ROTAVIRUS IMMUNIZATION AMONG CHILDREN: EXAMINATION OF COVERAGE AND IMPACT IN THE UNITED STATES

By

NISHA C. JANI

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ABSTRACT OF THE DISSERATION

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NISHA C. JANI, MPH

Dissertation Director:

William Halperin MD, DrPH, MPH

Context: Rotavirus is the most common cause of diarrhea and vomiting in infants and young children. The implementation of the rotavirus vaccination program in the United States has resulted in a marked reduction in diarrhea hospitalizations and related hospital costs among children nationally. There are several existing surveillance systems used by Public Health related to Rotavirus in the United States. Disease incidence can be tracked through medical records and passive reporting. The Vaccine Adverse Event Reporting System (VAERS) serves as an early warning system to ensure the safety of vaccines administered in the United States. Surveillance of national vaccine coverage is captured by the National Immunization Survey (NIS). The NIS is conducted annually and surveys households in the United States with children of ages between 19 and 35 months at the time of the interview. Vaccine coverage data can be a total in the determination of children at highest risk of under immunization. Examination of coverage rates by birth cohort can also supply valuable information regarding areas of need. The various existing surveillance systems can be incorporated into the larger Deming Cycle, as known as the

PDSA cycle. This Total Quality Management (TQM) can be applied to public health to focus on change and improvement at the procedural level.

Specific Aims: The aims of this dissertation were to examine rotavirus immunization coverage in among children in the United States. (1) Review the application of Total Quality Management (TQM) in public health practice and the implementation regarding the Rotavirus Vaccine United States of America. (2) Examination of demographic and health related risk factors among children who are not up-to-date with their rotavirus immunizations (3) Comparison of immunization rates cross sectionally and by birth cohort.

Methods: The first section examined current surveillance systems for the Rotavirus Vaccine. In particular focusing on the role of TQM and surveillance loops that can lead to the procedural improvements in public health practice. The data used for the analysis of the National Immunization Survey (NIS) for the years 2008-2014. Trends in rotavirus vaccination coverage were examined in children 19-35 months of age residing in the United States to assess changes in vaccine uptake in specific groups of participants. The primary outcome measure for this study is participant's rotavirus vaccination status. Descriptive analyses were performed among participants. Bivariate associations for all the risk factors by Rao Scott χ^2 were examined. Multivariable logistic regression was used for the binary up-to-date status for rotavirus vaccination.

Results: The overall coverage rates for rotavirus vaccination increased progressively across the NIS data collection years from 2010 to 2014 (59.2% to 71.7%) and across birth cohorts 2007-2009 (53.8% to 70.7%). The distribution of the covariates was consistent in both approaches. During both study periods children who were first born had greater odds of under immunization when compared with children born at a later birth order with OR =1.14 (CI 1.13-1.14) in NIS year 2010 and OR =1.21 (CI 1.05-1.39) among children born in 2010. A child being up to date with the 4:3:1:3:3:1 immunization series was shown to be more likely to have full coverage of rotavirus vaccination as well in each year: OR=0.32 (95% CI 0.32-0.32) in NIS year 2010 versus OR=0.20 (95% CI 0.20-0.20) in NIS year 2014. Likewise, this trend was evident when assessing the participants by year of birth. A child being up to date with this same six vaccine series was shown to be more likely to have full coverage of rotavirus vaccination in each year: OR=0.51 (95% CI 0.45-0.58) in birth year 2010 versus OR=0.31 (95% CI 0.26-0.36) in birth year 2012. The risk among children who live in households below the national poverty line decrease compared with households with incomes that lie above the national poverty line: OR =0.99 (95% CI 0.98-0.99) in 2010 versus OR =0.64 (CI 0.64-0.64) in 2014. The risk among children who live in households below the national poverty line decrease compared with household with incomes that lie above the national poverty line: OR =0.99 (95% CI 0.98-0.99) in 2010 versus OR =0.64 (CI 0.64-0.64) in 2014.

Conclusion: Surveillance is a core function of public health. It is the ongoing, systematic collection, analysis, and interpretation of health data which is essential to the planning and implementation of public health practice. To be truly effective it needs to include a

continuous ongoing system. One existing surveillance system for Rotavirus pretains to vaccine coverage. The National Immunization Survey is the primary source of vaccine estimates. It is conducted annually jointly by National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). The objective is to provide household, population-based, state and local area estimates of vaccination coverage among children 19-35 months of age. It assess the cumulative incidence of vaccine coverage for 14 childhood vaccines. The vaccines are selected based on recommendations from the Advisory Council of Immunization Practice (ACIP).

Rotavirus vaccine coverage rates have steadily increased annually. The comparison of the two different approaches of analysis show that non stratified analysis can give an inaccurate image of coverage rates. For instances, poverty appears to be confounded by year of birth. Therefore it is important to take year of birth into account since trends may not be similar when looking at the two different types of sequential cross sectional survey analysis.

ACKNOWLEDGEMENT

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INTRODUCTION

Background

Rotavirus is the most common cause of diarrhea and vomiting in infants and young children. [1] In the 1990s through early 2000s, rotavirus was responsible for more than 400,000 physician outpatient visits, 200,000 Emergency Department visits, and 55,000 to 70,000 hospitalizations. [2] Rotavirus is a double-stranded RNA virus transmitted by the fecal oral route. The incubation period ranges from one to three days. Symptoms include fever, vomiting, and watery diarrhea. Abdominal pain may also occur. The symptoms generally persist for three to nine days. Immunity to repeated rotavirus infection is incomplete, but repeat infections tend to be less severe than the original. There is no specific antiviral therapy available, however, fluids and electrolytes are given to prevent or correct dehydration. [1]

Prior to the introduction of the Rotavirus vaccine in 2006, a majority of children would be affected before 5 years of age.[3] By 2008, the Advisory Committee on Immunization Practices (ACIP) recommended Rotarix® and RotaTeq® for routine rotavirus vaccination for infants. Two or three doses of live oral rotavirus vaccines are recommended at ages 2, 4, and 6 months concurrently with other vaccines given at these ages.[4] The vaccines have high levels of efficacy against rotavirus gastroenteritis of any severity, 74% with RotaTeq and 87% with Rotarix; for severe rotavirus gastroenteritis, the efficacy was 98% and 96%, respectively.[4]

Surveillance of Disease Incidence

Public Health surveillance is a core function of modern public health.[5] It is the ongoing, systematic collection, analysis, and interpretation of health data, essential to the planning, implementation and evaluation of public health practice. It is closely integrated with the dissemination of these data to those who need to know and linked to prevention and control includes a continuous and systematic collection, analysis, and interpretation of health-related data [6] Surveillance can be conducted either actively or passively. Surveillance can be conducted either actively or passively.

The implementation of the rotavirus vaccination program in the United States has resulted in a marked reduction in diarrhea-related hospitalizations and associated hospital costs among children nationally. [7-9] An eighteen-state analysis of hospital discharge data for children under five years of age has indicated a forty-five percent decrease in the median rate of gastroenteritis hospitalization in 2008 compared with the years 2000-2006. [7] When the state-specific rates are examined, reductions in acute gastroenteritis hospitalizations are evident; however, the magnitude of the reductions vary greatly from state to state. The rate of acute gastroenteritis hospitalizations in 2008 ranged from 36.7 per 10,000 children in Maine to 98.6 per 10,000 in West Virginia. The difference from the period 2000-2006 and 2008 was a reduction of 17.1% in Arizona and of 61.3% in South Carolina.[8]

Surveillance of Vaccine Efficacy

The Vaccine Adverse Event Reporting System (VAERS) was established in 1990 to serve as an early warning system to ensure the safety of vaccines administered in the United States. The VAERS surveillance program is run by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA). The goals are to detect adverse events that happen after vaccination, monitor increases in side effects, identify potential patient risk factors for particular types of health problems related to vaccines, surveillance for unexpected or unusual patterns in adverse event reports, and assess the safety of newly licensed vaccines.

Approximately 30,000 VAERS reports are filed each year.[10] The data is obtained by reports received from any individual who either administers or receives a licensed vaccine in the United States. After the administration of a vaccine an adverse event can be reported even if it is uncertain to be caused by the vaccine. About 85-90% of the VAERS reports describe mild side effects associated with the rotavirus vaccines, such as fever, arm soreness, and crying or mild irritability. [10] If aggregate VAERS data identifies a vaccine safety signal, scientists may conduct further investigations to assess if the vaccine represents an actual risk.

A serious concern associated with rotavirus vaccines has been intussusception, a condition in which a segment of the intestine slides into an adjacent part of the intestine. This ‘telescoping’ often blocks food or fluid from passing through. If untreated this can lead to perforation of the bowel, infection, and death of the bowel tissue.[11] An assessment of VAERS data from 2006-2012 noted a clustering of intussusception events three to six days after dose one. Scientists have concluded that the benefits outweigh the low-level risk of intussusception.[12]

Surveillance of Vaccine Coverage

The National Immunization Survey (NIS) is the primary source for national vaccine coverage. The NIS is conducted jointly by the National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). NIS estimated that rotavirus vaccine coverage nationally was 68.6 percent in 2012. This marks an almost 14 percent increase from 2010, however, the coverage rates are lower than those for other ACIP recommended vaccines.[13-15]

The NIS is conducted annually and surveys households in the United States with children between 19 and 35 months of age at the time of the interview. The purpose of this cross-sectional design is to determine the vaccine coverage for participating child at that one point in time. This is irrespective of the actual age at which the child received the vaccine; it is only required that they are up-to-date at the time of the interview. Cross-sectional designs are valuable for providing information regarding overall coverage rates. However, this approach may not be ideal when assessing coverage rates for newly introduced vaccines.

Factors such as race, maternal factors, and access to medical care have been reported to be associated with under vaccination of children.[16-18] New vaccine have additional barriers to uptake due to misconceptions and/or lack of knowledge[19] Assessing immunization coverage in a newly introduced vaccine can provide information regarding groups requiring support to improve immunization rates and be used to monitor shifts, if any, over time as familiarity increases. In theory, each birth year group could an increased likelihood of receiving a timely immunization due to greater availability, increased physician knowledge, and increased familiarity with the vaccine. Analysis of immunization coverage by birth year may give researchers a better picture of the true uptake of a new vaccine and the children at highest risk of under immunization.

Surveillance Based on Total Quality Management

Total Quality Management (TQM) can be applied to public health to focus on improvement at the procedural level. A key aspect of TQM is the Deming Cycle, also known as the PDSA Cycle, a core principle of continuous quality improvement. This was based on thoughts introduced to Deming by his mentor Walter Shewhart.[20] The PDSA cycle is made up of four steps: plan, do, check and act.[20] First, one must recognize an opportunity and plan the new program or change. Then the new program/change should be implemented. Subsequently, it is necessary to study to see how the previous step conforms to the plan and act on what has been learned. It requires review of the action, analysis of the results and identifying what has been learned. Lastly, action should be taken based on what was learned in the check step. Determining whether the change was successful or an alternative plan should be implemented starts the cycle again. Other surveillance cycles associated with identification of disease, adverse events, and vaccine coverage can be incorporated into this total quality management approach to make improvements in overall reduction of Rotavirus.

Specifics Aims

This dissertation will examine rotavirus immunization coverage among children in the United States. It will assess the risk factors for underimmunzation and consider alternative methods to increasing vaccine uptake for rotavirus. Following are the specific aims.

Manuscript I - Application of Total Quality Management in Public Health Practice: Rotavirus Surveillance in the United States

1. Assessment of Total Quality Management in public health.
2. Application of the PDSA model in Rotavirus Vaccine Initiatives.

Manuscript II Examination of Rotavirus Vaccine Coverage among NIS Participating Children in the USA

1. Assess variations in rotavirus vaccine coverage cross-sectionally in five distinct NIS survey years.
2. Examine demographic and health related risk factors among children who are not up-to-date with their rotavirus immunizations.

Manuscript III Birth Cohort Analysis of Rotavirus Vaccine Coverage in the USA, 2007-2009

1. Assess the variations in rotavirus vaccine coverage by birth cohort in five distinct NIS survey years.

2. Exam demographic and health related risk factors among children who are not up-to-date with their rotavirus immunizations by birth cohort.

3. Comparison of immunization rates cross-sectionally (children from the 2010, 2011, 2012, 2013, and 2014 NIS) and by birth cohort (children born in 2007, 2008, and 2009)

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Manuscript I: Application of Total Quality Management in Public Health Practice:

Rotavirus Vaccine Coverage in the United States

INTRODUCTION

Public health surveillance is a core function of modern public health which has evolved over the years.[1] The surveillance of vaccine preventable diseases and coverage has greatly changed since the initial days of the small pox vaccine. When Edward Jenner introduced this vaccination in the late 1700s the process was limited to the distribution of vaccine.[2] There lacked a systematic approach to assess overall coverage and effectiveness.

The 1963 paper The Surveillance of Communicable Diseases of National Importance was an introduction to current surveillance.[3] In this paper Alexander Langmuir notes the importance of a systematic method which involves collecting data, analysis, and then usage. He was able to use epidemiology and surveillance to affect changes in public health policy. For instance, in late 1970s there was intense use of surveillance in the transmission of Measles in the United States.[4] This surveillance was impactful and guided the determination of the ideal age at measles immunization, the implementation of measles vaccination policy among military recruits, college entry immunizations, and booster dose of measles vaccine was added to the national guidelines.

The idea of Total Quality Management was introduced by Walter Shewart and expanded upon by W. Edwards Deming. [5] They created many of the most important ideas of quality control such as the PDSA cycle. This cycle is a tool for management and planners to have the knowledge they need to recognize when a problem is the result of an isolated glitch or fluctuation in an otherwise well-run organization; as opposed to when it is the result of deep-rooted systematic problems. [6]

What is currently missing in public health dialogue in reference to childhood immunizations and vaccine preventable diseases is the incorporation public health surveillance and TQM. There are many established surveillance systems currently in place however there is much to gain from the incorporation of TQM. These surveillance systems are all ongoing going processes in one larger system with the fundamental goal of increasing quality.

PUBLIC HEALTH SURVEILLANCE - DO, ANALYZE, AND USE

Public health surveillance is a core function of modern public health.[7] It is the ongoing, systematic collection, analysis, and interpretation of health data; essential to the planning, implementation and evaluation of public health practice. It is closely integrated with the dissemination of these data to those who need to know linked to prevention and control includes a continuous and systematic collection, analysis, and interpretation of health-related data.[8]

Alexander Langmuir wrote the landmark paper, The Surveillance of Communicable Diseases of National Importance, and has been said to have fathered Public Health Surveillance. In the paper, he addressed how surveillance can be used to address specific public health problems. An example is the 1955 Cutter Incident. [9] During this event 200,000 people infected by live virus polio. This led to 70,000 ill, 200 permanently paralyzed, and 10 deaths.[10] The Epidemic Intelligence Service (EIS) officers investigated every aspect of the outbreak including the disease onset, prior polio vaccination, and type of vaccines. It was later determined that the cases were caused by a contaminated batch of vaccines due to single manufacturer, Cutter Laboratories, in Berkeley, California.[9] Langmuir oversaw the prediction of expected size of the epidemic and the number of secondary cases that would occur.

