The History and Legacy of Vaccines:
An Overview of Vaccine Hesitancy in the United States

Ella Hagopian
St. Olaf College
May 4, 2020

Abstract

Vaccine distrust has existed for as long as modern vaccines have been produced. For many vaccines, there is currently a loss of confidence due to fear of adverse events and complacency regarding the severity of disease. The goal of this analysis is to identify groups who may be vaccine hesitant so that outreach programs can make the largest possible impact on vaccination rates. I used the CDC's National Immunization Survey data to examine the associations between a child's up to date status and several key explanatory variables, including the child's age, number of children in the house, mother's education, mother's age, mother's marital status, family income, insurance status, race, and U.S. region using logistic multivariate regression. I found significant associations with all of the listed variables except family income and race, with the biggest disparities in up to date status depending on insurance coverage. Using these results to tailor outreach programs such as the Vaccines for Children program may help increase vaccination rates by ensuring that parents who are vaccine hesitant are able to interact and have meaningful conversations with healthcare practitioners.

Introduction

History of Vaccine Distrust

Vaccines have been declared one of the top ten greatest public health achievements of the beginning of the century [1]. The Centers for Disease Control estimates that routine vaccination for children born between 1994 and 2013 will prevent 322 million illnesses, avoid 732,000 deaths, and save $1.4 trillion in social costs [2]. From the first smallpox vaccination to now, vaccines have become incredibly safe and effective. For as long as vaccines have existed, however, there have been people who have doubted or feared them.

The first modern vaccination was created by Edward Jenner in the 1790’s, using a less dangerous cowpox strain to protect people against the deadly smallpox [3]. After hearing that many dairymaids who were infected by cowpox were subsequently immune to smallpox, he performed an experiment with a young boy that became the basis for his smallpox vaccine. Understandably, people were skeptical. It required injecting pustule fluid into a small cut in the skin made by the healthcare provider. Some called the vaccine unchristian, some generally did not trust medicine, some believed smallpox was simply transmitted by miasma (bad air), and some thought vaccinations were a violation of their personal liberty [4]. These fears were one of the first instances of distrust in vaccines. On average, however, countries themselves have been fairly pro-vaccine even if individuals are anti-vaccine. For example, the U.S. Supreme Court case Jacobson v. Massachusetts ruled in 1905 that the right to refuse vaccinations is not guaranteed by the Fourteenth Amendment, so an individual’s right does not overrule a mandatory vaccine [5].

As more and more vaccines have been developed, individual opposition to them has not lessened. One of the main issues that people cite is the supposed side effects. The diphtheria-tetanus-pertussis (DTP) vaccine in particular generated a lot of controversy. The supposed side effects included epilepsy and mental disability [6]. Because of that, parents started filing lawsuits and many vaccine manufacturers started to stop vaccine production to avoid legal battles [7]. The complaints eventually spawned the Vaccine Injury Compensation Program in order to prevent vaccine shortages from lack of manufacturing and a drop in U.S. vaccination rates [8]. That program still exists today. The lawsuits against DTP generally claimed epilepsy or other atypical neurological functions afflicted their children after the child was vaccinated, thereby blaming the symptoms on the vaccine. Many of the cases that claimed epilepsy or an unspecified intellectual disability were eventually disproved by a 2006 study by Samuel Berkovic, a neurologist. Berkovic was the first to discover that the people claiming injury from DTP were most likely suffering from a neurological disorder called Dravet's Syndrome instead [6]. That discovery implied that a genetic disorder was the cause of the symptoms. It was a landmark discovery because vaccines cannot change genetics, so the DTP vaccine could not have been what caused the symptoms.

Despite the recognition that the DTP vaccine did not cause epilepsy or intellectual disability, parents still distrusted vaccines. Another example of this distrust is the debunked link between the measles, mumps, and rubella (MMR) vaccine and autism. Andrew Wakefield's famous study that claimed to confirm the link between the vaccine and autism only served to add fire to the flame [6]. Even though Wakefield's study has been debunked on multiple fronts – sloppy trial design, inability of other scientists to recreate the results, and the discovery of the link between Wakefield and a personal injury lawyer representing the families in the trial in cases against vaccine manufacturers – fear of the MMR vaccine swept up many families. Like with DTP, many parents filed complaints through the Vaccine Injury Compensation Program that the MMR vaccine and/or the thimerosal in several other vaccines caused their child to get autism. Thimerosal was removed from vaccines to assuage parent fears in an abundance of caution, yet the complaints kept coming [7]. These complaints eventually led to the Omnibus Autism Proceeding to examine the supposed causal link.

The Omnibus Autism Proceeding happened because the Vaccine Injury Compensation Program had been flooded with claims that the MMR vaccine or thimerosal caused autism. It involved a collection of cases believed to have the strongest claims to compensation. Even with the strongest cases, the judges presiding over the case all unanimously rejected their theories [6]. They found that the respondents, those fighting the causal claim, had stronger cases because "the expert witnesses presented by the respondent were far better qualified, far more experienced, and far more persuasive than the petitioners' experts, concerning the key points. The numerous medical studies concerning the issue of whether thimerosal causes autism, performed by medical scientists worldwide, have come down strongly against the petitioners' contentions" [9]. The outcome of the proceeding effectively shut down any further claims about autism as a result of vaccines.

Current State of Vaccine Distrust

For the most part, the United States has high vaccine coverage rates; for example, as of 2018, the median vaccination coverage for the DTaP vaccine was 95.1% and the MMR vaccine was 91.5% amongst kindergarteners [10]. However, the percentage of children who are up to date on the entire recommended vaccine schedule is lower. Only 70.4% were completely up to date for the entire series [10]. Despite an abundance of evidence on the general effectiveness and safety of a vaccine that enters the market, people still continue to advocate against vaccines [11, 12]. Of particular concern are the possible adverse events of vaccines. Some of the latest concerns are aluminum or formaldehyde in some vaccines, even though pears contain more naturally occurring formaldehyde than any vaccine [7]. Part of the distrust in vaccines is a result of their success. Figure 1 demonstrates the general lifecycle of vaccine use for a given vaccine. Once a vaccine is developed, the incidence of disease dramatically decreases, but that also means people do not have firsthand experience with that disease and thus start fearing the small incidence of adverse events more than the disease itself. That causes a loss of confidence where more outbreaks occur, prompting more people to fear the disease and resume vaccinations, which can finally bring about the disease's eradication.

