AN ESTIMATION OF COUNTY-LEVEL VACCINATION COVERAGE FOR HUMAN PAPILLOMAVIRUS VACCINE AMONG ADOLESCENTS AGED 13-17 YEARS IN SOUTH EASTERN UNITED STATES OF AMERICA USING BAYESIAN AND SPATIAL EFFECTS MODELS

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by

DAVID YANKEY

Under the Direction of Ruiyan Lou, PhD

ABSTRACT

This dissertation applies Bayesian Hierarchical (BH) methods and Spatial effects at both the state and county levels to estimate Human papillomavirus (HPV) vaccination initiation coverage at the county level in the ten Southeastern U.S. states (925 counties) using 2016 National Immunization Survey-Teen (NIS-Teen) adequate provider data. Small sample sizes yield inadequate precision for direct domain estimators. Bayesian methods allows indirect estimation with small sample size, missing values and covariates via the Markov Chain Monte Carlo (MCMC) method. The BH method, which allows the parameters of a prior distribution or a
population distribution themselves to be estimated from data, is one of the appropriate ways in handling small areas with sparse data because posterior inference is exact which does not rely on asymptotic arguments. We use the conditional autoregressive (CAR) model to capture the spatial correlation and study its role in modeling the HPV vaccination initiation coverage. Additionally, we applied Bayesian modeling of temporal trends of HPV vaccination initiation coverage over time (quarter of survey year) and space (in the 10 southeastern states in US) using NIS-Teen survey years 2011 to 2016 adequate provider data. These methods can be used in further analysis for the temporal trend of HPV vaccination initiation coverage at the county level.

INDEX WORDS: Bayesian Methods, Conditional Autoregressive (CAR), County-Level Vaccination, Deviance Information Criterion (DIC), Human Papillomavirus (HPV), Random Effect, Southeastern States, Temporal Trend.
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DAVID YANKEY

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in the College of Arts and Sciences Georgia State University 2018
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Office of Graduate Studies
College of Arts and Sciences
Georgia State University
May 2018
DEDICATION

I dedicate this dissertation to the Almighty God for making this PhD degree possible for me.
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1 INTRODUCTION

1.1 Background of the Study

1.1.1 Human Papillomavirus Vaccination and Significance

Human papillomavirus (HPV) refers to a group of more than 150 related viruses. Infection with some HPV viruses lead to development of warts and orogenital cancers including mouth/throat, anal/rectal, cervical, vaginal, vulvar, and penile cancers. Statistics from the Centers for Disease Control and Prevention (CDC) reveal that, each year in the United States, about 39,800 new cases of cancer (about 23,300 among women, and about 16,500 among men) are diagnosed in parts of the body where HPV is often found, and HPV causes about 31,500 of these incident cancers. Cervical cancer and oropharyngeal cancers are the commonest HPV associated cancers (de Sanjosé, Bruni, & Alemany, 2014). HPV is generally responsible for over 90% of anal and cervical cancers, almost 70% of vaginal and vulvar cancers, and more than 60% of penile cancers. Even though cancers of the head and neck are commonly caused by tobacco and alcohol use, recent studies show that about 70% of oropharyngeal cancers may be linked to HPV (Chaturvedi et al., 2011; Elrefaey, Massaro, Chiocca, Chiesa, & Ansarin, 2014; Pytynia, Dahlstrom, & Sturgis, 2014). Almost all cervical cancers are caused by HPV. The types of HPV virus that causes cervical cancers are predominantly HPV types 6, 11, 16, 18 with 16 and 18 causing almost 70% of all cervical cancers (Burd, 2003; Braaten & Laufer, 2008). It is estimated that about 79% of anal cancers are probably caused by two types of HPV: 16 and 18 and almost 8% of anal cancers are probably caused by HPV types 31, 33, 45, 52, and 58 (de Martel, Plummer, Vignat, & Franceschi, 2017). The distribution of rates of cancer associated with HPV during 2009 to 2013 by states in the United States (US) is shown in Figure 1-1 below:
Figure 1.1 HPV-Associated Cancer Rates by State During 2009 – 2013. HPV-Associated Cancer Rates by State During 2009 – 2013. (The states are divided into groups based on the rates at which people were diagnosed with an HPV-associated cancer. The rates are the average numbers out of 100,000 people who developed cancer each year. Reference: https://www.cdc.gov/cancer/hpv/statistics/state/index.htm)

