demographics and geographic levels. Fourth, there is a need to improve data collection and study methodologies to estimate adolescent

vaccination, particularly at the state and county levels. Further evaluations, with more recent data, are needed to monitor these trends while also accounting for the impact of the COVID-19 pandemic on adolescent vaccine uptake in Georgia.

References

1. Schuchat A. Human Vaccines and Their Importance to Public Health. *Procedia Vaccinol.* 2011;5:120-126. doi:10.1016/j.provac.2011.10.008
2. Bilukha OO, Rosenstein N, National Center for Infectious Diseases, Centers for Disease Control and Prevention (CDC). Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep.* 2005;54(RR-7):1-21.
3. Broder KR, Cortese MM, Iskander JK, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep.* 2006;55(RR-3):1-34.
4. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep.* 2013;62(RR-2):1-28.
5. Markowitz LE, Dunne EF, Saraiya M, et al. Quadrivalent Human Papillomavirus Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep.* 2007;56(RR-2):1-24.
6. Bernstein S, North A, Schwartz J, Niccolai LM. State-Level Voting Patterns and Adolescent Vaccination Coverage in the United States, 2014. *Am J Public Health.* 2016;106(10):1879-1881. doi:10.2105/AJPH.2016.303381
7. Centers for Disease Control and Prevention. National and state vaccination coverage among adolescents aged 13 through 17 years--United States, 2010. *MMWR Morb Mortal Wkly Rep.* 2011;60(33):1117-1123.
8. Nguyen KH, Santibanez TA, Stokley S, et al. Parental vaccine hesitancy and its association with adolescent HPV vaccination. *Vaccine.* 2021;39(17):2416-2423. doi:10.1016/j.vaccine.2021.03.048
9. Nguyen KH, Srivastav A, Vaish A, Singleton JA. Population Attributable Fraction of Nonvaccination of Child and Adolescent Vaccines Attributed to Parental Vaccine Hesitancy, 2018–2019. *Am J Epidemiol.* 2022;191(9):1626-1635. doi:10.1093/aje/kwac049
10. Nowak GJ, Cacciatore MA. State of Vaccine Hesitancy in the United States. *Pediatr Clin North Am.* 2023;70(2):197-210. doi:10.1016/j.pcl.2022.11.001
11. Pingali C, Yankey D, Elam-Evans LD, et al. National Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2021. *MMWR Morb Mortal Wkly Rep.* 2022;71. doi:10.15585/mmwr.mm7135a1

12. Santibanez TA, Nguyen KH, Greby SM, et al. Parental Vaccine Hesitancy and Childhood Influenza Vaccination. *Pediatrics*. 2020;146(6):e2020007609. doi:10.1542/peds.2020-007609
13. Seither R, Calhoun K, Yusuf OB, et al. Vaccination Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2021–22 School Year. *MMWR Morb Mortal Wkly Rep*. 2023;72. doi:10.15585/mmwr.mm7202a2
14. Vasudevan L, Ostermann J, Wang Y, et al. Predictors of HPV vaccination in the southern US: A survey of caregivers from 13 states. *Vaccine*. 2021;39(51):7485-7493. doi:10.1016/j.vaccine.2021.10.036
15. Centers for Disease Control and Prevention. Diphtheria, Tetanus, and Whooping Cough Vaccination: What You Should Know | CDC. Centers for Disease Control and Prevention. Published January 17, 2023. Accessed April 10, 2023. <https://www.cdc.gov/vaccines/vpd/dtap-tdap-tb/public/index.html>
16. Raderalazaso G. Trends in Pertussis Incidence in Georgia from 2010 – 2020 Based on the 2020 CSTE/CDC Case Definition. Published online 2021. doi:10.57709/24081774
17. Kamiya H, Cho BH, Messonnier ML, Clark TA, Liang JL. Impact and cost-effectiveness of a second tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine dose to prevent pertussis in the United States. *Vaccine*. 2016;34(15):1832-1838. doi:10.1016/j.vaccine.2016.02.027
18. Carrico J, Talbird SE, La EM, et al. Cost-benefit analysis of vaccination against four preventable diseases in older adults: Impact of an aging population. *Vaccine*. 2021;39(36):5187-5197. doi:10.1016/j.vaccine.2021.07.029
19. Centers for Disease Control and Prevention. Meningococcal Disease | CDC. Centers for Disease Control and Prevention. Published May 10, 2022. Accessed April 4, 2023. <https://www.cdc.gov/meningococcal/index.html>
20. Moore AE, MacNeil JR, Wang X, et al. Emergence of Localized Serogroup W Meningococcal Disease in the United States — Georgia, 2006–2016. *MMWR Morb Mortal Wkly Rep*. 2018;67. doi:10.15585/mmwr.mm6732a5
21. Martín-Torres F. Deciphering the Burden of Meningococcal Disease: Conventional and Under-recognized Elements. *J Adolesc Health*. 2016;59(2, Supplement):S12-S20. doi:10.1016/j.jadohealth.2016.03.041
22. Centers for Disease Control and Prevention. Human Papillomavirus (HPV) Vaccine. Centers for Disease Control and Prevention. Published December 2, 2019. Accessed April 10, 2023. <https://www.cdc.gov/hpv/parents/vaccine-for-hpv.html>
23. Centers for Disease Control and Prevention. HPV Vaccination: What Everyone Should Know | CDC. Centers for Disease Control and Prevention. Published May 6, 2022. Accessed February 16, 2023. <https://www.cdc.gov/vaccines/vpd/hpv/public/index.html>

24. Guo F, Cofie LE, Berenson AB. Cervical Cancer Incidence in Young U.S. Females After Human Papillomavirus Vaccine Introduction. *Am J Prev Med*. 2018;55(2):197-204. doi:10.1016/j.amepre.2018.03.013
25. Georgia Department of Public Health. *Cancers Attributable to Human Papillomavirus (HPV) Georgia 2011-2015*. Georgia Department of Public Health; 2018:1. <https://dph.georgia.gov/document/document/hpv-fact-sheet-2011-2015>
26. Kim JJ, Goldie SJ. Health and Economic Implications of HPV Vaccination in the United States. *N Engl J Med*. 2008;359(8):821-832. doi:10.1056/NEJMsa0707052
27. Chesson HW, Laprise JF, Brisson M, Martin D, Ekwueme DU, Markowitz LE. The Estimated Lifetime Medical Cost of Diseases Attributable to Human Papillomavirus Infections Acquired in 2018. *Sex Transm Dis*. 2021;48(4):278-284. doi:10.1097/OLQ.0000000000001379
28. Dennison C, King AR, Rutledge H, Bednarczyk RA. HPV Vaccine-Related Research, Promotion and Coordination in the State of Georgia: A Systematic Review. *J Community Health*. 2019;44(2):313-321. doi:10.1007/s10900-018-0589-7
29. Thomas TL, Strickland O, Diclemente R, Higgins M. An Opportunity for Cancer Prevention During Preadolescence and Adolescence: Stopping Human Papillomavirus (HPV)-Related Cancer Through HPV Vaccination. *J Adolesc Health*. 2013;52(5, Supplement):S60-S68. doi:10.1016/j.jadohealth.2012.08.011
30. Viens LJ, Henley SJ, Watson M, et al. Human Papillomavirus-Associated Cancers - United States, 2008-2012. *MMWR Morb Mortal Wkly Rep*. 2016;65(26):661-666. doi:10.15585/mmwr.mm6526a1
31. Machado BAS, Hodel KVS, Fonseca LM dos S, et al. The Importance of Vaccination in the Context of the COVID-19 Pandemic: A Brief Update Regarding the Use of Vaccines. *Vaccines*. 2022;10(4):591. doi:10.3390/vaccines10040591
32. Centers for Disease Control and Prevention. Tetanus Disease (Lockjaw) | CDC. Centers for Disease Control and Prevention. Published September 14, 2022. Accessed April 4, 2023. <https://www.cdc.gov/tetanus/index.html>
33. Centers for Disease Control and Prevention. Diphtheria | CDC. Centers for Disease Control and Prevention. Published September 9, 2022. Accessed April 10, 2023. <https://www.cdc.gov/diphtheria/index.html>
34. Pan American Health Organization. Diphtheria - PAHO/WHO | Pan American Health Organization. Pan American Health Organization. Published 2022. Accessed April 4, 2023. <https://www.paho.org/en/topics/diphtheria>
35. Centers for Disease Control and Prevention. Whooping Cough (Pertussis) | CDC. Centers for Disease Control and Prevention. Published 2023. Accessed April 4, 2023. <https://www.cdc.gov/pertussis/index.html>

36. Kapil P, Merkel TJ. Pertussis Vaccines and Protective Immunity. *Curr Opin Immunol*. 2019;59:72-78. doi:10.1016/j.coi.2019.03.006
37. Blain A, Tiwari T. Tetanus - Vaccine Preventable Diseases Surveillance Manual | CDC. Centers for Disease Control and Prevention (CDC). Published December 16, 2022. Accessed April 4, 2023. <https://www.cdc.gov/vaccines/pubs/surv-manual/chpt16-tetanus.html>
38. Hill HA, Chen M, Elam-Evans LD, Yankey D, Singleton JA. Vaccination Coverage by Age 24 Months Among Children Born During 2018-2019 - National Immunization Survey-Child, United States, 2019-2021. *MMWR Morb Mortal Wkly Rep*. 2023;72(2):33-38. doi:10.15585/mmwr.mm7202a3
39. World Health Organization. Tetanus vaccines: WHO position paper, February 2017 – Recommendations. *Vaccine*. 2018;36(25):3573-3575. doi:10.1016/j.vaccine.2017.02.034
40. McNamara LA, Potts C, Blain AE, et al. Detection of Ciprofloxacin-Resistant, β -Lactamase–Producing *Neisseria meningitidis* Serogroup Y Isolates — United States, 2019–2020. *MMWR Morb Mortal Wkly Rep*. 2020;69. doi:10.15585/mmwr.mm6924a2
41. National Cancer Institute. HPV and Cancer - NCI. National Cancer Institute. Published March 1, 2019. Accessed February 16, 2023. <https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer>
42. Centers for Disease Control and Prevention. How Many Cancers Are Linked with HPV Each Year? | CDC. Centers for Disease Control and Prevention. Published October 4, 2022. Accessed April 4, 2023. <https://www.cdc.gov/cancer/hpv/statistics/cases.htm>
43. Kombe Kombe AJ, Li B, Zahid A, et al. Epidemiology and Burden of Human Papillomavirus and Related Diseases, Molecular Pathogenesis, and Vaccine Evaluation. *Front Public Health*. 2021;8. Accessed April 4, 2023. <https://www.frontiersin.org/articles/10.3389/fpubh.2020.552028>
44. Meites E, Kempe A, Markowitz LE. Use of a 2-Dose Schedule for Human Papillomavirus Vaccination - Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 2016;65(49):1405-1408. doi:10.15585/mmwr.mm6549a5
45. Centers for Disease Control and Prevention. National Immunization Surveys (NIS) - Health, United States. Centers for Disease Control and Prevention. Published August 8, 2022. Accessed April 4, 2023. <https://www.cdc.gov/nchs/hus/sources-definitions/nis.htm>
46. Centers for Disease Control and Prevention. TeenVaxView Interactive! Centers for Disease Control and Prevention. Published 2017. <https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/index.html>
47. Brown J, Monasch R, Bicego G, Burton A, Boerma JT. *An Assessment of the Quality of National Child Immunization Coverage Estimates in Population-Based Surveys*. MEASURE Evaluation; 2002.

48. Holbrook AL, Krosnick JA, Pfent A. The Causes and Consequences of Response Rates in Surveys by the News Media and Government Contractor Survey Research Firms. In: Lepkowski JM, Tucker C, Brick JM, et al., eds. *Advances in Telephone Survey Methodology*. Wiley; 2008:499-528.
<https://web.stanford.edu/dept/communication/faculty/krosnick/docs/2007/2007%20TSMII%20chapter%20proof.pdf>
49. DeMaio T, Beck J. *The National Immunization Survey Evaluation Study Special Sworn Status Procedures: Focus Group Results*. U.S. Census Bureau; 2009.
<https://www.census.gov/content/dam/Census/library/working-papers/2009/adrm/ssm2009-13.pdf>
50. Conley AE, Amonson E, Ma Q, Elam-Evans LD, Smith C. *Evaluation of a \$10 vs. \$20 Incentive Promise on the National Immunization Survey-Child (NIS-Child)*.
51. Georgia Department of Public Health, Machado FR. *Georgia Adolescent Immunization Study, 2018*. Georgia Department of Public Health; 2018.
52. Georgia Department of Public Health. Immunization Study Reports. Georgia Department of Public Health. Published 2023. Accessed April 9, 2023.
<https://dph.georgia.gov/immunization-study-reports>
53. Glanz JM, Newcomer SR, Jackson ML, et al. White Paper on studying the safety of the childhood immunization schedule in the Vaccine Safety Datalink. *Vaccine*. 2016;34 Suppl 1:A1-A29. doi:10.1016/j.vaccine.2015.10.082
54. Irving SA, Groom HC, Dandamudi P, et al. A decade of data: Adolescent vaccination in the vaccine safety datalink, 2007 through 2016. *Vaccine*. 2022;40(9):1246-1252.
doi:10.1016/j.vaccine.2022.01.051
55. Hirth J. Disparities in HPV vaccination rates and HPV prevalence in the United States: a review of the literature. *Hum Vaccines Immunother*. 2019;15(1):146-155.
doi:10.1080/21645515.2018.1512453
56. Happe LE, Lunacsek OE, Kruzikas DT, Marshall GS. Impact of a Pentavalent Combination Vaccine on Immunization Timeliness in a State Medicaid Population. *Pediatr Infect Dis J*. 2009;28(2):98. doi:10.1097/INF.0b013e318187d047
57. Kulkarni AA, Desai RP, Alcalá HE, Balkrishnan R. Persistent Disparities in Immunization Rates for the Seven-Vaccine Series Among Infants 19–35 Months in the United States. *Health Equity*. 2021;5(1):135-139. doi:10.1089/heq.2020.0127
58. Centers for Disease Control and Prevention. Healthy People - Healthy People 2010. Centers for Disease Control and Prevention (CDC). Published December 10, 2021. Accessed April 10, 2023. https://www.cdc.gov/nchs/healthy_people/hp2010.htm

59. Betsch C, Schmid P, Heinemeier D, Korn L, Holtmann C, Böhm R. Beyond confidence: Development of a measure assessing the 5C psychological antecedents of vaccination. *PLoS ONE*. 2018;13(12):e0208601. doi:10.1371/journal.pone.0208601
60. Thomson A, Robinson K, Vallée-Tourangeau G. The 5As: A practical taxonomy for the determinants of vaccine uptake. *Vaccine*. 2016;34(8):1018-1024. doi:10.1016/j.vaccine.2015.11.065
61. Larson HJ, Gakidou E, Murray CJL. The Vaccine-Hesitant Moment. Longo DL, ed. *N Engl J Med*. 2022;387(1):58-65. doi:10.1056/NEJMra2106441
62. Siddiqui M, Salmon DA, Omer SB. Epidemiology of vaccine hesitancy in the United States. *Hum Vaccines Immunother*. 2013;9(12):2643-2648. doi:10.4161/hv.27243
63. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, Mangione-Smith R. The Relationship Between Parent Attitudes About Childhood Vaccines Survey Scores and Future Child Immunization Status: A Validation Study. *JAMA Pediatr*. 2013;167(11):1065-1071. doi:10.1001/jamapediatrics.2013.2483
64. SAGE Working Group. *Report of the SAGE Working Group on Vaccine Hesitancy*. World Health Organization; 2014. <https://thecompassforsbc.org/sbcc-tools/report-sage-working-group-vaccine-hesitancy>
65. Centers for Disease Control and Prevention. Bridged-Race Population Estimates - Data Files and Documentation. Centers for Disease Control and Prevention. Published November 5, 2021. Accessed February 27, 2023. https://www.cdc.gov/nchs/nvss/bridged_race/data_documentation.htm
66. Georgia Department of Public Health. Georgia Immunization Registry (GRITS). Georgia Department of Public Health. Published 2022. Accessed February 27, 2023. <https://dph.georgia.gov/immunization-section/georgia-immunization-registry-grits>
67. Microsoft Corporation. Microsoft Excel. Published online 2018.
68. SAS Institute. SAS Software. Published online 2013.
69. Georgia Department of Public Health. Public Health Districts. Georgia Department of Public Health. Published 2022. Accessed April 9, 2023. <https://dph.georgia.gov/public-health-districts>
70. Centers for Disease Control and Prevention. Immunization Schedules for 18 & Younger. Centers for Disease Control and Prevention. Published February 10, 2023. Accessed February 27, 2023. <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>
71. Georgia Department of Public Health. School Vaccines and Updates. Georgia Department of Public Health. Published 2022. Accessed April 3, 2023. <https://dph.georgia.gov/schoolvaccines>

72. White AA, Neelon B, Martin RH, et al. Spatial patterns of HPV and Tdap vaccine dose administration and the association of health department clinic access in Georgia counties. *Vaccine*. 2022;40(9):1352-1360. doi:10.1016/j.vaccine.2021.12.039
73. Adjei Boakye E, Fedorovich Y, White M, et al. Rural-Urban Disparities in HPV Vaccination Coverage Among Adolescents in the Central Part of the State of Illinois, USA. *J Community Health*. 2023;48(1):24-29. doi:10.1007/s10900-022-01136-x
74. Saelee R, MStat EZ, Murthy BP, et al. Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71. doi:10.15585/mmwr.mm7109a2
75. Senkomago V, Henley SJ, Thomas CC, Mix JM, Markowitz LE, Saraiya M. Human Papillomavirus–Attributable Cancers — United States, 2012–2016. *Morb Mortal Wkly Rep*. 2019;68(33):724-728. doi:10.15585/mmwr.mm6833a3
76. Gowda C, Dong S, Potter RC, Dombkowski KJ, Stokley S, Dempsey AF. A systematic evaluation of different methods for calculating adolescent vaccination levels using immunization information system data. *Public Health Rep Wash DC 1974*. 2013;128(6):489-497. doi:10.1177/003335491312800608
77. Kirtland KA, Raghunathan T, Patel Murthy B, et al. Estimating vaccination coverage for routinely recommended vaccines among children aged 24 months and adolescents aged 13 through 17 years using data from immunization information systems in the United States. *Vaccine*. 2022;40(52):7559-7570. doi:10.1016/j.vaccine.2022.10.070
78. Robinson S ann. Adapting to climate change at the national level in Caribbean small island developing state. *Isl Stud J*. 2018;13(1):79-100. doi:10.24043/isj.59
79. Georgia Department of Public Health. Georgia Immunization Registry (GRITS) Frequently Asked Questions. <https://dph.georgia.gov/immunization-section/georgia-immunization-registry-grits>
80. Centers for Disease Control and Prevention. Healthy People - Healthy People 2020. Centers for Disease Control and Prevention. Published April 18, 2022. Accessed April 10, 2023. https://www.cdc.gov/nchs/healthy_people/hp2020.htm
81. Jamison AM, Quinn SC, Freimuth VS. “You don’t trust a government vaccine”: Narratives of institutional trust and influenza vaccination among African American and white adults. *Soc Sci Med*. 2019;221:87-94. doi:10.1016/j.socscimed.2018.12.020
82. Siegel M, Critchfield-Jain I, Boykin M, et al. Racial/Ethnic Disparities in State-Level COVID-19 Vaccination Rates and Their Association with Structural Racism. *J Racial Ethn Health Disparities*. 2022;9(6):2361-2374. doi:10.1007/s40615-021-01173-7