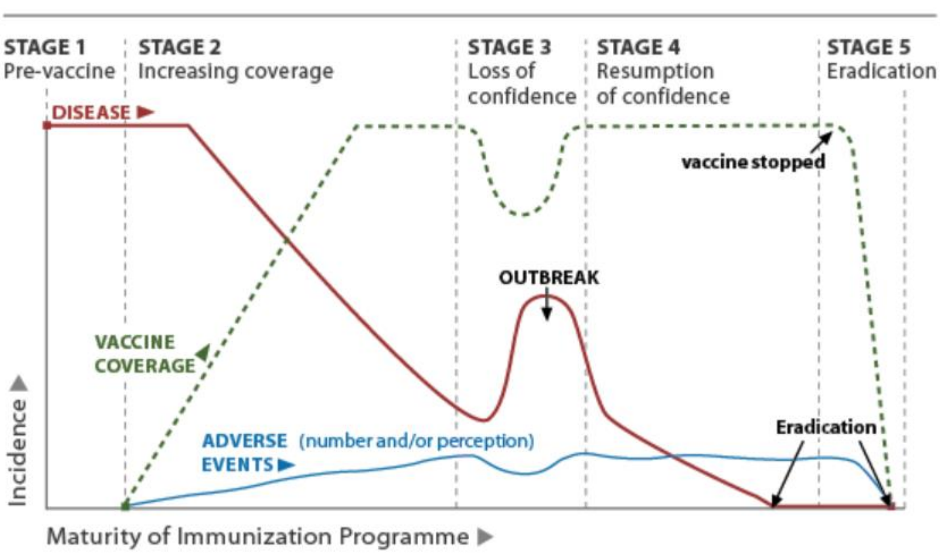

Figure 1. Natural evolution of a vaccination program from pre-vaccine to disease eradication. Reprinted from *Vaccine safety and false contraindications to vaccination*, by WHO/Europe [11].

Several communities have already felt the impact of the loss of confidence in some recommended vaccines. For example, in 2019 the U.S. experienced the highest number of measles cases since 1992. Most cases could be traced back to the New York outbreaks amongst communities with low vaccination rates [13]. Until a higher proportion of the population is vaccinated, outbreaks will continue to occur.

State exemptions are available for parents as well. As of right now, though all states have required vaccines for students except for medically necessary cases, 45 states have religious exemptions and 15 have philosophical exemptions [14]. Figure 2 illustrates the current exemption statuses of each state. Religious exemptions require vaccines to be against a tenant of one's faith, while philosophical exemptions are simply based on moral or personal beliefs. Some of these exemptions are currently under fire; in 2019, Washington removed philosophical exemptions, New York removed religious exemptions, and Maine removed both [14]. New York's removal happened in response to the measles outbreak. Exemptions often mean higher non-vaccination rates. Omer et al.'s 2006 study found that states that allow for personal exemptions had higher overall exemption rates, and states with more relaxed exemption requirements had a higher average number of vaccinations [15]. Removing or altering the easier exemption policies could mean higher vaccinations rates, and hopefully a future where eradication for more vaccines is possible.

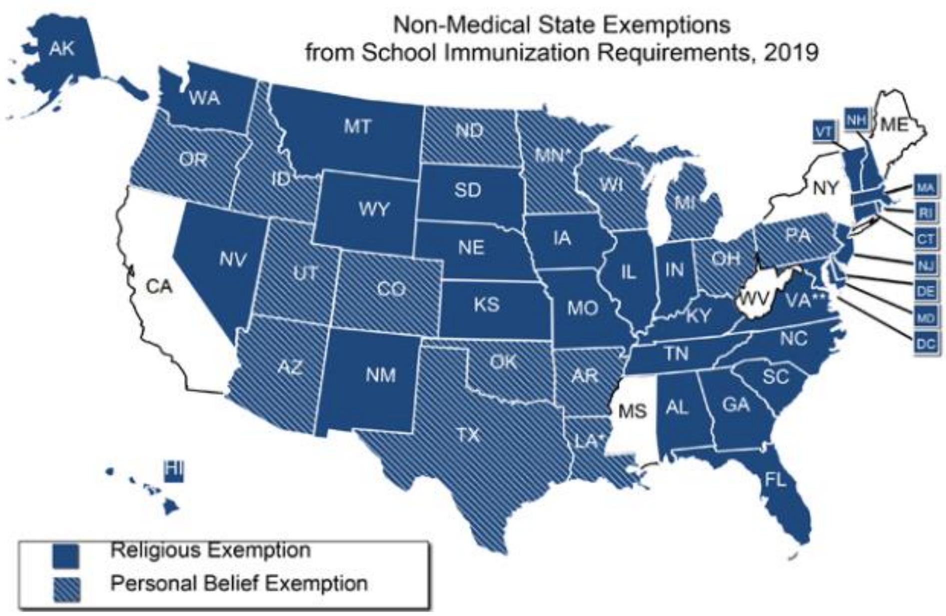

Figure 2. Map of United States and non-medical state exemption policies as of 2019. Reprinted from *Non-medical state exemptions from school immunization requirements, 2019,* by National Conference of State Legislatures [14].

In 2014, a group from the World Health Organization Strategic Advisory Group of Experts developed a working definition of vaccine hesitancy as a “delay in acceptance or refusal of vaccines despite availability of vaccine services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factor such as complacency, convenience, and confidence” [16]. This definition was meant to encompass the variety of reasons someone may be hesitant, including:

(1) concerns about the effectiveness and/or safety of vaccines,
(2) complacency when the perceived risk of a disease is low, or
(3) barriers to receiving a vaccine that may discourage seeking out vaccinations.

