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Effect of Race/Ethnicity, Poverty, and its Interaction on Missed Influenza Vaccine Receipt in 6-23 month U.S. Children

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Master of Public Health

Epidemiology

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Abstract

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By Nicole Ariel Richardson

Background

Children aged 6-23 months old are at high risk of influenza-associated hospitalization and death. In 2009, influenza vaccine recommendations were updated to include two doses of influenza, separated by four weeks, the first time a child, aged 6 to 23 months, is vaccinated. Racial and ethnic disparities have been documented for influenza vaccination in this population, but little is known about the combined impact of race/ethnicity and poverty-level disparities in influenza vaccine coverage in this age group.

Methods

Using provider-verified immunization history data from the 2013 National Immunization Survey, we assessed the independent effects of race/ethnicity and poverty status on influenza vaccine coverage among 6-23 month old children, as well as interaction of these factors. We conducted bivariate comparisons and evaluated the interaction of race/ethnicity and poverty status through multivariate logistic regression models.

Results

During the 2012-2013 influenza season, 60.8% of children aged 6 to 23 months were eligible for influenza vaccination. Of these eligible children, 61% did not get the influenza vaccine. In bivariate analysis, above poverty children were less likely to have not received influenza vaccine (odds ratio: 0.72, 95% confidence interval [CI]: 0.59, 0.88) compared to below poverty children. Compared to non-Hispanic white children, Non-Hispanic Black children had higher odds of missed vaccine receipt (odds ratio [OR]: 1.70, CI: 1.32, 2.19). In multivariate analysis, the only race/ethnicity and poverty level interaction group with a significantly increased odds of lack of influenza vaccine was Non-Hispanic Black children living above poverty compared to non-Hispanic white children living above poverty (OR: 1.62, 95% CI: 1.10, 2.38).

Conclusions

The findings on the interaction of race/ethnicity and poverty status highlight the need to address both of these factors in tandem, to better identify the role of programs such as Vaccines for Children (VFC) in improving vaccine uptake in a way that transcends racial lines.

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Chapter I: Background/Literature Review

Overview of Influenza

Influenza is a highly infectious disease, affecting about 10% of the world's population annually, corresponding to around 500 million people (1). Transmitted through inhalation of microdroplets, the influenza virus infects the respiratory system (1). Influenza virus infection usually results in mild symptoms such as high fever, greater than 37.8^{o}C, lasting a few days (2). There may also be respiratory symptoms such as cough or coryza as well as otitis media (3). At its most severe, influenza can result in pneumonia and even death (2). Influenza can be self-limited in older children and adults between 18-49 years of age, through the use of vaccines annually, but children under the age of three years have complications that result in hospitalization and/or death similar to the elderly population. These complications are a result of weakened or underdeveloped immune systems in these groups (3). Furthermore, influenza has a large economic burden in the United States for all age groups and populations, with 11 billion to 18 billion dollars spent in direct or indirect costs (3).

History of Influenza

Symptoms specific to influenza were noted by Hippocrates and Livy in 412 B.C. (4). These notes are said to be the first historical accounts of influenza pandemics. More common influenza pandemics that led to many deaths occurred in the 19th and 20th century, most notably, The Spanish Flu. The Spanish Flu pandemic occurred from 1918 to 1920 and caused over 40 million deaths worldwide, the most to date in history. Most of the deaths occurred in young people due to secondary bacterial pneumonia (4). This was thought to be because of poverty and malnutrition attributable to the war (2). The high levels of pneumonia occurring in otherwise healthy young adults was also thought to be caused by a cytokine storm, which is a rapid accumulation of proinflammatory cytokines after influenza infection (4). The cytokine storm led to an overactive immune system which in the lungs, cause immune cells to enter into the systemic circulation system producing systemic

sepsis. This results in acute lung injuries, hypotension, and death (5). In more recent years, there have been additional influenza pandemics, including the 1957 H2N2 pandemic and the 1968 H3N2 pandemic, responsible for six million deaths collectively (6). Additionally, in 2009, a novel H1N1 strain caused the first pandemic of the 21st century (7).

Influenza Virology

In 1933, scientists from the National Institute for Medical Research in London discovered and isolated the influenza virus (2). Influenza is a member of the Orthomyxoviridae family. Within the Orthomyxoviridae family are two genera, one including influenza A and B viruses and the other including influenza C. Influenza A has the ability to infect both human and animal host while influenza B and C infect only human host (2).

Influenza viruses are made of eight RNA sequences that frequently mutate due to a highly active RNA polymerase. RNA polymerase is responsible for replication of the influenza virus, RNA, for creation of new virions. However, RNA polymerases can make errors in the transcription process, leading to mutations that may slightly alter the new influenza virus. This process is known as antigenic drift. Antigenic drift occurs due to the misplacement of nucleotides, creating a new but similar gene sequence. The need to create these new vaccines in response to slightly altered influenza virus strains is the reason for the need to create new annual seasonal influenza vaccines. Additionally, because the influenza genome is segmented into 8 segments, it is possible animals inflected with more than one influenza type at the same time may provide the opportunity for viral replication to incorporate segments from different influenza strains into a novel strain. This is known as antigenic shift. The result is a novel virus, for which there is typically little immunity in the population, which can lead to influenza pandemics (8).

Vaccine Creation

While antigenic shift causes viral strains that usually cannot be predicted, vaccines are usually always available for each influenza season due to the predictability of antigenic drift, which necessitates routine surveillance of circulating influenza strains. Though surveillance aids in understanding the predictability of the virus, vaccine production is still tedious (1). Surveillance is under the control of the World Health Organization where the epidemiology of the influenza virus is monitored. This process started in 1947 and looks for evolution in the virus make up in both animal and human host for influenza A and B (1). Vaccine production takes about six months and approximately 250 million doses are put on the market annually in more than 100 countries (1). Unfortunately, on a global scale, 89% of the 195 countries received less than the target rate of 159 doses per 1,000 population (9).