Appendix

Methods

Sample Size by Birth Cohort

Birth Cohort	Census Age (Calculated Age on July 1, 2017)	Sample Size
First half of 1995	22	100621
1995-1996	21	108964
1996-1997	20	110975
1997-1998	19	119242
1998-1999	18	124320
1999-2000	17	128321
2000-2001	16	125987
2001-2002	15	126510
2002-2003	14	132943
2004-2005	13	128420
2005-2006	12	110906
2006-2007	11	62358
2007-2008	10	6585
2008	9	1464

Frequency and Percentage of Missingness by Variable

Variable	Frequency Missing	Percentage Missing (%)
Sex	2	0.0001
Ethnicity	469458	33.8320
Race	141158	10.1727
Health District/County	3363	0.2424

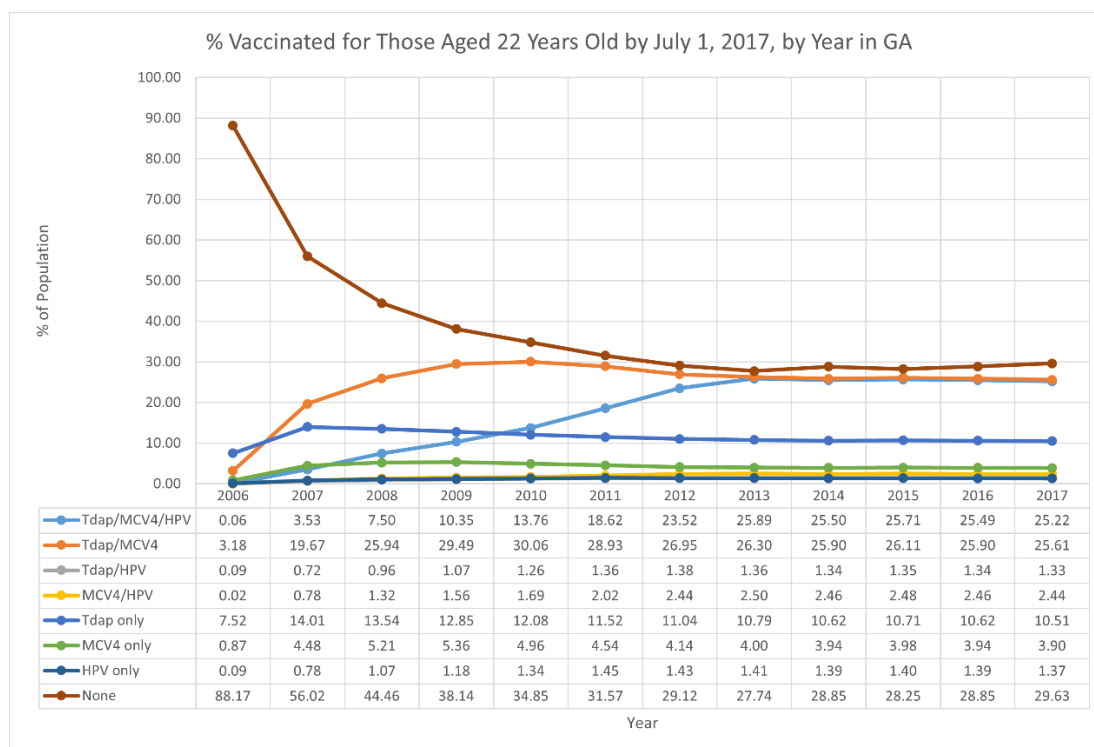
Age Matrix

Census Age	Birth Cohort	By 2006	By 2007	By 2008	By 2009	By 2010	By 2011	By 2012	By 2013	By 2014	By 2015	By 2016	By 2017
22	1995	11	12	13	14	15	16	17	18	19	20	21	22
21	1995/1996	10	11	12	13	14	15	16	17	18	19	20	21
20	1996/1997	9	10	11	12	13	14	15	16	17	18	19	20
19	1997/1998	8	9	10	11	12	13	14	15	16	17	18	19
18	1998/1999	7	8	9	10	11	12	13	14	15	16	17	18
17	1999/2000	6	7	8	9	10	11	12	13	14	15	16	17
16	2000/2001	5	6	7	8	9	10	11	12	13	14	15	16
15	2001/2002	4	5	6	7	8	9	10	11	12	13	14	15
14	2002/2003	3	4	5	6	7	8	9	10	11	12	13	14
13	2003/2004	2	3	4	5	6	7	8	9	10	11	12	13
12	2004/2005	1	2	3	4	5	6	7	8	9	10	11	12
11	2005/2006	0	1	2	3	4	5	6	7	8	9	10	11
10	2006/2007		0	1	2	3	4	5	6	7	8	9	10
9	2007/2008			0	1	2	3	4	5	6	7	8	9