Langmuir led to an increased focus on the use of epidemiology and surveillance to affect changes in public health policy. He oversaw surveillance in the transmission of Measles in the United States. This surveillance had an effect of determination of the age at measles immunization, the implementation of measles vaccination policy among military recruits, college entry immunizations, and booster dose of measles vaccine was added to the national guidelines. Additionally, during this time period there was the development of national surveillance systems. United States had no national surveillance system for any disease prior to the middle of the 20th century. First systems in place were Malaria surveillance system, Polio (1955), and Influenza (1957).[11] Langmuir pioneered work on the key is collaboration between federal, state, and local governments. Important model which now used globally.

TOTAL QUALITY MANAGEMENT

During this same time period Total Quality Management (TQM), an approach that views continuous improvement as an ongoing process instead of short term goals, gained more popularity. Walter Shewhart increased awareness of the TQM method of statistical analysis. It is to help minimize variation, control quality, and stress the importance of consistency. During his work at the Hawthorne Plant in Illinois he helped discover the "Hawthorne Effect".[12] This is the alteration of behavior by a subject of a study due to their awareness of being observed. An important contribution and a core principle of continuous quality improvement was the PDSA cycle.

The PDSA cycle is made up of four steps for improvement: plan, do, check and act.[13] As shown in Figure 2 it describes that organizations should first recognize an opportunity and plan the new program or change. Then the new program/change should be implemented. Subsequently, it is necessary to check to see how it conforms to the plan and act on what has been learned. It is needed to review the action, analyze the results and identify learning points. Lastly, action should be taken based on what you learned in the check step. It needs to be determined if the change was successful or an alternative plan should be implemented because the cycle starts again from the beginning.

Deming's work increased awareness on a method of statistical analysis that helped minimize variation and control the quality and consistency of a product.[14] All systems are subject to some inconsistency. These inconsistencies lead to a decline in results making it difficult to predict how its systems and strategies will perform. These inconsistencies can cause a degradation of quality and inevitably, negative results. The PDSA cycle is a tool for management and planners to have the knowledge they need to recognize when a problem is the result of an isolated glitch or fluctuation in an otherwise well-run organization; as opposed to when it is the result of deep-rooted systematic problems.[15]

BRINGING TOGETHER PUBLIC HEALTH SURVEILLANCE AND TQM

In nature TQM is an ongoing process. That continues and if done correctly the quality will improve over time. Figure 3 provides a visual description of the incorporation of TQM and surveillance. The entire train which is moving is representative of TQM. It continues to proceed uphill and overtime leads to better quality. Each wheel corresponds with a distinct surveillance system with its own PDSA cycle. Basically, we have our distinct surveillance systems in place for different aspects of childhood immunizations, ranging from disease incidence, vaccine side effects, to vaccine coverage. A PDSA is needed for each system to ensure that they are functioning effectively. However, when we take a step back we see that fundamentally they are all components which will lead to the same goal. Optimal quality for rotavirus can be found once all of the components are improved which leads to reduced incidence of disease, reduced adverse vaccine effects, and increased immunization coverage in the population.

ROTAVIRUS

Now we will discuss the benefit of this approach in reference to Rotavirus. Rotavirus is the most common cause of diarrhea and vomiting in infants and young children. This double-stranded RNA virus is transmitted by the fecal oral route.[16] Symptoms include fever, vomiting, and watery diarrhea. Immunity from infection is incomplete, but repeat infections tend to be less severe than the original infection.[17]

In the 1990s through early 2000s, RV was responsible for more than 400,000 outpatient physician visits, 200,000 Emergency Department visits, and 55,000 to 70,000 hospitalizations in the United States.[18] Since its introduction, the Rotavirus vaccine has had a substantial effect in reducing hospital admissions of young children because of diarrhea.[19-21] A reduction in hospitalizations due to diarrhea from 2001-2006 compared to 2007-2008 of 33% among children five years of age and below has been reported.[22] Two or three doses of live oral rotavirus vaccine is recommended at ages two, four, and six months concurrently with other vaccines given at this age.[23-24] The number of doses is dependent on the product received.

In the next sections, we will review surveillance systems currently in place and then apply the PDSA cycle to one component to show the possible use and real-world application.

IMMUNIZATION SURVEILLANCE SYSTEMS

Surveillance of Disease Incidence

Surveillance can be conducted either actively or passively. Since, rotavirus is not a nationally reportable disease, hospitalizations can be used to assess disease impact. The implementation of the rotavirus vaccination program in the United States has resulted in a marked reduction in diarrhea hospitalizations and related hospital costs among children nationally. An eighteen-state analysis of hospital discharge data for children under five years of age has indicated a forty-five percent decrease in the median rate of gastroenteritis hospitalization in 2008 compared with the years 2000-2006.[25] When the state-specific rates are examined, it demonstrates a reduction in acute gastroenteritis hospitalizations; however, the magnitude of this change varies greatly state to state. In a study looking at eighteen states, the rate of acute gastroenteritis hospitalizations in 2008 ranged from 36.7 per 10,000 children in Maine to 98.6 per 10,000 in West Virginia. The difference from the period 2000-2006 and 2008 was a reduction of 17.1% in Arizona and of 61.3% in South Carolina.[26]

Surveillance of Vaccine Efficacy: The Vaccine Adverse Event Reporting System (VAERS) was established in 1990 to serve as an early warning system to ensure the safety of vaccines administered in the United States. The VAERS surveillance program is run by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA). The goals are to detect adverse events that happen after vaccination, monitor increases in side effects, identify potential patient risk factors for particular types of health problems related to vaccines, watch for unexpected or unusual patterns in adverse event reports, and assess the safety of newly licensed vaccines.

Approximately 30,000 VAERS reports are filed each calendar year.[27] The data is obtained by reports received from any individual who either gives or received a licensed vaccine in the United States. After the administration of a vaccine an adverse event can be reported even if it is uncertain to be caused by the vaccine. About 85-90% of the reports describe mild side effects such as fever, arm soreness, and crying or mild irritability. [28] After assessing the aggregate VAERS data, if a vaccine safety signal is identified scientists may conduct further research to assess if the vaccine represents an actual risk.

A serious concern associated with rotavirus vaccines has been intussusception. This is a condition in which a segment of the intestine slides into an adjacent part of the intestine. This ‘telescoping’ often blocks food or fluid from passing through. If untreated this can lead to perforation of the bowel, infection, and death of the bowel tissue.[29] An assessment of VAERS data from 2006-2012 noted a persistent clustering of intussusception events three to six days after dose one. It is thought that this low-level risk of intussusception outweighs the documented benefits.

Surveillance of Vaccine Coverage: The National Immunization Survey (NIS) is the primary source for national vaccine coverage. The NIS is conducted jointly by the National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). NIS estimated that rotavirus vaccine coverage nationally was 68.6 percent in 2012. This marks an almost a 14 percent increase from 2010, however, the coverage rates are lower than those for other ACIP recommended vaccines.[30-31]

APPLICATION OF THE TOTAL QUALITY MANAGEMENT IN CHILDHOOD IMMUNIZATIONS

As demonstrated in the previous section there are several sources where one can obtain data of Rotavirus Vaccination Coverage among children. The underlying issue with all of these systems is the lack of complete coverage data for all children on a state or local level. This degree of data is vital is one wants to accurately assess immunization uptake and coverage. The PDSA model can be applied to this issue.

Plan: First the opportunity for change must be recognized. In this situation, we understand that there are gaps in our data collection process for childhood immunizations. Therefore, a new plan or program is needs to be created to address this issue. The IIS is a valuable tool for capturing necessary immunization related data. A national IIS would create a repository of person level data for immunization history, demographics, and health care utilization. This system would ideally be able to replace the NIS, individual state IIS, and school audit reporting needs.

Do: Next, this national IIS needs to be implemented. It would be most effective if a federal agency would create and oversee this standardized IIS. This would also entail a large-scale education component to ensure IIS user understand the purpose of this revised system and the benefits on a universal method to collect this data.

Study: Subsequently, the program needs to be studied to assess it impact on coverage estimates. The IIS should be analyzed to look at completeness of data, the number and background of users, and overall compliance. Additionally, the coverage estimates of this new IIS should be compared existing systems as a form of quality insurance.

Act: Lastly, action should be taken based on what was learned in the previous step. If the coverage estimates among these various sources are similar to the new IIS and it is being properly utilized it may be appropriate for the other system to be phased out. However, if the opposite is shown or if participation in IIS steeply declines the other systems need to remain in place until a better substitute can be developed.

CONCLUSION

Surveillance is a core function of public health. It is the ongoing, systematic collection, analysis, and interpretation of health data which is essential to the planning and implementation of public health practice. To be truly effective it needs to include a continuous ongoing system. One existing surveillance system for Rotavirus pretains to vaccine coverage. Beyond this is it important for public health efforts to focus on change and improvement on the procedural level as well. The incorporation of TQM and the PDSA cycle with public health surveillance can have a positive impact on immunizations.

Vaccinations has been identified as one of the greatest public health achievements of the 20th century. In public health, we understand their importance. Therefore, much has been done to improve the coverage and quality of immunizations. Many surveillance systems are currently established which allow for the collection of data, analysis, and mechanism for action.

Rotavirus is the most common cause of diarrhea and vomiting in infants and young children. There are several existing surveillance systems used by Public Health related to rotavirus in the United States. One important component is vaccine coverage. The implementation of the rotavirus vaccination program in the United States has resulted in a marked reduction in diarrhea hospitalizations and related hospital costs among children nationally.

Rotavirus vaccine coverage rates have steadily increased annually. The rotavirus vaccine was added to the National Immunization Survey (NIS), the primary source of vaccine estimates, in 2007. However, all methods of surveillance should be examined to ensure that the most efficient and accurate estimates are being captured.

Figure 1: Rotavirus: Cascade of Prevention

Primary Prevention	Clean drinking water
	Education
	Vaccine for Children (VFC)
	Public immunization programs
	Proper hand hygiene
	Immunization
Secondary Prevention	Case: Early diagnosis of disease
	Cases: Hydration and early treatment
	Epidemic: Early detection
	Epidemic: Reduce spread
Tertiary Prevention	Intense Hydration
	Advanced medical treatment

Figure 2: Plan Do Study Act Cycle

1) Plan: One must recognize an opportunity and plan the new program or change

2) Do: The new program/change should be implemented

3) Study: Study to see how the previous step conforms to the plan

4) Act: Act on what has been learned. It is needed to review the action, analyze the results and identify learnings.

Lastly, action should be taken based on what you learned in the check step. It needs to be determined if the change was successful or an alternative plan should be implemented because the cycle starts again from the beginning.

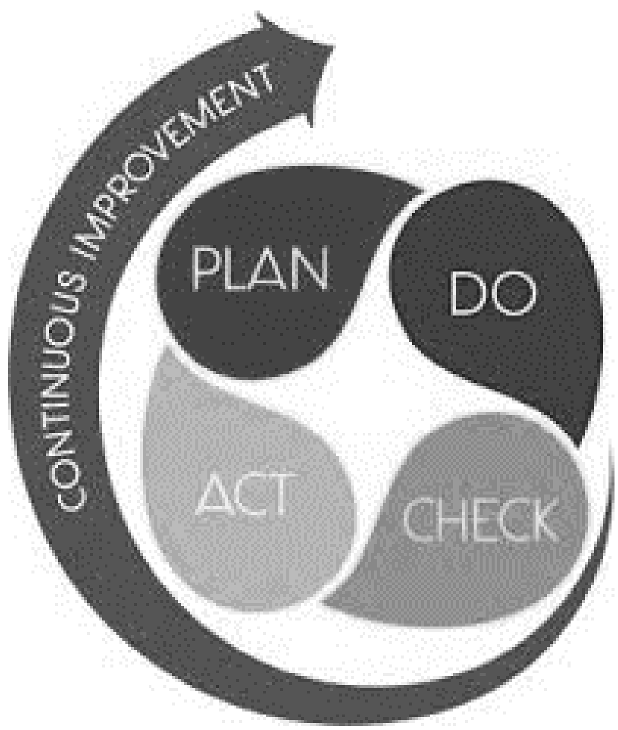

Table 1 Rotavirus Surveillance Systems

Surveillance System	Goal	Agency	Strength	Limitation
Pediatric Bacterial Meningitis Network & sentinel surveillance networks for pneumococcal & RV disease	Assesses disease burden	WHO	Works with hospitals/labs to obtain information on confirmed cases and genotyping when possible	Limited participating countries
Disease Incidence	Assesses disease burden	Multiple		Passive system leading to underestimate of disease
Vaccine Adverse Event Reporting System (VAERS)	Detect adverse events post vaccination	CDC	National surveillance program	Passive reporting system
National Immunization Survey (NIS)	Vaccination Coverage	CDC	Nationally representative sample	Limited information obtained and cannot make local inferences

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MANUSCRIPT II: Examination of rotavirus vaccine coverage among National Immunization Survey participating children in the United States

ABSTRACT

Background: Rotavirus is the most common cause of diarrhea and vomiting in infants and young children in the United States.[1] Prior to the introduction of the rotavirus vaccine in 2006, 95% of children would have been affected before the age of five years.[2] Coverage rates for rotavirus immunizations have increased since its introduction, however, rates still lag that of other vaccines recommended by the Advisory Committee on Immunization Practices (ACIP). [3,4,5] Much research has been done on groups at highest risk for under immunization. However, it is unclear if these groups are also at high risk when immunizations are first introduced into circulation. Does the early adopter effect have an influence on the timely immunization of a child?

Methods: The National Immunization Surveys (NIS) from 2010-2014 were used in this study. Trends in rotavirus vaccination coverage were examined in children 19-35 months of age residing in the United States to assess changes in vaccine uptake in specific groups of participants. The primary outcome measure for this study is participant's rotavirus vaccination status. Descriptive analyses were performed among participants. Bivariate associations for all the risk factors by Rao Scott χ^2 were examined. Multivariable logistic regression was used for the binary up-to-date status for rotavirus vaccination.

Results: The overall coverage rates for rotavirus vaccination increased progressively across the NIS data collection years from 2010 to 2014 (58.3% to 71.7%). During the five-year study period, the risk of under immunization declined for all groups.

Children who were first born had greater odds of under immunization when compared with children born of a later birth order with OR =1.14 (CI 1.13-1.14) in NIS year 2010. A child being up to date with the 4:3:1:3:3:1 immunization series was shown to be more likely to have full coverage of rotavirus vaccination as well in each year: OR=0.32 (95% CI 0.32-0.32) in NIS year 2010 and OR=0.20 (95% CI 0.20-0.20) in NIS year 2014. Children who live in households below the national poverty line had UTD rate of 51.5% in 2010 which improved to 62.8% by 2014 compared to 62.9% among those above poverty in 2010 increasing to 76.9% UTD in 2014 ; adjusted models indicated that those below poverty were more likely to be vaccinated compared to households with incomes that lie above the national poverty line when adjusted for other factors OR =0.64 (CI 0.64-0.64) in 2014.

Conclusion: Overall coverage rates for the rotavirus vaccine have increased steadily over the five-year period examined in this study. There remains to be groups of children who are at greater risk for not receiving a newly introduced vaccine. Public health officials must be certain that newer vaccines are available to lower income populations. There should be increased education to physicians in both the private and public sector to ensure proper vaccine coverage.