The first influenza vaccine was manufactured in 1946 from inactivated influenza viruses replicated on mice pulmonary cells and then eventually on the embryo of a hen's egg. Currently, two of the three vaccines in production still use eggs to grown the virus. The inactivated influenza vaccine, administered as an injectable vaccine, and the live attenuated vaccine, administered as a nasal spray, are made from influenza vaccine initially grown in hen eggs (10). In these processes, the viral strain is harvested in the embroynated egg to reduce contamination. Next, the strains are sequences to make sure they are similar to the reference influenza viral strain. If they are suitable, the strains are further tested to see if they replicate at necessary levels and keep their antigenic stability through the inactivation and purification procedures. If this process is successful, bulk manufacturing of the vaccine begins (1).

There are also cell-based influenza vaccines that grow the vaccine viruses within cultured cells instead of incubating them in hen eggs. Because this vaccine only uses eggs for initial replication, less eggs are used overall and therefore this vaccine takes less time to manufacture than regular egg based vaccines. Lastly and more recently, recombinant influenza vaccines do not use eggs at all for production but rather isolate the hemagglutinin (HA) protein from the influenza virus. HA is the

protein that stimulates the human immune response. This manufacturing process takes the shortest amount of time to produce, because it is not dependent on eggs, and it is the only egg free vaccine which is beneficial for individuals with severe egg allergies (10).

Vaccine Effectiveness

Influenza vaccine effectiveness continues to be an issue despite the biannual meetings that discuss the best viral strains to add to the influenza vaccines each year. Due to manufacturing times, it is possible that the influenza vaccine circulating during influenza season may be different from those selected for the vaccine, as was seen in the 2014-2015 influenza season (11). Vaccine effectiveness (VE), which is the measure of protection against disease in a population, depends on various factors. Such factors include: age, immunocompetence, and the similarity between the circulation and the vaccine administered (12). In the United States, since 2005, VE has not risen over 60%. In 2012-2013, VE was only 51% (13).

Chung et al did a study which compared the effectiveness of the live attenuated influenza vaccine (LAIV) versus the inactivated influenza vaccine (IIV) in children between the ages of 2 and 17 years of age. The authors found that the odds of influenza was significantly higher among children with LAIV compared to IIV during the 2009 H1N1 pandemic. During milder seasonal influenza seasons, when H3N2 or B influenza took precedence, the odds of influenza was similar for both LAIV and IIV (14). Despite low levels of vaccine effectiveness, the influenza vaccines are the best interventions we have to date.

Vaccine Recommendation

To achieve the best protection against influenza, the Advisory Committee on Immunization Practices (ACIP) recommends vaccination for all individuals 6 months and older. The ACIP meets three times a year to discuss recommendations that pertain to various vaccines, including influenza. As a result, ACIP advises influenza vaccine administration at the very start of influenza activity,

which can occur in the fall months. ACIP recommends that receipt occurs as early as possible, with at least the first receipt of vaccine in October, when the influenza season usually begins (12).

For children who receive influenza vaccine for the first time, between the ages of six months and eight years old, two doses, four weeks apart, are recommended for optimal immune response. Studied in 2009, with one vaccine dose, protective antibody response levels were at 50% for children 6-35 months and 75% for those 3-9 years of age. To increase protection, two doses separated by at least four weeks will increase the antibody response (12).

For other populations, as mentioned previously, all individuals should receive the vaccine. Those who are pregnant can receive the vaccine but should not take the live attenuated influenza vaccine. If an individual has an egg allergy, between the ages of 18-49 years old, the normal influenza vaccine is still recommended as long as the allergy is mild. For allergies that are more severe, the recombinant influenza vaccine, which is made without the use of hen eggs, can be used (12).

When vaccine supply is low or the United States is facing a pandemic and priorities are necessary, those at highest risk of being an outpatient for an influenza related illness are first to receive vaccines. This population of individuals includes: children 6-59 months, all people 50 years of age or older, individuals with chronic conditions such as asthma and diabetes mellitus, individuals who are immunosuppressed, and women who are or will be pregnant (12).

Burden of Disease

The United States experiences an average of 30,000 deaths and more than 100,000 hospitalizations from influenza related illness and complications (15). When more virulent strains (e.g. Influenza A/H3N2) are in circulation, the numbers of deaths often rise. For the H3N2 influenza A strain prominent seasons, there were 7,722 influenza associated deaths compared to the 2,856 deaths when that strain was not prominent (16). Similarly, during the H1N1 pandemic, there were 12,469 deaths and 274,304 hospitalizations (17). For children under the age of 5 years old, influenza most commonly caused outpatient medical visits (15).

During the 2012-2013 influenza season, a total of 12,377 hospitalizations occurred due to confirmed influenza. In 2012-2013, among children aged 0-4 years, 66.2 cases/100,000 reported influenza while in children aged 5-17 years, 14.5 cases/100,000 reported. In adults aged 18-49 years, 16.4 cases/100,000 reported influenza. While in children, the rate of hospitalizations decreases as children age, this trend is not true in adults. Among adults aged 50-64 years, 41.2 cases/100,000 reported influenza while 191.2 cases/100,000 reports occurred in individuals of the age of 64 years (18).

In the United States, pediatric (aged 18 and younger) deaths are tracked. In the 2012-2013 influenza season, there were 149 laboratory confirmed influenza associated deaths. Among these deaths, 29 deaths occurred in children aged 6-23 months of age (18). As of May 2015, for the 2014-2015 influenza season, there were 141 laboratory confirmed influenza deaths in children under the age of 18, with 23 deaths in children aged 6-23 months (19).