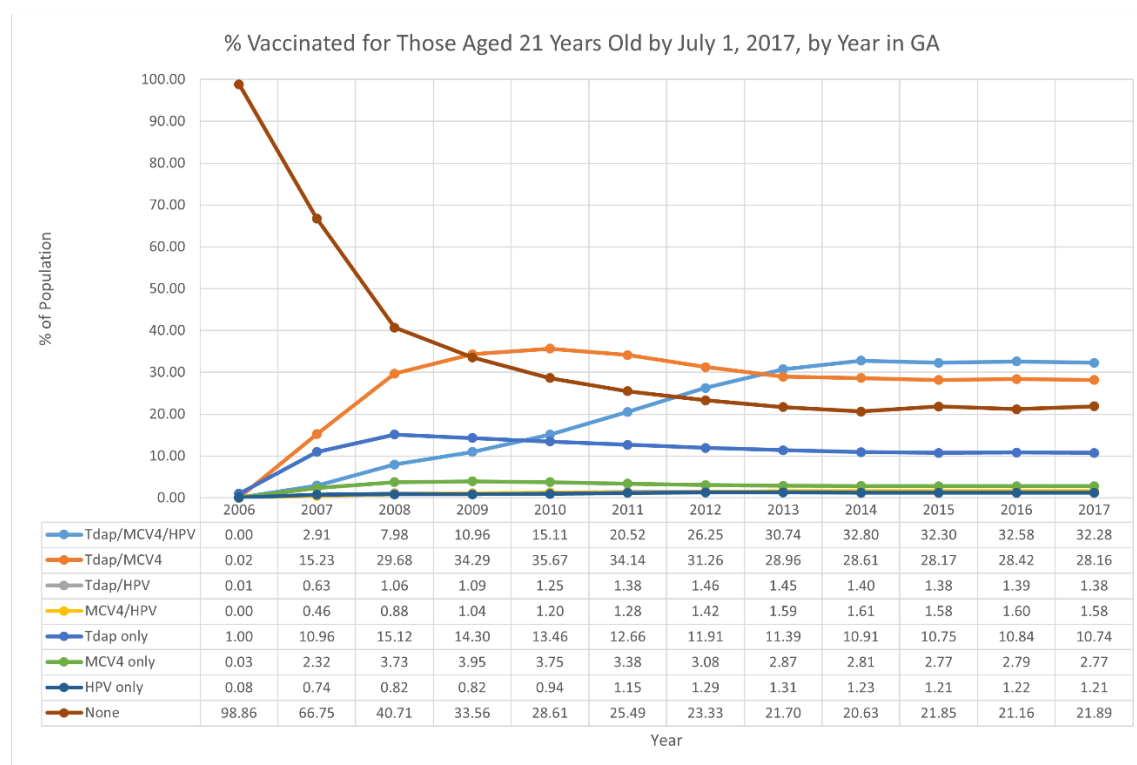
Aged out
Within Age Range
Too Young

Concomitant Vaccination Over Time

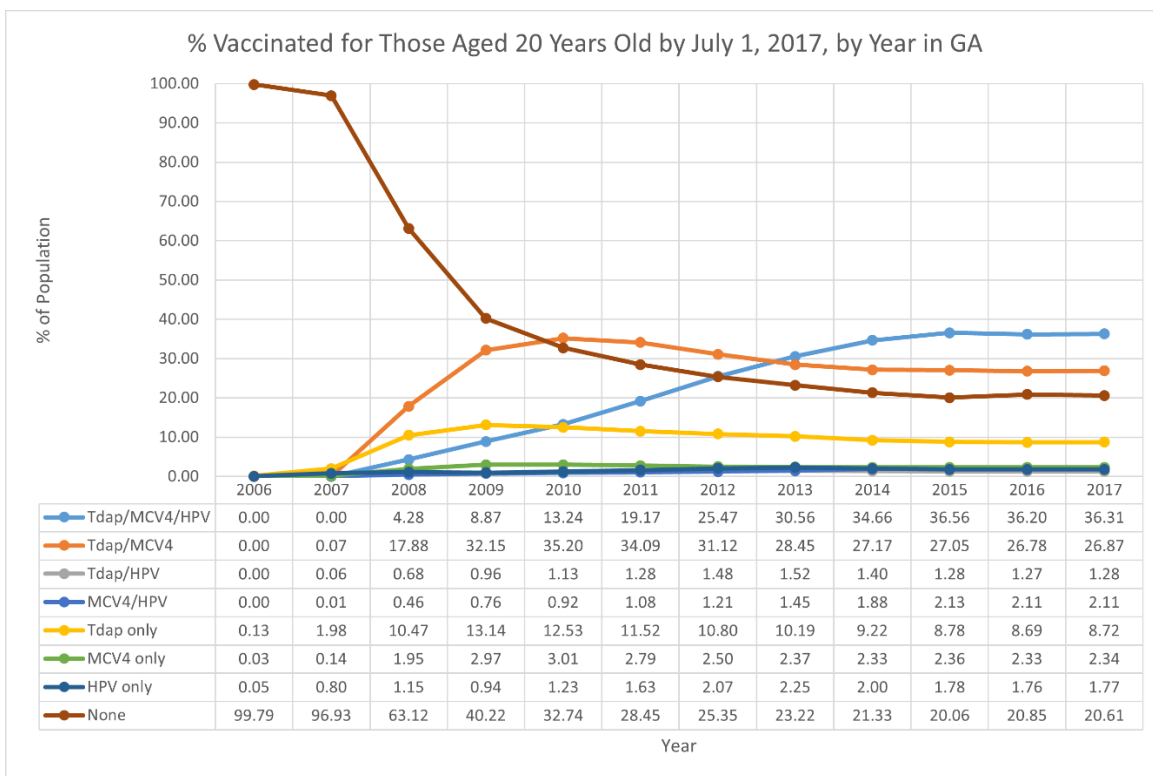
Age 22



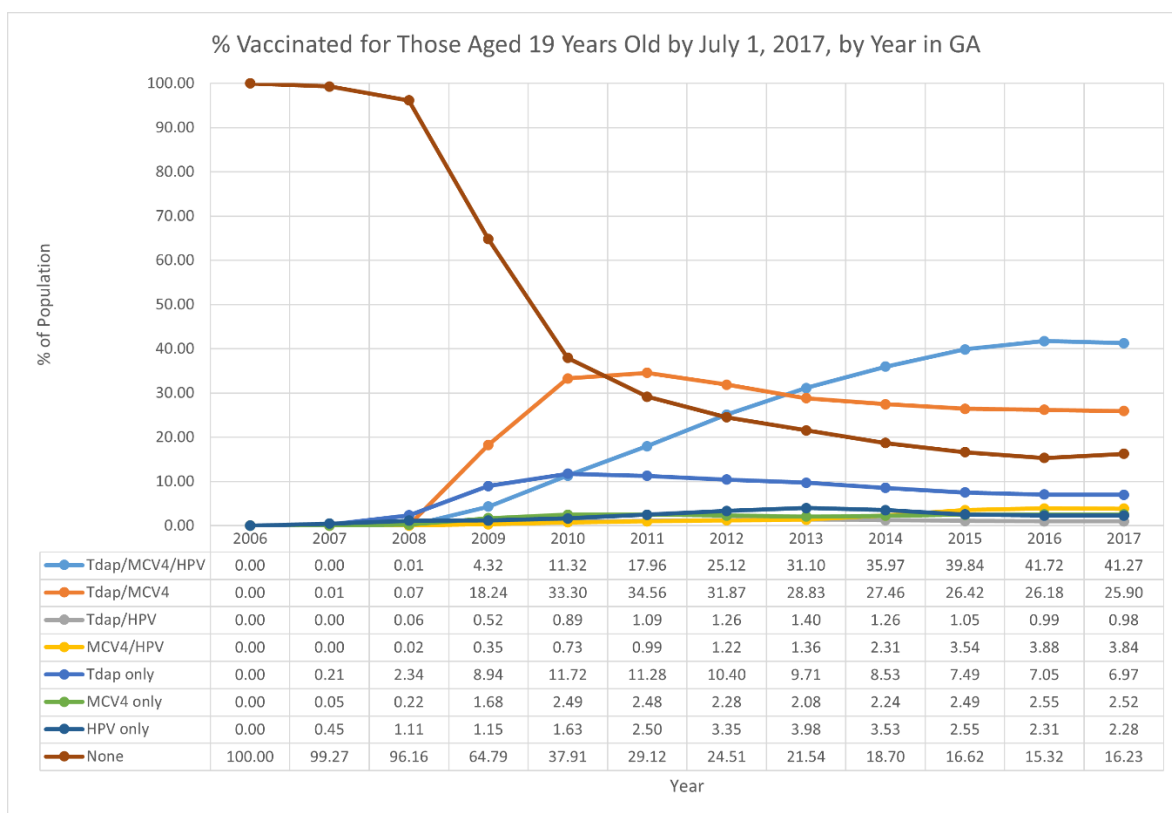
Age 21



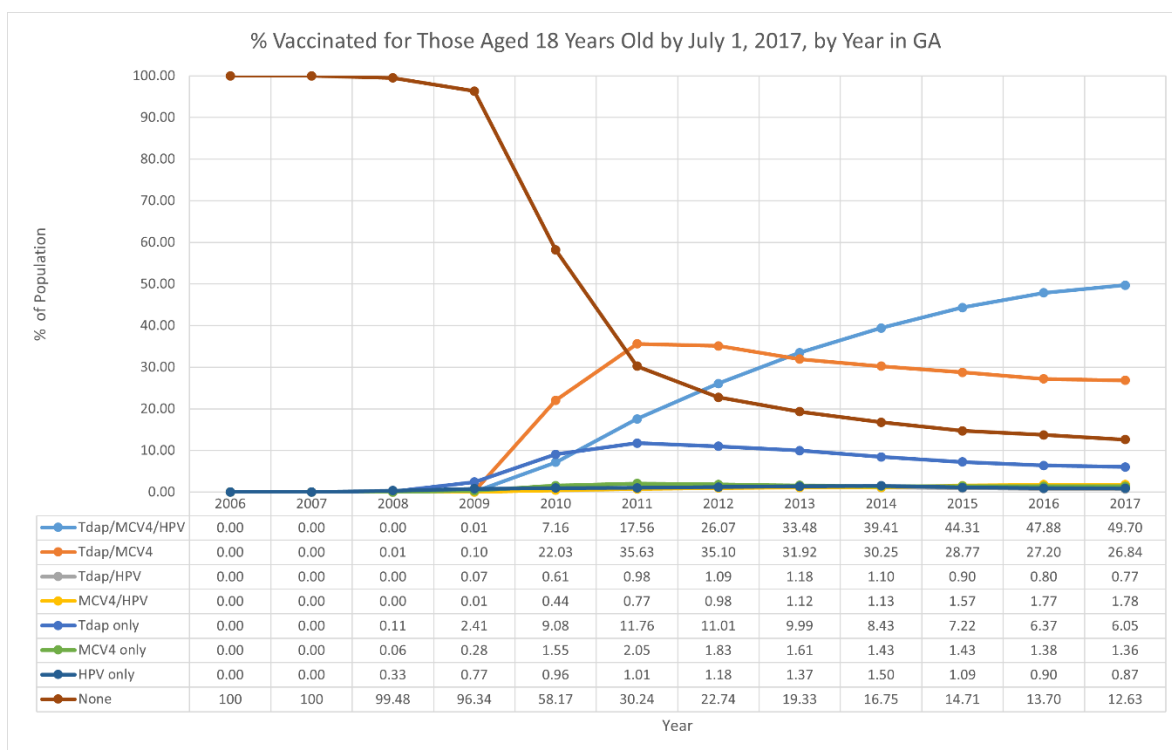
Age 20



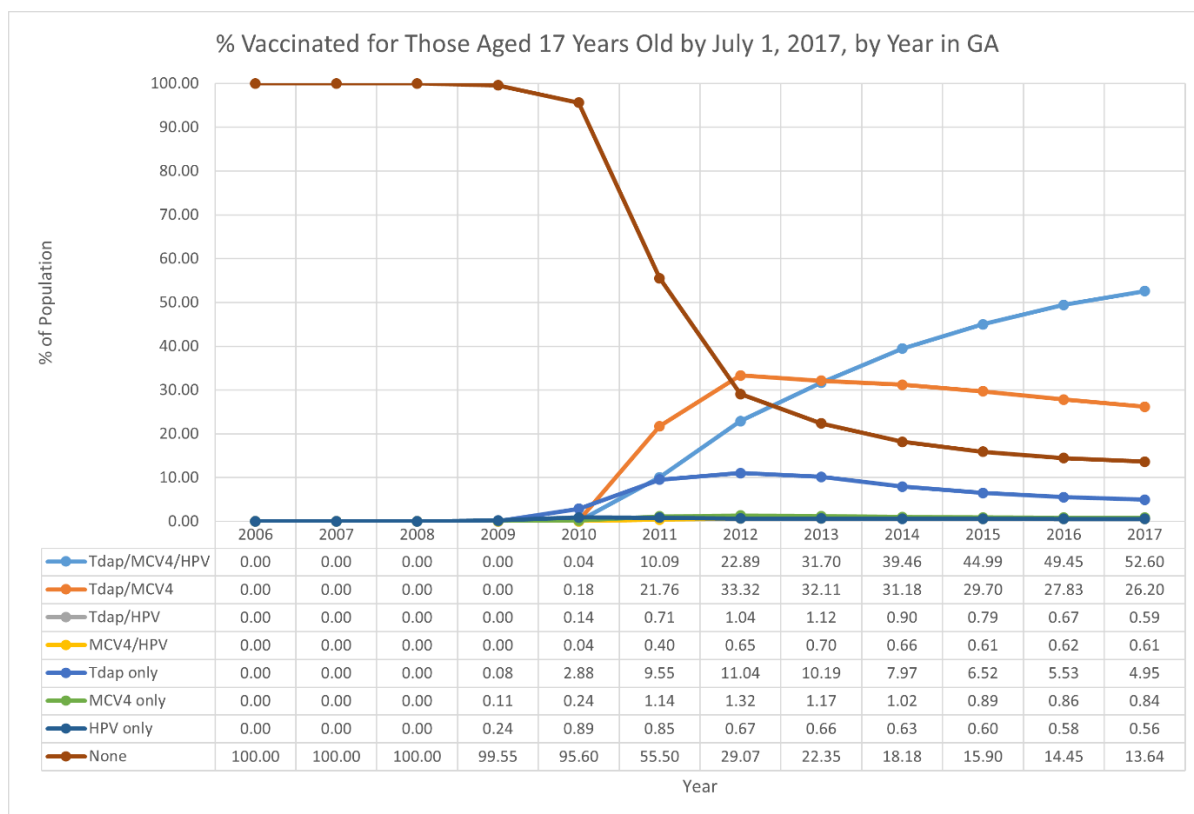
Age 19



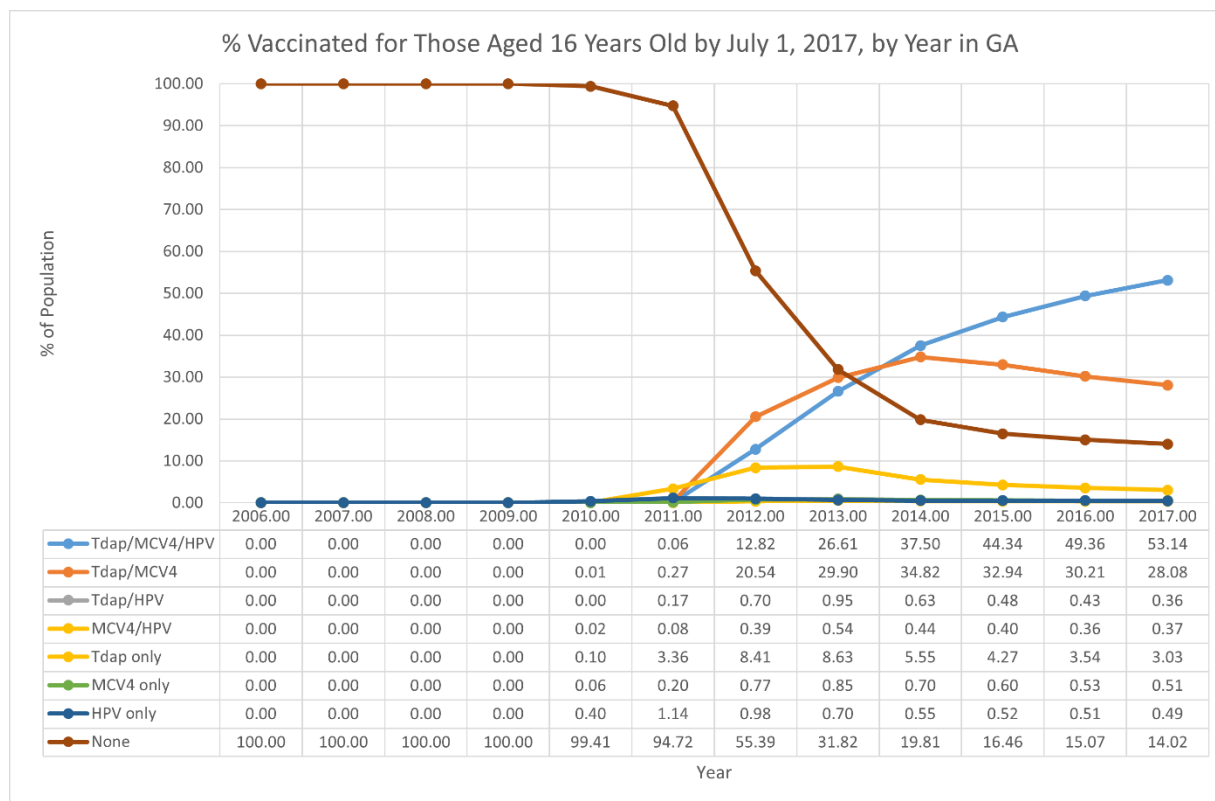
Age 18



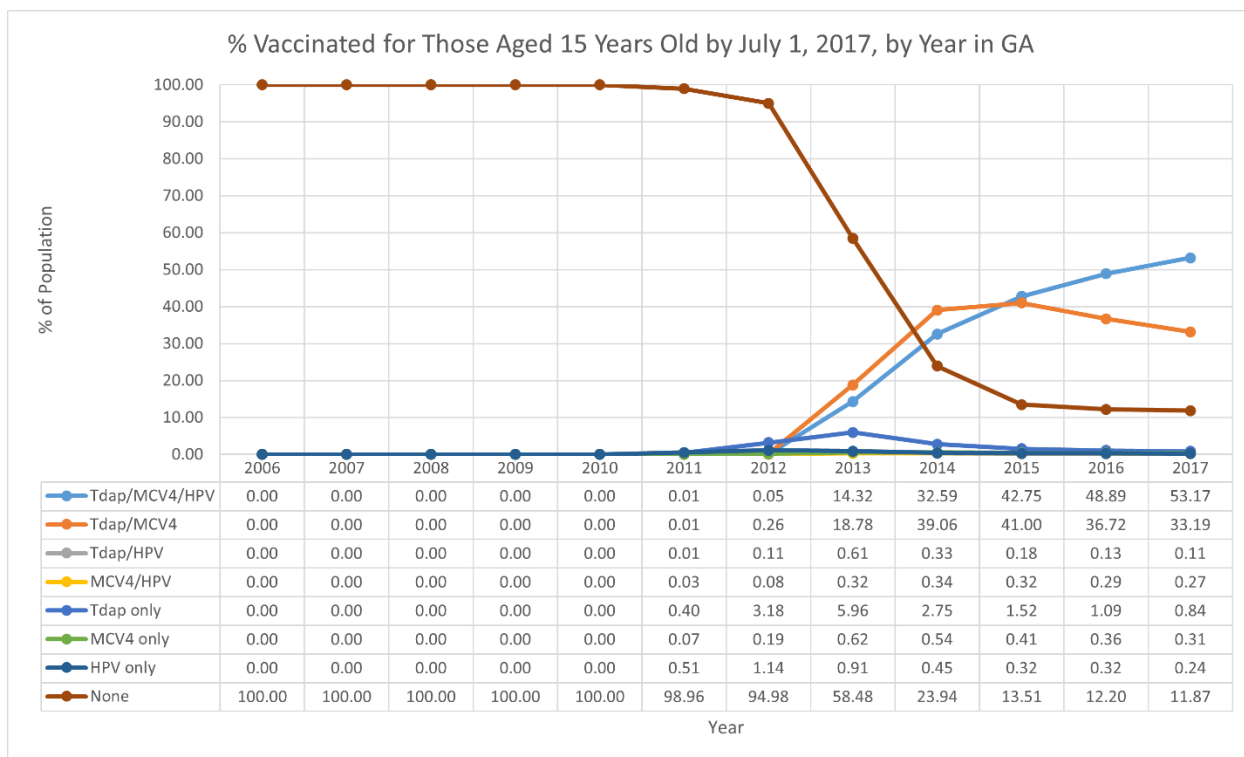
Age 17



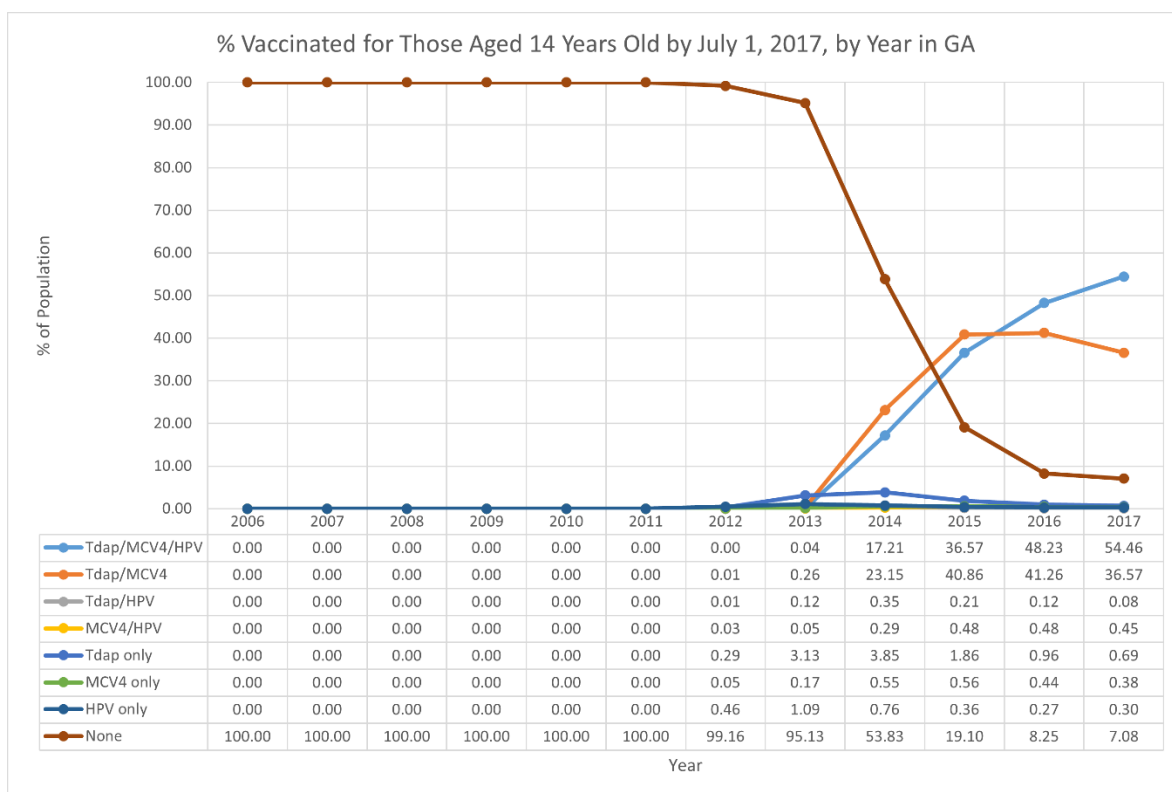