The most common sexually transmitted infection in the US is HPV, with an estimated incidence of about 14 million cases each year (Revzina & DiClemente, 2005; Satterwhite et al., 2013). For the period 2013 – 2014, prevalence of any HPV infection was 45.2% for men compared to 39.9% for women aged 18 – 59 years. The prevalence during this same period for high-risk HPV infection was 25.1% and 20.4%, respectively, for this cohort of men and women (McQuillan, 2017). Racial disparities in prevalence also exist. For example, any oral HPV was more prevalent among non-Hispanic black adults (9.7%) and lowest among non-Hispanic Asian adults (2.9%). The CDC states that “HPV is so common that nearly all sexually active men and women get the virus at some point in their lives”.

Protection against warts and orogenital cancers can be achieved with HPV vaccines. The Advisory Committee on Immunization Practices (ACIP) HPV vaccine workgroup commenced review of data on epidemiology and natural history of HPV in 2004, and final recommendations and minor recommendation were presented to ACIP at the June 2006 ACIP meeting. The ACIP recommends routine HPV vaccination at ages 11 or 12 years (vaccination can be given starting at 9 years). Children with a history of sexual abuse or assault are recommended to initiate HPV vaccination at age 9 years. HPV vaccination is also recommended as catch-up vaccination for females through 26 years and for males through age 21 years (males aged 22 through 26 years may also be vaccinated) who were not adequately vaccinated previously. Persons initiating vaccination before age 15 years, are recommended to receive two doses of HPV vaccine (second dose should be administered 6 to 12 months after the first dose; 0, 6-12 month schedule). Persons initiating vaccination on or after age 15 years or persons with immune compromising conditions are recommended immunization schedule of 3 doses of HPV vaccine (0, 1–2, 6-month schedule). For persons with interrupted vaccination schedules, the number of recommended doses is based on age at administration of the first dose (Meites, Kempe, & Markowitz, 2016a).

The U.S. Food and Drug Administration (FDA) approved the quadrivalent vaccine - Gardasil (4vHPV), for four types of HPV, in 2006. In 2009, FDA approved another vaccine that protects against two high-risk types of HPV - Cervarix (2vHPV) and in 2014, a 9-valent vaccine (9vHPV) – Gardasil 9 (Meites, Kempe, & Markowitz, 2016b).
1.1.2 HPV Vaccination Coverage in the United States

HPV vaccination coverage is estimated in dose counts, commonly, ≥1 dose, ≥2 doses and ≥3 doses by the CDC. In 2016, the coverage for HPV vaccination with 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV) vaccines were 60.4 (59.2–61.6) for ≥1, 49.2 (47.9–50.4) for ≥2, and 37.1 (35.9–38.4) for ≥3 dose measures, for females and males combined. Previous rates were comparatively lower 56.1 (54.9–57.4) for ≥1, 45.4 (44.2–46.7) for ≥2, and 34.9 (33.7–36.1) for ≥3 dose measures (Walker et al., 2017).

1.1.3 HPV--Associated Cervical Cancer, Oropharyngeal Cancer, and HPV Vaccination

Coverage by States

Age-adjusted rates of cervical cancer among women per 100,000 population using data from the cancer registry show that during 2009 – 2013, the southeastern states (apart from Georgia, North Carolina and Virginia), Wyoming, and New York had a comparatively higher rate of cervical cancer (7.57 – 12.11) than the other states (Viens et al., 2016). Rates for the other states ranged from 4.43 -7.56 per 100,000 population. The distribution of HPV-associated cervical cancer rates among women in the US by states is shown in Figure 1-2 below. There is no estimate available for Nevada (Viens et al., 2016).

Age-adjusted rates of oropharyngeal cancers among men per 100,000 population using data from the cancer registry during 2009 – 2013, show a similar pattern. For men, the southeastern states (apart from Virginia), Arkansas, Indiana, Louisiana, Maine, Massachusetts, Missouri and Oregon, show rates ranging from 8.42 – 10.03. All the other states have rates ranging from 4.84 – 8.41. The distribution of HPV-associated oropharyngeal cancer rates
among men in the US by states is shown in Figure 1-3 below. There is no estimate available for Nevada (Viens et al., 2016).