From this definition, it is easy to see that vaccine hesitancy is a complex issue with no easy solution. However, it is also a useful starting point for considering why people may not keep their children up to date on vaccinations.

Purpose

One of the main reasons for hesitancy is concerns about safety and effectiveness, so one of the most valuable resources for parents on the safety of vaccines is their child’s primary healthcare provider [17]. It is important that healthcare providers identify parents who may not trust vaccines or have concerns about vaccines so that they can spend the time needed to assuage their doubts. To that end, the goal of this paper is to explore demographics that are more likely to be vaccine hesitant and not fully up to date on vaccines. Previous studies have found that some of the major reasons for hesitancy are more often based on opinions than assessments; top reasons include safety concerns (such as the number of shots per visit) or fear of side effects, lack of knowledge on vaccines or not understanding the scientific evidence, and socioeconomic/cultural issues [17, 18]. Gust et al.’s 2008 study found that those who were white, younger, had a lower income, and had less education were most likely to have delayed their child’s vaccine schedule or had doubts about vaccines [19]. Using these previous results, I hypothesize that insurance status, income, number of children, mother’s education, mother’s age, marital status, and race are associated with a lower average number of vaccines for their child.

Methods

I am using 2018 data (n=28,971) from the CDC's National Immunization Survey that monitors vaccine coverage for children ages 19-35 months. The survey data provides individual-level information on demographics and vaccine coverage. I selected the child's age, number of children in the house, mother's education, mother's age, mother's marital status, family income, insurance status, race, and U.S. region to include as predictors in my models (table 1). I filtered out observations where there were missing values for a given vaccine due to the researchers being unable to reach the doctor, which brought the number of observations down to 15,333. I additionally removed observations from the same household so that each household was only represented one time in order to ensure independent observations, which further lowered the number of observations to 15,174.

My response variable is a binary yes/no variable for if the child is up to date on their vaccines. In this case, up to date is defined as 4+ DT-containing shots, 3+ polio-containing shots, 1+ measles-containing shots, 3+ HIB-containing shots, 3+ hepatitis B-containing shots, and 1+ varicella-containing shot at age 12+ months. This indicator does not consider rotavirus, mumps, rubella, or hepatitis A-containing shots that are also recommended by age 35 months [20]. I used logistic regression as my final model and chose $\alpha = 0.05$ as my cutoff for significance. After initially including all predictors of choice in my model, I removed variables one by one for those with a p-value greater than 0.05. After each variable was removed, I used a nested F-test to confirm that omitting that variable would not hurt the model. All analyses were performed in RStudio, version 1.2.5033.

Results

The data was evaluated with a logistic regression model using the child's age, number of children in the house, mother's education, mother's age, mother's marital status, insurance status, and U.S. region to predict the child's up to date status. The child's age is purely a control variable; based on regular vaccine schedules, children receive more total vaccines the older they are. The U.S. region was also used as a control variable to account for differences in location and general exemption policies. The number of children in the house has a strong association with up to date status after controlling for the other variables. For each additional child in the house, the odds of a particular child being up to date decreases by approximately 30% ($z = -9.9$, $p < 0.001$), holding age, mother's education, mother's age, marital status, insurance status, and region constant.

Several explanatory variables related to the mother are associated with the child's up to date status. First, the mother's education level has a significant association with the child's up to date status. For each additional level of education defined as less than 12 years, 12 years, some college, or college graduate, the odds of their child being up to date on vaccines increases by 13% ($z=4.7$, $p < 0.001$) holding all other variables constant. Second, the mother's age has a positive association with the child's up to date status. The odds of a child being up to date with a mother over 30 years old was 18% higher ($z = 3.4$, $p < 0.001$) as compared to children with younger mothers after accounting for all other variables. Third, the mother's marital status has a correlation with the child's up to date status. Compared to those who are married, the odds of the children of those who are not married decreases by 12% ($z = -2.3$, $p = 0.024$) after controlling for the other variables.

Additionally, the odds of a child being up to date varied with different insurance types. As compared to no insurance, having insurance is associated with greatly increased odds of being up to date after controlling for the other variables. Having Medicaid means the child's odds increase by 155% ($z = 9.0$, $p < 0.001$) compared to no insurance. Similarly, having other insurance such as military is associated with a 110% increase in the odds ($z = 6.1$, $p < 0.001$). Private insurance is associated with an even higher increase in the odds of 213% ($z = 10.6$, $p < 0.001$) as compared to no insurance.

Discussion

Conclusions

My results mostly align with my hypothesis. The results of the model confirm that insurance status, number of children in the household, mother's education, mother's age, and marital status all have an association with the odds of the child being up to date on a 4:3:1:3:3:1 vaccine schedule. In general, currently married mothers over 30 years old with higher education, fewer total children, and private insurance have higher odds of keeping their child up to date on vaccines. These findings are similar to previous studies examining demographics and delayed vaccine schedules [21, 22, 23]. Knowing the demographics of parents who are more likely to be vaccine hesitant is valuable for public health officials and healthcare practitioners. For example, launching public health campaigns that speak to certain groups or educating practitioners on how to effectively start conversations with vaccine hesitant parents could mean that more parents ultimately feel comfortable vaccinating their children. Previous studies have shown that some of the major reasons for hesitancy include safety concerns or simply a lack of knowledge, so being able to reach parents who are likely to be hesitant could make a large impact on their decisions regarding vaccinating their children.

The single most important predictor I found is insurance status. There is a huge disparity in the odds of a child without insurance being up to date and the odds of a child with private insurance being up to date. This indicates that the U.S. may be able to achieve even higher vaccination rates if more people have access to insurance and regular healthcare. Programs such as the Vaccines for Children program, which provides vaccines to children whose families may otherwise be unable to afford it, could be targeted as a way to improve vaccination rates [2].