Age 16



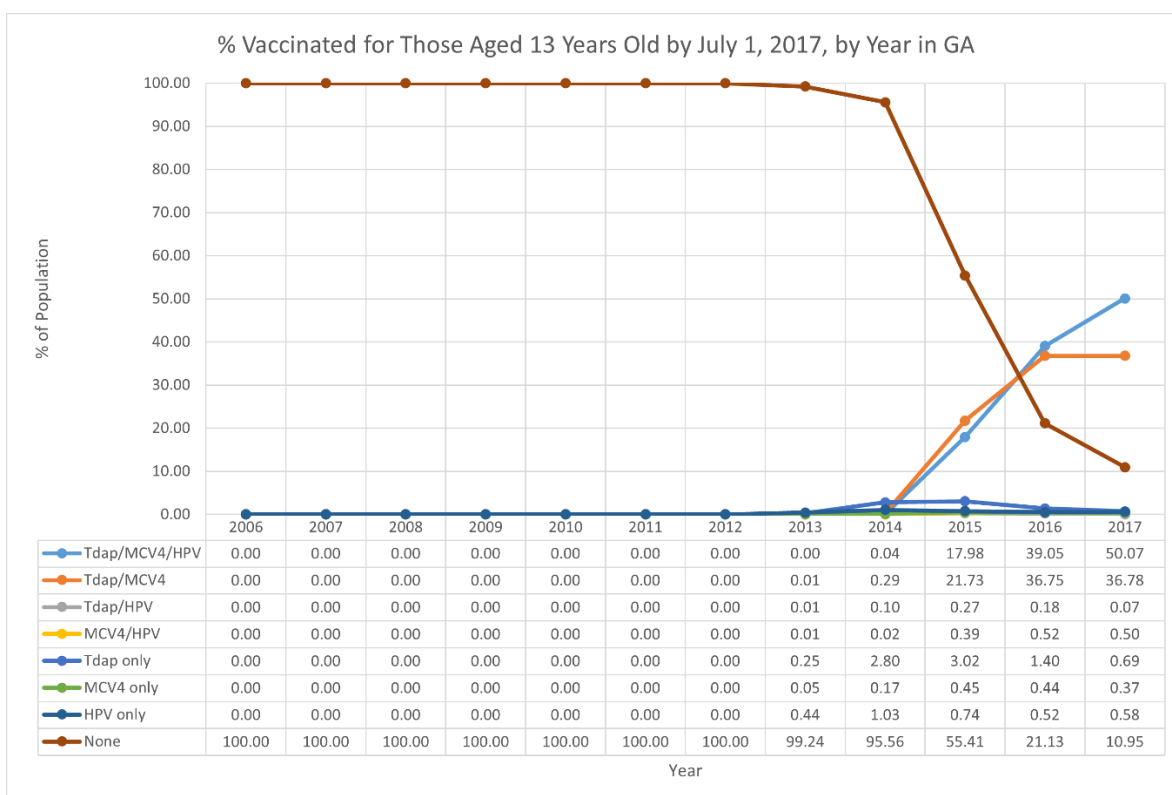
Age 15



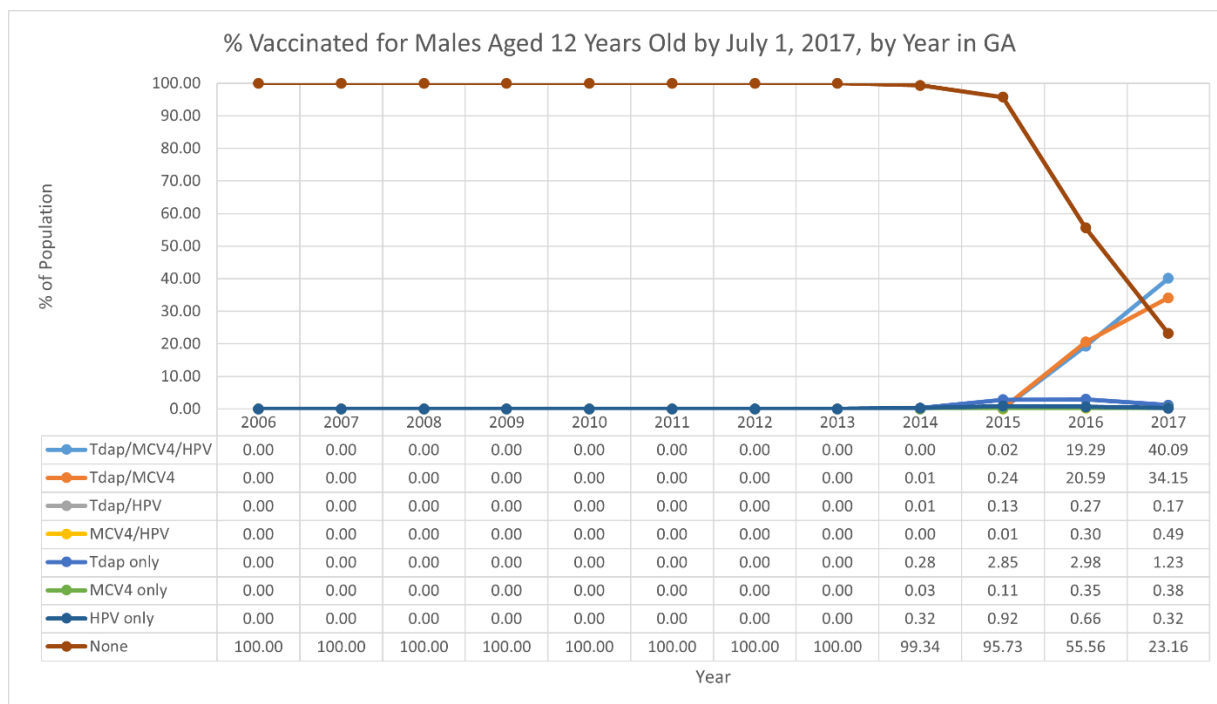
Age 14



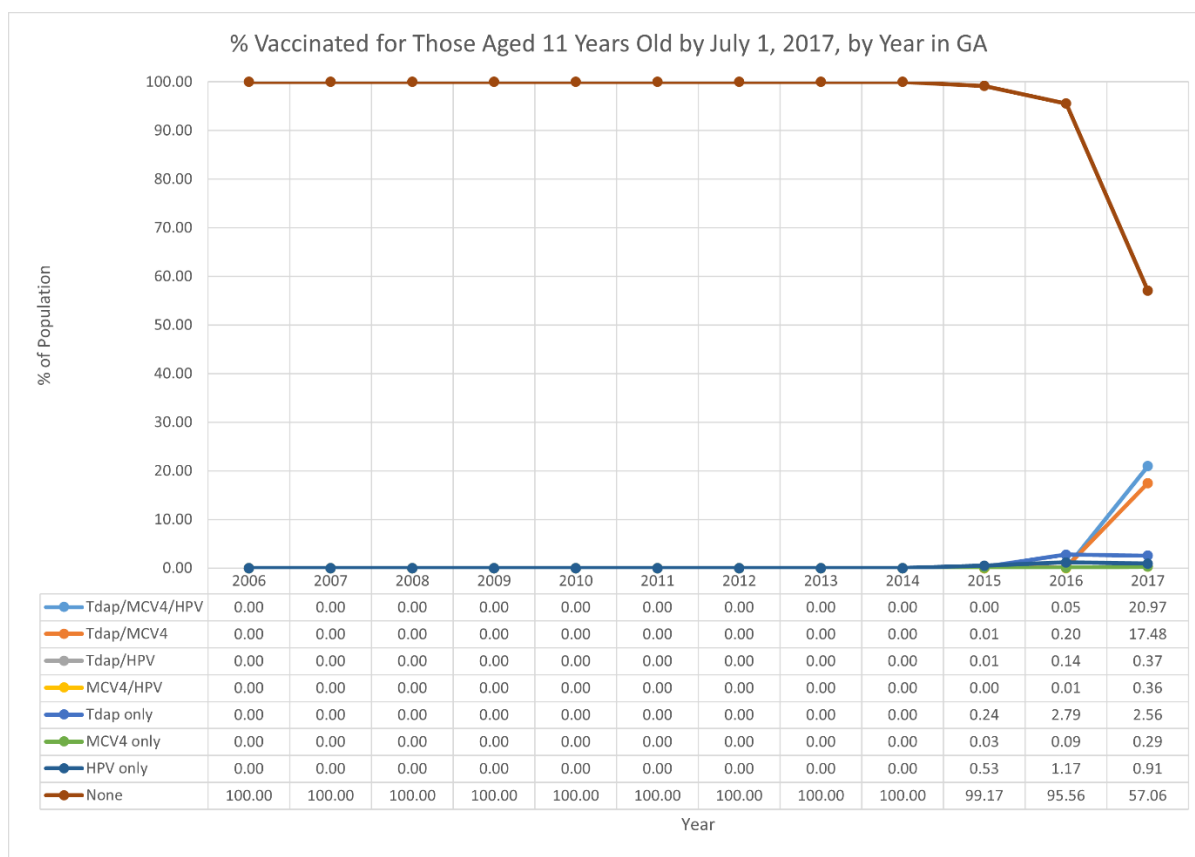
Age 13

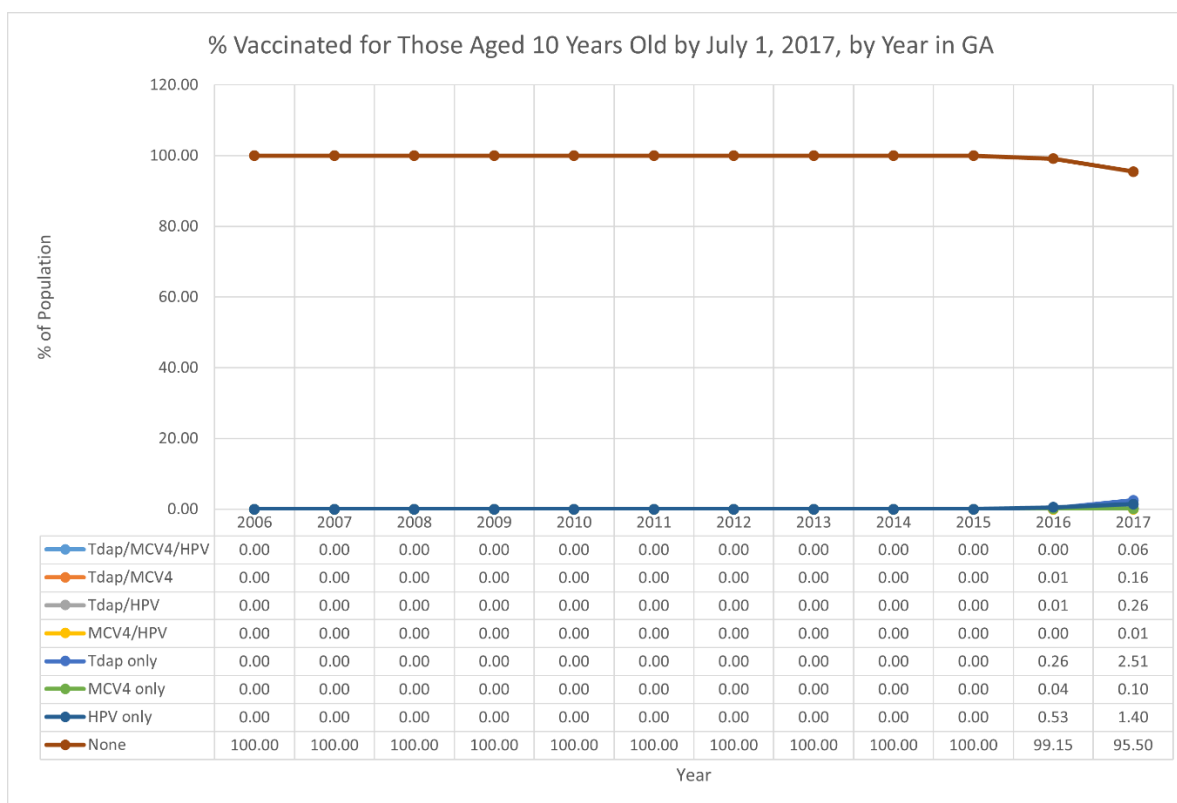
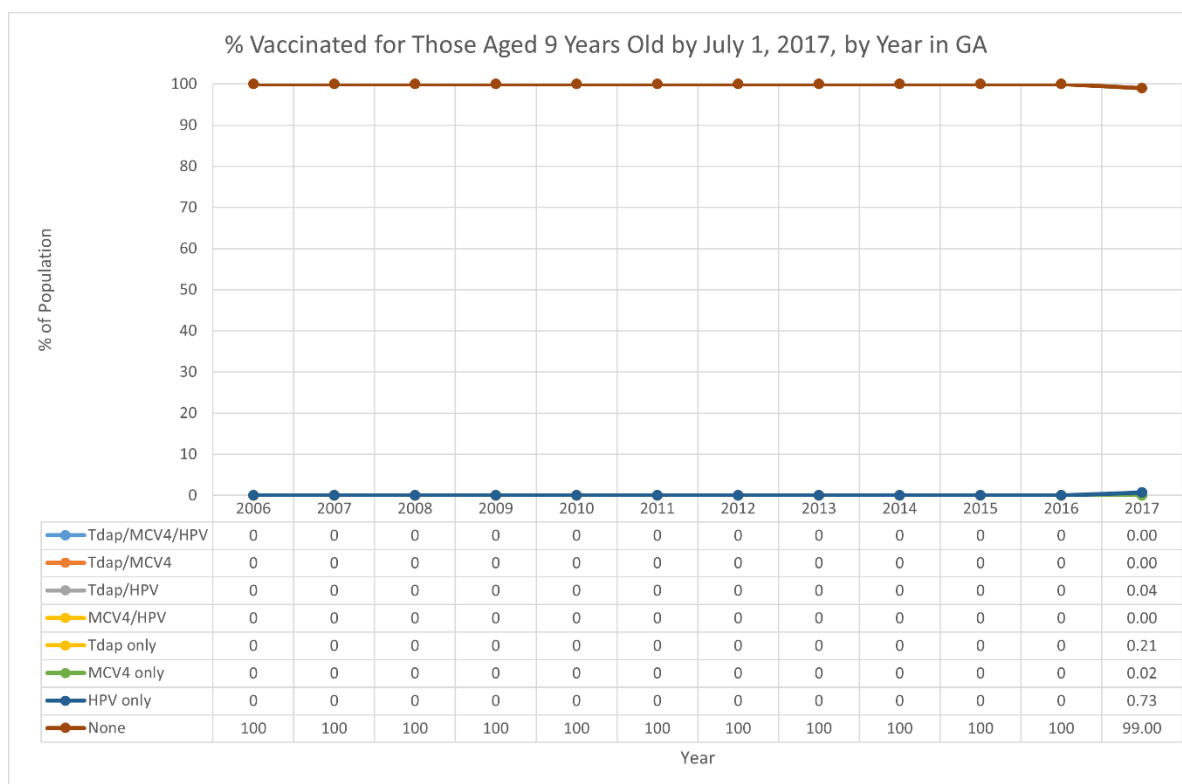


Age 12



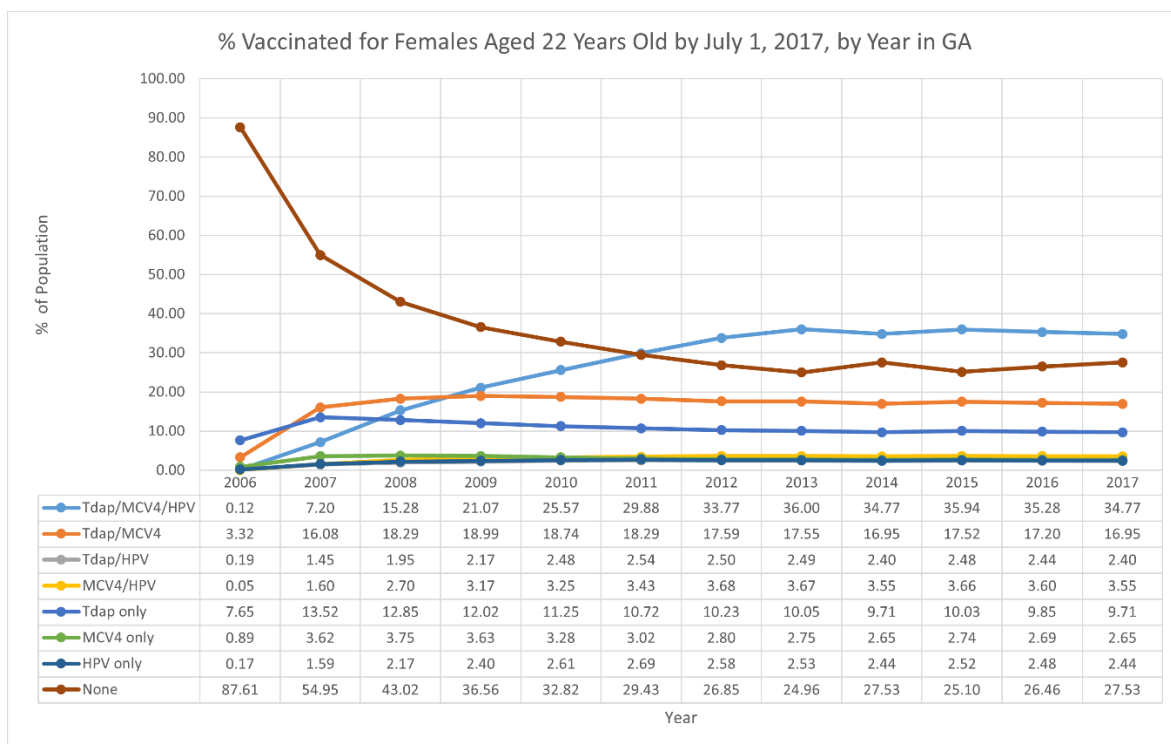
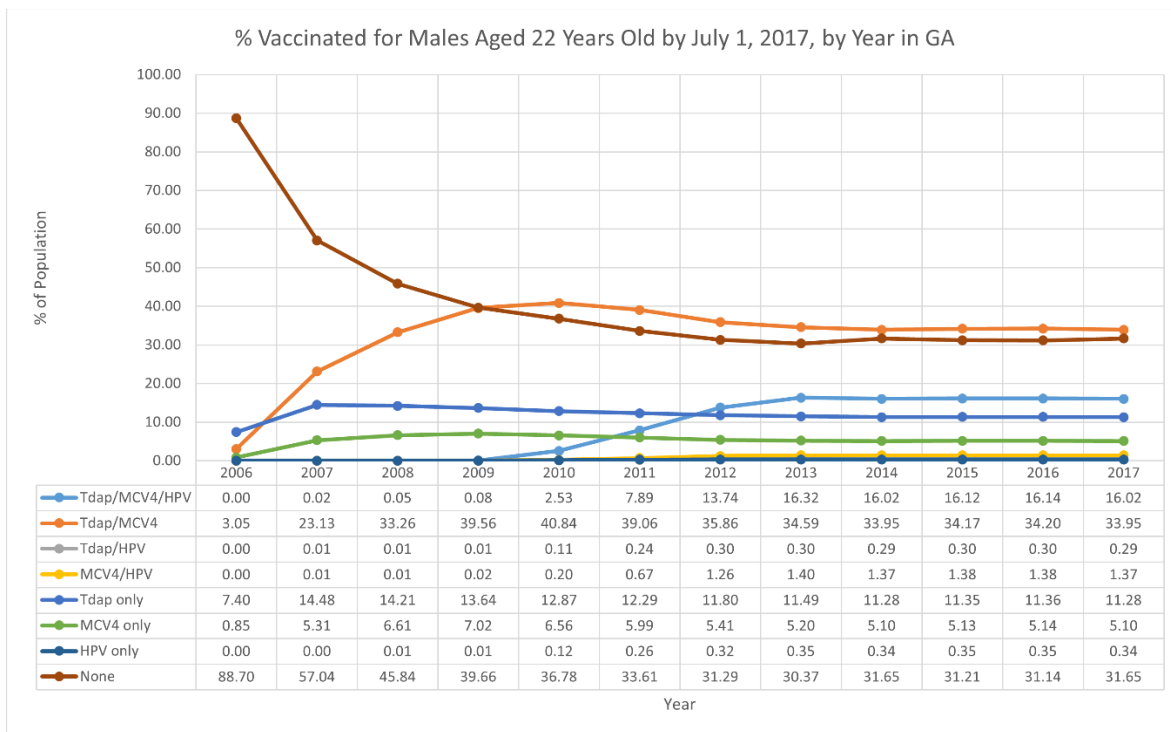
Age 11



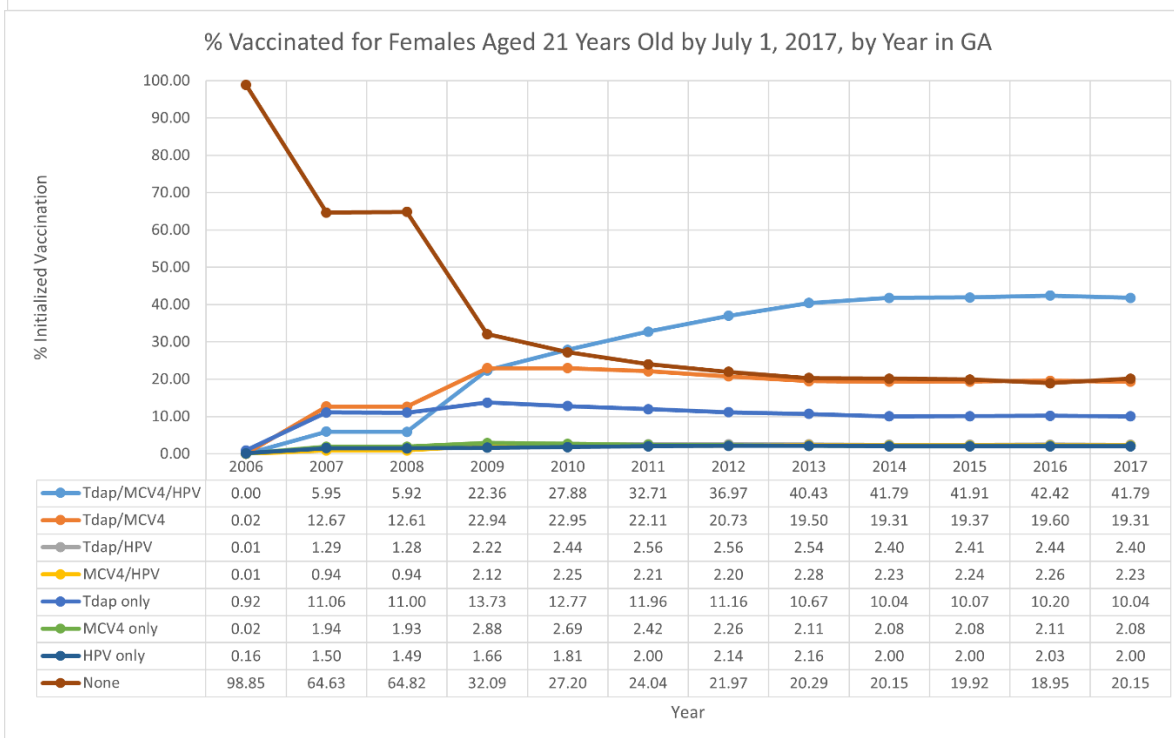
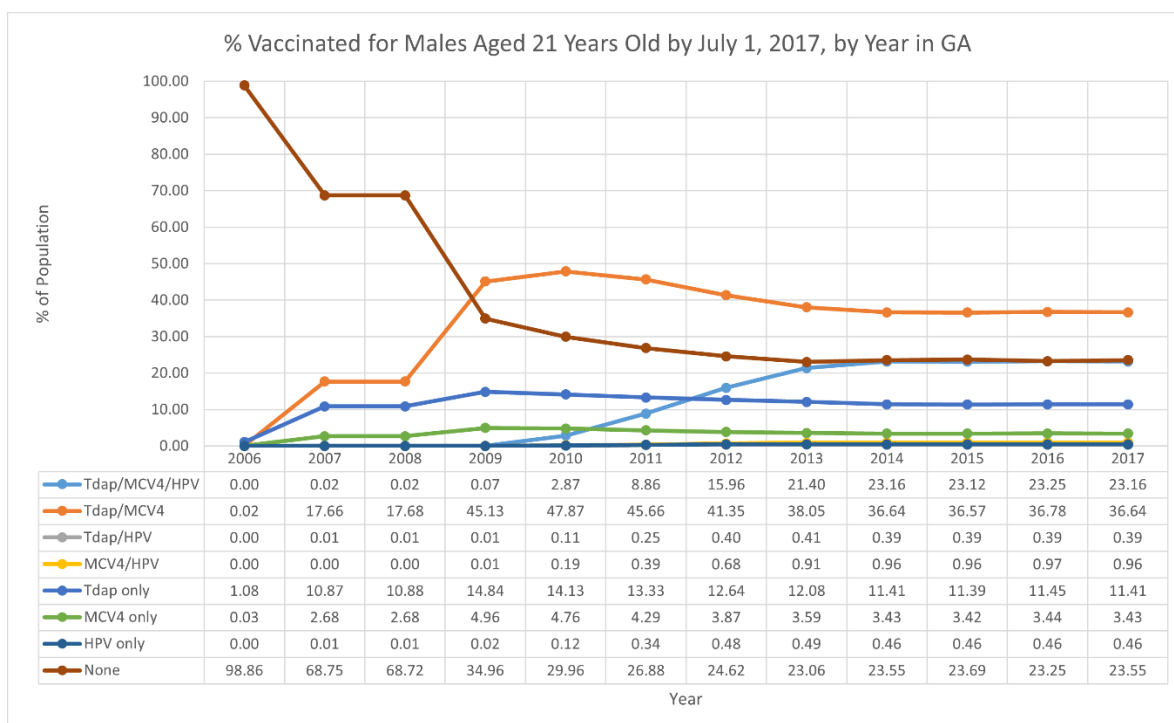
Age 10Age 9