For women, age-adjusted rates of oropharyngeal cancers per 100,000 population in the southeastern states (apart from Tennessee, Virginia and West Virginia), Arkansas, Louisiana, Maine, Massachusetts, Missouri, and Montana are from 1.86 – 2.43. All the other states show rates from 0.82 – 1.85. The distribution of HPV-associated oropharyngeal cancer rates among women in the US by states is shown in Figure 1-4 below. There is no estimate available for Nevada (Viens et al., 2016).

Figure 1.2 HPV-Associated Cervical Cancer Rates Among Women in the US by States During 2009 – 2013. (The states are divided into groups based on the rates at which women were diagnosed with an HPV-associated cervical cancer. The rates are the average numbers out of 100,000 people who developed cancer each year. Reference: https://www.cdc.gov/cancer/hpv/statistics/state/cervical.htm)
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State-level coverage for HPV vaccination among persons aged 13 – 17 years in 2016 show that southeastern states are among states with the lowest coverage. Southeastern states have coverage rates for ≥1 dose below 59.0% apart from Georgia (67.3%); for ≥2 doses below 47.5% apart from Georgia (52.9%) and for ≥3 doses below 35.9% apart from Georgia (36.6%) (Viens et al., 2016). HPV vaccination coverage among persons aged 13 – 17 years in 2016 for ≥1 dose, ≥2 doses, and ≥3 doses by states are shown in Figures 1-5, 1-6, and 1-7 respectively below.

Figure 1.4 HPV-Associated Oropharyngeal Cancer Rates Among Women in the US by States During 2009 – 2013. (The states are divided into groups based on the rates at which men were diagnosed with an HPV-associated oropharyngeal cancer. The rates are the average numbers out of 100,000 people who developed cancer each year. Reference:  https://www.cdc.gov/cancer/hpv/statistics/state/oropharyngeal.htm)
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ACIP recommends routine vaccinations for adolescents aged 11 – 12 years for the following vaccine antigens: tetanus, diphtheria and acellular pertussis vaccine (Tdap), meningococcal conjugate vaccine (MenACWY), and HPV vaccine (updated to a 2-dose schedule for immunocompetent adolescents initiating the vaccination series before age 15 years), a booster dose of MenACWY at age 16 years and catch-up vaccination of hepatitis B vaccine, measles, mumps, and rubella (MMR) vaccine, and varicella vaccine for adolescents lacking up-to-date childhood vaccinations (Robinson, Romero, Kempe, & Pellegrini, 2017).
Incidence and prevalence of vaccine preventable diseases especially among children have decreased substantially because of vaccination programs that have increased vaccine coverage (Ventola, 2016). However, the situation is not so for adolescents and young adults aged 11 – 39 years. Focusing on vaccination coverage among adolescents is hence an important step in ensuring that adolescents reduce their risks of contracting vaccine preventable diseases through adulthood and life. These especially include infections that are acquired through sexual activity. Most people get infected with these infections during age of adolescence when they become sexually active. Vaccine preventable diseases that are transmitted sexually include Hepatitis B and HPV. Adolescents are also vulnerable to meningitis and require adequate uptake of the MenACWY vaccine.

Reports from the National Immunization Survey-Teen (NIS-Teen) show that the different vaccines have uneven coverage among adolescents and some vaccination rates are below the Healthy People 2020 target (Reagan-Steiner et al., 2015). These include the HPV vaccine series for males and females, the MenACWY booster dose at age 16 years, and the annual influenza vaccine for all individuals aged 6 months and older. High vaccination coverage among adolescents aged 13 – 17 years was achieved in 2014 for Tdap (86.0%) and MenACWY (79.3%) (Reagan-Steiner et al., 2015). Disparities in state-level vaccination coverage were however evident (Reagan-Steiner et al., 2015). Coverage for influenza vaccination was also low, at 59.3% for children ages 6 months through 17 years in 2014–2015. Undoubtedly, barriers to effective uptake of these vaccines exist and need to be addressed. Barriers predominantly include misconceptions as side effects and perceived possible childhood disability associated with vaccination (Bronfin, 2008). Misconceptions on vaccination effectiveness are associated
with parent’s educational level and access to information on vaccination. Other barriers to vaccine uptake include cost or availability of health insurance. Beliefs, cultural preferences and vaccine hesitancy (Dubé et al., 2013) are also significant barriers to vaccine uptake ultimately affecting vaccination coverage. Variation in healthcare systems are also associated with vaccine uptake. Healthcare systems factors associated with vaccine uptake include healthcare provider availability, healthcare provider recommendation, awareness of vaccination programs and access to healthcare institutions that provide vaccination to name a few (Chando, Tiro, Harris, Kobrin, & Breen, 2013).