Contrary to my original hypothesis, race and income do not have a noticeable impact on the child's up to date status. It is possible that insurance already captures what income could have contributed to the model; those with low incomes might be less likely to have good insurance coverage and thus have lower odds of keeping their children up to date on vaccines. While this goes against previous findings on racial disparities in vaccine attitudes, it could be because the data is predominantly white as shown in table 2 [19, 24].

Limitations

There are several limitations to my modeling process. One important potential limitation for my model is that there was no way to know why a certain child was not up to date. In general, my interpretations make the assumption that a child who is not up to date has parents who are vaccine hesitant. It could be the case that some children need medical exemptions or are even just a little behind schedule for a reason not related to vaccine distrust. It is also important to note that the data only represents families living in the United States with young children. These results cannot be extrapolated to other countries that may have different cultural considerations or healthcare systems.

Additionally, a large component of vaccine hesitancy is not based on demographics but opinions. Many studies examining vaccine hesitancy tend to focus on opinions and fears rather than demographics [16, 17]. My data did not include any such information, so I cannot make any assumptions about why a particular child is under vaccinated or unvaccinated based on parental opinions.

Future Considerations

While it is important to be able to identify parents who are more likely to be vaccine hesitant or outright anti-vaccines, it is also crucial to remember that those who are vaccine hesitant represent a broad range of people and are not one homogenous group. Further, vaccine hesitancy represents a spectrum of beliefs rather than one particular view on vaccinations. The anti-vaccination movement may seem to be a large movement, but only approximately 1% of parents are denying all of the recommended vaccines [7]. One third of U.S. parents are not staunchly anti-vaccine, but vaccine hesitant. That group is reachable; providing information and actively listening to and responding to their concerns and questions is a valuable way to assuage their fears [7]. Many vaccines have been around long enough that the U.S. is in stage 3 of the maturity of an immunization program, or fears of adverse events are starting to outweigh the fear of the disease itself. So long as vaccine hesitant parents aren't dismissed as resolutely anti-vaccine, it is still possible to have productive outreach programs and continue working towards eradication.

While most vaccines have existed long enough that many don't remember the impact of the diseases they prevent, the coronavirus pandemic has ushered in a new facet to the vaccine debate. Many are eagerly awaiting the vaccine so that life can get back to normal, but others believe that the possibility of mandatory vaccinations infringes on individuals' rights. COVID-19 is unusual in that we are still in stage 1, where no vaccine has been developed and the disease is running rampant. It may be the factor that pushes more states to remove some non-medical exemptions, or it may be what causes anti-vaxxers to fight even more fiercely for exemptions. It is possible that some states will make the vaccine mandatory, especially because *Jacobson v. Massachusetts* already established the legality of a state making a vaccination required [7]. While the coronavirus may become another disease that people eventually forget about, it is crucial to continuously combat vaccine hesitancy at all stages in the immunization life cycle.

Acknowledgements

First and foremost, a huge thank you to my advisor, Susan Huehn. Thank you so much for everything: enthusiastically taking me on as a second individual major advisee, sharing your connections so my project could flourish, helping me lay out realistic goals, and supporting me whenever I felt overwhelmed. My experience as an individual major and my time at St. Olaf has been greatly enhanced by you.

To all the wonderful professors who have helped me explore what I love – Julie Legler, Eric Fure-Slocum, Sharon Lane-Getaz, Marc David, Paul Roback, Melissa Mendez, Sara Clifton, Matt Richey, and more – thank you for bringing your passion of your field to the classroom and truly caring about your students every day. Learning from amazing professors is such a privilege and I am so grateful that I was able to explore my passions with such kind and caring people.

To my teammates, my coaches, and my friends and family, thank you for all the laughs and memories that have helped to shape me during my time at St. Olaf. I couldn't have done it without you.

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Appendix I: Relevant Tables

Table 1. All variables considered during initial phase of the project. "Total" was manually computed from other variables in the original dataset not mentioned in this table.

Name	Variable Role	Definition	Values
Age	Explanatory	Age category of child	1 = 19-23 months 2 = 24-29 months 3 = 30-35 months
Sex	Explanatory	Sex of child	0 = male 1 = female
Num_child	Explanatory	Number of children less than 18 years in household	1 = one child 2 = two to three children 3 = four or more
Educ	Explanatory	Education of mother	1 = <12 years 2 = 12 years 3 = > 12 years, non-college grad 4 = college grad
M_age	Explanatory	Mother's age group	1 = <=29 years 2 = >= 30 years
Marital	Explanatory	Marital status of mother	0 = married 1 = not currently married
Income	Explanatory	Family income categories	3 = $0 - $7.5K 4 = $7,501 - $10K 5 = $10,001 - $17.5K 6 = $17,501 - $20K 7 = $20,001 - $25K 8 = $25,001 - $30K 9 = $30,001 - $35K 10 = $35,001 - $40K 11 = $40,001 - $50K 12 = $50,001 - $60K 13 = $60,001 - $75K 14 = $75,001+
Race	Explanatory	Race of child	1 = white only 2 = black only 3 = other/multiple races
Insurance	Explanatory	Family's insurance status	Private, Medicaid, other Insurance, uninsured
Region	Explanatory	U.S. region	Northeast, South, Midwest, West
UTD	Response	Up to date flag for 4:3:1:3:3:1 by 36 months of age, excluding any vaccinations after interview date	0 = not UTD 1 = UTD
Total	Response	Total number of hepatitis A, hepatitis B, rotavirus, DT, HIB, polio, MMR, varicella, and seasonal flu-containing shots	Discrete values from 0 - 25 Median = 23

Table 2. Sample demographics in original data.