Influenza Vaccination Coverage

Despite the need for annual influenza vaccination in the United States, vaccine coverage levels never reach the US Department of Health and Human Services target goal of 80% in healthy individuals. (20). During the 2012-2013, children between the ages of 6 months to 4 years had 63.5% vaccine coverage. As age increases, these coverage rates decline (21).

Vaccination Disparities

Insurance Coverage

Lack of adequate insurance coverage is among one of the most prominent reasons for a lack of vaccination coverage. During the 2012-2013 influenza season, 56.6% of children ages 6 months to 17 years received influenza vaccination, increasing from 43.7% during the 2009-2010 influenza season. Though an increase in coverage, target goals still were not reached. It is thought that the main reason for the gain in coverage in children is due to the use of the Vaccine for Children (VFC)

program. The VFC program works to reduce disparities by allowing children who are Medicaid-eligible, underinsured, uninsured, and American Indians to be vaccinated free of charge at their medical home or specific clinics. Studies show that children with health insurance have higher vaccine coverage than children without insurance (22).

In a study by Srivastav et al, authors researched differences between VFC entitled children compared to privately insured children. Results show similar coverage between VFC children and privately insured children, 56.0% to 57.2% respectively. Focusing on the VFC eligible group, uninsured children had lower vaccine coverage compared to those who were Medicaid eligible, 44.8% versus 58.6%, during the 2012-2013 influenza season (22).

During the same influenza season, influenza vaccine coverage was similar for private insurance and VFC entitled children. However, there were important subgroup differences in vaccine coverage among these children. Compared to VFC-entitled children, coverage was higher among privately insured children who were aged 6-23 months or aged 2-4 years, children who were non-Hispanic whites or non-Hispanic other race/multiple race, male, or who were above the federal poverty level. Despite differences by socio-demographics within insured or VFC-eligible children, the most significant disparity is found among the uninsured but VFC-eligible children. This lack of coverage may be due to a lack of awareness of the VFC program (22).

Negative Beliefs/Attitudes about Influenza Vaccines

Aside from the lack of insurance coverage among certain populations, attitudes about influenza vaccines lead to lower coverage than target goals. In a study done by Nyhan et al, authors focus on the notion that the influenza vaccine itself causes the influenza. In a study population of 1,000 participants chosen to represent the demographics of the U.S. adult population in 2012, 43% agreed with the statement that the vaccine itself causes the influenza. When offered corrective information about the vaccine, vaccination intent decreased among those already heavily concerned

with vaccine side effects. Among those who already had a low level of concern regarding the vaccine side effects, vaccination intent did not change (23).

The large percentages of individuals with negative perceptions about the vaccine have great consequence for vaccine coverage of 6-23 month old children, who are vaccinated under the discretion of parents and guardians. If vaccination intent did not change, even after corrective information, there must be more research on what information specifically causes aversion and how it can be restructured to encourage vaccine uptake (23).

Provider Initiated Discussion about Influenza Vaccines

Another element leading to disparities in influenza vaccine uptake is provider initiated discussion. A study done in Los Angeles looking at vaccine uptake during the height of H1N1, analyzed the primary reasons for lack of coverage among a population of poverty stricken, ethnic/racial minorities, low education, and uninsured adults. This specific population was the focus of study because minority groups are underserved and highly vulnerable for influenza illness and/or death, whether uninsured or insured/VFC-eligible. While the fear of vaccines causing influenza was of primary concern, results indicate that lack of trust of the provider is also a major concern in this population (24). This is important because a health care provider recommendation is one of the strongest predictors of vaccine acceptance (25).

Based on the study, cases where providers initiated the conversation with regard to vaccines, there was better receptiveness and receipt of the vaccine as compared to those who did not have conversations or had to initiate the conversation themselves. The issue that arises is that many underserved people do not have insurance and therefore do not have routine contact with providers who can give more corrective information on influenza vaccine safety and receipt. This lack of trust may be due to a lack of interaction then and if those relationships can be fostered more, then when there is interaction, vaccine coverage may increase in these populations. Increased interaction among

this population would have direct positive results on children 6-23 months of age who rely on their parents for all vaccine decisions (24).

Location of Provider

Concerning ethnic/racial minorities, despite many studies noting their negative opinions and beliefs regarding influenza vaccination, studies found that minority populations respond better to vaccine recommendations when assured by physicians and other medical staff in provider office based settings compared to other establishments where vaccine is administered, such as grocery store pharmacies. As a result, minorities are often in the position for missed opportunities for influenza vaccination if providers are not present and offering or recommending the vaccine. This is similar to the previous statement that noted how vaccine acceptance increases when providers initiate conversations on the vaccine. Findings according to this study show that the increase of uptake when in office based settings would lower the racial/ethnic disparities by almost half among minority populations (26).

Similarly, ease of vaccination for children impacts vaccine uptake. In 2010, there was a Connecticut law passed that required child care facilities, like preschools, to vaccinate children. This was an attempt to decrease the number of missed opportunities, this time among children 6 to 59 months of age. This age group was chosen because preschool aged children are at an increased risk of influenza illness or death due to the close proximity children with each other, which facilitates transmission. During the 2012-2013 influenza season, this age group had influenza vaccination coverage of 69.8% which was among the lowest vaccination coverage levels for this age group, only above rotavirus and hepatitis A vaccines. Using surveillance systems that monitor the uptake of influenza vaccine, the passage of this law in Connecticut resulted in an increase in vaccine uptake of 16.3 percentage points since the 2009-2010 influenza season (from 67.8% to 84.1%) (27).