1.3 HPV Vaccination Coverage Among Adolescents

Low coverage among adolescents for routine HPV vaccination is reported, albeit slowly improving. Three-dose HPV series initiation coverage for girls was 60% and 41.7% for boys aged 13 to 17 years in 2014. Coverage for HPV series completion was 69.3% for girls and 57.8% for boys (Reagan-Steiner et al., 2015).

Factors associated with HPV vaccination coverage include: age, sex, race, poverty, parent’s education, religion, and insurance. Research conducted by Wilson, A.R. and colleagues (2016) show that variables associated with HPV vaccine initiation and completion include age, marital status, religion, knowledge on HPV transmission and the connection between HPV and cervical cancer, belief in the importance of vaccination, and doctors’ recommendation for vaccination (Wilson et al., 2016). In their study, knowledge of HPV transmission (OR = 6.3) and connection between HPV and cervical cancer (3.9) showed the strongest associations compared to an odds ratio ranging from 1.2 – 3.6 for the other indicators.
Race is a significant factor associated with vaccine completion. In a research study conducted by Ekeledo S., and colleagues (2016) in the Georgia’s south central health district, more white individuals completed HPV vaccine schedule compared to other racial groups (Ekeledo, Best, Norman, Bazemore, & Schwind, 2016).

1.4 Purpose of the Study

In contemporary times, scarce resources make data collection for direct estimation of several health indicators in small areas a challenge. Increasingly, there is a demand for reliable small area estimates to allow for policy development, planning, and adequate resource distribution. This demand for small area estimates spans across public and private institutions, including researchers and grant awardees. Public institutions need information on small area indicators for policy formulation and resource allocation, whereas the private sector needs information on small area indicators for business decisions. Research institutions and grant awardees need information on small area indicators for implementation and evaluation of programs.

Vaccination against vaccine preventable diseases is one of the ten achievements of public health (CDC, 2011; Greenwood, 2014). As a primary prevention activity, vaccination is one of the successful ways of preventing disease and keeping the population healthy from several infectious diseases that otherwise can spread and lead to increases in morbidities and mortalities with a huge economic burden (Andre et al., 2008). Whereas information on
vaccination at the national- and state-levels are readily available, that for local or small areas is scarce. This inadvertently makes it difficult to strategically plan and efficiently allocate resources at local levels to solve vaccination needs and reduce vaccination associated disparities.

Small area vaccination coverage estimates are essential in assessing the impact of vaccination programs. Without vaccine coverage information on small areas, it is generally difficult to target areas with low vaccination coverage for intervention during outbreaks or epidemics of vaccine preventable diseases.

Since their introduction, overall HPV vaccination coverage has not been increasing at the rate at which tetanus and meningitis vaccination coverage uptake has. Coverage of HPV vaccination is an important determinant of the rates and spread of HPV-associated cancers and conditions. Information at local levels on HPV coverage is scarce.

The purpose of this study is to estimate HPV vaccination coverage at local levels in the southeastern states of US. State averages show that in the US, the southeastern states have high rates of HPV-related cancers and low HPV vaccination coverage rates, compared to other states in the US. Information on HPV vaccination coverage at local levels or various domains in the southeastern states, can help with planning and policies to address issues that promote vaccine uptake and reduce incidence of HPV associated cancers.
Statistical models can be used to estimate vaccination coverage. Studies have used various model-based approaches including multilevel (individual, county, public health region) random-intercept logit models (Eberth et al., 2013) to estimate vaccine coverage at the local levels.