Variable	Labels	Count	Percent (%)
Age	19-23 months	8,326	28.7
	24-29 months	8,727	30.1
	30-35 months	11,918	41.4
Sex	Male	14,992	51.7
	Female	13,979	48.3
Num_child	1	7,968	27.5
	2-3	16,940	58.5
	4+	4,063	14.0
Educ	< 12 years	2,922	10.1
	12 years	5,237	18.1
	> 12 years, non-college grad	7,302	25.2
	College grad	13,510	46.6
M_age	<= 29 years	9,649	33.3
	>= 30 years	19,322	66.7
Marital	Married	20,355	70.3
	Not currently married	8.616	29.7
Income	$0 - $7.5K	1,001	3.5
	$7,501 - $10K	954	3.3
	$10,001 - $17.5K	1,303	4.5
	$17,501 - $20K	1,163	4.0
	$20,001 - $25K	1,067	3.7
	$25,001 - $30K	1,304	4.5
	$30,001 - $35K	888	3.1
	$35,001 - $40K	1,222	4.2
	$40,001 - $50K	1,791	6.2
	$50,001 - $60K	1,612	5.6
	$60,001 - $75K	2,276	7.9
	$75,001+	11,990	41.4
	Don't know/refused	2,400	8.3
Race	White only	21,108	72.9
	Black only	3,120	10.8
	Other + multiple	4,743	16.4
Insurance	Private	7,966	27.5
	Medicaid	5,851	20.2
	Other	1,324	4.6
	Uninsured	516	1.8
	Missing	13,314	46
Region	Northeast	5,147	17.8
	Midwest	5,710	19.7
	South	12,204	42.1
	West	5,910	20.4
UTD	Not UTD	3,003	10.4
	UTD	12,654	43.7
	Missing	13,314	46.0

Table 3. Coefficient estimates, confidence interval, test statistic, and p-value for final logistic regression model.

	Estimate	**2.5%**	**97.5%**	**Z value**	**P value**
(Intercept)	-0.035	-0.37	0.30	-0.21	0.83
Age	0.28	0.23	0.34	10.65	< 0.001
Num_child	-0.36	-0.43	-0.29	-9.87	< 0.001
Educ	0.12	0.073	0.18	4.73	< 0.001
M_age	0.17	0.071	0.27	3.38	< 0.001
Marital	-0.13	-0.24	-0.017	-2.27	0.024
Insurance Medicaid	0.94	0.73	1.14	9.00	< 0.001
Insurance Other	0.74	0.50	0.98	6.13	< 0.001
Insurance Private	1.14	0.93	1.35	10.63	< 0.001
Region Northeast	0.12	-0.038	0.25	1.45	0.15
Region South	0.06	-0.061	0.17	0.95	0.34
Region West	-0.25	-0.38	-0.12	-3.76	< 0.001

Appendix II: Plots from Exploratory Data Analysis

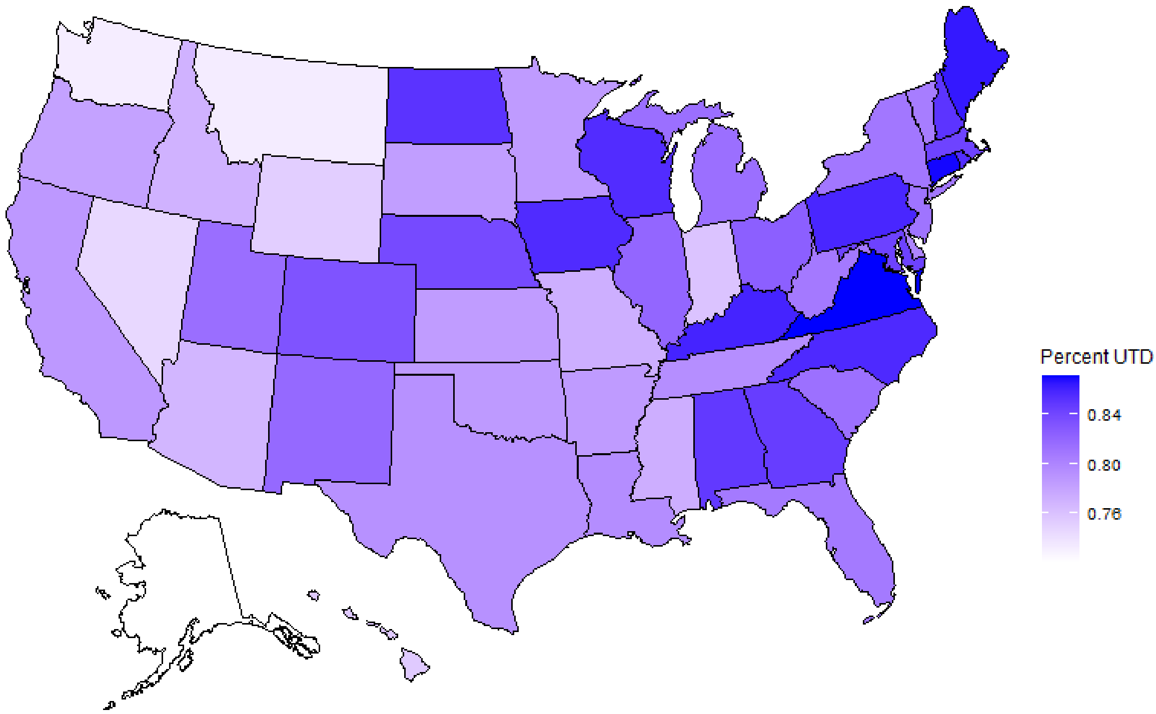

Figure 3. Map of the United States and up to date (UTD) percentages of children by state.