Concomitant Vaccination Over Time Stratified by Sex

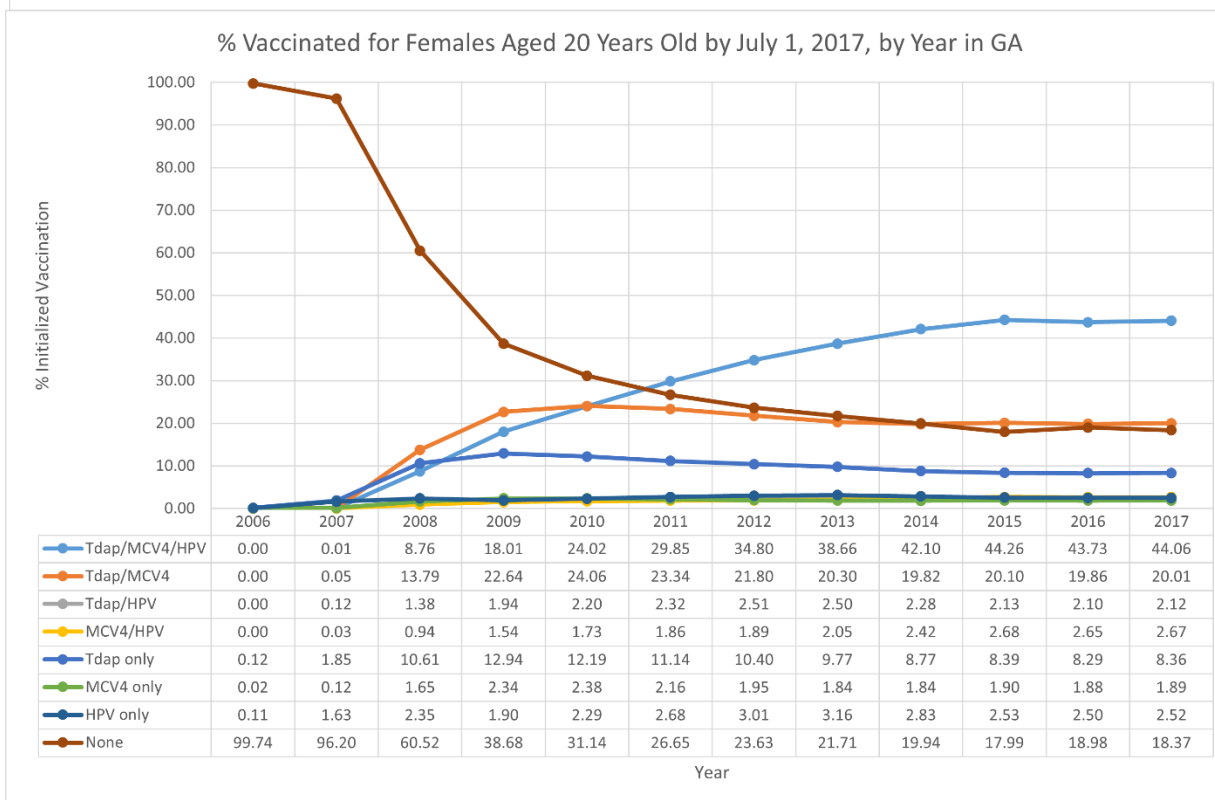
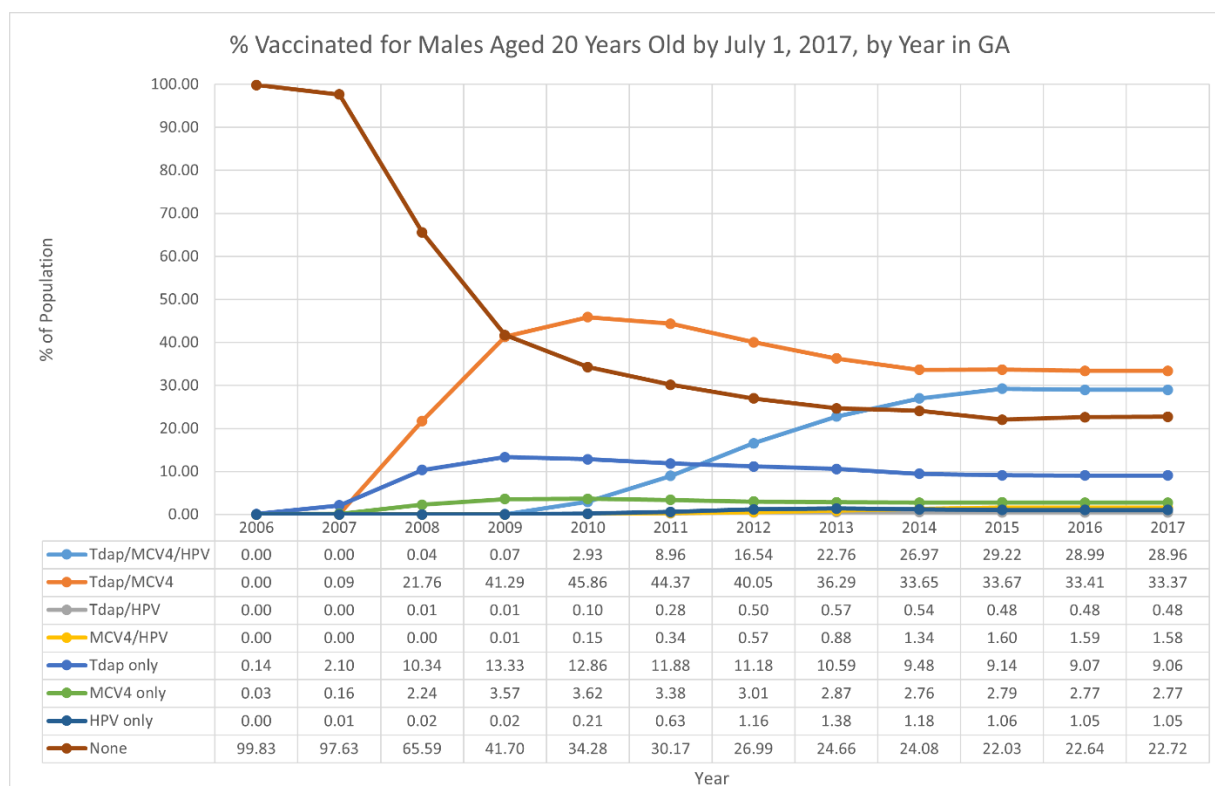
Age 22



Age 21

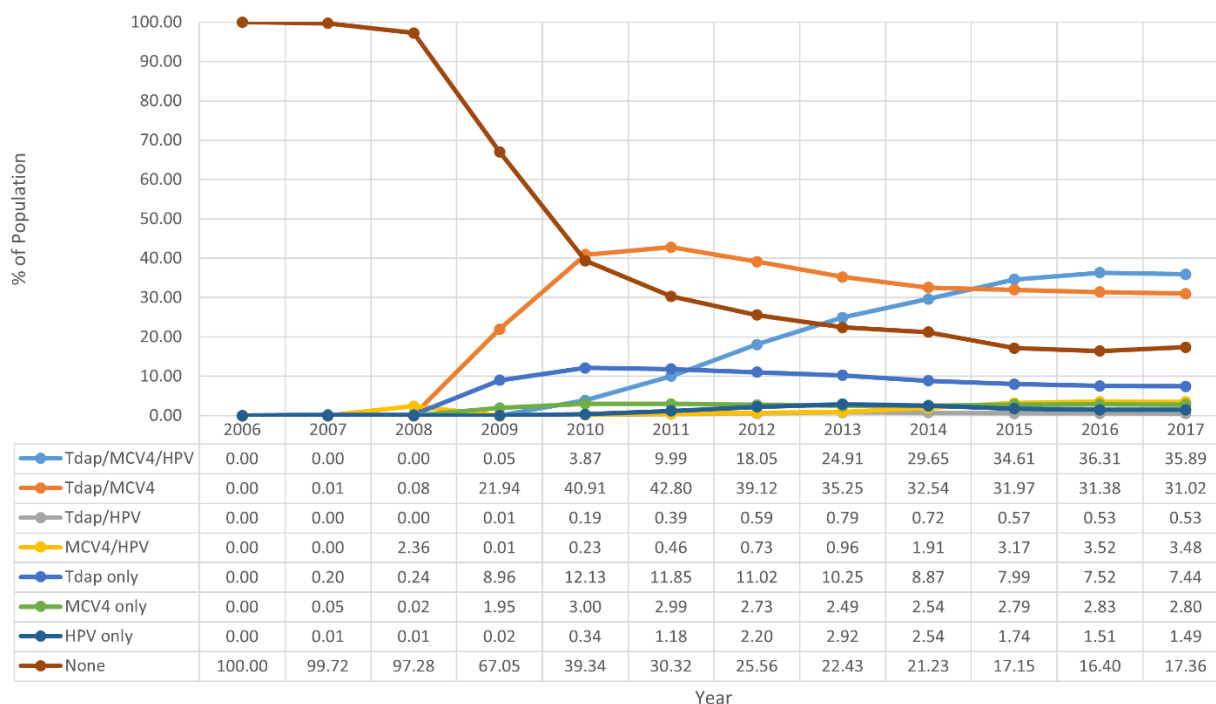


Age 20

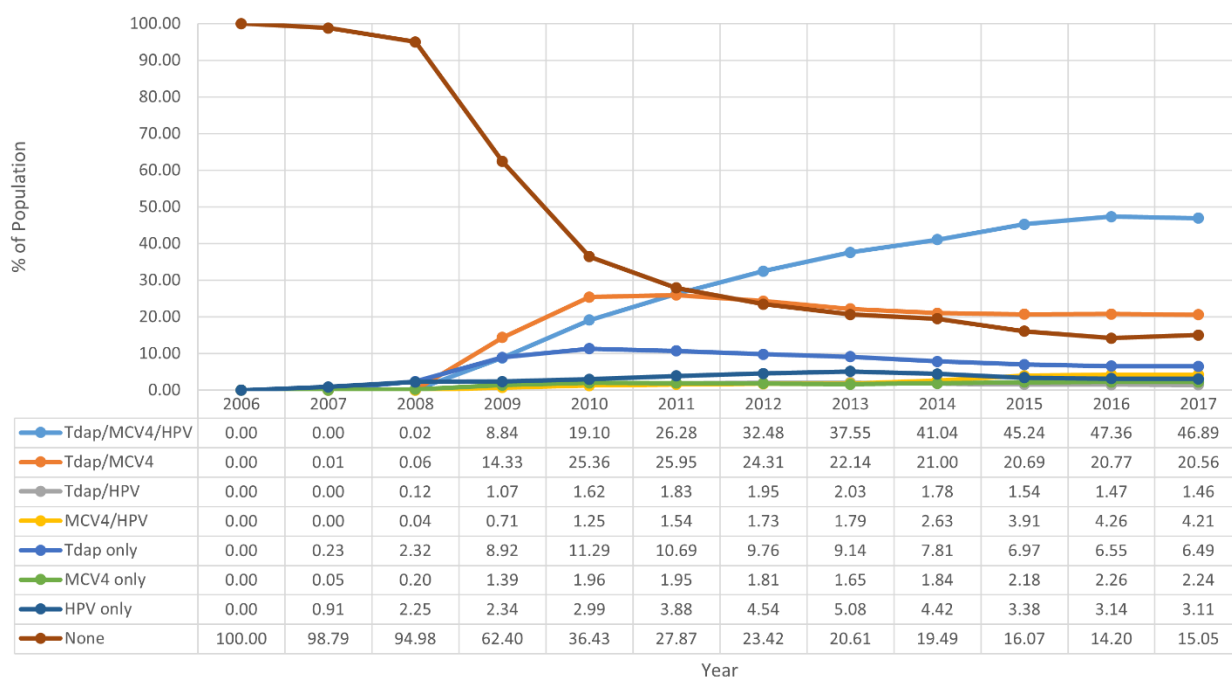


Age 19

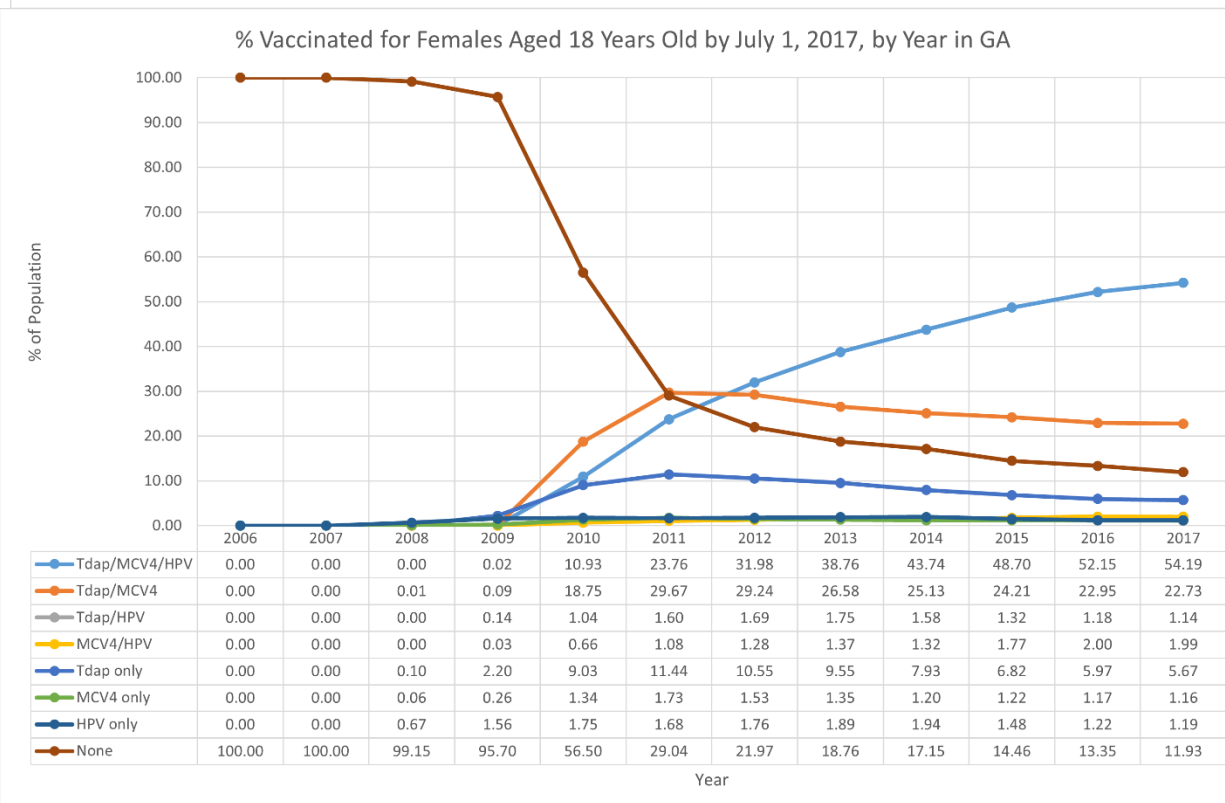
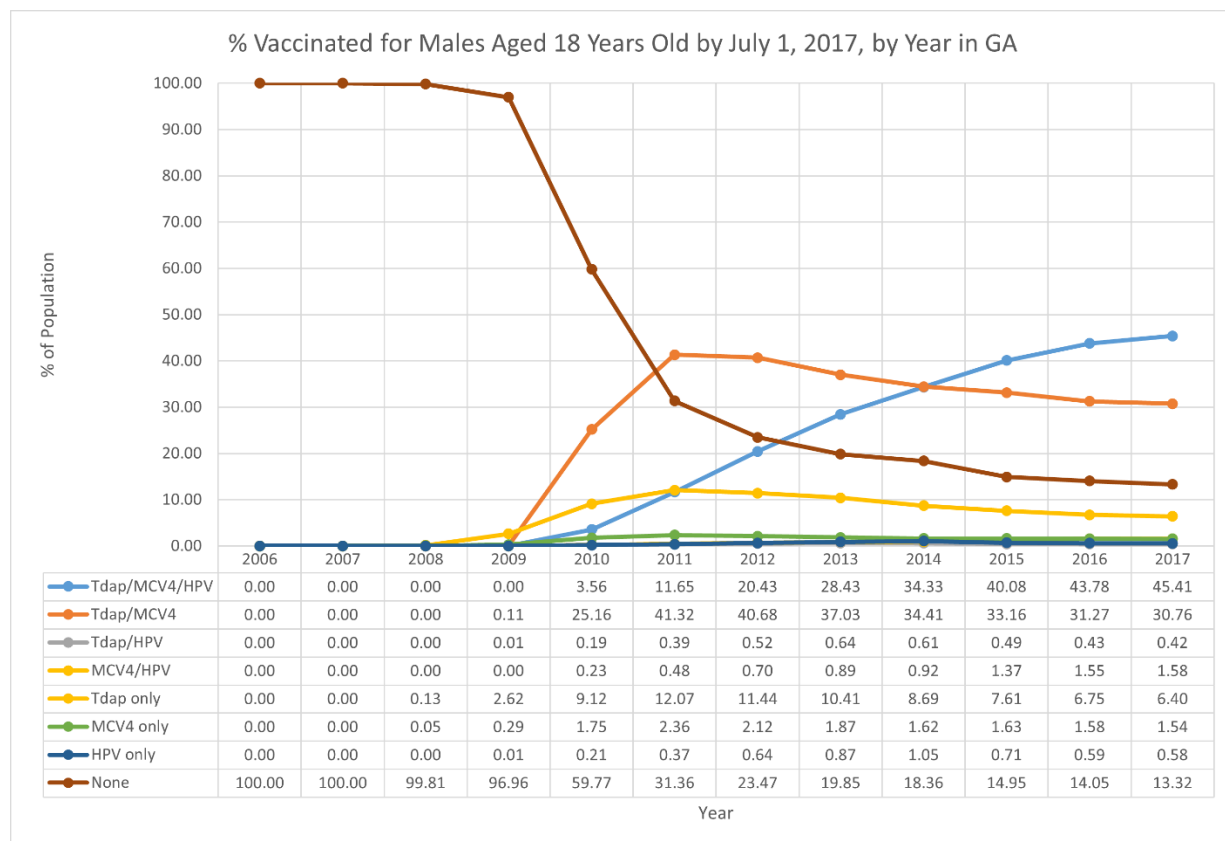
% Vaccinated for Males Aged 19 Years Old by July 1, 2017, by Year in GA