Bayesian methods allows for estimation with small sample size, missing values and covariates via Markov Chain Monte Carlo (MCMC) method. This method has been used in other studies to estimate county-level coverage for other health conditions or determinants (Lawson, 2013). This dissertation uses the Bayesian and Spatial effects model to estimate the small area vaccination coverage for HPV in the Southeastern states of US using NIS-Teen survey data for the year 2016.

1.5 Spatial Models

Ecological and environmental scientists use spatial models extensively in their research. Epidemiologists also use spatial models to study how the risk of disease varies consistently over areas or having spatial varying predictors like socio-economic factors or environmental exposures. The rapid development of powerful computational computers and software applications have revolutionized the use of MCMC methods in which the simulation of unknown quantities from their appropriate distribution are possible (Lawson, 2013). The MCMC method is used to generate a sequence of dependent samples from the target distribution and computes quantities by using Monte Carlo based on the samples.

1.5.1 Small Area Estimation

Sample surveys are used to estimate populations as well as subpopulations (domains). Domains may either reflect geographic areas or socio-demographic groups. Whereas direct
estimates are mostly design-based which use survey weights and associated measures of inference for large populations, direct estimates may not be appropriate for small areas, since they may not yield adequate precision (Rao, 2003). Sample size for small areas are generally very small or non-existent (practically zero). This necessitates the use of indirect estimates which make use of values of variables of interest from related areas also termed as covariates, thereby increasing effective sample size for small area estimation. These values are imputed in varied models for relevant estimation.

1.5.2 Bayesian Inference

Bayesian inference is the process of fitting a probability model to any set of data (i.e., continuous or categorical) and estimating the results by a probability distribution on the parameters of the model and on unobserved quantities such as predictions for new observation. Bayesian Hierarchical (BH) method, which allows the parameters of a prior distribution or a population distribution themselves to be estimated from data, is one of the appropriate ways in handling small areas with sparse data because posterior inference is exact which does not rely on asymptotic arguments (Gomez-Rubino, Best, Richardson, & Li).

In Bayesian statistics, parameters are treated as random variables expressed in terms of probabilities. Let $y$ represent a vector of $n$ observations and $\beta = (\beta_1, \ldots, \beta_k)$ represent a vector of $k$ parameters on which the distribution of the observations depends. Then according to Bayes’ theorem;

$$ p(\beta|y) \propto p(\beta) \, p(y|\beta) $$

where $p(\beta|y)$ denotes the posterior distribution of the parameters given the data $p(\beta)$ denotes the prior density of $\beta$
\( p(y|\beta) \) denotes the data likelihood given \( \beta \).

We sample from the posterior distribution \( p(\beta|y) \). MCMC method is one of the most reliable and general methods for simulating a suitable iterative approximation distribution samples from a complex Bayesian posterior distribution. For all \( t \), a sequence of random variables \( \beta^{(0)}, \beta^{(1)}, \beta^{(2)}, \ldots \) forms a Markov chain if the distribution of the \((t + 1)th\) variable in the sequence is given by \( \beta^{(t+1)} \sim p_{\text{trans}}(b | \beta^{(t)} = b^{(t)}) \), which is, conditional on the value of \( \beta^{(t)} \), the distribution of \( \beta^{(t+1)} \) is independent of all other preceding values, \( \beta^{(t-1)}, \beta^{(t-2)}, \beta^{(t-3)}, \ldots, \beta^{(0)} \). We call \( p_{\text{trans}}(b | \beta^{(t)} = b^{(t)}) \) as the transition distribution of Markov chain which defines the conditional probability of moving to any new values given the current values in the chain. The marginal distribution of \( \beta^{(t+1)} \) will converge to a unique stationary distribution as \( t \to \infty \).

One of the most widely used algorithms for simulating Markov chains is the Gibbs sampler which proceeds as follows:

1. Suppose we have a set of arbitrary starting values \( \{\beta_1^{(0)}, \ldots, \beta_k^{(0)}\} \) for each component, where the subscripts denote the sub-components of \( \beta \) and the superscripts denote the iteration number where the initial state of Markov chain is iteration zero.