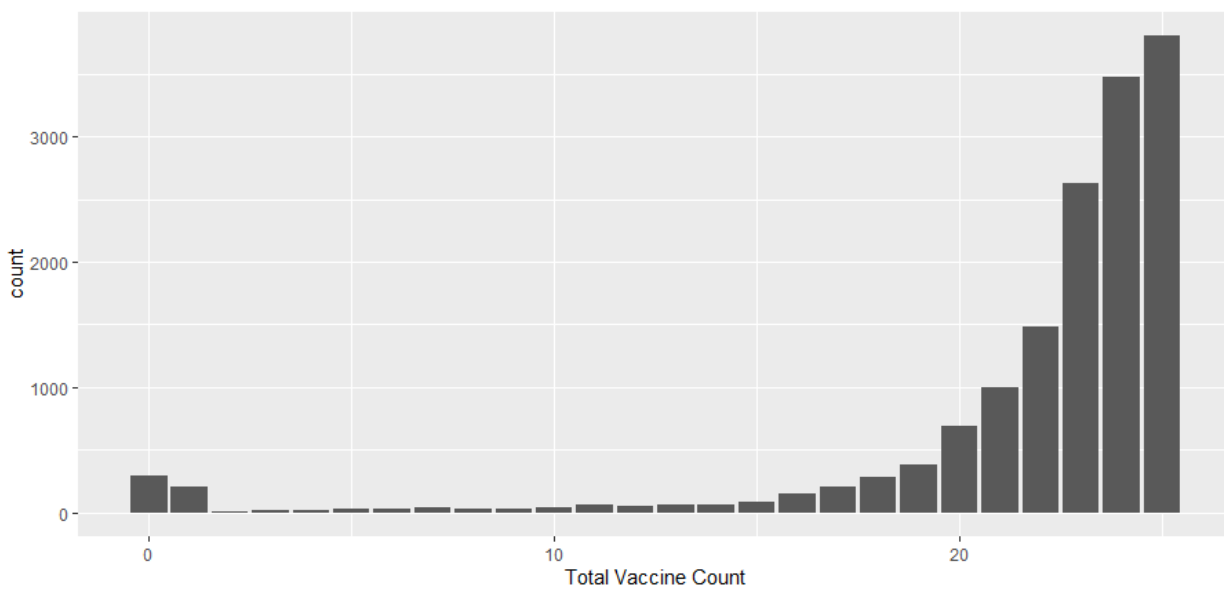

Figure 4. Histogram showing distribution for each child's total vaccine count. Range is from 0 to 29 cumulative doses of standard vaccines.

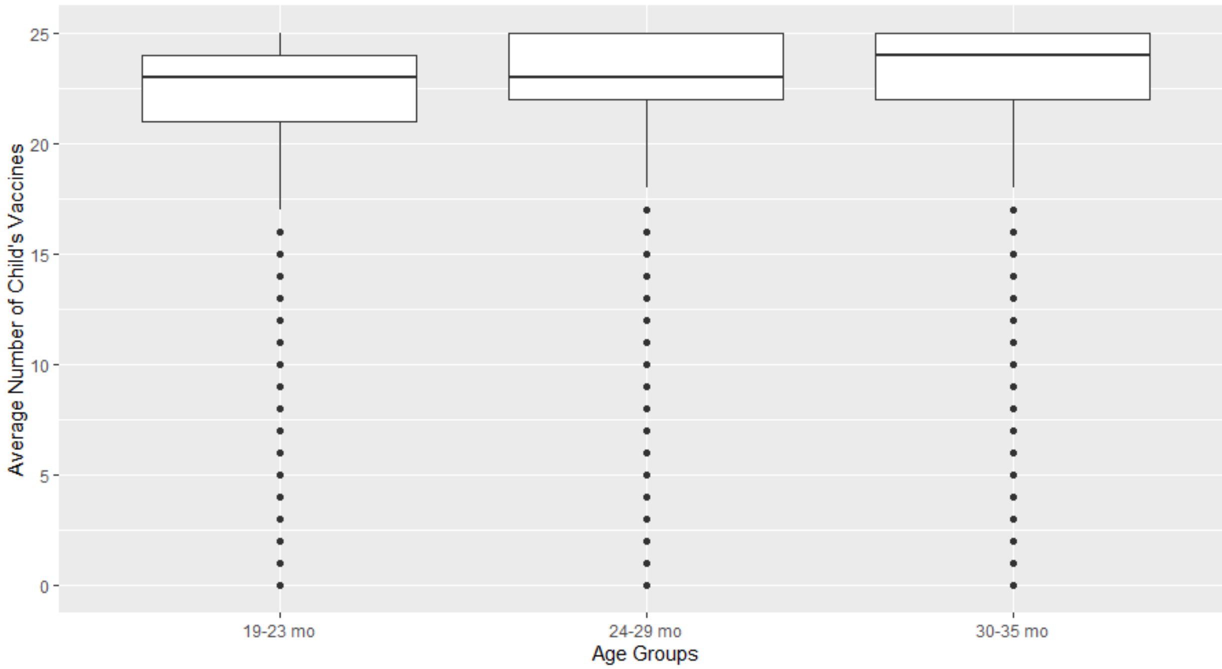

Figure 5. Boxplot showing distribution of average total vaccine count by age group.