Research Question

As illustrated from the previous information, the annual burden of disease from influenza virus infection in the United States is great. Though vaccination is recommended by the ACIP, there are still various disparities that impede optimal vaccine coverage. While this data is available, certain information is not known about the 6-23 month old population that can future determine vaccine uptake issues.

Specifically, in most studies, the 6-23 month old population is usually combined with older children. For this population, it is of interest to determine if there are any age specific factors leading to suboptimal vaccination uptake, or if these data mirror that of the broader pediatric population, including older children. Furthermore, there is still much information unknown regarding the impact of socio-demographic characteristics on influenza vaccination in these young children. While data has shown significant statistics on the effect of racial background or poverty status on the receipt of influenza vaccination, there is no data on the interaction between these two variables. The research question for this analysis is: how does the race/ethnicity, poverty, and the interaction of race and poverty affect eligible children's vaccine coverage? The hypothesis is that below poverty individuals of minority populations will have poorer vaccine coverage despite interventions as compared to above poverty, white individuals in the United States. This question was evaluated using National Immunization Survey-provided vaccination coverage and race and poverty status data.

Chapter II: Manuscript

Effect of Race/Ethnicity, Poverty, and its Interaction on Missed Influenza Vaccine Receipt in 6-23 month U.S. Children

Nicole Ariel Richardson

ABSTRACT

Background

Children aged 6-23 months old are at high risk of influenza-associated hospitalization and death. In 2009, influenza vaccine recommendations were updated to include two doses of influenza, separated by four weeks, the first time a child, aged 6 to 23 months, is vaccinated. Racial and ethnic disparities have been documented for influenza vaccination in this population, but little is known about the combined impact of race/ethnicity and poverty-level disparities in influenza vaccine coverage in this age group.

Methods

Using provider-verified immunization history data from the 2013 National Immunization Survey, we assessed the independent effects of race/ethnicity and poverty status on influenza vaccine coverage among 6-23 month old children, as well as interaction of these factors. We conducted bivariate comparisons and evaluated the interaction of race/ethnicity and poverty status through multivariate logistic regression models.

Results

During the 2012-2013 influenza season, 60.8% of children aged 6 to 23 months were eligible for influenza vaccination. Of these eligible children, 61% did not get the influenza vaccine. In bivariate analysis, above poverty children were less likely to have not received influenza vaccine (odds ratio: 0.72, 95% confidence interval [CI]: 0.59, 0.88) compared to below poverty children. Compared to non-Hispanic white children, Non-Hispanic Black children had higher odds of missed vaccine receipt (odds ratio [OR]: 1.70, CI: 1.32, 2.19). In multivariate analysis, the only race/ethnicity and poverty level group with a significantly increased odds of lack of influenza vaccine was Non-Hispanic Black children living above poverty compared to non-Hispanic white children living above poverty (OR: 1.62, 95% CI: 1.10, 2.38).

Conclusions

The findings on the interaction of race/ethnicity and poverty status highlight the need to address both of these factors in tandem, to better identify the role of programs such as Vaccines for Children (VFC) in improving vaccine uptake in a way that transcends racial lines.

KEYWORDS: Seasonal influenza vaccine; vaccine coverage disparities; race/ethnicity and poverty interaction; 6-23 month old children; NIS

INTRODUCTION

Influenza is a highly infectious disease, infecting about 10% of the world's population annually (1). During the 2012-2013 influenza season, a total of 12,377 hospitalizations occurred due to confirmed influenza. Influenza can disproportionately impact young children. In the 2012-2013 influenza season, among children aged 0-4 years, there were 66.2 influenza hospitalizations per 100,000 population. Furthermore, there were 149 laboratory confirmed deaths in children with 29 deaths occurring in children aged 6-23 months (18).

In the United States, the Advisory Committee on Immunization Practices (ACIP) recommends annual vaccination for all individuals 6 months and older, as early in the influenza season as possible (12). For children who are between the ages of six months and eight years old who are receiving influenza vaccine for the first time, two doses of vaccine, administered four weeks apart, are recommended (12). Despite the great importance of influenza vaccination in children, coverage levels have not consistently reached the US Department of Health and Human Service goals in all age groups (20, 21).

Additionally, there are various subpopulations with continued vaccine coverage disparities. Though influenza vaccine coverage disparities have been studied in general, there has not been a specific focus on the interrelationship of these disparities in the 6-23 month age population. Known disparities include those related to race/ethnicity and poverty, but little is known about the interaction between these factors. Understanding the interaction of these factors will help to identify groups for which specific interventions to improve influenza vaccine coverage should be developed and implemented. We describe the evaluation of the interaction between race/ethnicity and poverty status with regard to influenza vaccine coverage among children aged 6-23 months in the United States in 2013.

METHODS

Research Question and Hypothesis

This research addressed the question: how does the interaction of race and poverty affect eligible children's vaccine coverage? We hypothesized that racial and ethnic minority individuals living below poverty will have lower vaccine coverage compared to white individuals living above poverty, and that within racial and ethnic groups, individuals living below poverty will have lower influenza vaccine coverage than those living above poverty.

Survey Description

We analyzed data from the 2013 National Immunization Survey (NIS). The NIS was created by the National Center for Immunization and Respiratory Diseases (NCIRD) and the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). The target population for the NIS is parents of children between the ages of 19 and 35 months living in households throughout the United States during the time of the interview. The NIS uses both landline and cell phone samples. To conduct the interview, the NIS uses random digit dialing to contact households with children in the target age range. A household interview is used to gather information on demographics and vaccine coverage, and parents are asked if the child's provider(s) can be contacted to verify immunization information. With parental consent, the NIS contacts the child's health care provider(s) to request information regarding the child's vaccinations via the child's medical records. For the present analysis, we restricted the data to children for whom provider verified immunization records were obtained. Child and household demographic information is self-reported from parents/guardians (28).