INTRODUCTION

Rotavirus (RV) is the most common cause of diarrhea and vomiting in infants and young children. This double-stranded RNA virus is transmitted by the fecal oral route. Symptoms include fever, vomiting, and watery diarrhea. Immunity from infection is incomplete, but repeat infections tend to be less severe than the original infection.[1]

In the 1990s through early 2000s, RV was responsible for more than 400,000 outpatient physician visits, 200,000 Emergency Department visits, and 55,000 to 70,000 hospitalizations.[2] Since its introduction, the RV vaccine has had a substantial effect in reducing hospital admissions of young children because of diarrhea.[3-5] A reduction in hospitalizations due to diarrhea from 2001-2006 compared to 2007-2008 of 33% among children five years of age and below has been reported.[6] By 2008, the Advisory Committee on Immunization Practices (ACIP) recommended Rotarix® and RotaTeq® for routine rotavirus vaccination of infants. Two or three doses of live oral rotavirus vaccine is recommended at ages two, four, and six months concurrently with other vaccines given at these ages.[7,8]

The National Immunization Survey (NIS), conducted jointly by the National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), estimates childhood immunization coverage rates in the United States for children 19 to 35 months of age. Rotavirus vaccine coverage rates have increased since its introduction, however still lag behind other ACIP recommended vaccines.[9-11]

Factors such as race, maternal factors, and access to medical care have been reported to be associated with the under vaccination of children.[12-14] The introduction of a new vaccine adds barriers due to misconceived perceptions and/or lack of knowledge.[15] Information regarding the RV vaccine was added to the NIS in 2010 and is the most recent addition to the survey.[16] Assessing immunization in a newly introduced vaccine can provide information regarding groups at highest risk for underimmunzation and be used to observe shifts, if any, over time as familiarity increases.

Much research has been done on groups at highest risk for under immunization. However, it is unclear if these groups are also at high risk when immunizations are first introduced into use, i.e., whether the early adopter effect has an influence on the timely immunization of a child.

METHODS

Data Sources

National Immunization Survey (NIS) is a nationally representative survey which estimates childhood immunization coverage rates in the United States, District of Columbia, U.S. Virgin Islands, Guam, and Puerto Rico. It is conducted jointly by the National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC).[17]

The first component of NIS is a list-assisted random-digit-dialing telephone survey administered to households in the United States with children of ages between 19 and 35 months at the time of the interview. This computer-generated list of telephone numbers includes both land lines and cell phones. A parent or guardian of an eligible child is interviewed regarding the child's immunization history, demographic, and health care information.

Upon completion, the interviewer asks for permission to contact the child's medical provider to verify immunization history. During follow-up, a mailed survey is sent to the child's immunization provider. An immunization history from providers is obtained. [18-22] Data from immunization providers are used to validate the child's immunization history reported by the parent/guardian in the Household Telephone Survey. Only provider validated data was used in this study.

Discrepancies between household and provider reported vaccination histories are reconciled. Immunization data that are not consistent between NIS reports and state registry reports are flagged. First, an electronic procedure is used to correct minor errors. Then, medical providers are contacted for either all or a sample of inconsistent cases to verify discrepant data. The combined household and provider reports are used to form "best value" estimates of vaccination coverage. Estimates for childhood immunization coverage are produced for the nation and non-overlapping geographic areas consisting of the 50 states, the District of Columbia, and selected large urban areas. NIS also contains demographic, socio-economic, and geographic variables for participating children and households. On the health systems level, NIS collects data on provider characteristics and health insurance. [23-27]

Study Design

The annual NIS estimates vaccine coverage for children aged 19-35 months. In this study, we limited the data to children residing in the 50 states and participating in the 2010, 2011, 2012, 2013, or 2014 NIS. RV vaccine coverage data was not available prior to 2010.[23]

The primary outcome measure for this study is a record of a child being up-to-date (UTD) for their rotavirus vaccine. A child is considered UTD if they received ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]) by 36 months of age.[28]

Child level risk factors for noncompliance with the rotavirus vaccination were assessed. The covariates assessed for association with coverage were selected based on previously published peer reviewed studies.[30-33] Characteristics of the child included age group on the day of the initial interview; sex and first-born status; race/ethnicity classified as Hispanic, non-Hispanic white only, non-Hispanic black-only or other/multiple races. The region of residence is represented by the census region corresponding with the state.

Covariates pertaining to the mother include age, which is categorized into three groups: under 20 years, 20-29 years, and 30 and above; marital status which was constructed into a dichotomous variable of married and not married (never married/widowed/divorced); education of mother in four groups less than 12 years, 12 years, greater than 12 but non-college graduate, and college graduate and/or greater; poverty status based on the census poverty thresholds from the previous year (there were three categories: above poverty line, at or below the poverty line, and unknown poverty status); and number of people in household recoded to two categories: 2-3 people and four or greater.[23-27]

Health-related information included insurance status. This variable was constructed by combining several distinct variables related to insurance using a hierarchical selection process as seen in Figure 1. In the first step, a child was classified as ‘uninsured’ if they did not have medical insurance at any time. Next, a child would be classified as ‘Medicaid/S-Chip’ if they participated in either program. “Insured” children were those who had health insurance provided through employer or union; covered by Indian health service, military health care, Tricare, Champus, or Champ-VA; or other health insurance or health care plan. The remaining children were categorized as missing/other. The category of ‘Other’ represents interviewees who stated having ‘some other type of insurance’. While there is an open-ended follow-up question asking for the name of this other insurance, we do not have access to this response. Up-to-date with the full vaccine series was selected at 4:3:1:3:3:1 defined as at least four doses of DTaP (Diphtheria, Tetanus, and Acellular Pertussis), three doses of Polio, one dose of MMR (Measles, Mumps, and Rubella), three doses of Hib (Haemophilus Influenza Type b), three doses of Hepatitis B, and one dose of Varicella.

The pneumococcal conjugate vaccine (PCV7) was not included in this study to avoid possible bias in estimates caused by a shortage in Prevnar, the PCV7 vaccine, in the early 2000s. In February 2004, the CDC recommended that the 7-valent PCV vaccine be administered to healthy children on an abbreviated schedule in order to conserve the limited supplies. The Woman Infant Child (WIC) variable was categorized as using WIC benefits, not using WIC benefits, and other. The Other category is comprised of never heard of WIC, do not know, and refused to answer. Provider facility was self-reported by the physician and was classified as entirely public health facilities, entirely private, entirely hospital based facilities, military/other, and mixed facility type.

Statistical Analysis

All statistical analyses were performed using SAS version 9.4. Descriptive analyses were conducted for all NIS participants by study year and further by study year among those who have completed the rotavirus vaccine series. Bivariate analysis assessed relationships between the covariates and the outcome of rotavirus vaccine status using the Rao Scott χ^2 statistic to determine the statistical significance. Cramer's V was also used for each variable to test for possible collinearity. A Rao Scott χ^2 p-value cutoff of 0.20 was the cutoff for a covariate to be studied in multivariate analysis using logistic regression. The Survey Logistic SAS procedure was used to estimate odds ratio of not being UTD for rotavirus vaccination. Weight and strata statements were used to consider the weighted and stratified nature of this data.

RESULTS

Study Population

Table 1 shows the demographic characteristics among NIS participants by year. The number of NIS participants by year ranged from 5,710,556 to 6,159,994 participants (Table 1). Consistently, during the five-year period of this study, participants were approximately 51% male and 48% non-Hispanic white. In 2010, 19.6% lived in households with two to three residents but this percentage rose over time to 26.2% in 2014. From 2010-2014, there was an increase in the percentage of children surveyed who were first born (54% to 60%), who ever received WIC benefits (54.7% to 57.6%) and children going to providers based in public (10.9% to 11.7%) or hospital (9.3% to 12.4%) facilities. There was a 3.7% increase in coverage for the 4:3:1:3:3:1 series from 2010-2014 from 74.9% to 78.6%. Rotavirus coverage increased as well during this time period; the lowest coverage rate for rotavirus was 59.2% in 2010 and highest at 72.6% in 2013.

Vaccination Coverage

Among children who were up-to-date with their rotavirus vaccine over the five-year study period (Table 2), 50.4% to 50.7% were male, 47.1% to 50.1% non-Hispanic white, and 39.5% to 38.9% lived in the Southern region of the United States. Among types of provider facilities, most children went to providers practicing exclusively at a private facility (54.2% - 57.6%) and were covered under a private health insurance carrier (57.4% - 61.4%). The greatest improvement in Rotavirus coverage over the five-year study period was among Hispanics; coverage went from 60.5% in 2010 to 71.3% in 2015, a difference of 10.8% (95% CI 10.75-10.85) but their coverage remained below that of non-Hispanic whites (74.8%). Being UTD on 4:3:1:3:3:1:2 substantially increased the probability of being up-to-date with 66.4% vs 37.7% among those not UTD for 4:3:1:3:3:1:2 in 2010 (p<0.0001). While those UTD for 4:3:1:3:3:1:2 were more likely to have been vaccinated for rotavirus in 2010, they substantially increased to 79.9% in 2014, a 13.5% (95% CI: 13.45%-13.44%) increase, whereas among those not-UTD 4:3:1:3:3:1:2 in 2010 only had modest gains from 37.9% to 41.6% in 2014, a 3.9% (95% CI: 3.84-3.96) increase (Table 3)

Factors Associated with Under-immunizations

In each NIS year, greater than 75% of children whom were up-to-date with the rotavirus vaccine had also completed the 4:3:1:3:3:1 series. Table 4 shows significant associations between rotavirus vaccination coverage and covariates that had Cramer's V values below 0.20. We found no evidence of collinearity and all covariates were included in statistical models.

Multivariable analysis showed that risk differences among groups over the study period. (Table 5). In 2010, children living in larger households (OR = 1.20 (CI 1.19-1.20)), and children who were first born (OR = 1.14 (CI 1.13-1.48) had higher risks of under coverage vs their counterparts. A child being up to date with the 4:3:1:3:3:1 immunization series was shown to be more likely to have full coverage of rotavirus vaccination as well in each year OR=0.32 (95% CI 0.32-0.32) in 2010 to OR=0.20 (95% CI 0.20-0.20) in 2014.

At the end of the five-year study period, many children who had factors associated with lower income and lower health care utilization had seen an increase in immunization coverage. However, their odds for being underimmunized was still greater than children from higher socio-economic status.

CONCLUSION

The goal of this study was to examine immunization coverage for the rotavirus vaccine. The RV vaccine was added to the NIS in 2007 and is the most recent addition to the survey.[16] The introduction of a new vaccine is often accompanied by misconceived perceptions and/or lack of knowledge.[15] Assessing immunization coverage in a newly introduced vaccine can provide information regarding groups at highest risk for underimmunzation and be used to observe shifts, if any, over time as familiarity increases. Much research has been done on groups at highest risk for under immunization. Factors such as race, maternal status and access to medical care have been reported to be associated with the under vaccination of children.[12-14] This analysis was done to assess if these risk factors are also associated with under vaccination when immunizations are first introduced into use or if other factors can influence their coverage.

During this five-year study period, the overall rotavirus coverage rate was 58.3% in 2010 increased each year to 71.7 in 2014. However, the odds of certain groups to not be immunized are considerable higher than their peers. Factors associated with health care access to groups with a lower socio-economic status demonstrated increased levels of risk during the study period. Children whom were ever enrolled in WIC, received Medicaid/S-Chip benefits, were uninsured at any point, and/or received health care at public based providers initially had lower levels of risk or showed a protected effect which decreased over time.

WIC is a program within the Department of Agriculture which provides assistant to low income pregnant, postpartum and breast-feeding women, infants, and children up to age five who are at nutritional risk. In an average month in 2012, WIC served an estimated 63.1 percent of those eligible for services.[34, 35] The results of this study showed that children who ever received WIC benefits in 2012 were not less likely to be vaccinated with the rotavirus vaccine than those that did not. However, the risk increased in subsequent years and may be an underestimate. It has been reported that WIC eligible children who never received WIC benefits had the lowest vaccine coverage when compared to children who receive benefits and children who are ineligible.[36]

In the initial NIS year, children who were uninsured or on Medicaid/S-Chip were more likely to be fully covered for Rotavirus than those with private insurance. Children were considered uninsured if they did not have health insurance coverage at any point prior to the administration of the NIS questionnaire so it is possible that a child was uninsured for a brief period of time before getting another public or private insurance. Seeing a provider based in a public facility such as a government funded health clinic was protective.

Children whom are uninsured and underinsured can be eligible for the Vaccine for Children (VFC) program. VFC is a federally funded program that provides vaccine at no cost to children who might not otherwise be vaccinated because of inability to pay.[40] The ability of VFC to remove financial and logistical barriers hindering vaccination for low-income children likely plays a significant role in increasing vaccine coverage.[41] Additionally, receiving the vaccine at no cost to the physician may be an incentive to begin delivering new vaccines which may not yet be required. This can also be associated with the reduced risk among children with providers in public facilities, such as a local health department or a public health clinic, versus than private providers.

Consistently throughout the study period, full coverage of the 4:3:1:3:3:1 vaccine series is the strongest predictor for rotavirus vaccine coverage. The coverage rate of these six vaccines tends to be higher since they have been on the schedule longer and are mandated for most school admissions in the United States. Rotavirus vaccine is only mandated for admission to schools in three states: Idaho, Louisiana, and Rhode Island; however, rotavirus vaccine coverage positively benefited from school based mandates for other childhood vaccines.

This study shows that the factors which influence the coverage and uptake of vaccines differ immediately after vaccine introduction. Therefore, it may not be appropriate to apply our current knowledge pertaining to the groups at greatest risk for under-immunization under these circumstances. Past vaccination efforts have focused on lower income households, the uninsured, and using government supplied aid. Many resources have been allotted to resolve this gap. There has been an increased focus on incorporating immunization education and/or delivery during WIC visits.[37,38,39] This action may be having a positive impact on vaccine coverage. Women receiving WIC may have better access, or be more inclined, to utilize other public health services available to them.

This study shows that typical approaches may not work when introducing a new vaccine. Public health officials must recognize the reasons for the noncompliance to the rotavirus vaccine may differ from that of other more established vaccines. As new vaccines are introduced, it is important to note the various factors which can affect coverage. Once early and late adopters are identified, proper public health strategies can be planned. The knowledge of the barriers in coverage be used to change public health policy and procedures by allowing resources to be focused on developing more effective methods of increasing overall vaccine coverage for children.

Typically, the introduction of a new vaccine triggers the addition of resources available to communities with lower socio-economic status known to have challenges with access to care. In this study, our hypothesis is that once the funding for these 'start up' resources to initiate new programs are exhausted there is a significant negative impact on the children in these communities. Any progress made in these high-risk groups diminish over time and children in these groups are at higher risk for not being proper immunized against rotavirus.

Private providers cannot be ignored either. This study shows a slow decline in disparity of risk among children who go to private providers. Low compliance in medical practices may be due to the lack of a physician's knowledge and familiarity with the new vaccine. Physicians can play a large role in increasing vaccine coverage, especially when newly introduced. Physician counseling, aid in parental decision-making, and continuing the physician-patient relationship suggest initiatives that could increase confidence in immunization programs.[42] Focused education of physicians serving communities which may not typically be considered ‘high risk’ may be important for increasing compliance.

Strengths of this study include the use of the NIS database, a large national database which has been reviewed and validated. The weighted sample enables the results to be generalizable for all children aged 19 to 35 months in the United States. The use of multiple years of data allows the assessment of trends and patterns. All data given during the telephone surveys are confirmed with a child's medical care provider to insure accuracy in the immunization estimates for each child in this study.