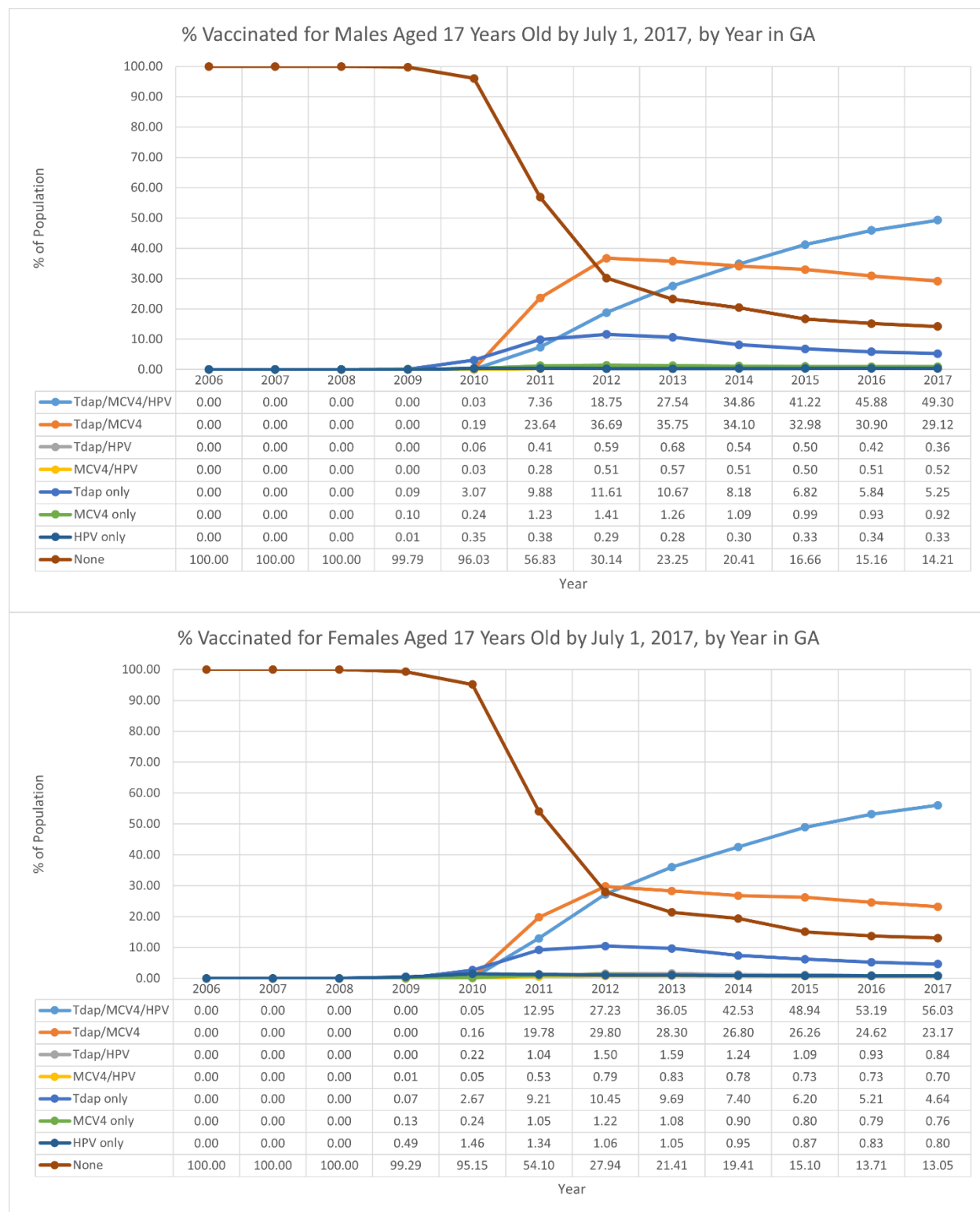
% Vaccinated for Females Aged 19 Years Old by July 1, 2017, by Year in GA



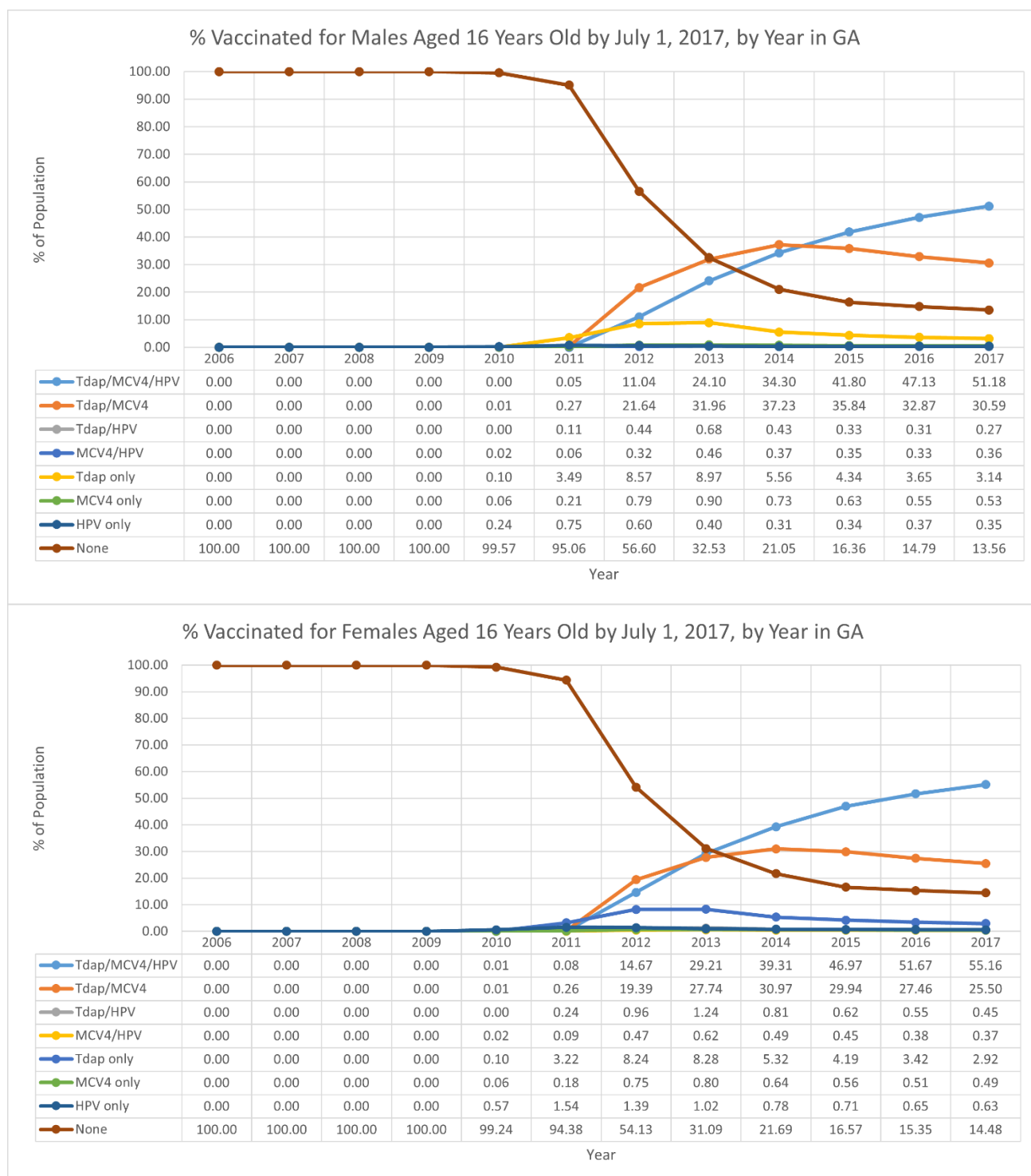
Age 18



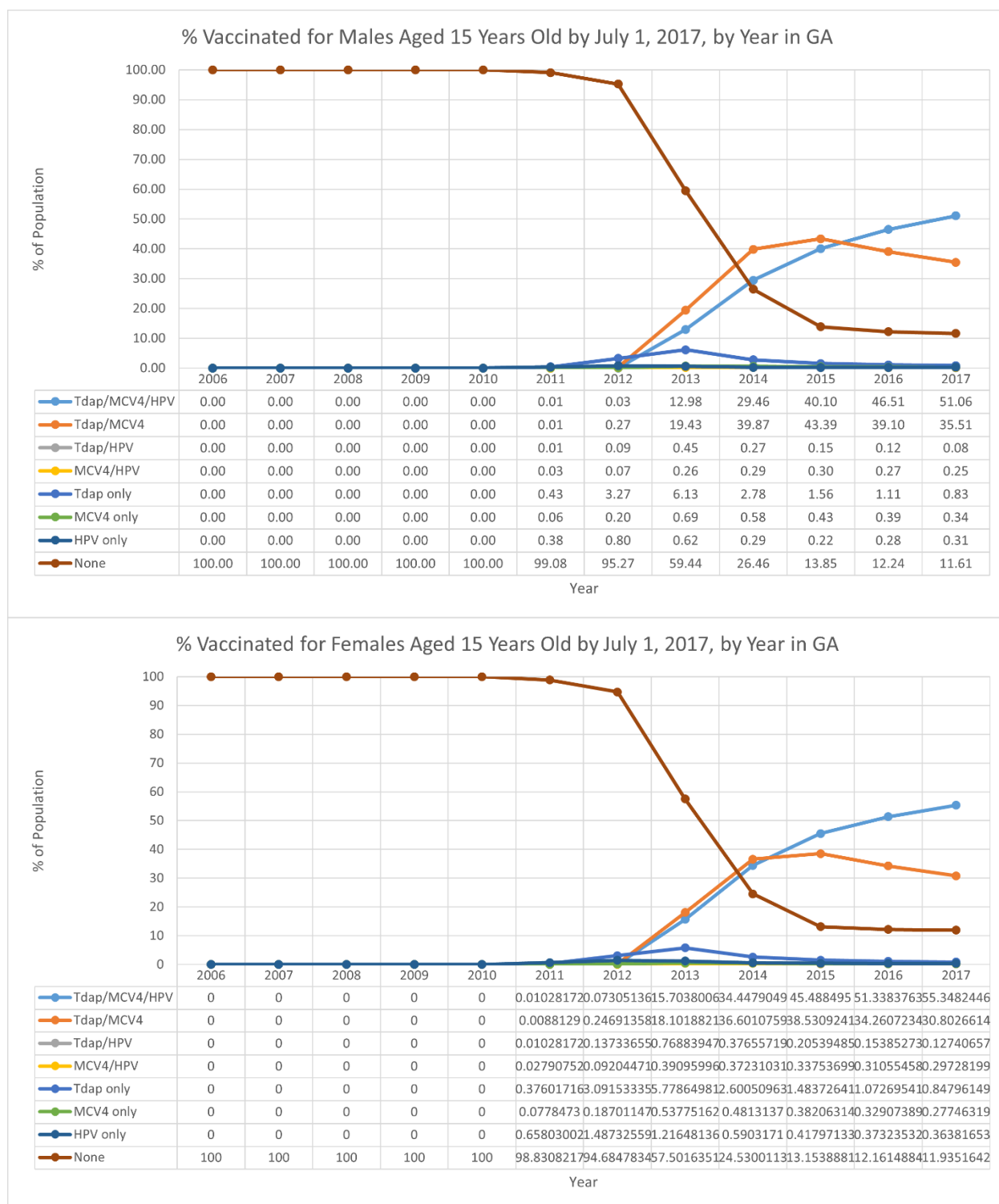
Age 17



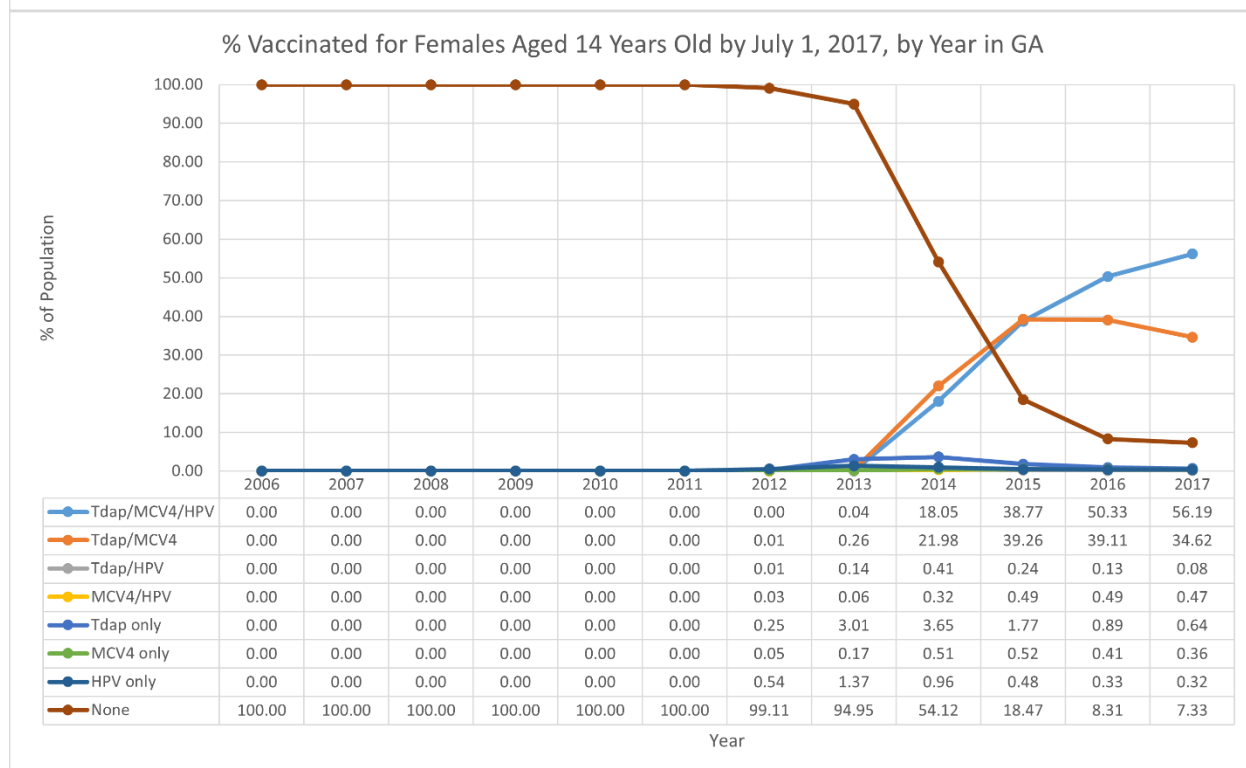
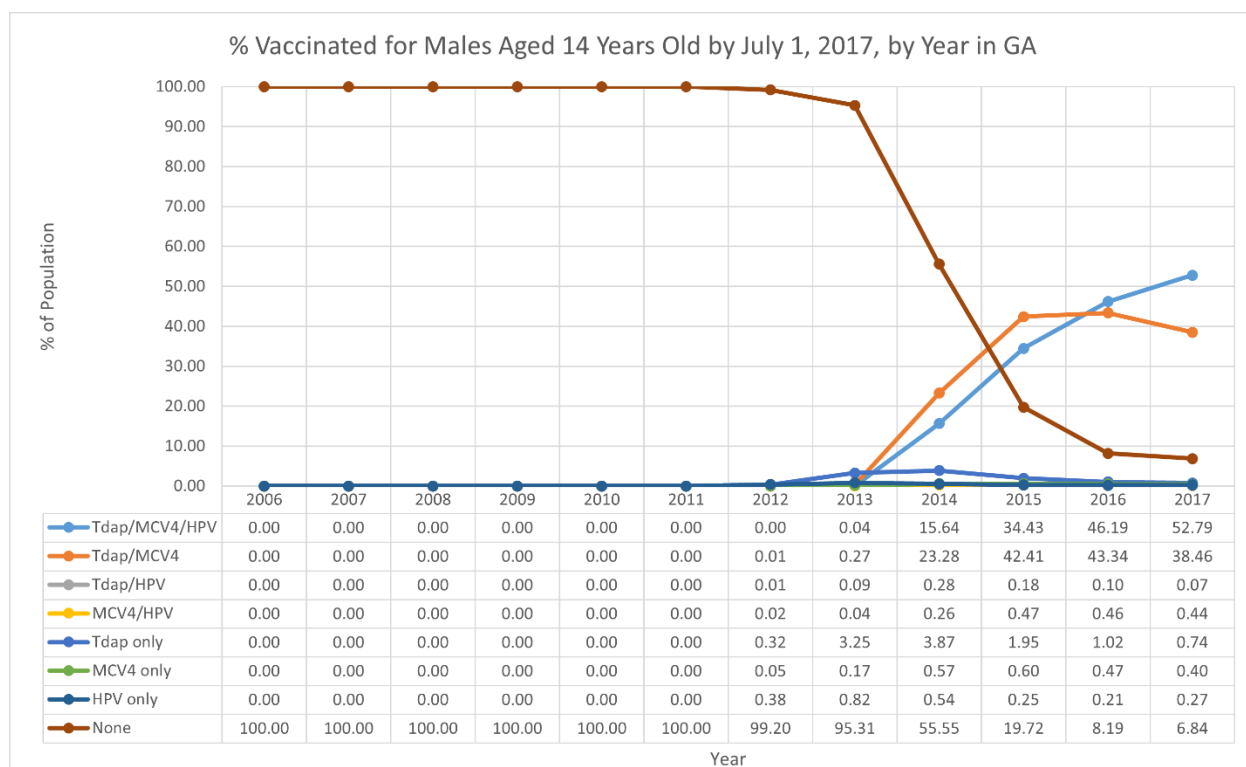
Age 16