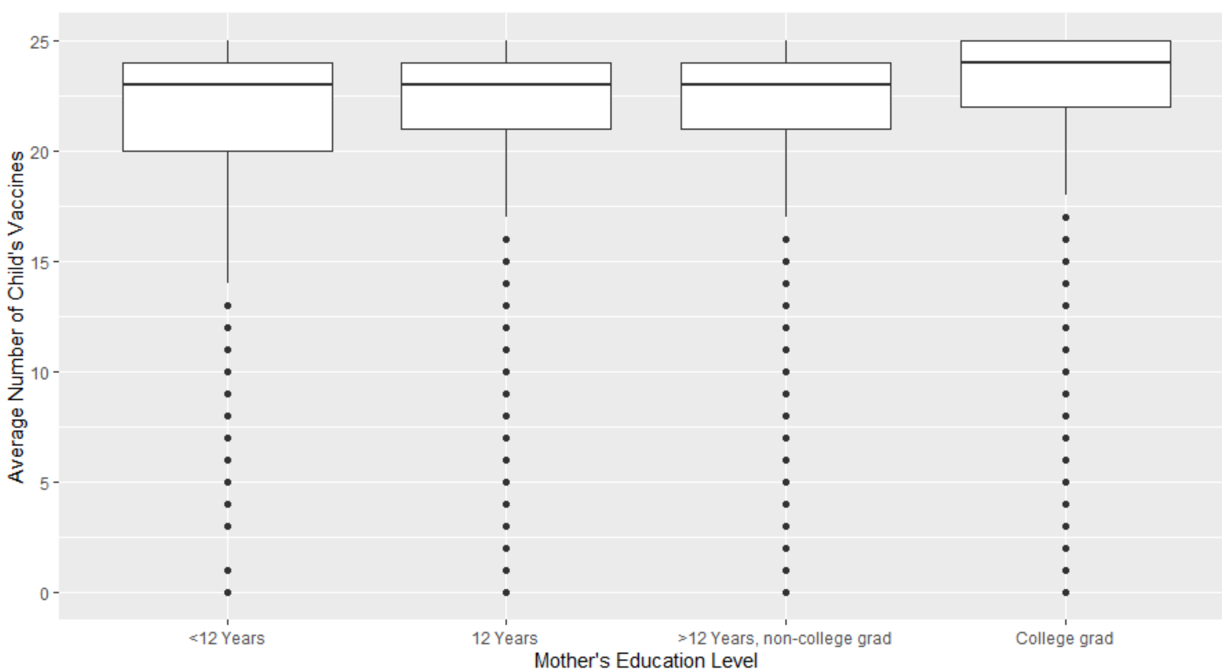

Figure 6. Boxplot showing distribution of average total vaccine count by mother's education level.

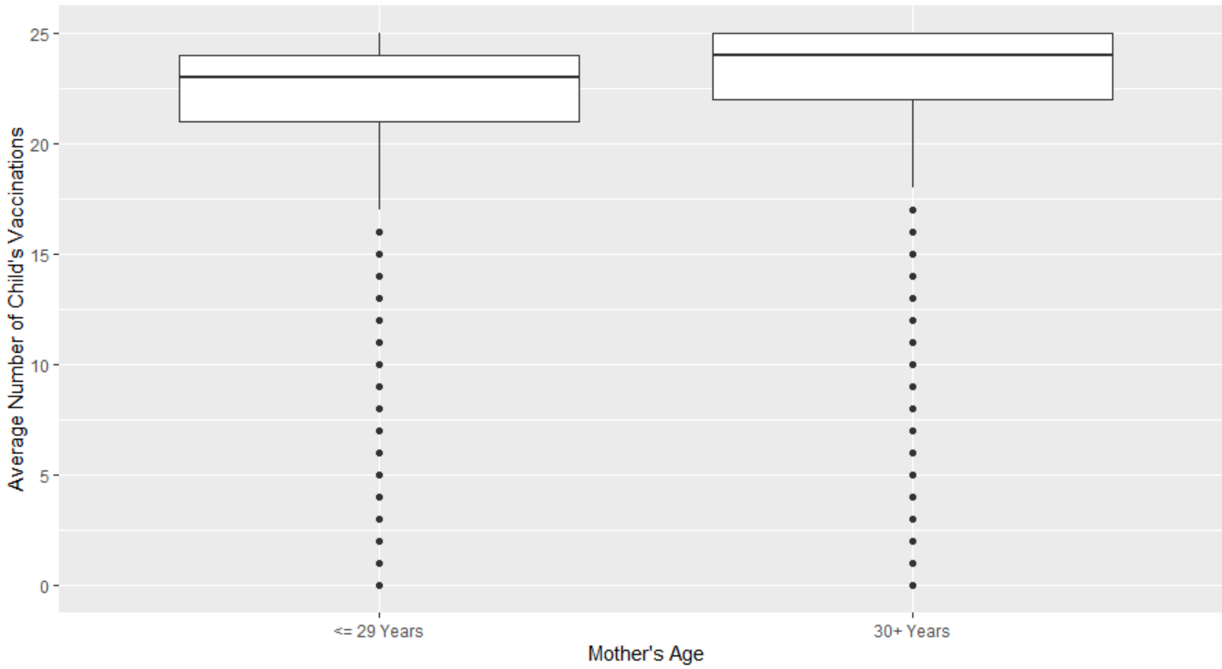

Figure 7. Boxplot showing distribution of average total vaccine count by mother's age group.

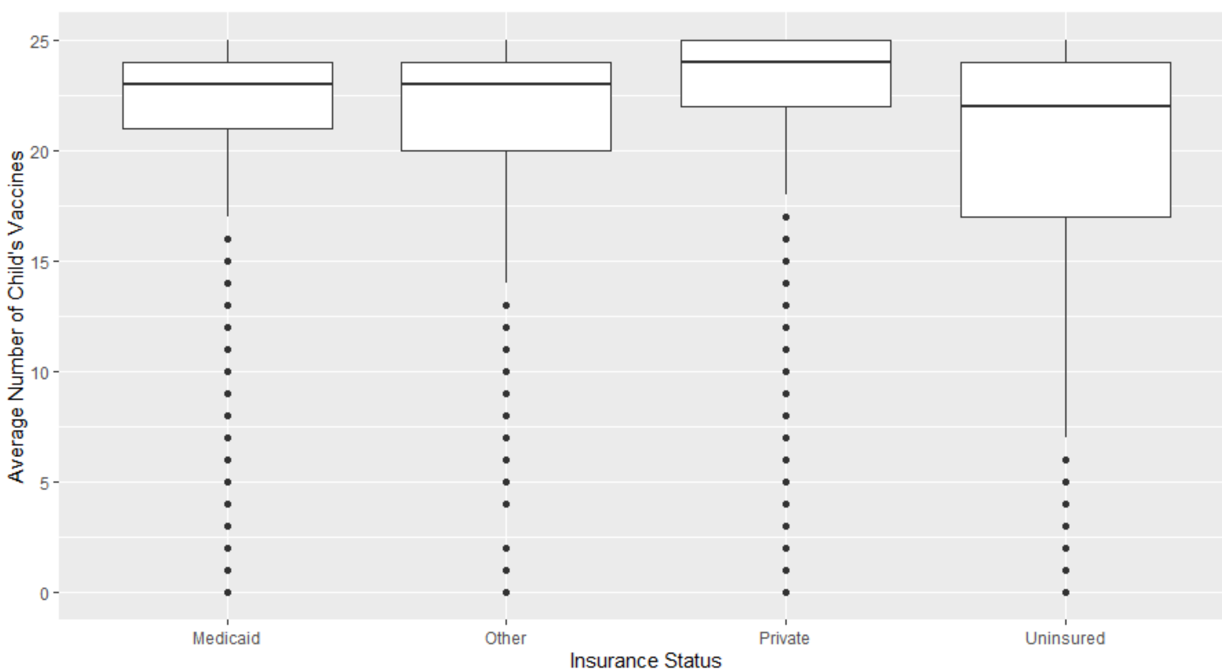

Figure 8. Boxplot showing distribution of average total vaccine count by family's insurance status.