Table 1: Characteristics of National Immunization Survey (NIS) Participants and their mothers, 2010-2014										
	NIS Year									
Characteristic	2010		2011		2012		2013		2014	
Total No.	6,159,994		5,993,201		5,807,171		5,724,087		5,710,556	
Age group										
19-23 mo.	1,813,955	(29.4)	1,773,326	(29.6)	1,723,242	(29.7)	1,715,872	(30.0)	1,736,453	(30.4)
24-29 mo.	2,113,019	(34.3)	2,049,374	(34.2)	1,967,752	(33.9)	1,942,753	(33.9)	1,927,367	(33.8)
30-35 mo.	2,233,021	(36.3)	2,170,501	(36.2)	2,116,177	(36.4)	2,065,462	(36.1)	2,046,736	(35.8)
Sex										
Male	3,150,335	(51.1)	3,067,051	(51.2)	2,971,551	(51.2)	2,930,735	(51.2)	2,920,393	(51.1)
Female	3,009,659	(48.9)	2,926,150	(48.8)	2,835,619	(48.8)	2,793,352	(48.8)	2,790,163	(48.9)
Race/Ethnicity										
Hispanic	1,699,619	(27.6)	1,670,570	(27.9)	1,587,486	(27.3)	1,557,218	(27.2)	1,498,053	(26.2)
Non-Hispanic White	3,034,077	(49.3)	2,871,542	(47.9)	2,735,977	(47.1)	2,741,628	(47.9)	2,672,351	(46.8)
Non-Hispanic Black	811,572	(13.2)	788,223	(13.2)	791,267	(13.6)	724,461	(12.7)	775,979	(13.6)
Other/Multiple	614,726	(10.0)	662,866	(11.1)	692,441	(11.9)	700,781	(12.2)	764,174	(13.4)
First born										
Yes	3,330,242	(54.1)	3,662,080	(61.1)	3,562,536	(61.3)	3,439,677	(60.1)	3,429,328	(60.1)
No	2,829,752	(45.9)	2,331,121	(38.9)	2,244,634	(38.7)	2,284,411	(39.9)	2,281,228	(39.9)
No. in household										
2-3	1,208,077	(19.6)	1,400,911	(23.4)	1,471,285	(25.3)	1,486,591	(26.0)	1,493,879	(26.2)
4+	4,951,917	(80.4)	4,592,290	(76.6)	4,335,886	(74.7)	4,237,496	(74.0)	4,216,677	(73.8)
Age of mother (yrs.)										
≤ 19	168,605	(2.7)	170,234	(2.8)	139,086	(2.4)	114,847	(2.0)	38,597	(0.7)
20-29	2,292,152	(37.2)	2,639,367	(44.0)	2,449,060	(42.2)	2,442,793	(42.7)	2,388,482	(41.8)
≥30	3,699,238	(60.1)	3,183,601	(53.1)	3,219,025	(55.4)	3,166,447	(55.3)	3,283,477	(57.5)
Marital status										
Married	4,124,236	(67.0)	3,762,689	(62.8)	3,635,529	(62.6)	3,580,172	(62.5)	3,589,753	(62.9)
Never/widowed/ divorced	2,035,758	(33.0)	2,230,512	(37.2)	2,171,641	(37.4)	2,143,915	(37.5)	2,120,803	(37.1)
Region of residence										
Northeast	972,717	(15.8)	955,714	(15.9)	935,572	(16.1)	929,020	(16.2)	920,956	(16.1)
Midwest	1,276,519	(20.7)	1,250,291	(20.9)	1,210,220	(20.8)	1,194,587	(20.9)	1,191,591	(20.9)
South	2,367,100	(38.4)	2,301,767	(38.4)	2,229,784	(38.4)	2,190,295	(38.3)	2,195,481	(38.4)
West	1,543,659	(25.1)	1,485,429	(24.8)	1,431,594	(24.7)	1,410,186	(24.6)	1,402,528	(24.6)
Education of mother										
<12 yrs.	1,204,497	(19.6)	1,185,927	(19.8)	1,106,221	(19.0)	1,058,210	(18.5)	1,014,514	(17.8)
12 yrs.	1,820,422	(29.6)	1,681,552	(28.1)	1,568,678	(27.0)	1,469,898	(25.7)	1,437,348	(25.2)
>12 yrs. Non-college grad	1,181,187	(19.2)	1,293,511	(21.6)	1,297,074	(22.3)	1,266,611	(22.1)	1,350,971	(23.7)
College grad	1,953,888	(31.7)	1,832,211	(30.6)	1,835,197	(31.6)	1,929,368	(33.7)	1,907,724	(33.4)

Poverty status										
Above poverty	3,874,960	(62.9)	3,509,844	(58.6)	3,392,243	(58.4)	3,502,470	(61.2)	3,484,281	(61.0)
Below poverty	1,938,599	(31.5)	2,131,187	(35.6)	2,139,478	(36.8)	1,912,947	(33.4)	1,914,564	(33.5)
Unknown	346,435	(5.6)	352,169	(5.9)	275,450	(4.7)	308,670	(5.4)	311,711	(5.5)
Insurance status										
Insured	3,094,539	(50.2)	2,825,000	(47.1)	2,740,609	(47.2)	2,747,654	(48.0)	2,675,469	(46.9)
Medicaid/S-CHIP	907,259	(14.7)	1,006,393	(16.8)	957,746	(16.5)	921,755	(16.1)	2,878,896	(50.4)
Uninsured at any point	555,594	(9.0)	521,959	(8.7)	512,219	(8.8)	483,459	(8.4)	64,079	(1.1)
Missing/other	1,602,602	(26.0)	1,639,849	(27.4)	1,596,596	(27.5)	1,571,218	(27.4)	4,527	(0.1)
UTD Rotavirus[1]										
Yes	3,643,884	(59.2)	4,032,953	(67.3)	3,983,105	(68.6)	4,155,803	(72.6)	4,092,521	(71.7)
No	2,516,111	(40.8)	1,960,247	(32.7)	1,824,066	(31.4)	1,568,284	(27.4)	1,618,036	(28.3)
UTD 4:3:1:3:3:1[2]										
Yes	4,612,028	(74.9)	4,611,927	(77.0)	4,395,763	(75.7)	4,444,854	(77.7)	4,489,235	(78.6)
No	1,547,966	(25.1)	1,381,274	(23.0)	1,411,407	(24.3)	1,279,233	(22.3)	1,221,321	(21.4)
Child ever received WIC Benefits										
Yes	3,371,123	(54.7)	3,557,698	(59.4)	3,422,825	(58.9)	3,321,371	(58.0)	3,291,711	(57.6)
No	2,769,320	(45.0)	2,417,523	(40.3)	2,360,820	(40.7)	2,383,802	(41.6)	2,387,601	(41.8)
Never heard of WIC	10,028	(0.2)	10,881	(0.2)	9,698	(0.2)	8,651	(0.2)	11,157	(0.2)
Do not know	8,996	(0.1)	7,074	(0.1)	13,482	(0.2)	10,263	(0.2)	20,088	(0.4)
Refused to answer	527	0.0	24	0.0	346	0.0	897	0.0	1,267	0.0
Provider facility type										
All public	671,854	(10.9)	751,554	(12.5)	704,377	(12.1)	722,361	(12.6)	667,075	(11.7)
All hospital	571,939	(9.3)	610,813	(10.2)	657,331	(11.3)	711,758	(12.4)	709,397	(12.4)
All private	3,338,089	(54.2)	3,409,839	(56.9)	3,347,740	(57.6)	3,218,465	(56.2)	3,153,727	(55.2)
Military/Other	677,099	(11.0)	364,533	(6.1)	121,900	(2.1)	137,289	(2.4)	175,398	(3.1)
Mixed	859,962	(14.0)	808,607	(13.5)	929,178	(16.0)	893,323	(15.6)	961,601	(16.8)

[1] Receive ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]) by 36 months of age.

[2] Based on 4:3:1:3:3:1 series – 4+ DTaP (Diphtheria, Tetanus, and Acellular Pertussis), 3+ Polio, 1+ MMR (Measles, Mumps, and Rubella), 3+ Hib (Haemophilus Influenza Type b), 3+ HepB (Hepatitis B), and 1+ Varicella

Table 2: Characteristics of National Immunization Survey (NIS) Participants and their mothers who are up-to-date with Rotavirus Vaccination[1], 2010-2014

	NIS Year									
Characteristic	2010		2011		2012		2013		2014	
Total no.	3,643,884		4,032,953		3,983,105		4,155,803		4,092,521	
Age group										
19-23 mo.	1,184,797	(32.5)	1,229,067	(30.5)	1,182,982	(29.7)	1,273,398	(30.6)	1,270,054	(31.0)
24-29 mo.	1,255,777	(34.5)	1,378,911	(34.2)	1,350,273	(33.9)	1,407,330	(33.9)	1,390,538	(34.0)
30-35 mo.	1,203,310	(33.0)	1,424,975	(35.3)	1,449,850	(36.4)	1,475,076	(35.5)	1,431,928	(35.0)
Sex										
Male	1,835,355	(50.4)	2,058,005	(51.0)	2,039,350	(51.2)	2,391,925	(57.6)	2,075,116	(50.7)
Female	1,808,529	(49.6)	1,974,949	(49.0)	1,943,755	(48.8)	1,763,878	(42.4)	2,017,404	(49.3)
Race/Ethnicity										
Hispanic	1,028,501	(28.2)	1,140,359	(28.3)	1,087,388	(27.3)	1,148,361	(27.6)	1,068,469	(26.1)
Non-Hispanic White	1,825,063	(50.1)	1,960,527	(48.6)	1,876,042	(47.1)	2,051,951	(49.4)	1,999,963	(48.9)
Non-Hispanic Black	427,628	(11.7)	492,549	(12.2)	541,702	(13.6)	449,906	(10.8)	478,436	(11.7)
Other/Multiple	362,692	(10.0)	439,519	(10.9)	473,989	(11.9)	505,585	(12.2)	545,652	(13.3)
First born										
Yes	1,883,522	(51.7)	2,372,909	(58.8)	2,441,643	(61.3)	2,391,925	(57.6)	2,379,019	(58.1)
No	1,760,362	(48.3)	1,660,045	(41.2)	1,541,462	(38.7)	1,763,878	(42.4)	1,713,501	(41.9)
No. in household										
2-3	795,371	(21.8)	1,010,432	(25.1)	1,007,726	(25.3)	1,154,660	(27.8)	1,150,647	(28.1)
4+	2,848,513	(78.2)	3,022,522	(74.9)	2,975,379	(74.7)	3,001,142	(72.2)	2,941,873	(71.9)
Age of mother(yrs.)										
≤ 19	91,134	(2.5)	124,120	(3.1)	95,595	(2.4)	56,794	(1.4)	24,170	(0.6)
20-29	1,258,180	(34.5)	1,623,326	(40.3)	1,680,870	(42.2)	1,686,403	(40.6)	1,606,925	(39.3)
≥30	2,294,570	(63.0)	2,285,507	(56.7)	2,206,640	(55.4)	2,412,606	(58.1)	2,461,426	(60.1)
Marital status										
Married	2,514,009	(69.0)	2,613,552	(64.8)	2,493,424	(62.6)	2,681,692	(64.5)	2,665,292	(65.1)
Never/widowed/ divorced	1,129,875	(31.0)	1,419,402	(35.2)	1,489,681	(37.4)	1,474,111	(35.5)	1,427,228	(34.9)
Region of residence										
Northeast	560,661	(15.4)	638,542	(15.8)	641,280	(16.1)	702,375	(16.9)	664,693	(16.2)
Midwest	763,065	(20.9)	824,898	(20.5)	828,486	(20.8)	854,068	(20.6)	853,081	(20.8)
South	1,438,669	(39.5)	1,559,038	(38.7)	1,529,512	(38.4)	1,551,487	(37.3)	1,592,075	(38.9)
West	881,489	(24.2)	1,010,475	(25.1)	983,827	(24.7)	1,047,875	(25.2)	982,673	(24.0)
Education of mother										
<12 yrs.	648,170	(17.8)	705,271	(17.5)	756,790	(19.0)	678,643	(16.3)	680,563	(16.6)
12 yrs.	990,855	(27.2)	1,105,340	(27.4)	1,075,438	(27.0)	1,039,430	(25.0)	944,680	(23.1)
>12 yrs, non-college	693,465	(19.0)	854,059	(21.2)	888,232	(22.3)	887,037	(21.3)	932,725	(22.8)
College grad	1,311,394	(36.0)	1,368,283	(33.9)	1,258,661	(31.6)	1,550,693	(37.3)	1,534,553	(37.5)

Poverty status										
Above poverty	2,437,990	(66.9)	2,495,092	(61.9)	3,393,605	(85.2)	2,694,132	(64.8)	2,677,695	(65.4)
Below poverty	997,630	(27.4)	1,301,267	(32.3)	1,465,783	(36.8)	1,229,535	(29.6)	1,202,043	(29.4)
Unknown	208,264	(5.7)	236,594	(5.9)	187,206	(4.7)	232,136	(5.6)	212,782	(5.2)
Insurance status										
Insured	1,999,025	(54.9)	2,086,676	(51.7)	2,043,333	(51.3)	2,149,918	(51.7)	2,080,654	(50.8)
Medicaid/S-CHIP	488,347	(13.4)	601,396	(14.9)	394,327	(9.9)	638,264	(15.4)	671,546	(16.4)
Uninsured at any point	270,059	(7.4)	311,836	(7.7)	235,003	(5.9)	1,064,160	(25.6)	316,020	(7.7)
Missing/other	886,452	(24.3)	1,033,044	(25.6)	697,043	(17.5)	1,596,596	(38.4)	1,024,300	(25.0)
UTD 4:3:1:3:3:1:2										
Yes	3,060,990	(84.0)	3,415,347	(84.7)	3,015,210	(75.7)	3,606,605	(86.8)	3,584,876	(87.6)
No	582,893	(16.0)	617,606	(15.3)	967,895	(24.3)	549,199	(13.2)	507,645	(12.4)
Child ever received WIC benefits										
Yes	1,859,580	(51.0)	2,286,753	(56.7)	2,346,049	(58.9)	2,285,072	(55.0)	2,222,315	(54.3)
No	1,776,395	(48.8)	1,735,615	(43.0)	1,621,124	(40.7)	1,858,264	(44.7)	1,850,209	(45.2)
Never heard of WIC	4,749	(0.1)	6,650	(0.2)	7,966	(0.2)	6,519	(0.2)	6,576	(0.2)
Do not know	3,065	(0.1)	3,911	(0.1)	7,966	(0.2)	5,949	(0.1)	13,421	(0.3)
Provider Facility Types										
All Public	319,020	(8.8)	428,678	(10.6)	410,260	(10.3)	465,289	(11.2)	450,571	(11.0)
All Hospital	347,897	(9.5)	416,430	(10.3)	414,243	(10.4)	492,596	(11.9)	470,001	(11.5)
All Private	2,090,055	(57.4)	2,431,787	(60.3)	2,445,626	(61.4)	2,462,786	(59.3)	2,421,615	(59.2)
Military/Other	358,794	(9.8)	209496.5	(5.2)	87,628	(2.2)	88,720	(2.1)	110,705	(2.7)
Mixed	528,117	(14.5)	546561	(13.6)	629,331	(15.8)	646,412	(15.6)	639,629	(15.6)

[1] Receive ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]) by 36 months of age.