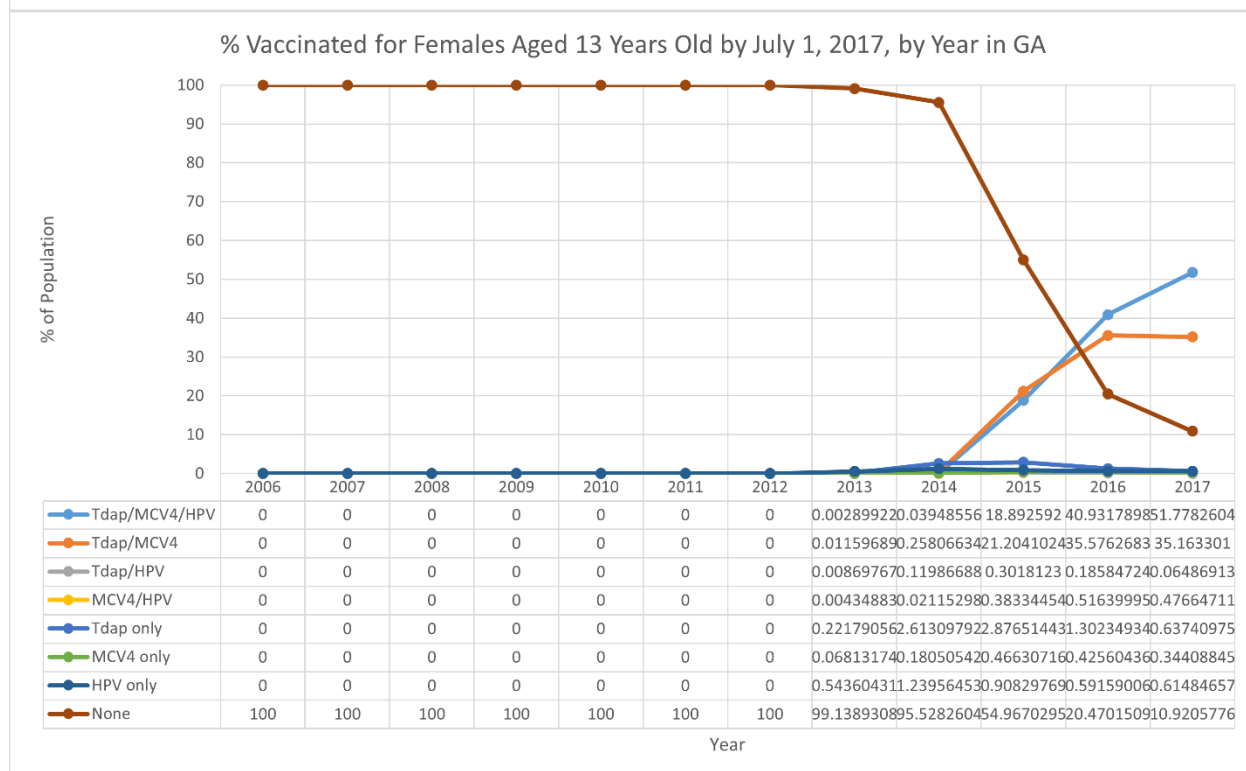
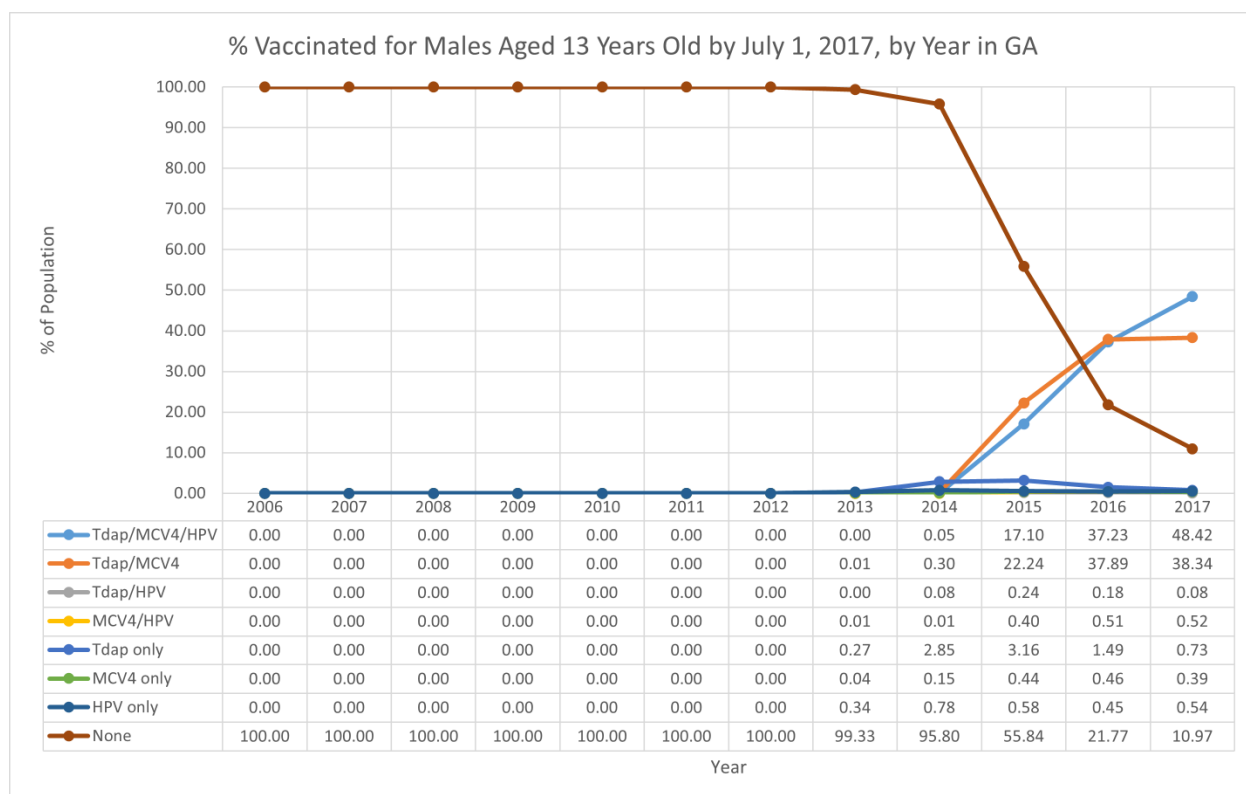
Age 15

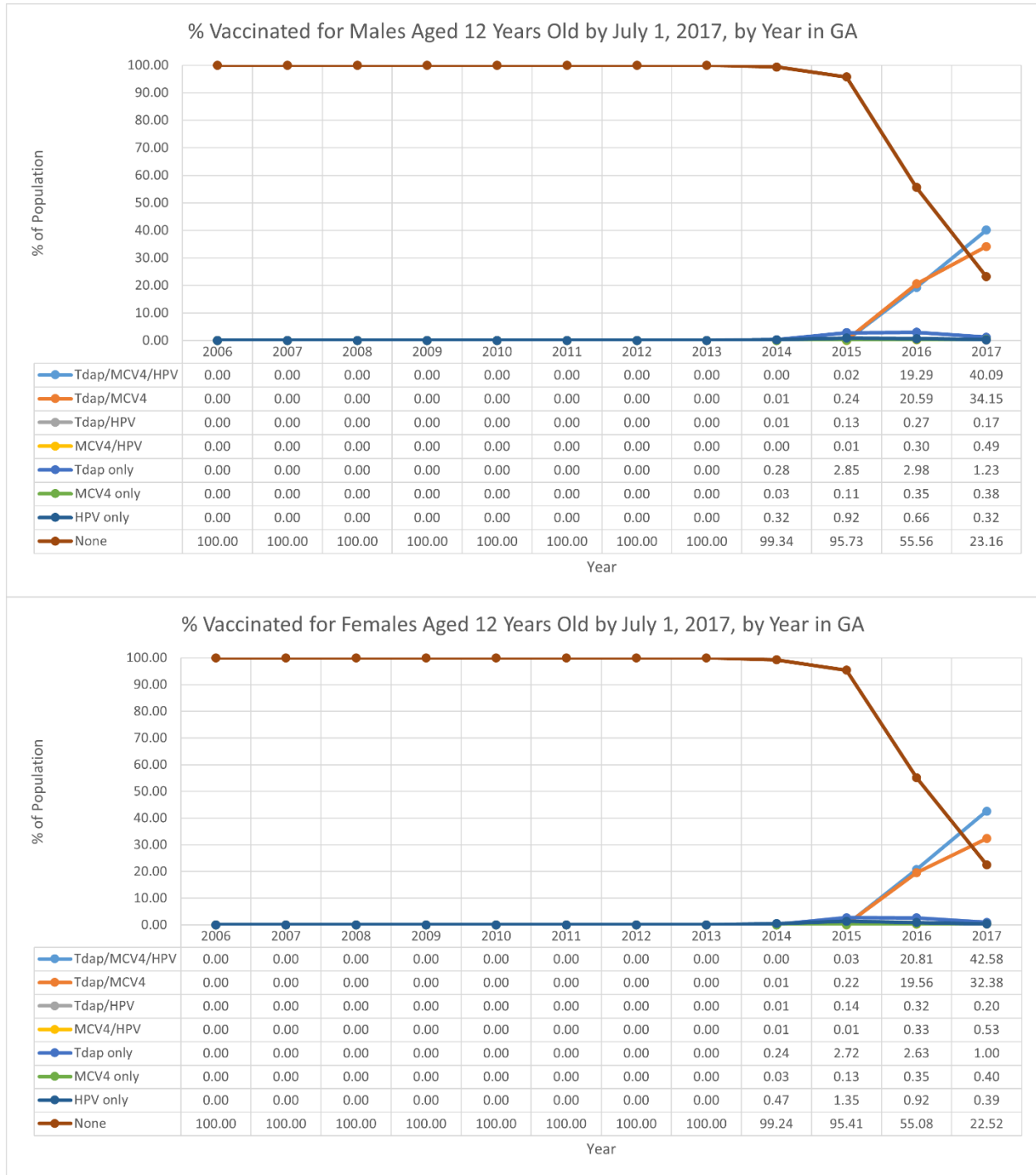


Age 14

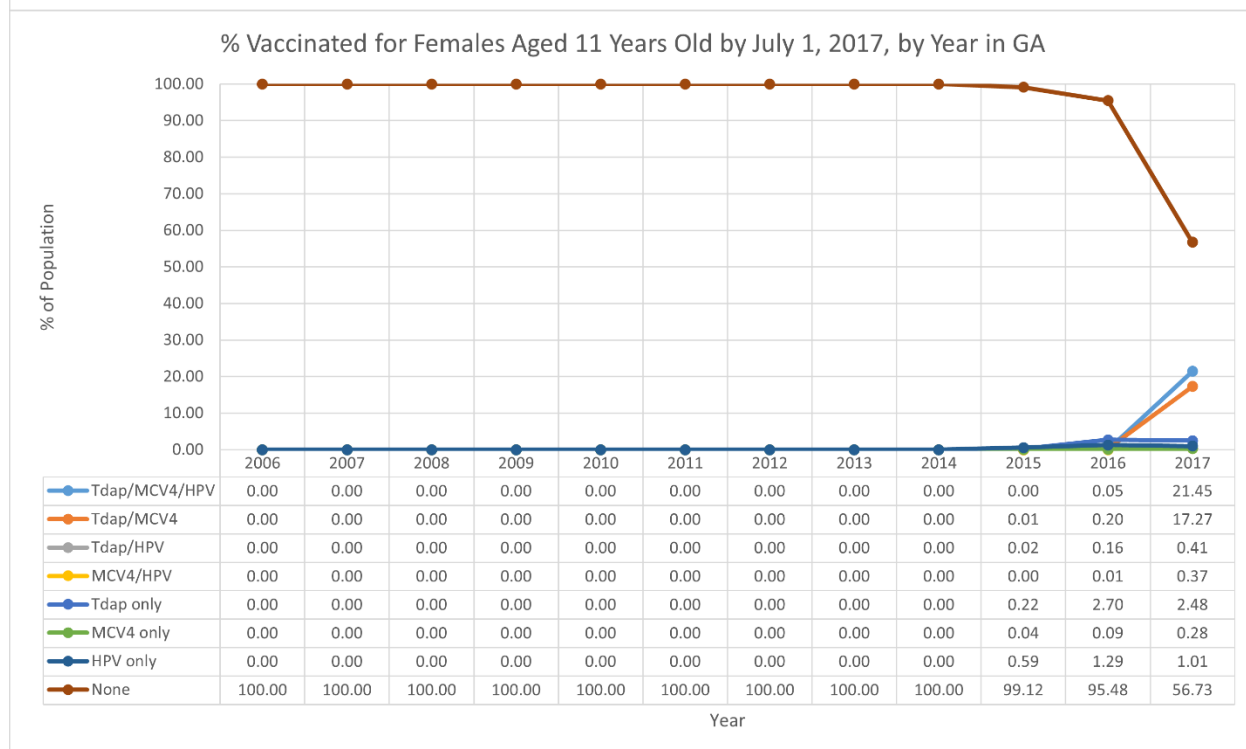
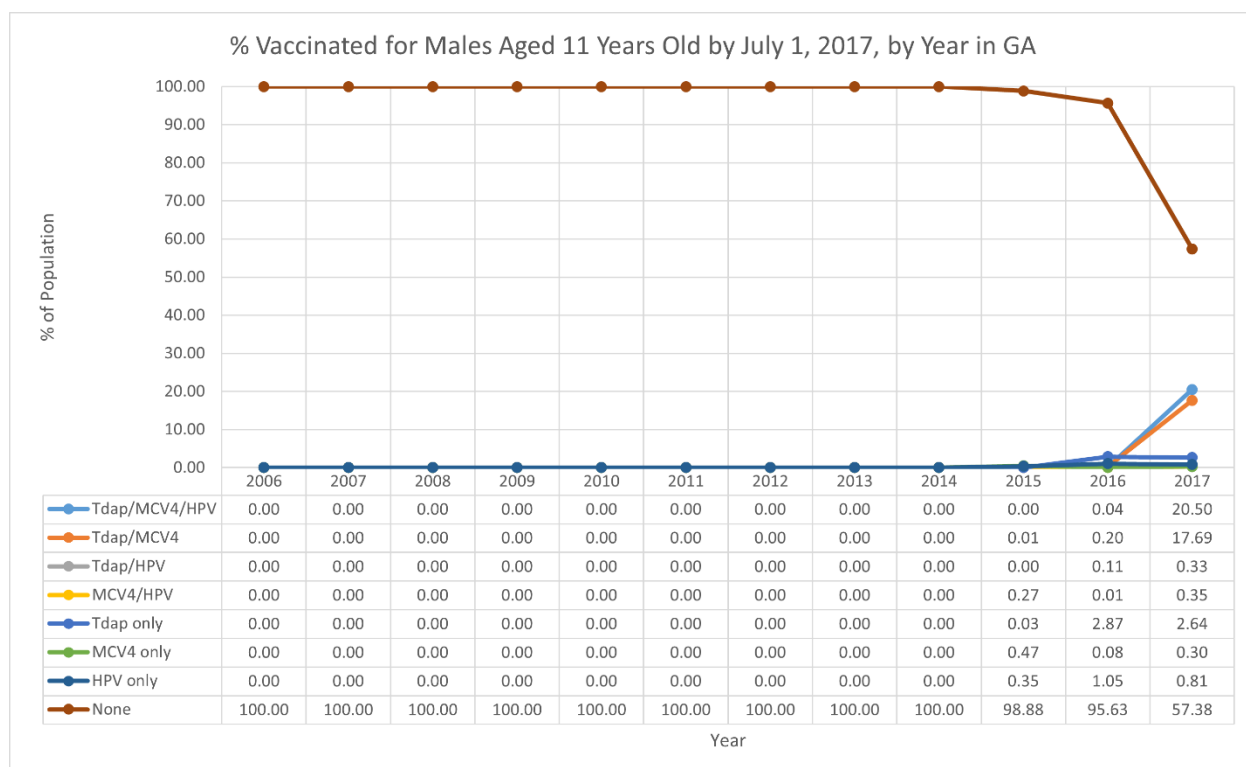