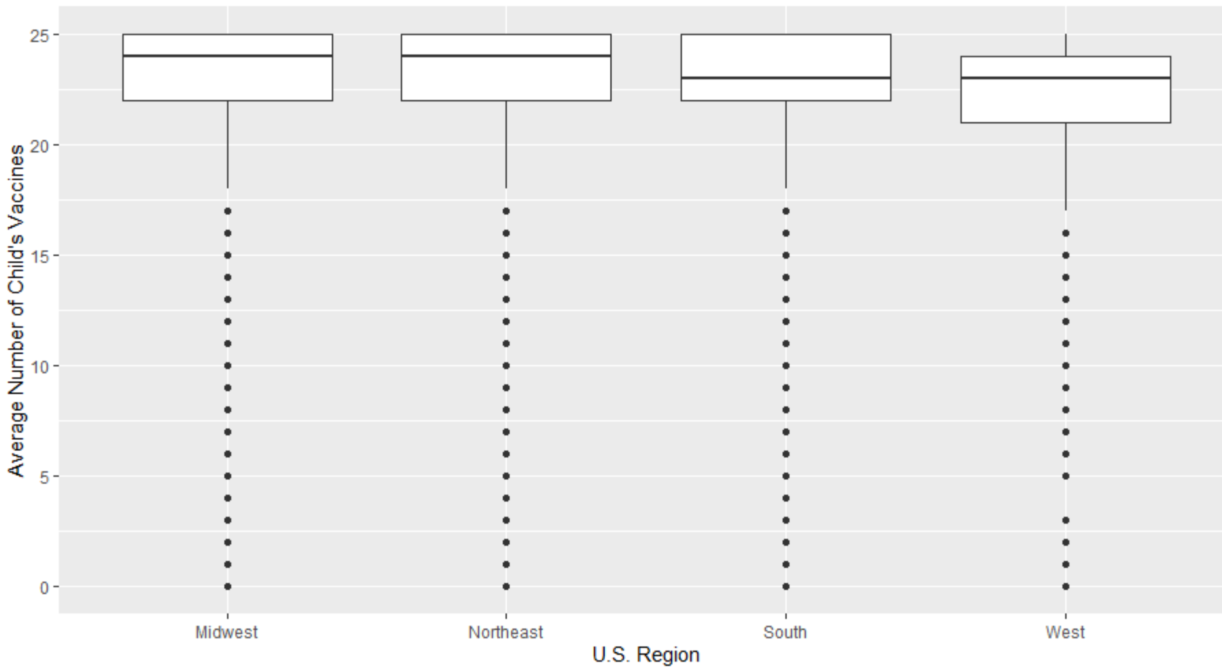

Figure 9. Boxplot showing distribution of average total vaccine count by U.S. region where family lives.

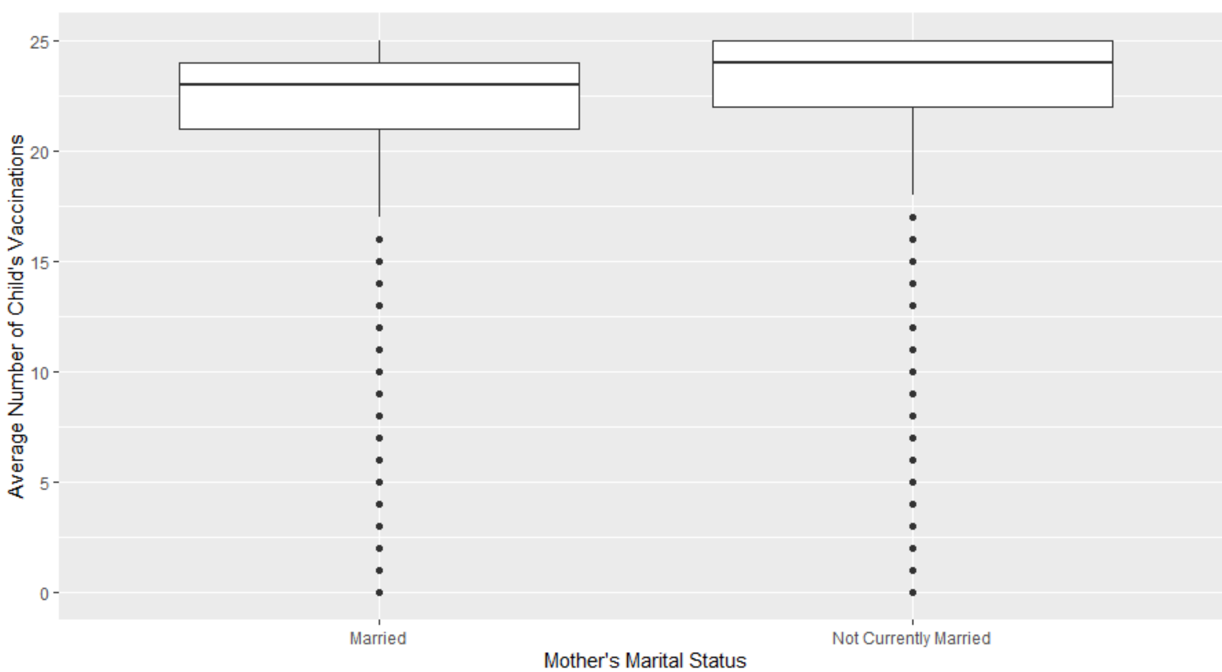

Figure 10. Boxplot showing distribution of average total vaccine count by mother's marital status.