Influenza Vaccination Eligibility Criteria

To be defined as eligible for this analysis, children had to be between the ages of 6 and 23 months during the 2012-2013 influenza season, defined from October of 2012 to February of 2013.

This age range was chosen as it is directly assessed within the NIS. The NIS determined which children were eligible using birthdate information that was reported by the household and provider during the interview process (28).

Statistical Methods

The NIS identified 13,611 children that had healthcare provider data on vaccination coverage. In this study, we wanted to evaluate children who were eligible for vaccination, defined above, which resulted in 8,188 children for further analysis. We used the influenza vaccine receipt data for each child to classify children according to our outcome measure: having received either no doses of influenza vaccine or at least one dose of influenza vaccine during the 2012-2013 influenza season.

Our exposures of interest were race/ethnicity, poverty status, and the interaction of these variables. Race/ethnicity level classification included Hispanic, Non-Hispanic Black, Non-Hispanic White, and Non-Hispanic Other/ Multiple Race. Poverty Level was originally a tertiary variable (above poverty/greater than $75, 000 annual income; above poverty/greater than federal poverty level but less than $75,000 annual income; below poverty) and was redefined as a dichotomous variable, above and below poverty level.

Additionally, we included as covariates the following sociodemographic variables that may be associated with vaccine coverage: number of children in a household, medical facility, maternal education level, primary language spoken, census region, and current age of child. All sociodemographic variables were self-reported. Number of children in the household was classified as one, two or three, or four or more. Medical facilities were all public, all private, all military/other, or mixed facilities. Maternal education ranged from under twelve years of education to obtaining a college degree. Languages included English, Spanish, and other. Census region included Northeast, South, West, and the Midwest. The current age of the child at time of interview ranged from 19

month to 35 months of age. For the analysis, all continuous variables were categorized. Dummy variables were used for all categorical variables with more than two levels.

We computed weighted proportions of the outcome, exposures of interest, and covariates using PROC SURVEYFREQ with weights provided in the NIS dataset, according to the NIS Data Users Guide (28). Similarly, to evaluate the effect of eligibility on not receiving the influenza vaccine, we calculated odds ratios and 95% confidence intervals by the various covariates, using PROC SURVEYLOGISTIC in the regression analyses. The interaction of race/ethnicity and poverty status was included in the regression models using dummy variables for race/ethnicity, and stratum-specific estimates were computed using contrast statements. SAS (SAS Institute, Inc., Cary, NC, version 9.4) was used for all analyses, and all statistical analysis was conducted at the $\alpha = 0.05$ level.

This analysis utilized previously collected and public use data. As a result, this study was considered to be non-human subjects research and therefore did not require institutional review board approval.

RESULTS

Demographics of Eligible Children 6-23 months of age

We restricted this analysis to children for whom adequate healthcare provider data was available (13,611/23,248, 58.5%). Among these children, 8,188 children were categorized within the NIS as eligible to receive the influenza vaccination based on their birthdates for the 2012-2013 influenza season, and were the focus of this analysis. Approximately 61% of the eligible population did not get the influenza vaccine during the 2012-2013 influenza season. The demographic composition of the eligible sample was 60% Non-Hispanic Whites, 59% Hispanics, 64% Non-Hispanic Blacks, and 62% Non-Hispanic Other/Multiple Race; additionally, 62% were below poverty while 60% were above poverty children. In the non-eligible population approximately 28% did not get the influenza vaccine during the 2012-2013 influenza season. Furthermore, the demographic composition of the non-eligible sample was 40% Non-Hispanic Whites, 41%

Hispanics, 36% Non-Hispanic Blacks, and 38% Non-Hispanic Other/Multiple Race. Within the non-eligible population, 40% were above poverty and 38% were below (Table 1).

Bivariate Analysis among Vaccinated and Unvaccinated Eligible Children

In bivariate analysis, unvaccinated children with parents at or above the poverty level had lower odds of missed vaccine uptake. This association was statistically significant. Compared to households with only one child, children living in households with four or more children were more likely to not be vaccinated (Table 2).

Non-Hispanic Black children have 70% higher odds of missed vaccine uptake as compared to non-Hispanic White children (odds ratio: 1.7 [95% confidence interval (CI) 1.32, 2.19]). This was the only significant racial or ethnic difference identified (Table 2).

Compared to English speaking households, households in which the NIS interview was conducted in Spanish had lower odds of missed influenza vaccination (odds ratio: 0.63 [95% CI 0.42, 0.94]). No difference was observed for other interview languages. Higher educated mothers, with at least a college degree, were less likely to have children unvaccinated against influenza, relative to mothers with less than a high school diploma. (Table 2).

The interaction between Race/Ethnicity and Poverty

Using multivariate logistic regression, adjusting for all covariates in the analysis, Non-Hispanic Black children living above the poverty line were more likely to not receive influenza vaccine compared to their White above poverty counterparts (odds ratio: 1.62 [1.10, 2.38]). For below poverty children, Multiple Race/Other Race children were less likely than Non-Hispanic White children to have not received influenza vaccine. Interestingly, there were little difference comparing across both race/ethnicity and poverty status difference (e.g. Non-Hispanic Black below poverty compared to Non-Hispanic White above poverty) (Table 3). Despite the higher odds in above poverty Non-Hispanic Black children compared to above poverty Non-Hispanic White

children, the absolute coverage illustrates relatively high levels of missed influenza receipt in both levels of poverty for Non-Hispanic Black children as well as below poverty Non-Hispanic White Children, compared to Hispanic children, Non-Hispanic Other/Multiple Race children, and Non-Hispanic White children above poverty (Table 4).