Age 13



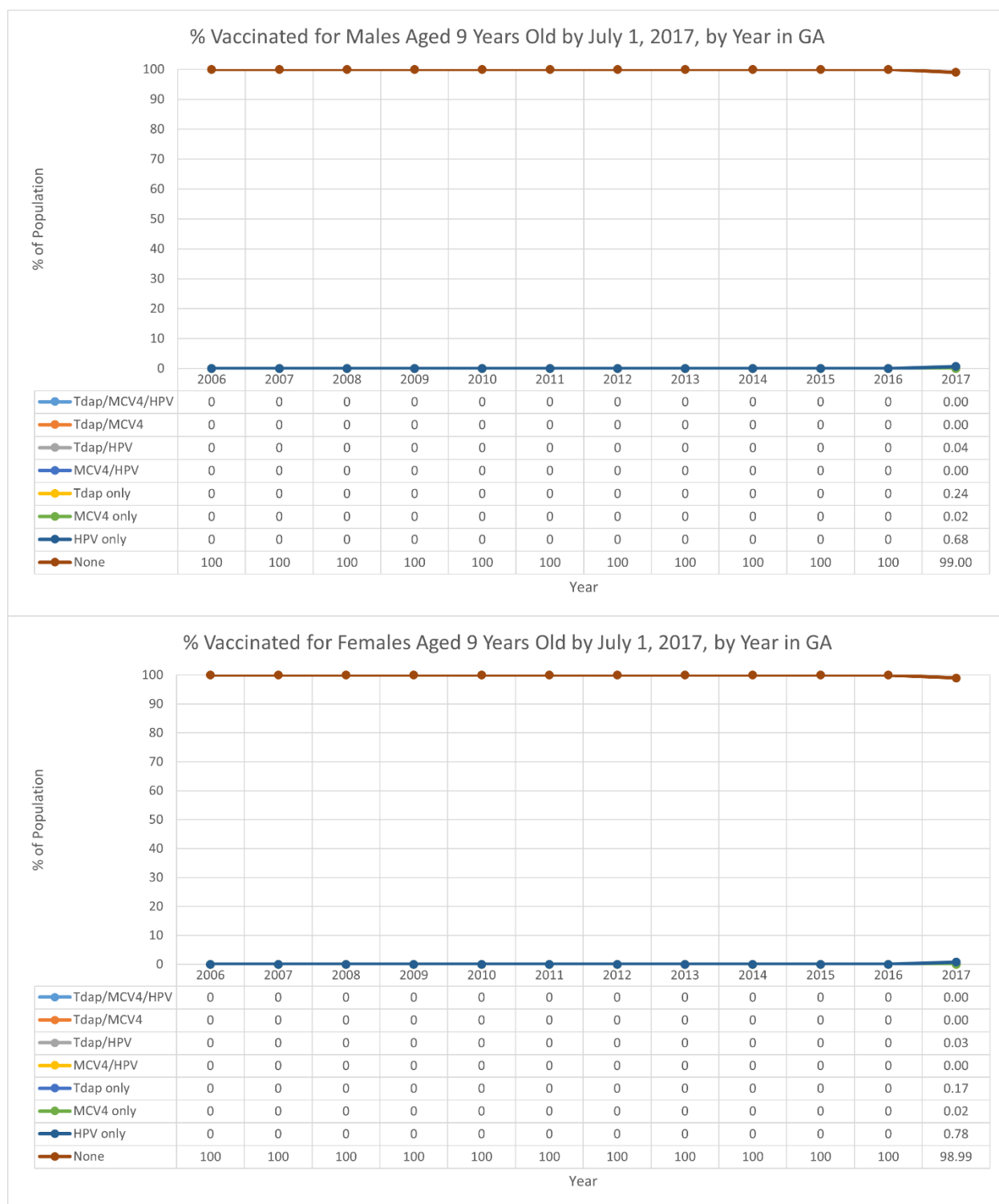
Age 12

Age 11



Age 10

Age 9



Concomitant Vaccination by Health District for Full Cohort in 2017

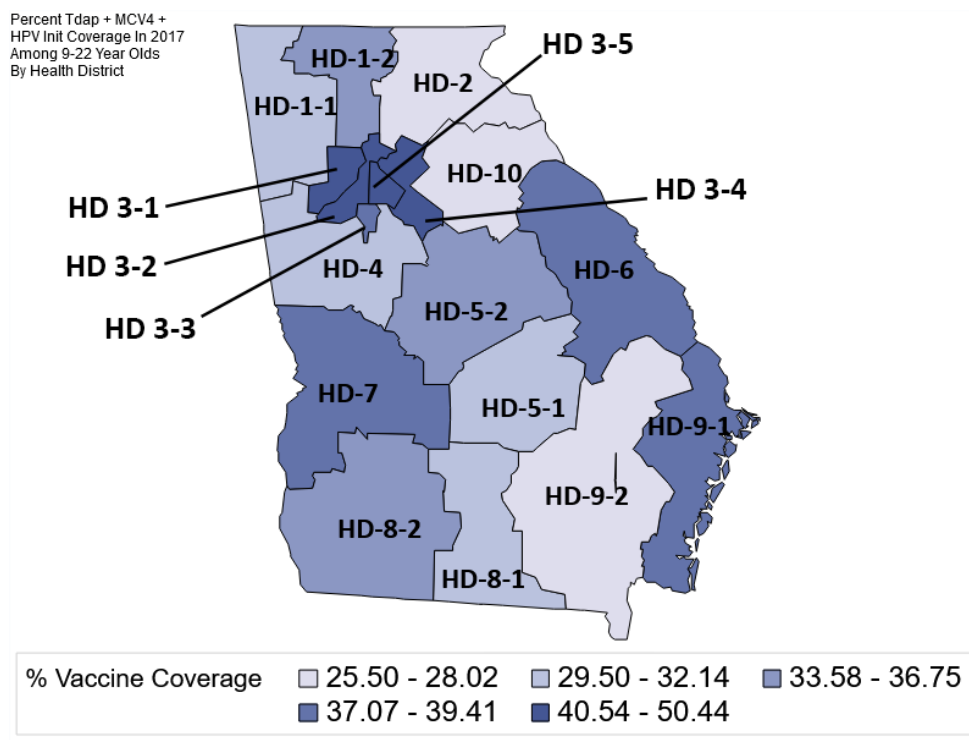
Table

		Tdap/MCV4/ HPV	Tdap/MCV4	Tdap/HPV	MCV4/HPV	Tdap Only	MCV4 Only	HPV Only	None
Health District	Pop.	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
1-1 Northwest (Rome)	126,734	42,183 (33.28)	36,450 (28.76)	1,437 (1.13)	1,643 (1.30)	8,039 (6.34)	3,427 (2.70)	2,164 (1.71)	31,391 (24.77)
1-2 North Georgia (Dalton)	90,009	35,797 (39.77)	26,553 (29.50)	884 (0.98)	1,254 (1.39)	5,618 (6.24)	2,207 (2.45)	1,136 (1.26)	16,560 (18.40)
2 North (Gainesville)	137,769	38,873 (28.22)	38,225 (27.75)	1,334 (0.97)	1,532 (1.11)	11,668 (8.47)	3,413 (2.48)	1,771 (1.29)	40,953 (29.73)
3-1 Cobb- Douglas	170,765	82,243 (48.16)	64,922 (38.02)	2,013 (1.18)	4,408 (2.58)	12,381 (7.25)	8,717 (5.10)	3,486 (2.04)	0*
3-2 Fulton	192,312	87,665 (45.58)	55,725 (28.98)	2,326 (1.21)	5,035 (2.62)	10,500 (5.46)	7,261 (3.78)	3,689 (1.92)	20,111 (10.46)
3-3 Clayton	59,419	25,177 (42.37)	17,840 (30.02)	465 (0.78)	1,083 (1.82)	3,962 (6.67)	2,507 (4.22)	1,017 (1.71)	7,368 (12.40)
3-4 GNR (Lawrenceville)	234,343	102,446 (43.72)	75,395 (32.17)	2,803 (1.20)	6,917 (2.95)	17,581 (7.50)	11,144 (4.76)	4,248 (1.81)	13,809 (5.89)
3-5 DeKalb	126,712	68,946 (54.41)	43,106 (34.02)	1,747 (1.38)	3,836 (3.03)	11,469 (9.05)	7,153 (5.65)	2,446 (1.93)	0*
4 District 4	172,307	55,438 (32.17)	54,025 (31.35)	1,965 (1.14)	2,694 (1.56)	13,521 (7.85)	5,831 (3.38)	2,956 (1.72)	35,877 (20.82)
5-1 South Central (Dublin)	25,952	9,065 (34.93)	9,489 (36.56)	359 (1.38)	380 (1.46)	3,805 (14.66)	739 (2.85)	340 (1.31)	1,775 (6.84)
5-2 North Central (Macon)	101,213	38,796 (38.33)	29,268 (28.92)	980 (0.97)	2,081 (2.06)	6,733 (6.65)	3,760 (3.71)	2,005 (1.98)	17,590 (17.38)
6 East Central (Augusta)	90,772	37,446 (41.25)	27,055 (29.81)	1,201 (1.32)	1,658 (1.83)	6,081 (6.70)	3,032 (3.34)	1,616 (1.78)	12,683 (13.97)

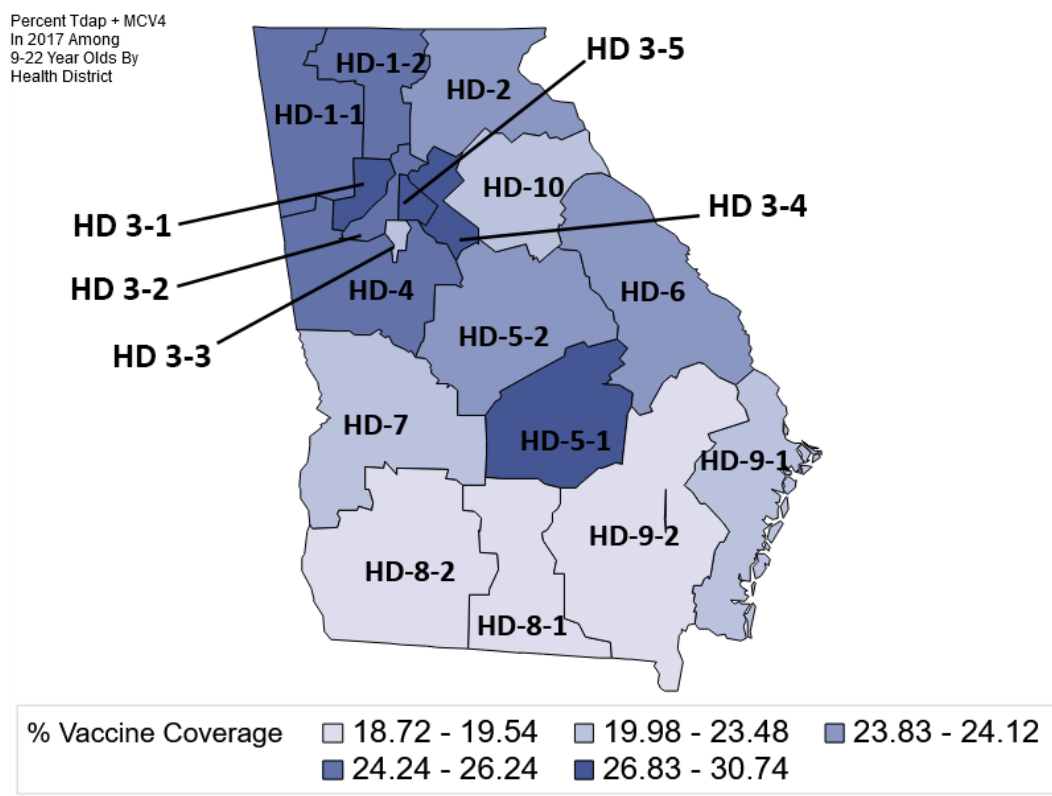
		Tdap/MCV4/ HPV	Tdap/MCV4	Tdap/HPV	MCV4/HPV	Tdap Only	MCV4 Only	HPV Only	None
7 West Central (Columbus)	67,812	27,924 (41.18)	18,578 (27.40)	697 (1.03)	1,412 (2.08)	5,279 (7.78)	2,240 (3.30)	1,103 (1.63)	10,579 (15.60)
8-1 South (Valdosta)	53,919	18,659 (34.61)	12,312 (22.83)	450 (0.83)	498 (0.92)	2,565 (4.76)	872 (1.62)	456 (0.85)	18,107 (33.58)
8-2 Southwest (Albany)	65,131	24,116 (37.03)	15,963 (24.51)	475 (0.73)	1,080 (1.66)	3,250 (4.99)	2,231 (3.43)	975 (1.50)	17,041 (26.16)
9-1 Coastal (Savannah)	114,977	47,774 (41.55)	33,239 (28.91)	1,384 (1.20)	2,099 (1.83)	10,738 (9.34)	4,324 (3.76)	1,965 (1.71)	13,454 (11.70)
9-2 Southeast (Waycross)	75,818	23,410 (30.88)	18,585 (24.51)	1,184 (1.56)	1,128 (1.49)	7,504 (9.90)	1,991 (2.63)	1,633 (2.15)	20,383 (26.88)
10 Northeast (Athens)	106,151	29,289 (27.59)	24,659 (23.23)	1,058 (1.00)	1,229 (1.16)	5,986 (5.64)	2,217 (2.09)	1,865 (1.76)	39,848 (37.54)

* These districts had an excess vaccinated population recorded in GRITS compared to Census data estimates; therefore, estimates may be inaccurate.

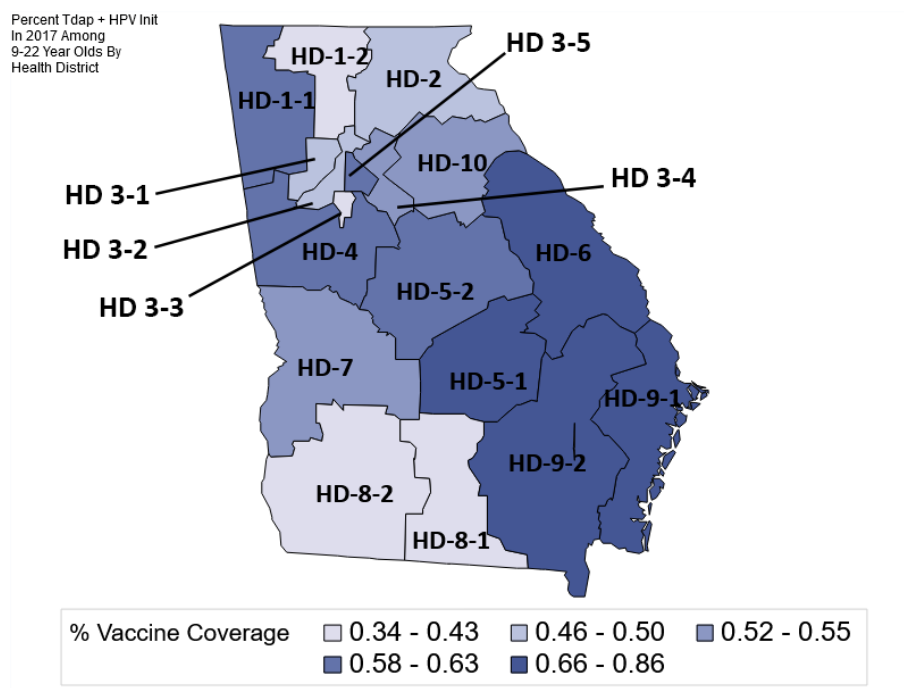
Tdap/MCV4/HPV Map



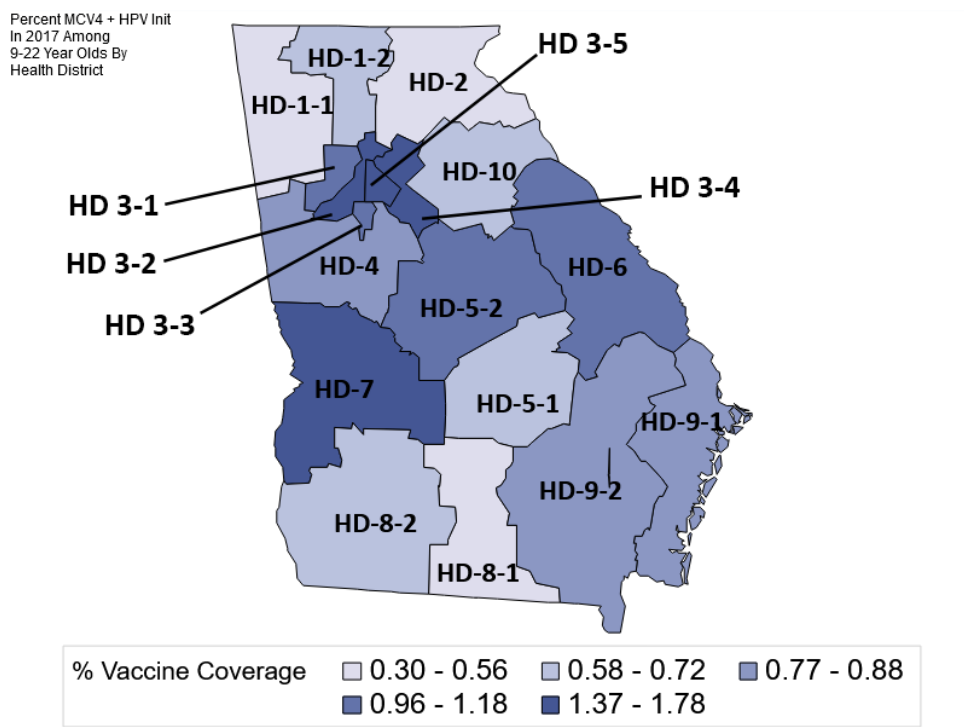
Tdap/MCV4 Map



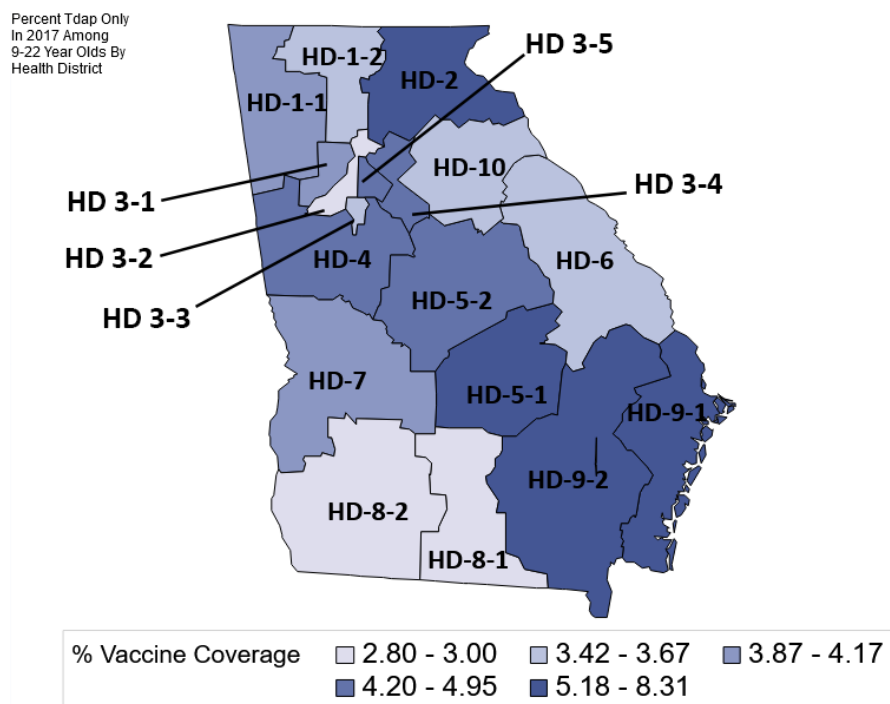
Tdap/HPV Map



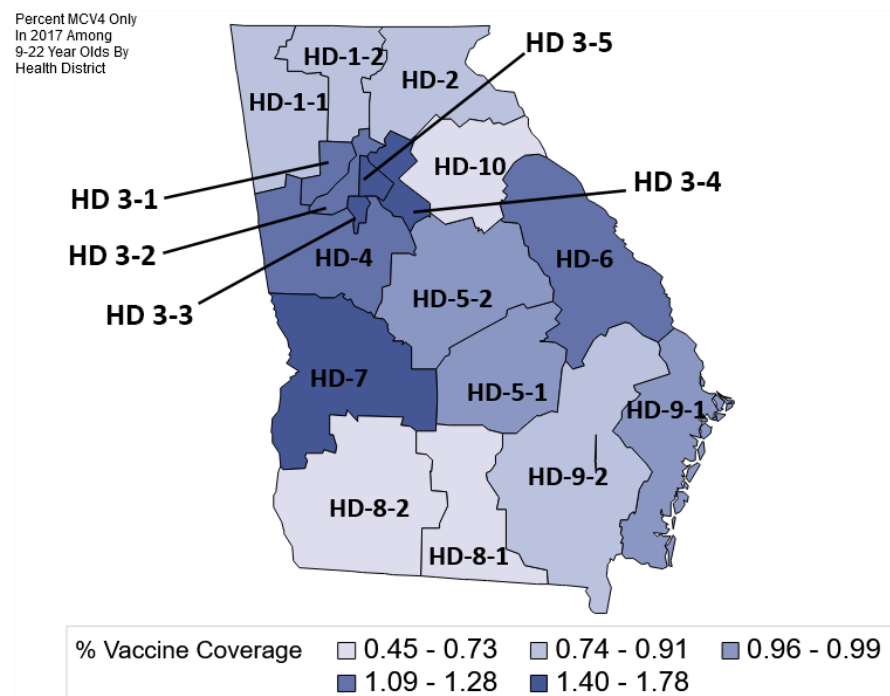
MCV4/HPV Map



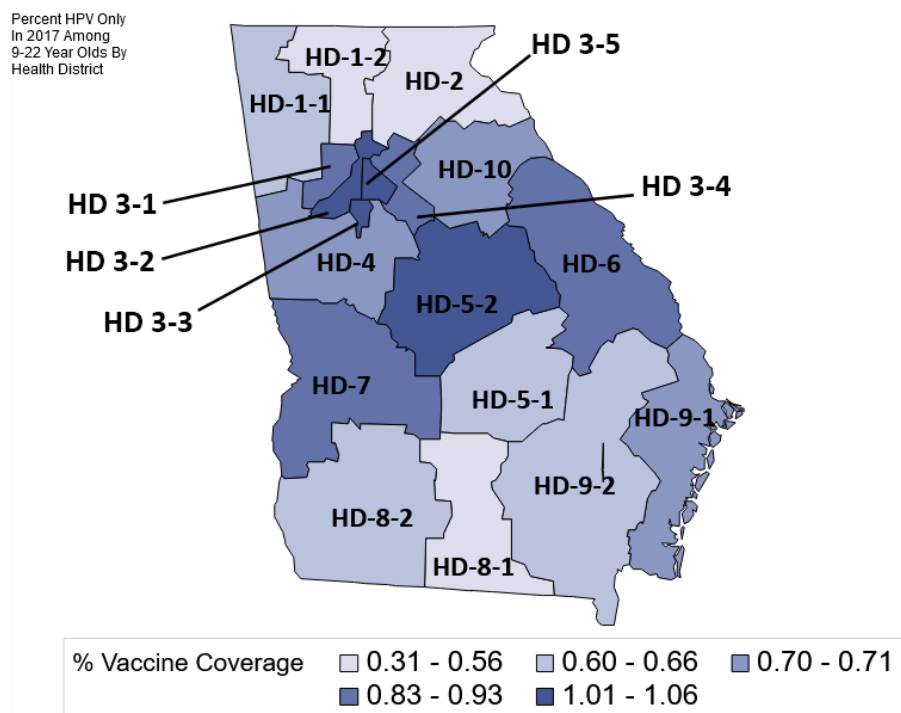
Tdap Only Map



MCV4 Only Map



HPV Only Map



None Map