[2] Based on 4:3:1:3:3:1 series – 4+ DTaP (Diphtheria, Tetanus, and Acellular Pertussis), 3+ Polio, 1+ MMR (Measles, Mumps, and Rubella), 3+ Hib (Haemophilus Influenza Type b), 3+ HepB (Hepatitis B), and 1+ Varicella

Table 3: Change in Rotavirus Vaccine Coverage 2010 vs 2014 among NIS Participants					
	2010	2014	Difference	Confidence Interval	
Sex					
Male	58.30	71.10	12.80	12.75	12.85
Female	58.30	72.30	14.00	13.95	14.05
Race/Ethnicity					
Hispanic	60.50	71.30	10.80	10.75	10.85
Non-Hispanic White	60.20	74.80	14.60	14.55	14.65
Non-Hispanic Black	52.70	61.70	9.00	8.94	9.06
Other/Multiple	59.00	71.40	12.40	12.35	12.45
First Born					
Yes	56.60	69.40	12.80	12.74	12.86
No	62.20	75.10	12.90	12.85	12.95
No. in Household					
2-3	65.80	77.00	11.20	11.15	11.25
4+	57.50	69.80	12.30	12.24	12.36
Age of Mother(yrs.)					
<= 19	54.10	62.60	8.50	8.44	8.56
20-29	54.90	67.30	12.40	12.34	12.46
>=30	62.00	75.00	13.00	12.95	13.05
Marital Status					
Married	61.00	74.20	13.20	13.15	13.25
Never/widowed/ divorced	55.50	67.30	11.80	11.74	11.86
Education of Mother					
<12 yrs.	53.80	67.10	13.30	13.24	13.36
12 yrs.	56.50	67.30	11.30	11.24	11.36
College grad	67.10	80.40	13.30	13.25	13.35
Poverty Status					
Above poverty	62.90	76.90	14.00	13.95	14.05
Below Poverty	51.50	62.80	11.30	11.24	11.36
Unknown	60.10	68.30	8.20	8.14	8.26
UTD 4:3:1:3:3:1:2					
Yes	66.40	79.90	13.50	13.45	13.55
No	37.70	41.60	3.90	3.84	3.96
WIC Benefits					
Yes	55.20	67.50	12.30	12.24	12.36
No	64.00	77.30	13.30	13.25	13.35
Provider Facility Types					
All Public	60.80	66.30	5.50	5.44	5.56
All Hospital	62.60	76.80	14.20	14.15	14.25
All Private	53.00	63.10	10.10	10.04	10.16
Military/Other	61.40	66.50	5.10	5.04	5.16
Mixed	64.60	77.30	12.70	12.65	12.75

Table 4: Bivariate Analysis: Rotavirus Vaccine coverage by participant characteristics among NIS Participants										
	Percentage UTD with Rotavirus Vaccine NIS Year									
Characteristic	2010		2011		2012		2013		2014	
Total No.	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value
Age Group		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
19-23 mo.	65.3		69.3		69.6		74.2		73.1	
24-29 mo.	59.4		67.3		70.4		72.4		72.1	
30-35 mo.	53.9		65.7		66.2		71.4		70.0	
Sex		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Male	58.3		67.1		68.6		74.0		71.1	
Female	58.3		67.5		68.5		70.7		72.3	
Race/Ethnicity		<0.0001		0.03		<0.0001		0.03		<0.0001
Hispanic	60.5		68.3		70.0		73.7	0.03	71.3	
Non-Hispanic White	60.2		68.3		70.5		74.8		74.8	
Non-Hispanic Black	52.7		62.5		60.4		62.1		61.7	
Other/Multiple	59.0		66.3		66.9		72.1		71.4	
First Born		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Yes	56.6		64.8		66.2		69.5		69.4	
No	62.2		71.2		72.4		77.2		75.1	
No. in Household		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
2-3	65.8				72.2		77.7		77.0	
4+	57.5		65.8		67.4		67.4		69.8	
Age of Mother(yrs.)		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
<= 19	54.1		72.9		60.4		60.4		62.6	
20-29	54.9		61.5		65.0		65.0		67.3	
>=30	62.0		71.8		71.7		71.7		75.0	
Marital Status		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Married	61.0		69.5		72.0		72.0		74.2	
Never/widowed/ divorce	55.5		63.6		62.9		62.9		67.3	
Education of Mother		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
<12 yrs.	53.8		59.5		60.6		60.6		67.1	
12 yrs.	56.6		65.9		67.0		67.0		67.4	
College grad	67.1		74.7		76.2		76.2		80.4	
Poverty Status		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Above poverty	62.9		71.1		72.5		72.5		76.9	
Below Poverty	51.5		61.1		63.0		63.0		62.8	
Unknown	60.1		67.2		63.7		63.7		68.3	
Insurance Status		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Insured	64.6		73.9		74.6		74.6		77.3	
Medicaid/ S-CHIP	53.8		59.8		60.3		60.3		69.0	
Uninsured at any point	48.6		59.7		66.7		66.7		62.2	
Missing/other	55.3		63.0		63.8		63.8		66.6	

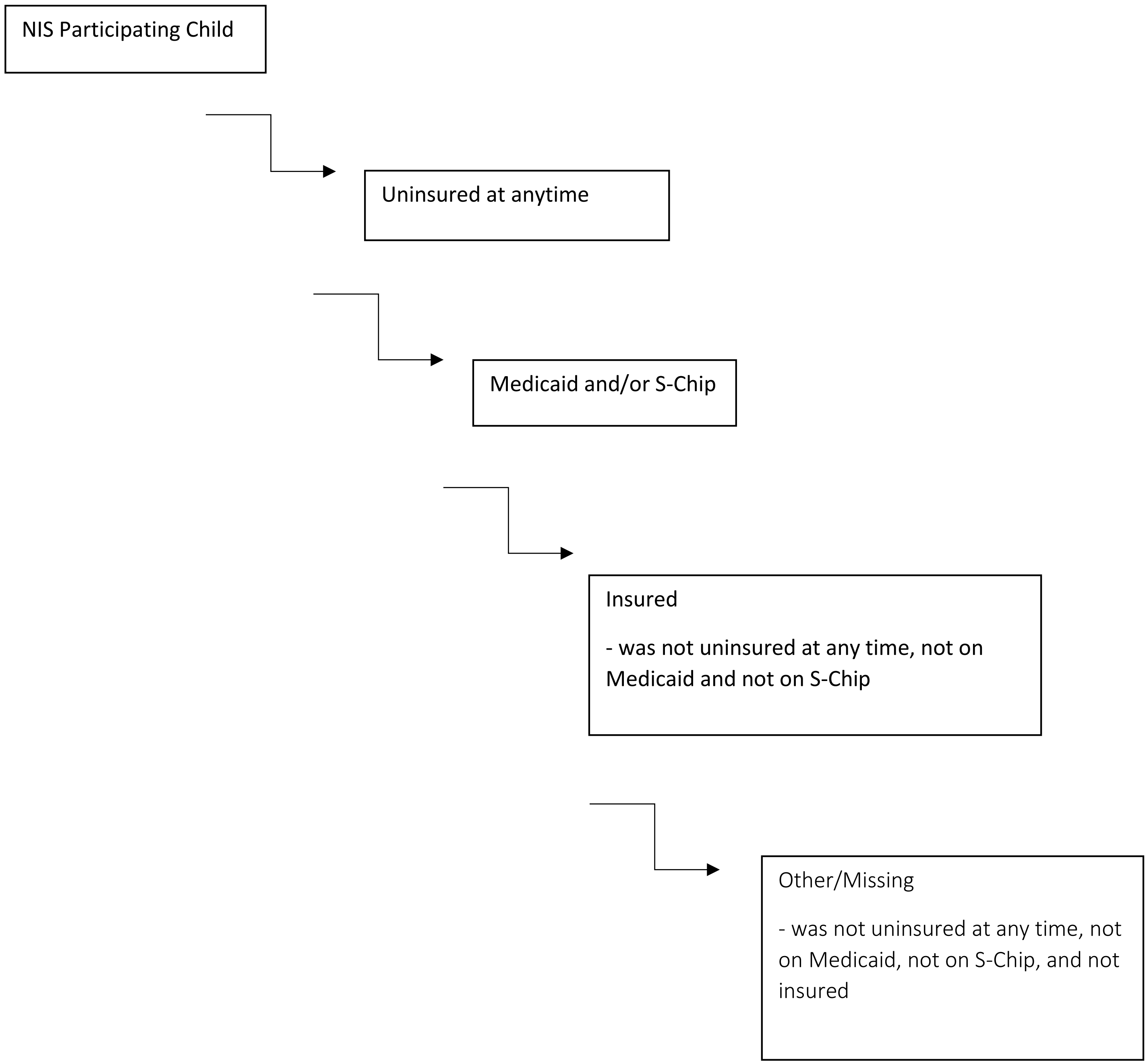
UTD 4:3:1:3:3:1:2		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Yes	66.4		74.1		76.6		76.6		79.9	
No	37.7		44.7		43.6		42.9		41.6	
WIC Benefits		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
Yes	55.2		64.3		64.8		68.8		67.5	
No	64.0		71.7		74.0		77.9		77.3	
Never heard of WIC	42.7		67.8		79.3		60.2		49.7	
Provider Facility Types		<0.0001		<0.0001		<0.0001		<0.0001		<0.0001
All Public	60.8		68.2		63.0		69.2		66.3	
All Hospital	62.6		71.3		73.0		76.5		76.8	
All Private	53.0		57.5		72.2		64.6		63.1	
Military/Other	61.4		67.6		67.7		72.4		66.5	
Mixed	64.6		73.9		74.6		78.2		77.3	

Table 5: Multivariable Analysis: Lack of Rotavirus Vaccine Coverage by characteristics of children, mothers and families among NIS Participants*

		2010			2011			2012			2013			2014		
Effect		Odds Ratio	95% CI		Odds Ratio	95% CI		Odds Ratio	95% CI		Odds Ratio	95% CI		Odds Ratio	95% CI	
Race Ethnicity	Hispanic vs white	0.8	0.8	0.8	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.6	0.6	0.6
	black vs white	1.3	1.2	1.3	1.3	1.3	1.3	1.4	1.4	1.4	1.3	1.3	1.3	1.0	1.0	1.0
	other/multiple vs. white	1.0	1.0	1.0	1.0	0.9	1.0	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
First Born	yes vs no	1.1	1.1	1.1	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.1	1.0	1.1
No. Household	2-3 vs 4+	1.2	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.1	1.3	1.3	1.3	1.4	1.4	1.5
Maternal Age group	≤19 vs ≥30	0.9	0.9	0.9	1.4	1.4	1.4	0.9	0.9	0.9	0.6	0.6	0.6	1.0	1.0	1.0
	20-29 vs ≥30	0.8	0.9	0.9	0.7	0.7	0.7	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
Maternal Marital Status	married vs other	1.1	1.1	1.1	1.0	1.0	1.0	0.9	0.8	0.9	1.0	1.0	1.0	0.9	0.9	0.9
Maternal Education	<12 Years vs College grad	0.9	0.9	0.9	1.3	1.3	1.3	1.2	1.2	1.2	1.3	1.3	1.3	0.9	0.9	0.9
	12 Years vs College grad	1.1	1.1	1.2	1.3	1.3	1.3	1.3	1.3	1.3	1.2	1.2	1.2	1.0	1.0	1.0
Poverty Status	Below vs. Above poverty	1.0	1.0	1.0	0.8	0.8	0.9	1.0	1.0	1.0	0.7	0.7	0.7	0.6	0.6	0.6
	Unknown vs. Above poverty	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	1.0	0.5	0.5	0.5	0.4	0.4	0.4
Insurance	insured vs uninsured	0.8	0.8	0.8	0.6	0.6	0.6	0.7	0.7	0.7	1.1	1.1	1.1	1.1	1.1	1.1
	Medicaid/S-CHIP vs uninsured	0.7	0.7	0.7	0.6	0.6	0.6	0.9	0.9	0.9	0.6	0.6	0.6	0.9	0.8	0.9
	Other/missing vs uninsured	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	1.0	1.0	1.0
UTD 431331	yes vs no	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2
WIC	yes vs no	1.0	1.0	1.0	1.3	1.3	1.3	1.0	1.0	1.0	1.0	1.0	1.1	1.2	1.2	1.2
	other vs no	0.4	0.4	0.4	0.6	0.6	0.7	0.6	0.6	0.6	0.5	0.5	0.5	0.8	0.8	0.8
Provider Facility	public vs private	0.7	0.7	0.7	0.6	0.6	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.8	0.8	0.8
	hospital vs private	1.1	1.1	1.1	1.0	1.0	1.0	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
	military/ other vs private	0.7	0.6	0.7	0.7	0.7	0.7	1.1	1.1	1.1	0.6	0.6	0.6	0.5	0.5	0.5
	mixed vs private	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.6	0.6	0.6

*Logistic regression was used to fit multivariable models and estimate odds ratios (OR) for the outcome of being not up-to-date using the SURVEYLOGISTIC procedure in SAS with weight and strata statements to account for the study design.

Figure 1: Categorization of Insurance Status of NIS participating children



MANUSCRIPT III: Birth Cohort Analysis of Rotavirus Vaccine Coverage in the United States, 2007-2009

ABSTRACT

BACKGROUND: Rotavirus is the most common cause of diarrhea and vomiting in infants and young children in the United States.[1] Prior to the introduction of the rotavirus vaccine in 2006, 95% of children would have been infected before the age of five years.[2] Coverage rates for rotavirus immunizations have increased since its introduction, however, rates still lag behind other vaccines recommended by the Advisory Committee on Immunization Practices (ACIP). [3,4,5] Currently the National Immunization Survey (NIS) is conducted annually to the vaccination coverage rates of children in the United States between 19 and 35 months of age. Surveys with cross-sectional designs are a valuable way to obtain information regarding overall coverage rates. However, this approach may not be ideal when assessing coverage rates for a vaccine newly introduced into circulation. In theory, each birth year group has a likelihood of receiving a timely immunization. There are many causes for this, such as, greater availability, increased physician knowledge, and more familiarity of the vaccine. Analysis of immunization coverage by birth year may give researchers a better picture of the true uptake of a new vaccine and the children at highest risk of under immunization.

METHODS: Study participants were children born in 2007-2009 who participated in the National Immunization Survey (NIS) in 2008-2011. Trends in rotavirus vaccination coverage were examined in children 19-35 months of age residing in the United States to assess changes in vaccine uptake in specific groups of participants. The primary outcome measure for this study is participant's rotavirus vaccination status. Descriptive analyses

were performed among participants. Bivariate associations for all the risk factors by Rao Scott χ^2 were examined. Multivariable logistic regression was used for the binary up-to-date status for rotavirus vaccination.

RESULTS: The overall coverage rates for rotavirus vaccination increased progressively across study years. During the three-year study period, change in risk varied among groups. (Table 5). Among children born in 2007, children who were first born (OR 1.21 (CI 1.05-1.39)), lived in households above the federal poverty line (OR 1.24 (CI1.01-1.53)), and have mothers whom are college graduates (OR 1.81 (CI 1.40-2.34) all had higher risks of under coverage. In comparison to provides in public facilities, having a private insurance provider was a protective factor for children in 2009. The odds of underimmunzation for Rotavirus was lower among mother who were college graduates (OR 1.62 (CI 1.22 – 2.14) compared those with lower educational achievement. Have a provider based in a private facility remained a risk factor over the three years. There was a protective effect when public facilities were compared to private (OR 0.68 (CI 0.55-0.84) to (OR 0.66 (CI 0.52-0.84)). A child being up-to-date with the 4:3:1:3:3:1 immunization series was shown to be highly protective for having full coverage of rotavirus vaccination vs those not up-to-date for that series.