DISCUSSION

Despite consistent ACIP recommendations for influenza vaccination in individuals 6 months of age and older, this study adds to the literature concerning lack of influenza vaccine coverage primarily in minority populations (12, 20-27). There have not been many studies, to our knowledge, that focus specifically on the 6-23 month age group for influenza vaccine coverage, especially focusing on the effects of race/ethnicity, poverty status, and its interaction on missed vaccination uptake in the United States.

In this study, Non-Hispanic Black children, as compared to Non-Hispanic White children had the highest odds of missed vaccine receipt, whereas Hispanic children did not have a documented disparity in influenza vaccine receipt. These findings were consistent with other findings in literature, both for children in our specific age group as well as the individuals in all age groups (22, 24, 26). Similarly, above poverty children were less likely to have missed influenza vaccine receipt consistent with the established literature (22, 24, 26). However, the interaction between race/ethnicity and poverty status has not been widely studied in vaccine coverage evaluations.

Even after adjusting for known covariates that may impact influenza vaccine uptake, Non-Hispanic Black children living above poverty had a higher odds of missed vaccine receipt compared to their Non-Hispanic White above poverty counterparts. These findings identify the gaps in our current studies as well as possible interventions to address these issues. Many of the studies we reference point out the below poverty individuals most at risk or that there are ethnic/racial minorities in need for vaccination interventions, however the truth is more complicated. Not only are Non-Hispanic Black children, in both poverty levels, more likely to miss influenza vaccination, but Non-Hispanic

White children below poverty are as well. The Vaccines for Children program aims to reduce economic barriers for vaccination yet children below poverty, particularly those whom are Non-Hispanic White or Black, are still not getting influenza vaccination at the frequency of Hispanics and Non-Hispanic Other/Multiple Races (29). For Non-Hispanic Black children specifically, both levels of poverty are at approximately equal frequency of missed vaccination which indicates that poverty level alone does not protect against missed vaccine receipt. The successes of the VFC program cannot be denied but a large segment of our population in the United States is still missing influenza vaccine receipt and that should be addressed through more interventions (29).

One such intervention is the Affordable Care Act (ACA). Though this intervention stipulates that preventative services, such as immunizations, are to be provided with no cost sharing, the effects of the law may not have been fully realized at the time this iteration of the NIS was conducted. The implementation of ACA especially in more recent years has resulted in higher coverage of vaccination for those not previously insured in America (30). Though this was not part of this study, it would be an important next step in research to determine what factors specifically affect Non-Hispanic children and their parents who are above the federal poverty line. Studying the coverage of influenza receipt in years after the ACA may demonstrate the effectiveness of the law on children maintaining higher vaccination coverage in the United States. It would also be necessary to study specific factors that affect Non-Hispanic Black children whom are above poverty and their ability to receive influenza vaccination. Similarly, Non-Hispanic Other/Multiple Race children are also exceeding all coverage barriers, both above and below poverty. Again, though beyond the scope of this study, it would be important to analyze the factors contributing to this group's success in influenza vaccination coverage and how that could possibly be applied or understood in other racial and poverty groups with vaccination coverage problems.

STRENGTHS & LIMITATIONS

There were a few limitations regarding this study worth addressing. The primary limitation is non-bias response. The NIS uses adjusted weights to take into account non-response for households and/or providers. Though the dual frame uses weight to produce an accurate estimate, it does not take into account all of the potential non-response bias such as: the amount of non-working/non-residential cell phone numbers and the lack of cell phone users being sent advance letters about the survey. Furthermore, the outcome variable did not fully assess ACIP influenza vaccine recommendations regarding two-dose vaccine receipt when a child is vaccinated for the first time. The outcome of interest is the number of flu shot doses received, categorized into either one or more doses or no doses. Though for the purpose of the study, we focused on those who did not get any doses, relative to children who received at least one influenza vaccine dose. However, this does not address whether children actually are following recommendations and getting two doses or are just getting one dose. Lastly, the analysis used provider data for all vaccine related information as a way to receive less biased data. Despite this, it is possible that some vaccine information could be missed, possibly if the child does not have a stable medical home or the influenza vaccine was not received by their main provider and rather a clinic or pharmacy that did not keep their records on file.

Despite these limitations, there are several strengths for this analysis. Among these is the NIS data using weighted sampling to produce nationally representative estimates. Furthermore, the NIS also uses a large national sample which produces a highly representative population similar to that of the United States' total population. Lastly, due to the use of provider verified vaccination data, bias as a result of self-reporting was negligible.

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Table 1. Demographic data of children 6-23 months old during National Immunization Survey (NIS) 2012-2013. (N= 13,611)

Variable of Interest	*Weighted Percentages (%)*	*Weighted Percentages (%)*
Children eligible for influenza vaccine		
Eligible	60.80	
Non-eligible	39.20	
	Among eligible participants:	***Among non-eligible participants:***
Did not receive influenza vaccine		
Got at least one flu shot	60.70	39.30
Did not get a flu shot	61.06	38.94
Poverty level of participants		
Above Poverty	60.14	39.86
Below poverty	61.97	38.03
Medical facility types		
All Public Facilities	63.32	36.68
All Hospital Facilities	61.07	38.93
All Private Facilities	59.80	40.20
All Military/Other Facilities	65.86	34.14
Mixed Facilities	61.68	38.32
Region where participants are located		
Northeast	63.66	36.34
Midwest	61.71	38.29
South	59.40	40.60
West	60.33	39.67
Age groups of children at time of interview		
19-23mo	89.55	10.45
24-29mo	79.86	20.14
30-35mo	18.99	81.01
Number of children living in the household		
One	63.73	36.27
Two or Three	59.89	40.11

Four or More	58.35	41.65
Race/Ethnicity of participants		
Hispanic	59.47	40.53
Non-Hispanic White	60.37	39.63
Non-Hispanic Black	63.66	36.34
Non-Hispanic Other/Multiple Race	62.49	37.51
Language In Which Interview was Conducted		
English	61.28	38.72
Spanish	56.82	43.18
Other	66.19	33.81
Education of mother		
<12 Years	59.79	40.21
12 Years	61.66	38.34
>12 Years, Non-College Grad	57.74	42.26
College Grad	62.71	37.29

Source: CDC, NCRID and NCHS (2015), 2014 National Immunization Survey.

Note: Frequencies are weighted

Table 2. Unadjusted Bivariate Logistic Regression Analysis among Eligible Participants, National Immunization Survey (NIS) 2012-2013. (N=8,188)

	Percentage Unvaccinated	Percentage Vaccinated	Unvaccinated Children	
	%	%	OR	95% CI
Poverty Status				
Above Poverty	26.42	73.58	0.72	0.59 , 0.88
Below Poverty	33.25	66.75	--	--
Age groups of children at Interview				
19-23 mo	31.03	68.97	Referent	--
24-29 mo	27.91	72.09	0.86	0.70, 1.05
30-35 mo	23.07	76.93	0.67	0.50, 0.89
Number of children living in the household				
One	27.39	72.61	Referent	--
Two or Three	27.34	72.66	1.00	0.80, 1.24
Four or More	38.26	61.74	1.64	1.24, 2.18
Education of mother				
<12 Years	33.78	66.22	Referent	--
12 Years	32.31	67.69	0.94	0.68, 1.29
>12 Years, Non-College Grad	30.22	69.78	0.85	0.63, 1.15
College Grad	22.54	77.46	0.57	0.43, 0.76
Medical facility types				
All Public Facilities	34.10	65.90	Referent	--
All Hospital Facilities	30.47	69.53	0.85	0.59, 1.22
All Private Facilities	28.22	71.78	0.76	0.57, 1.02
All Military/Other Facilities	30.75	69.25	0.86	0.51, 1.44
Mixed Facilities	21.51	78.49	0.53	0.38, 0.75
Race/Ethnicity of participants				

Hispanic	27.16	72.84	0.94	0.72, 1.22
Non-Hispanic White	28.49	71.51	Referent	--
Non-Hispanic Black	40.42	59.58	1.70	1.32, 2.19
Non-Hispanic Other/Multiple Race	20.75	79.25	0.66	0.49, 0.89
Language In Which Interview was Conducted				
English	29.74	70.26	Referent	--
Spanish	20.90	79.10	0.63	0.42, 0.94
Other	32.78	67.22	1.15	0.51, 2.61
Region where participants are located				
Northeast	17.78	82.22	Referent	--
Midwest	28.01	71.99	1.80	1.41, 2.29
South	37.17	62.83	2.74	2.16, 3.46
West	24.11	75.89	1.47	1.04, 2.08

Source: CDC, NCRID and NCHS (2015), 2014 National Immunization Survey.

Note: Frequencies are weighted

-- = no data

OR = odds ratio

CI = confidence interval

Table 3. Adjusted Multivariate Analysis of Interaction of Race/Ethnicity and Poverty Status on odds of not receiving influenza vaccine among Eligible 6-23 month old children, National Immunization Survey (NIS) 2012-2013. (N=8,188)

	Unvaccinated Children	
	OR	**95% CI**
Hispanic, Above Poverty vs. White, Above Poverty	1.01	0.67, 1.52
Black, Above Poverty vs. White, Above Poverty	1.62	1.10, 2.38
Other, Above Poverty vs. White, Above Poverty	0.71	0.47, 1.06
Hispanic, Below Poverty vs. White, Below Poverty	0.99	0.61, 1.61
Black, Below Poverty vs. White, Below Poverty	1.05	0.71, 1.56
Other, Below Poverty vs. White, Below Poverty	0.52	0.31, 0.86
Hispanic, Above Poverty vs. White, Below Poverty	0.82	0.52, 1.29
Black, Above Poverty vs. White, Below Poverty	1.30	0.84, 2.30
Other, Above Poverty vs. White, Below Poverty	0.57	0.36, 0.90
Hispanic, Below Poverty vs. White, Above Poverty	1.23	0.79, 1.94
Black, Below Poverty vs. White, Above Poverty	1.30	0.91, 1.88
Other, Below Poverty vs. White, Above Poverty	0.64	0.40, 1.04

Source: CDC, NCRID and NCHS (2015), 2014 National Immunization Survey.

OR = odds ratio

CI = confidence interval

Table 4. Frequency of Vaccination Coverage in Eligible 6-23 month old Children by Race/Ethnicity and Poverty Status Interaction, National Immunization Survey (NIS) (N=8,188)

	Unvaccinated Children Frequency	Vaccinated Children Frequency
Hispanic, Above Poverty	26.77	73.23
Hispanic, Below Poverty	29.21	70.79
Non-Hispanic White, Above Poverty	25.86	74.14
Non-Hispanic White, Below Poverty	35.94	64.06
Non-Hispanic Black, Above Poverty	40.37	59.63
Non-Hispanic Black, Below Poverty	41.78	58.22
Non-Hispanic Other/Multiple Race, Above Poverty	20.06	79.94
Non-Hispanic Other/Multiple Race, Below Poverty	24.55	75.45

Source: CDC, NCRID and NCHS (2014), 2013 National Immunization Survey.

Note: Frequencies are weighted

Chapter III: Summary, Public Health Implications, Possible Future Directions

CONCLUSIONS

In conclusion, among eligible 6-23 months children in the United States, those with the highest odds of missed vaccine uptake were those who identified as Non-Hispanic Black. This association held in bivariate analysis as well as in the adjusted multivariate analysis among above poverty Non-Hispanic Blacks and Whites. In the bivariate analysis, those who identified as other or multiple race consistently had lower odds of missed vaccine uptake. In the adjusted multivariate analysis, this association held for below poverty multiple race/other individuals and Non-Hispanic White individuals, as well as multiple race/other individuals that were above poverty compared to Non-Hispanic Whites below poverty.