CONCLUSION: Overall coverage rates for the rotavirus vaccine have increased steadily. There are clear groups of children who are at greater risk for not receiving a newly introduced vaccine. These groups do not follow necessarily reflect the groups which are typically expected to be at high risk for underimmunzation. Public health officials must be certain that newer vaccines are available to lower income populations. There should be increased education to physicians in both the private and public sector to ensure proper vaccine coverage.

INTRODUCTION

Rotavirus (RV) is the most common cause of diarrhea and vomiting in infants and young children. This double-stranded RNA virus is transmitted by the fecal oral route. Symptoms include fever, vomiting, and watery diarrhea. Immunity from infection is incomplete, but repeat infections tend to be less severe than the original infection.[1]

In the 1990s through early 2000s, RV was responsible for more than 400,000 outpatient physician visits, 200,000 Emergency Department visits, and 55,000 to 70,000 hospitalizations.[2] Since its introduction, the RV vaccine has substantially reduced hospital admissions of young children for diarrhea.[3-5] A reduction in hospitalizations due to diarrhea from 2001-2006 compared to 2007-2008 of 33% among children five years of age and below has been reported.[6] By 2008, the Advisory Committee on Immunization Practices (ACIP) recommended Rotarix® and RotaTeq® for routine rotavirus vaccination of infants. Two or three doses of live oral rotavirus vaccine is recommended at ages two, four, and six months concurrently with other vaccines given at these ages.[7,8]

The NIS is conducted annually and surveys households in the United States. The purpose of this cross-sectional design is to determine the vaccine coverage for each child at that one point in time. This is irrespective of the actual age the child received the vaccine. It is only required that they are up-to-date at the time of the interview. Rotavirus vaccine coverage rates have increased since its introduction, however still lags behind other ACIP recommended vaccines.[9-11]

Cross-sectional designs are valuable to obtain information regarding overall coverage rates. However, this approach may not be ideal when assessing coverage rates for a vaccine newly introduced into circulation. In theory, each birth year group may have an increased likelihood of receiving a timely immunization from greater availability, increased physician knowledge, and more familiarity of the vaccine. Analysis of immunization coverage by birth year may give researchers a better picture of the true uptake of a new vaccine and the children at highest risk of under immunization.

METHODS

Data Sources

National Immunization Survey (NIS) is a nationally representative survey which estimates childhood immunization coverage rates in the United States, District of Columbia, U.S. Virgin Islands, Guam, and Puerto Rico. It is conducted jointly by the National Center for Immunizations and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC).[12]

The first component of NIS is a list-assisted random-digit-dialing telephone survey administered to households in the United States with children of ages between 19 and 35 months at the time of the interview. This computer-generated list of telephone numbers includes both land lines and cell phones.

A parent or guardian of an eligible child is interviewed regarding the child's immunization history, demographic, and health care information. Upon completion, the interviewer asks for permission to contact the child's medical provider to verify immunization history. During follow-up, a mailed survey is sent to the child's immunization provider. An immunization history from providers is obtained.[13-18] Data from immunization providers are used to validate the child's immunization history reported by the parent/guardian in the Household Telephone Survey. Only provider validated data was used in this study.

Discrepancies between household and provider reported vaccination histories are reconciled. Immunization data that are not consistent between NIS reports and state registry reports are flagged. First, an electronic procedure is used to correct minor errors. Then, medical providers are contacted for either all or a sample of inconsistent cases to verify discrepant data. The combined household and provider reports are used to form "best value" estimates of vaccination coverage. Estimates for childhood immunization coverage are produced for the nation and non-overlapping geographic areas consisting of the 50 states, the District of Columbia, and selected large urban areas. NIS also contains demographic, socio-economic, and geographic variables for participating children and households. On the health systems level, NIS collects data on provider characteristics and health insurance. [13-22] Data from NIS surveys in years 2008 to 2011 are used for this study.

Study Design

In this study, we limited the data to children residing in the 50 states born in 2007-2009. The proper birth cohort is determined based on the month and year of birth. For instance, a child born in 2007 are eligible for participation in 2008, 2009, or 2010 NIS rounds based on their date of birth and age 19 to 35 months criteria eligibility for NIS participation. Therefore the 2007 birth cohort contains has data from 2007-2009 NIS years. Figure 1 is a lexis diagram describing NIS years contributing to each birth cohort.

The primary outcome measure for this study is a record of a child being up-to-date (UTD) for their rotavirus vaccine. A child is considered UTD if they received ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]) by 36 months of age.[23] Child-level risk factors for noncompliance with the rotavirus vaccination were assessed among children born in 2007, 2008, and 2009.

The covariates assessed for association with coverage were selected based on previously published peer reviewed studies.[24-27] Characteristics of the child included age group on the day of the initial interview; sex and first-born status; race/ethnicity classified as Hispanic, non-Hispanic white only, non-Hispanic black-only or other/multiple races. The region of residence is represented by the census region corresponding with the state.

Covariates pertaining to the mother include age, which is categorized into three groups: under 20 years, 20-29 years, and 30 and above; marital status which was constructed into a dichotomous variable of married and never married/widowed/divorced; education of mother in four groups less than 12 years, 12 years, greater than 12 but non-college graduate, and college graduate and/or greater; poverty status based on the census poverty thresholds from the previous year (there were three categories: above poverty line, at or below the poverty line, and unknown poverty status); and number of people in household recoded to two categories: 2-3 people and four or greater.[18-22]

Health-related information included insurance status. This variable was constructed to combine several distinct variables related to insurance using a hierarchical selection process as seen in Figure 1. In the first step, a child was classified as 'uninsured' if they did not have medical insurance at any time. Next, a child would be classified as 'Medicaid/S-Chip' if they participated in either program. "Insured" children were those who had health insurance provided through employer or union; covered by Indian health service, military health care, Tricare, Champus, or Champ-VA; or other health insurance or health care plan. The remaining children were categorized as missing/other. The category of 'Other' represents interviewees who stated having 'some other type of insurance'. While there is an open-ended follow-up question asking for the name of this other insurance, we do not have access to this response. Up-to-date with the full vaccine series was selected at 4:3:1:3:3:1 defined as at least four doses of DTaP (Diphtheria, Tetanus, and Acellular Pertussis), three doses of Polio, one dose of MMR (Measles, Mumps, and Rubella), three doses of Hib (Haemophilus Influenza Type b), three doses of Hepatitis B, and one dose of Varicella.

The Woman Infant Child (WIC) variable was categorized as yes using WIC benefits, not using WIC benefits, and other. Other is comprised of never heard of WIC, do not know, and refused to answer. Provider facility was self-reported by the physician and was classified as entirely public health facilities, entirely private, entirely hospital based facilities, military/other, and mixed facility type.

Statistical Analysis

All statistical analyses were performed using SAS version 9.4. Descriptive analyses were conducted for all NIS participants by study year and further by study year among those who have completed the rotavirus vaccine series. Bivariate analysis assessed relationships between the covariates and the outcome of rotavirus vaccine status using the Rao Scott x^2 to determine the statistical significance of the covariates. Cramer's V was also used to test for possible collinearity among variables. A cutoff p-value of 0.20 was set to study associations in multivariable logistic regression. A Rao Scott χ^2 was calculated to examine the difference between observed and expected frequencies. The Survey Logistic Procedure in SAS was used to obtain estimates of odds ratio of not being UTD for rotavirus vaccination. Weight and strata statements were used to take into account the weighted and stratified nature of this data.

RESULTS

Study Population

Table 1 shows the demographic characteristics among NIS participants by birth year. In each birth cohort, the size ranged from 4,038,283 to 4,477,438 participants (Table 1). Consistently, during the three birth year groups, participants were approximately 51% male and 55% non-Hispanic white. In the 2007 birth year group

21.8% lived in households with two to three residents at the time of the NIS survey. This number rose to 24.2% for the 2009 birth year. There was an increase in children who were first born (53.3% to 60.3%), children who ever received WIC benefits (39.4% to 46.4%) and children going to providers based in public (8.6% to 9.3%) or hospital (10.5% to 10.9%) facilities with birth year.

There was a 7.9% increase in coverage for the 4:3:1:3:3:1 series from 2010-2014. Rotavirus coverage increased as well during with birth year. The lowest coverage rate for rotavirus was 53.8% in the 2007 birth year to a high of 70.7% in the 2009 birth year.

Vaccination Coverage

Among children who were up-to-date with their rotavirus vaccine (Table 2) most were male (range 50.3% to 51.2%) and non-Hispanic white (range 60.7.1% to 55.5%). The maternal and household characteristics of subjects that were UTD differed by cohort. For example, for children born in 2009, mothers of children were up-to-date for rotavirus tended to be older (60.6% were 30 years or older), married (70.5%), more educated (39.8% graduated college) and more likely to live above poverty (69.0% lived about poverty line).

In each cohort, greater than 76% of children whom were up-to-date with the rotavirus vaccine had also completed the 4:3:1:3:3:1 series. Among types of provider facilities, most children exclusively went to providers practicing at a private facility (64.1% - 63.8%) and were covered under a private health insurance carrier (96.2% - 99.2%).

The greatest increase in coverage over three-year study period was among Whites. The difference in coverage rates between 2007 and 2008 was 14.6% (CI 14.5-14.6). By the end of the five years the smallest improvement was among children who were not up to date for the 4:3:1:3:3:1vaccine series with a difference of 3.9% (CI 3.8-3.9). (Table 3)

Factors Associated with Under immunization

Table 4 shows significant associations between rotavirus vaccination coverage and covariates that had Cramer's V p-values below 0.20. Collinearity was not to be found and all covariates were included in statistical models.

For the three-birth year groups, odds of under immunization among groups changed. (Table 5) Children born in 2007, were first born (OR 1.21 (CI 1.05-1.39)), lived in households that are above the federal poverty line (OR 1.24 (CI1.01-1.53)), and had mothers who are college graduates (OR 1.81 (CI 1.40-2.34) all had higher risks of under immunization.

There was a consistent protective effect when public facilities were compared to private: OR =0.68 (CI 0.55-0.84) in 2007, OR = 0.70 (CI 0.56-0.88) in 2008, and OR = 0.66 (CI 0.52-0.84) in 2009. A child being up-to-date with the 4:3:1:3:3:1 immunization series was shown to be highly protective for having full coverage of rotavirus vaccination in each birth year group.

CONCLUSION

This study demonstrates the impact of the birth cohort effect in the assessment of vaccine coverage in the United States. It shows the importance of using alternative approaches to properly examine the uptake of newly introduced vaccines. The populations at greatest risk for underimmunzation may not be the groups which we typically would assume to see based on past research.

The effect of birth cohort in the prevalence of disease has been noted.[28, 29] When comparing the decline in prevalence of latent tuberculosis infection (LTBI) it was noted that although older age groups have higher rates of tuberculosis infections when compared to younger in the United States observed LTBI prevalence in this group represents an underestimate of infection.[30] This has been contributed to the birth cohort effect and waning immunologic reactivity over time.

NIS has a cross-sectional design which is valuable in obtaining information regarding overall coverage rates. Cross-sectional studies are relatively inexpensive and can be conducted faster since researchers can survey many people of different age ranges at the same time.[31] Yearly comparisons were used to determine where the gaps are in immunization coverage. However, this approach may not be ideal when assessing coverage rates for a vaccine newly introduced into circulation.

In theory, each birth year group has an increased likelihood of receiving a timely immunization. In respect to the introduction of the Rotavirus vaccine, it was first available in 2006. Children born 2007 had greater odds of receiving this vaccine due to greater due to factors such as greater availability, increased physician knowledge, and more familiarity of the vaccine. Analysis of immunization coverage by birth year may give researchers a better picture of the true uptake of a new vaccine and the children at highest risk of under immunization.

Consistently over the three birth cohorts, full coverage of the 4:3:1:3:3:1 vaccine series is the strongest predictor for rotavirus vaccine coverage. The overall coverage rate for these six vaccines tend to be higher since they have been on the schedule longer and are mandated for school admissions to the vast majority of schools in the United States. Rotavirus vaccine is only mandated for admission to schools in three states: Idaho, Louisiana, and Rhode Island, however, it still seems to positively benefit from school-based mandates from other childhood vaccines.

Factors associated with health care access to groups with a lower socio-economic status tend to demonstrate increased levels of risk. Children who were ever enrolled in WIC, received Medicaid/S-Chip benefits, were uninsured at any point, and/or received health care at public based providers initially typically have higher levels of risk. In this study, among children born in 2007, households who fall above the poverty line and children whose mothers have graduated college tended to be at greater risk of not being up-to-date with the Rotavirus vaccine. Seeing a provider based in a private facility showed to be a risk factor. This impact continued over the study period.

Typically, the introduction of a new vaccine triggers the addition of resources available to communities with lower SES and known to have challenges with access to care. In this study, our hypothesis is that once the funding for these ‘start up’ are exhausted there is a significant negative impact on the children in these communities.

Additionally, private providers cannot be ignored either. This study shows a slow decrease in risk among children who go to private providers. Low compliance in medical practices may be due to the lack of a physician's knowledge and familiarity to the new vaccine. Physicians can play a crucial role in increasing vaccine coverage, especially, when newly introduced. Physician counseling, aid in parental decision-making and continuing the physician-patient relationship are initiatives that could increase confidence in immunization programs.[42] Focused education of physicians in communities which may not typically be considered 'high risk' may be important in increasing compliance.

Strengths of this study include that the NIS database is a large national database which has been reviewed and validated. This weighted sample enables the results to be statistically generalizable for all children aged 19 to 35 months in the United States. The use of multiple years of data enable the assessment of trends and patterns. Examining the data based on birth cohort allows us to see the gradual impact of the ACIP recommendations for the rotavirus vaccination for children under the age of 12 months. Additionally, all data obtained via telephone surveys were confirmed with a child's medical care provider to insure accuracy in the immunization estimates for each child in this study.

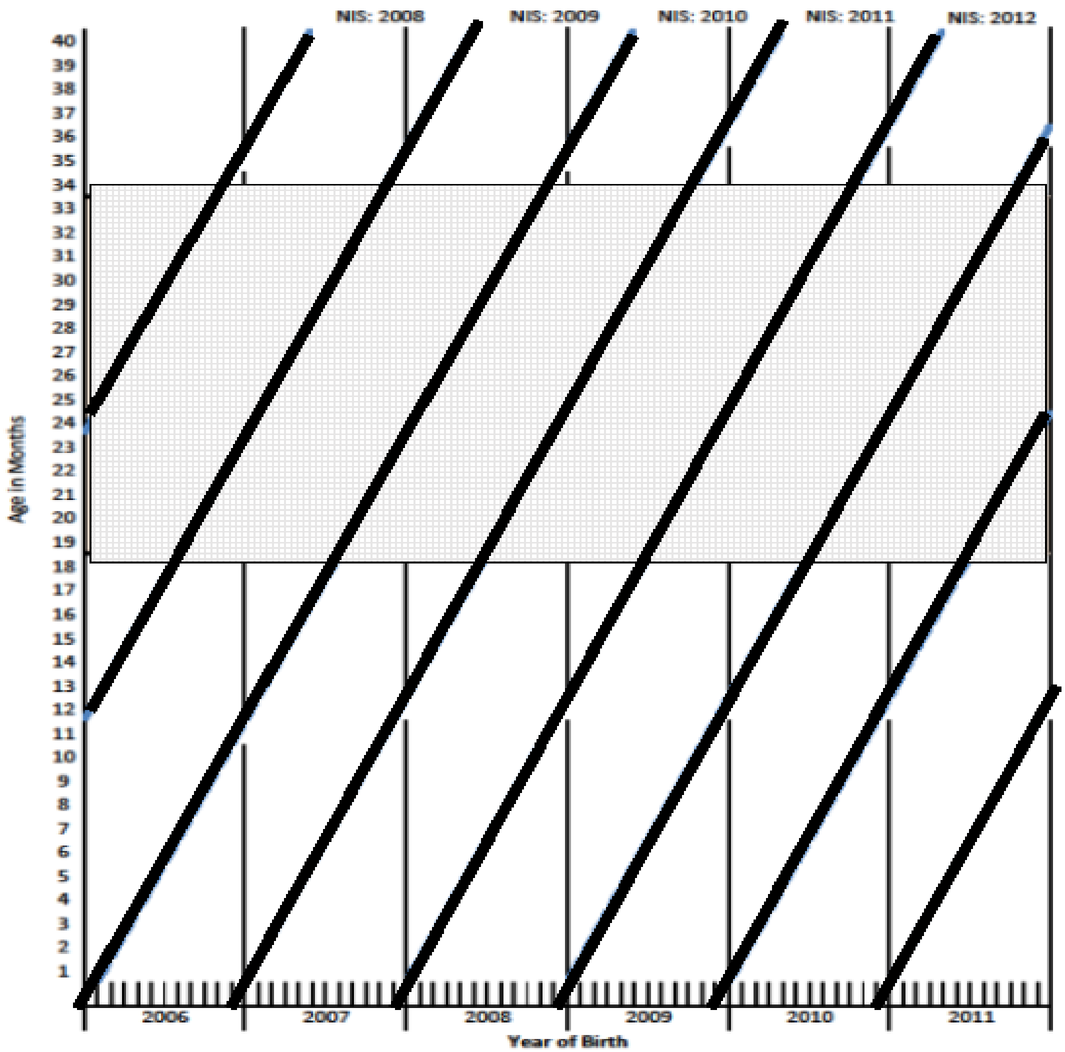
This study does have limitations. The NIS is a random digit dial telephone survey; therefore, bias may remain due to households without telephones even after statistical adjustments. Only children with vaccination histories confirmed by their provider were included for analysis which can result in underestimates of vaccination coverage.

There has been extensive research on the effectiveness of the rotavirus vaccine. This study examines the coverage of the rotavirus vaccine throughout the United States. Incidence of rotavirus infections among children have declined since the introduction of the vaccine. The reduction has resulted in the reduction of hospitalizations and death due to complications. [32,33,34] However, despite the availability of two effective rotavirus vaccines and national immunization recommendations for vaccination at age 19-35 months, rotavirus vaccination remains underutilized for infants. [35,36] Targeted short and long-term strategies tailor to various demographics is important to increase coverage rates. Different types of approaches are needed to have a prolonged positive impact on coverage rates.[37]

Public health officials must be cognizant of the fact that the reasons for the noncompliance to the rotavirus vaccine may differ from that of other more established vaccines. As research continues and new vaccines are introduced, it is important to note the various factors that can affect coverage and uptake in a population. Once early and late adopters are identified, proper public health strategies can be planned. The knowledge of the barriers in coverage can have an immediate impact on public health policy and procedures for developing more effective methods of increasing overall vaccine coverage for children.

The factors which influence the coverage and uptake of vaccines differ immediately after vaccine introduction. Therefore, it may not be appropriate to apply our current knowledge pertaining to the groups at greatest risk for under-immunization under these circumstances.

Figure 1 Lexis Diagram Depicting the Creating of Birth Cohorts



NIS participants born 2007, 2008, and 2009 were included in the analysis. Each NIS annual survey contains data from multiple birth cohorts. The corresponding NIS years

2008 (partial), 2009, 2010, 2011, and 2012 (partial). The rotavirus vaccine was first approved by ACIP in 2006, therefore 2007 is the earliest NIS which can be used

Figure 2: Categorization of Insurance Status of NIS participating children

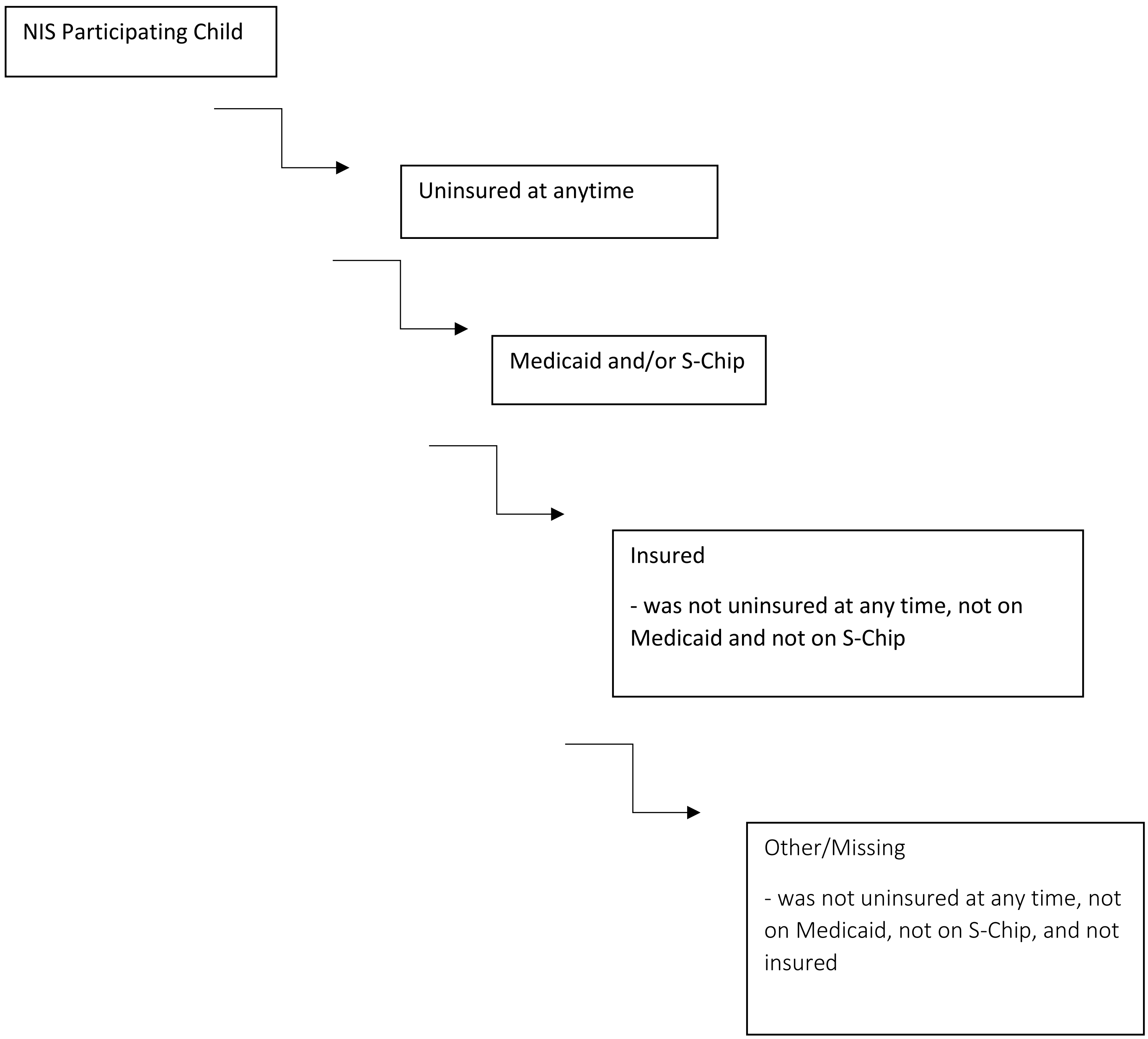


Table 1: Demographic Characteristics at the time of Participation in National Immunization Survey (NIS)						
	Birth Year					
Characteristic	2007		2008		2009	
Total No.	4,477,438		4,395,595		4,038,283	
Age group at time of NIS participation n (%)						
19-23 months	1,349,691	(30.1)	1,376,963	(31.3)	1,188,378	(29.4)
24-29 months	1,485,377	(33.2)	1,450,105	(33.0)	1,396,568	(34.6)
30-35 months	1,642,370	(36.7)	1,568,527	(35.7)	1,453,336	(36.0)
Sex n (%)						
Male	2,300,307	(51.4)	2,230,177	(50.7)	2,063,483	(51.1)
Female	2,177,131	(48.6)	2,165,418	(49.3)	2,063,483	(51.1)
Race/Ethnicity n (%)						
Hispanic	942,649	(21.1)	924,477	(21.0)	883,788	(21.9)
Non-Hispanic White	2,593,370	(57.9)	2,446,012	(55.6)	2,184,089	(54.1)
Non-Hispanic Black	509,107	(11.4)	556,075	(12.7)	481,006	(11.9)
Other/Multiple	432,312	(9.7)	469,031	(10.7)	489,401	(12.1)
First born n (%)						
Yes	2,385,907	(53.3)	2,437,706	(55.5)	2,435,172	(60.3)
No	2,091,531	(46.7)	1,957,889	(44.5)	1,603,111	(39.7)
No. people in household n (%)						
2-3	977,653	(21.8)	964,719	(21.9)	975,878	(24.2)
4+	3,499,785	(78.2)	3,430,875	(78.1)	3,062,405	(75.8)
Age of mother (yrs.) n (%)						
<= 19	93,535	(2.1)	87,022	(2.0)	77,367	(1.9)
20-29	1,382,150	(30.9)	1,504,575	(34.2)	1,512,779	(37.5)
>=30	3,001,754	(67.0)	2,803,998	(63.8)	2,448,137	(60.6)
Marital status n (%)						
Married	3,181,300	(71.1)	3,223,335	(73.3)	2,846,664	(70.5)
Never/widowed/ divorced	1,296,138	(28.9)	1,172,260	(26.7)	1,191,619	(29.5)
Education of mother n (%)						
<12 Years	590,610	(13.2)	619,541	(14.1)	532,414	(13.2)
12 Years	2,048,288	(45.7)	1,991,726	(45.3)	1,900,272	(47.1)
College grad	1,838,540	(41.1)	1,784,328	(40.6)	1,605,596	(39.8)
Poverty status n(%)						
Above poverty	3,338,994	(74.6)	3,155,612	(71.8)	2,785,869	(69.0)
Below poverty	921,124	(20.6)	1,018,014	(23.2)	1,043,472	(25.8)
Unknown	217,320	(4.9)	221,969	(5.0)	208,942	(5.2)
Insurance status n (%)						
Insured	2,261,106	(50.5)	2,189,006	(49.8)	1,966,644	(48.7
Medicaid/S-CHIP	680,571	(15.2)	703,295	(16.0)	666,317	(16.5)
Uninsured at any point	775,559	(34.3)	748,640	(34.2)	684,392	(34.8)
UTD Rotavirus[1] n (%)						
Yes	2,410,255	(53.8)	2,773,934	(63.1)	2,853,228	(70.7)
No	2,067,183	(46.2)	1,621,661	(36.9)	1,185,054	(29.3)
UTD 4:3:1:3:3:1[2] n(%)						
Yes	3,089,707	(69.0)	3,354,517	(76.3)	3,104,060	(76.9)
No	1,387,731	(31.0)	1,041,078	(23.7)	934,223	(23.1)

Child Ever Received WIC						
Yes	1,764,194	(39.4)	1,923,844	(43.8)	1,871,932	(46.4)
No	2,697,738	(60.3)	2,465,242	(56.1)	2,465,242	(61.0)
Other	15,506	(0.3)	6,509	(0.1)	4,172	(0.1)
Provider Facility Types n (%)						
All Public Facilities	384,189	(8.6)	429,176	(9.8)	376,403	(9.3)
All Hospital Facilities	468,114	(10.5)	423,185	(9.6)	441,593	(10.9)
All Private Facilities	2,760,954	(61.7)	2,579,887	(58.7)	2,458,006	(60.9)
Military Facilities/Other	268,769	(6.0)	382,245	(8.7)	210,472	(5.2)
Mixed	562,804	(12.6)	550,221	(12.5)	515,865	(12.8)

[1] Receive ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for

[2] Based on 4:3:1:3:3:1 series – 4+ Dtap (Diphtheria, Tetanus, and Acellular Pertussis), 3+ Polio, 1+ MMR (Measles, Mumps, and Rubella), 3+ Hib (Haemophilus Influenza Type b), 3+ HepB (Hepatitis B), and 1+ Varicella

[3] Includes NIS years 2008-2012

Table 2: Characteristics at the Time of Participation in National Immunization Survey (NIS) for all Participants Born in 2007-2009 and their mothers who are up-to-date with Rotavirus Vaccination

	Birth year					
Characteristic	2007		2008		2009	
Total No.	2,410,255		2,773,934		2,853,228	
Age at NIS participation n (%)						
19-23 months	732,245	(30.4)	876,194	(31.6)	856,850	(30.0)
24-29 months	820,935	(34.1)	903,524	(32.6)	982,503	(34.4)
30-35 months	857,075	(35.6)	994,216	(35.8)	1,013,875	(35.5)
Sex n (%)						
Male	1,211,235	(50.3)	1,389,079	(50.1)	1,460,263	(51.2)
Female	1,199,020	(49.7)	1,384,855	(49.9)	1,392,965	(48.8)
Race/Ethnicity n (%)						
Hispanic	472,025	(19.6)	605,203	(21.8)	622,574	(21.8)
Non-Hispanic White	1,463,027	(60.7)	1,547,936	(55.8)	1,582,445	(55.5)
Non-Hispanic Black	242,981	(10.1)	320,913	(11.6)	305,881	(10.7)
Other/Multiple	232,222	(9.6)	299,881	(10.8)	342,328	(12.0)
First born n(%)						
Yes	1,209,440	(50.2)	1,479,353	(53.3)	1,650,995	(57.9)
No	1,200,815	(49.8)	1,294,581	(46.7)	1,202,234	(42.1)
Number people in household n (%)						
2-3	576,822	(23.9)	674,981	(24.3)	726,807	(25.5)
4+	1,833,434	(76.1)	2,098,953	(75.7)	2,126,421	(74.5)
Age of mother(yrs.) n (%)						
≤ 19	42,427	(1.8)	54,261	(2.0)	46,395	(1.6)
20-29	685,754	(28.5)	875,095	(31.5)	985,729	(34.5)
≥30	1,682,075	(69.8)	1,844,578	(66.5)	1,821,105	(63.8)
Marital status n (%)						
Married	1,792,704	(74.4)	2,092,405	(75.4)	2,087,440	(73.2)
Never/widowed/ divorced	981,230	(40.7)	162,841	(5.9)	765,788	(26.8)
Education of mother n (%)						
<12 Years	233,615	(9.7)	339,985	(12.3)	308,046	(10.8)
12 Years	1,035,164	(42.9)	1,192,876	(43.0)	1,290,735	(45.2)
College grad	1,141,476	(47.4)	1,241,072	(44.7)	1,254,448	(44.0)
Poverty status n (%)						
Above poverty	1,917,499	(79.6)	2,081,878	(75.1)	2,074,077	(72.7)
Below Poverty	384,139	(15.9)	558,657	(20.1)	635,138	(22.3)
Unknown	108,617	(4.5)	133,399	(4.8)	144,014	(5.0)
Insurance status n (%)						
Insured	1,272,615	(52.8)	1,550,629	(55.9)	1,480,825	(51.9)
Medicaid/S-CHIP	359,128	(14.9)	380,029	(13.7)	405,158	(14.2)
Uninsured at any point	411,055	(32.3)	471,391	(30.4)	502,000	(33.9)
UTD 4:3:1:3:3:1[2] n(%)						
Yes	1,838,632	(76.3)	2,347,058	(84.6)	2,405,177	(84.3)
No	571,623	(23.7)	426,876	(15.4)	448,051	(15.7)
Child Ever Received WIC benefits						
Yes	832,051	(34.5)	1,109,776	(40.0)	1,216,578	(42.6)
No	1,569,785	(65.1)	1,661,930	(59.9)	1,633,485	(57.3)
Other	8,419	(0.3)	2,228	(0.1)	3,166	(0.1)
Provider Facility Types n(%)						
All Public	150,719	(6.3)	225,772	(8.1)	213,117	(7.5)
All Hospital	262,148	(10.9)	270,612	(9.8)	307,343	(10.8)
All Private	1,544,937	(64.1)	1,706,156	(61.5)	1,821,235	(63.8)
Military Facilities/Other	130,375	(5.4)	223,476	(8.1)	137,877	(4.8)
Mixed	322,076	(13.4)	347,918	(12.5)	373,656	(13.1)