FUTURE DIRECTIONS

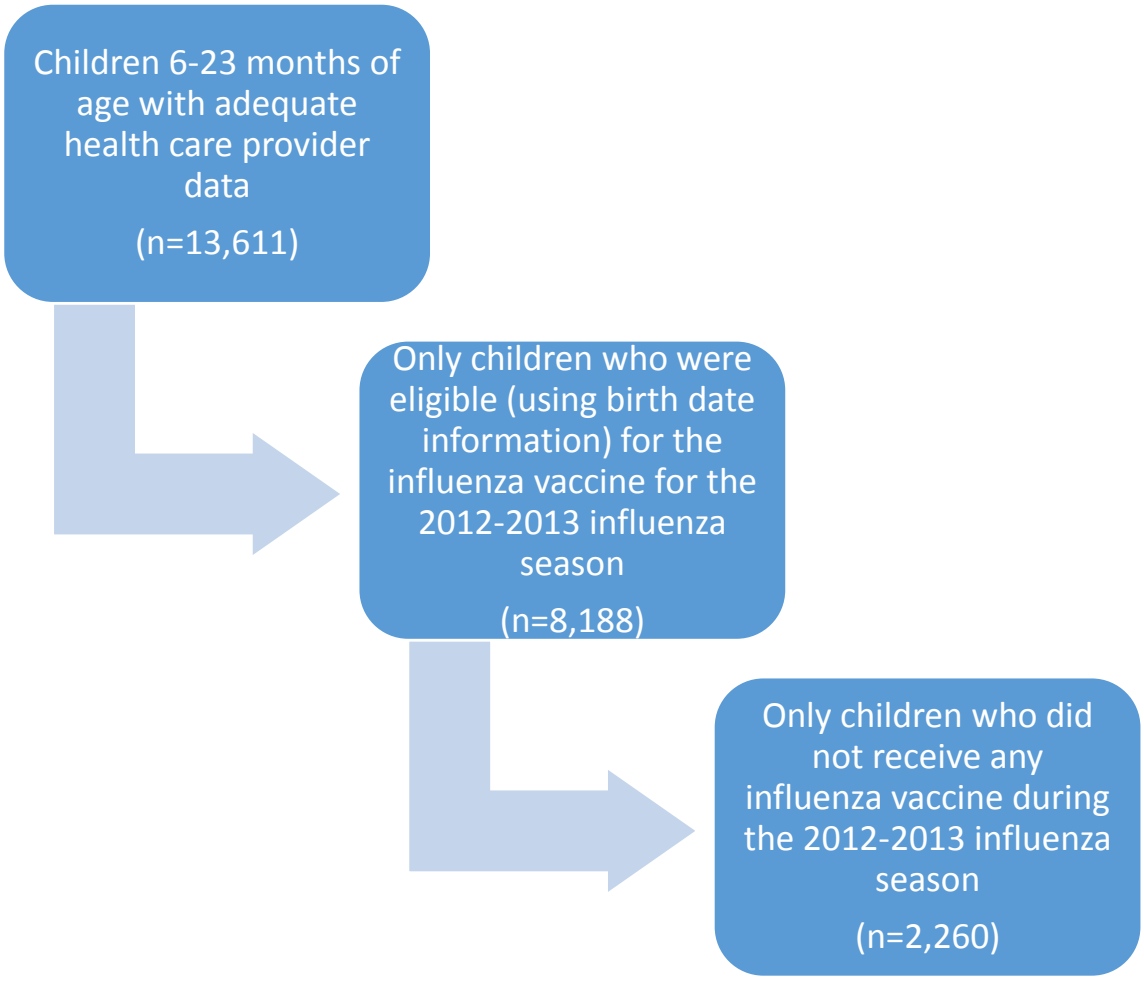
Non-Hispanic Blacks are consistently pointed out in literature as not having high vaccination coverage, at various age groups. In the adjusted multivariate analysis, this held true for children above poverty compared to Non-Hispanic Whites. This association did not hold for below poverty children. In the assessment of absolute influenza vaccination coverage, Non-Hispanic Black children of both poverty levels and Non-Hispanic White children whom are below poverty had the lowest coverage frequencies. Interventions such as the Vaccines for Children (VFC) are an important factor in reducing the vaccination disparities in below poverty children. However, there are still racial and poverty groups more likely to miss receipt opportunities. More studies should be done to assess the specific risk factors associated with missed vaccine uptake in above poverty, Non-Hispanic Black children. The results should be used for further interventions in this population to increase vaccination. Similarly, the NIS clustered multiple race individuals, Alaska Natives, Pacific Islanders together as the "other" group. This group consistently had lower odds for missed vaccine uptake among below poverty children as well as above poverty other/multiple race versus below poverty

Non-Hispanic Whites. Further studies into the ethnicities/races of this group should be done. There may be specific interventions or factors that influence vaccination rates worth assessing for research and implementation in other racial groups experience coverage problems.

PUBLIC HEALTH IMPLICATIONS

As a result of this research, Non-Hispanic Black children, aged 6-23 months of age, are still below the necessary protective influenza vaccination coverage and at risk for serious hospitalizations and death. It is important that interventions are reaching this population at both levels of poverty. Furthermore, programs such as Vaccines for Children, should continue to provide services for below poverty children and even focus much of their efforts on reaching the Non-Hispanic White and Black population yet to be covered.

Appendix



Supplementary Fig. 1. Flowchart of the methodology used to determine eligible children who did not receive influenza vaccine during the 2012-2013 influenza season.