[1] Receive ≥2 or ≥3 doses, depending on the product received (≥2 doses for Rotarix [RV1] or ≥3 doses for RotaTeq [RV5]) by

[2] Based on 4:3:1:3:3:1 series – 4+ Dtap (Diphtheria, Tetanus, and Acellular Pertussis), 3+ Polio, 1+ MMR (Measles, Mumps,

[3] Includes NIS years 2008-2012

Table 3: Change in Rotavirus Vaccine Coverage 2007 vs 2009 among NIS Participants

	2007	2009	Difference	Confidence Interval	
Sex					
Male	52.70	70.80	18.10	18.03	18.17
Female	55.10	67.50	12.40	12.33	12.47
Race/Ethnicity					
Hispanic	50.10	70.40	20.30	20.23	20.37
Non-Hispanic White	56.40	72.50	16.10	16.04	16.16
Non-Hispanic Black	47.70	63.60	15.90	15.83	15.97
Other/Multiple	53.70	69.90	16.20	16.13	16.27
First Born					
Yes	50.70	67.80	17.10	17.03	17.17
No	57.40	75.00	17.60	17.54	17.66
No. in Household					
2-3	59.00	74.50	15.50	15.44	15.56
4+	52.40	69.40	17.00	16.93	17.07
Age of Mother(yrs.)					
<= 19	45.40	60.00	14.60	14.53	14.67
20-29	49.60	65.20	15.60	15.53	15.67
>=30	56.00	74.40	18.40	18.34	18.46
Marital Status					
Married	56.40	73.30	16.90	16.84	16.96
Never/widowed/ divorced	64.30	75.70	11.40	11.46	11.34
Education of Mother					
<12 yrs.	39.60	57.90	18.30	18.23	18.37
12 yrs.	50.50	67.90	17.40	17.33	17.47
College grad	62.10	78.10	16.00	15.94	16.06
Poverty Status					
Above poverty	57.40	74.40	17.00	16.94	17.06
Below Poverty	41.70	60.90	19.20	19.13	19.27
Unknown	50.00	68.90	18.90	18.83	18.97
UTD 4:3:1:3:3:1:2					
Yes	59.50	77.50	18.00	17.94	18.06
No	41.20	48.00	6.80	6.73	6.87
WIC Benefits					
Yes	47.20	65.00	17.80	17.73	17.87
No	58.20	66.30	8.10	8.03	8.17
Provider Facility Types					
All Public	39.20	56.60	17.40	17.33	17.47
All Hospital	56.00	69.60	13.60	13.53	13.67
All Private	56.00	74.10	18.10	18.04	18.16
Military/Other	48.50	65.50	17.00	16.93	17.07
Mixed	57.20	72.40	15.20	15.14	15.26

Table 4: Bivariate Analysis: Rotavirus Vaccine coverage by participant characteristics among NIS participants

Percentage UTD with Rotavirus Vaccine						
Year of Birth						
Characteristic	2007		2008		2009	
Total No.	%	p-value	%	p-value	%	p-value
Age Group n(%)		<0.0001		<0.0001		<0.0001
19-23 months	54.3		63.6		72.1	
24-29 months	55.3		62.3		70.4	
30-35 months	52.2		63.4		69.8	
Sex n(%)		0.518		<0.0001		<0.0001
Male	52.7		62.3		70.8	
Female	55.1		64.0		67.5	
Race/Ethnicity n(%)		<0.0001		<0.0001		<0.0001
Hispanic	50.1		65.5		70.4	
Non-Hispanic White	56.4		63.3		72.5	
Non-Hispanic Black	47.7		57.7		63.6	
Other/Multiple	53.7		63.9		69.9	
First Born n(%)		<0.0001		<0.0001		<0.0001
Yes	50.7		60.7		67.8	
No	57.4		66.1		75.0	
No. People in Household n(%)		<0.0001		<0.0001		<0.0001
2-3	59.0		70.0		74.5	
4+	52.4		61.2		69.4	
Age of Mother(yrs.) n(%)		<0.0001		<0.0001		<0.0001
≤ 19	45.4		62.4		60.0	
20-29	49.6		58.2		65.2	
≥30	56.0		65.8		74.4	
Marital Status n(%)		<0.0001		<0.0001		<0.0001
Married	56.4		64.9		64.3	
Never/widowed/ divorced	75.7		63.9		73.3	
Education of Mother n(%)		<0.0001		<0.0001		<0.0001
<12 Years	39.6		54.9		57.9	
12 Years	50.5		59.9		67.9	
College grad	62.1		69.6		78.1	
Poverty Status n(%)		<0.0001		<0.0001		<0.0001
Above poverty	57.4		66.0		74.4	
Below poverty	41.7		54.9		60.9	
Unknown	50.0		60.1		68.9	

Insurance Status n(%)		<0.0001		<0.0001		<0.0001
Insured	54.6		62.8		70.9	
Medicaid/SCHIP	38.7		69.2		69.8	
Uninsured at any point	45.5		58.2		58.1	
UTD 4:3:1:3:3:1[2] n(%)		<0.0001		<0.0001		<0.0001
Yes	59.5		70.0		77.5	
No	41.2		41.0		48.0	
Child Ever Received WIC n(%)		<0.0001		<0.0001		<0.0001
Yes	47.2		57.7		65.0	
No	58.2		67.4		66.3	
Other	54.3		34.2		75.9	
Provider Facility Types n(%)		<0.0001		<0.0001		<0.0001
All Public Facilities	39.2		52.6		56.6	
All Hospital	56.0		63.9		69.6	
All Private	56.0		66.1		74.1	
Military/Other	48.5		58.5		65.5	
Mixed	57.2		63.2		72.4	

Table 5: Multivariable Analysis: Lack of Rotavirus Vaccine Coverage among NIS Participants

		2007			2008			2009		
	Effect	Point Est	95% CI		Point Est	95% CI		Point Est	95% CI	
Race Ethnicity	Hispanic vs white	0.96	0.79	1.15	1.33	1.11	1.61	1.23	1.00	1.51
	black vs. white	0.86	0.69	1.05	0.88	0.71	1.10	0.90	0.71	1.15
	other/multiple vs. white	0.97	0.79	1.18	0.99	0.79	1.24	0.89	0.72	1.09
First Born	yes vs no	1.21	1.05	1.39	1.16	1.00	1.36	1.40	1.16	1.69
No. in Household	4+ vs. 2-3	1.03	0.87	1.23	1.28	1.06	1.55	1.00	0.80	1.25
Maternal Age group	<=19 vs >=30	1.06	0.62	1.81	1.13	0.71	1.79	0.80	0.46	1.37
	20-29 vs >=30	1.01	0.87	1.18	0.88	0.75	1.03	0.77	0.65	0.91
Maternal Marital Status	married vs other	1.00	0.89	1.12	0.94	0.77	1.14	0.97	0.80	1.18
Maternal Education	12 Years vs <12 Years	1.32	1.05	1.67	1.10	0.88	1.37	1.28	1.00	1.64
	College grad vs. <12 Years	1.81	1.40	2.34	1.36	1.05	1.77	1.62	1.22	2.14
Poverty Status	Above poverty vs. below poverty	1.24	1.01	1.53	1.20	0.98	1.47	1.22	0.98	1.53
	Unknown vs. below poverty	1.11	0.80	1.54	1.11	0.75	1.65	1.14	0.77	1.68
Insurance	insured vs uninsured	1.47	0.99	2.18	0.57	0.41	0.79	0.74	0.53	1.04
	Medicaid/S-CHIP vs uninsured	1.21	0.51	2.89	0.64	0.32	1.29	0.52	0.22	1.21
UTD 431331	yes vs no	0.51	0.45	0.58	0.32	0.28	0.37	0.31	0.26	0.36
WIC	yes vs no	1.00	0.83	1.20	0.84	0.70	1.01	0.90	0.74	1.10
	other vs no	0.86	0.42	1.76	0.41	0.14	1.17	0.63	0.29	1.37
Provider Facility	public vs private	0.68	0.55	0.84	0.70	0.56	0.88	0.66	0.52	0.84
	hospital vs private	1.17	0.96	1.43	1.11	0.89	1.37	0.94	0.75	1.17
	military/other vs private	0.95	0.81	1.13	0.87	0.74	1.03	0.91	0.76	1.09

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CONCLUSION

Surveillance is a core function of public health. It is the ongoing, systematic collection, analysis, and interpretation of health data which is essential to the planning and implementation of public health practice. To be truly effective it needs to include a continuous ongoing system. One existing surveillance system for Rotavirus pretains to vaccine coverage. Beyond this is it important for public health efforts to focus on change and improvement on the procedural level as well. The incorporation of TQM and the PDSA cycle with public health surveillance can have a positive impact on immunizations. This will incorporate the various surveillance systems, allow for the evaluation, and constant improvement over time to increase the quality of the one primary outcome.

Rotavirus is the most common cause of diarrhea and vomiting in infants and young children. There are several existing surveillance systems used by Public Health related to rotavirus in the United States. One important component is vaccine coverage. The implementation of the rotavirus vaccination program in the United States has resulted in a marked reduction in diarrhea hospitalizations and related hospital costs among children nationally.

Rotavirus vaccine coverage rates have steadily increased annually. The rotavirus vaccine was added to the National Immunization Survey (NIS), the primary source of vaccine estimates, in 2007 and assess the cumulative incidence of vaccine coverage for fourteen childhood vaccines. In these studies, we further examined the methods behind immunization coverage for the rotavirus vaccine and assessed the groups at greatest odds of being under immunized. We looked at this serial cross-sectional survey to assess the impact of the stratification of NIS data by year of birth. It has been shown that year a child is born can provide important additional information. In both methods of analysis, the overall rotavirus coverage rate increased each year. Both methods demonstrated that odds of certain groups to not be immunized are considerable higher than their peers. However, the actual groups varied in some instances.

Consistently throughout the study period, full coverage of the 4:3:1:3:3:1 vaccine series was the strongest predictor for rotavirus vaccine coverage. It is believed that the coverage rate of these six vaccines tends to be higher since it represents vaccines which have been on the schedule longer. The six vaccines in this series are also all mandated for most school admissions in the United States. Rotavirus vaccine is only mandated for admission to schools in three states: Idaho, Louisiana, and Rhode Island; however, rotavirus vaccine coverage has been positively benefited from school based mandates for other childhood vaccines.

In both approaches, birth order influences the odds of being fully immunized for rotavirus. Children who were first born had greater odds of under immunization when compared with children who were born at a later birth order. A possible reason for this could be the increased familiarity with the vaccines and the vaccination process after the first child.

Seemingly the type of facility in which the physician or vaccine provider practices can also be a factor leading to proper coverage. A child who goes to a private provider has greater odds of being timely immunized than a public based facility. Low compliance in medical practices may be due to the lack of a physician's knowledge and familiarity with the new vaccine. Physicians can play a large role in increasing vaccine coverage, especially when newly introduced. Physician counseling, aid in parental decision-making, and continuing the physician-patient relationship suggest initiatives that could increase confidence in immunization programs. Focused education of physicians serving communities which may not typically be considered 'high risk' may be important for increasing compliance.

The impact of household income differs depending on the method of analysis. Using the conventional serial cross-sectional approach children who live in households which fall below the poverty level tend to be more immunized for rotavirus when compared with children who live in households which lay above the federal poverty line. This protective effect increased during the five-year study period.

In contrast, analysis by birth cohort shows that living in households below the federal poverty line is associated with under immunization. This risk seems to be fairly constant and unchanged over the three year period which was examined.

NIS has a cross-sectional design which is valuable in obtaining information regarding overall coverage rates. Cross-sectional studies are relatively inexpensive and can be conducted faster since researchers can survey many people of different age ranges at the same time. Yearly comparisons of coverage data can be useful in determining where the gaps are in immunization coverage.

This study demonstrates the impact of the birth cohort effect in the assessment of vaccine coverage in the United States. It shows the importance of using alternative approaches to properly examine the uptake of newly introduced vaccines. The populations at greatest risk for underimmunzation may not be the groups which we typically would assume to see based on past research. In theory, each birth year group has an increased likelihood of receiving a timely immunization. In respect to the introduction of the Rotavirus vaccine, it was first available in 2006. Children born 20009 had greater odds of receiving this vaccine due to greater due to factors such as greater availability, increased physician knowledge, and more familiarity of the vaccine. Analysis of immunization coverage by birth year may give researchers a better picture of the true uptake of a new vaccine and the children at highest risk of under immunization.

Strengths of this study include that the NIS database is a large national database which has been reviewed and validated. This weighted sample enables the results to be statistically generalizable for all children aged 19 to 35 months in the United States. The use of multiple years of data enable the assessment of trends and patterns. Examining the data based on birth cohort allows us to see the gradual impact of the ACIP recommendations for the rotavirus vaccination for children under the age of 12 months. Additionally, all data obtained via telephone surveys were confirmed with a child's medical care provider to insure accuracy in the immunization estimates for each child in this study.

This study does have limitations. The NIS is a random digit dial telephone survey; therefore, bias may remain due to households without telephones even after statistical adjustments. Only children with vaccination histories confirmed by their provider were included for analysis which can result in underestimates of vaccination coverage.

Public health officials must be cognizant of the fact that the reasons for the noncompliance to the rotavirus vaccine may differ from that of other more established vaccines. As research continues and new vaccines are introduced, it is important to note the various factors that can affect coverage and uptake in a population. Once early and late adopters are identified, proper public health strategies can be planned. The knowledge of the barriers in coverage can have an immediate impact on public health policy and procedures for developing more effective methods of increasing overall vaccine coverage for children.

The factors which influence the coverage and uptake of vaccines differ immediately after vaccine introduction. Therefore, it may not be appropriate to apply our current knowledge pertaining to the groups at greatest risk for under-immunization under these circumstances.