2. Draw new values for element of \( \beta \) by cycling through the following steps:
   - Draw a new value for \( \beta_1 \), from the full conditional distribution of \( \beta_1 \) given the most recent values of all other elements of \( \beta \) and the data:
     \[
     \beta_1^{(1)} \sim p(\beta_1 | \beta_2^{(0)}, \beta_3^{(0)}, \ldots, \beta_k^{(0)}, y).
     \]
• Draw a new value \( \beta_2^{(1)} \) for the second component of \( \beta \), from its full conditional distribution \( p(\beta_2 | \beta_1^{(1)}, \beta_3^{(0)}, \ldots, \beta_k^{(0)}, y) \). Note that as a new value for \( \beta_1 \) has been drawn, it is the current value that is conditioned together with the starting values for all other elements of \( \beta \).

• 

• Draw \( \beta_k^{(1)} \) from \( p(\beta_k | \beta_1^{(1)}, \beta_2^{(1)}, \ldots, \beta_{k-1}^{(1)}, y) \).

This completes one iteration of the Gibbs sampler. After one iteration we have

\[
(\beta_1^{(1)}, \beta_2^{(1)}, \ldots, \beta_k^{(1)}).
\]

3. Repeat 2, many times conditioning on the most recent value of other parameters.

After \( t \) such iterations we obtain \( (\beta_1^{(t)}, \beta_2^{(t)}, \ldots, \beta_k^{(t)}) \).

The Gibbs sampling algorithm outlined above can be summarized as follows:

\[
(\beta_1^{(t)}, \beta_2^{(t)}, \ldots, \beta_k^{(t)}) \overset{d}{\rightarrow} [\beta_1, \beta_2, \ldots, \beta_k] \text{ as } t \rightarrow \infty.
\]

The Bayesian Using Gibbs Sampling (BUGS) project which began in Cambridge, United Kingdom in 1989 uses Gibbs sampler as an algorithm that sequentially generates samples from a joint distribution of two or more random variables which is often used in Bayesian inference (Lunn, Jackson, Best, Thomas, & Spiegelhalter, 2013). Bayesian methodology has seen great advances since the introduction of BUGS and then WinBUGS. WinBUGS is a free software package that allows the development and fitting of relatively complex hierarchical Bayesian models (Lawson, 2013). MCMC method using the Gibbs Sampler algorithm is used in WinBUGS to produce sample drawings from the joint posterior
density once it has converged to stationarity. Samples before convergence are discarded by specifying a statement in the model using the “burn-in” statement. We can then estimate summaries of interest from the posterior distribution directly from the simulations.

1.5.3 Conditional Autoregressive Models

Spatial interactions between neighboring areas can be defined as using the simultaneous autoregressive (SAR) models (Whittle 1954; Ord 1975; Haining 1990, 2003) or the Gaussian conditionally autoregressive (CAR) models (Besag 1974; Besag et al. 1991; Haining 1990, 2003). WinBUGS (version 1.4) supports various spatial models including intrinsic (improper) CAR (ICAR) and proper CAR (PCAR).

Our focus will be on the ICAR model which we will refer to as CAR model for simplicity. Let \( S = (S_1, S_2, \ldots, S_n) \) to be a vector of random variables associated with location \( i = 1, \ldots, n \). CAR models specify how each \( S_i \) is related to the \( S_j \) at all other locations using a set of univariate conditional distributions. Let \( \{w_{i,j}: i, j = 1, \ldots, n\} \) denote a 0-1 contiguity matrix \( (W) \) in which \( w_{i,j} = 1 \) if \( i \) and \( j \) are neighbors and \( w_{i,j} = 0 \) otherwise, and \( w_{i,i} = 0 \).

The most commonly used distribution formulated by Besag et al., 1991 is as follows

\[
S_i | S_j = s_j, \ j \neq i, \ j \ is \ a \ neighbour \ of \ i \sim \text{Normal} \left( \bar{s}_i, \frac{\omega_S^2}{m_i} \right).
\]

That is the conditional distribution of \( S_i \) given \( S_j \) is normal with mean \( \bar{s}_i = \sum_{j \neq i} \frac{w_{i,j}s_j}{m_i} \) and variance \( \frac{\omega_S^2}{m_i} \), where \( m_i = \sum_j w_{i,j} \) is the number of neighbors of area \( i \). The variance parameter \( \omega_S^2 \) controls the amount of variability in \( S_i \). The variance \( \frac{\omega_S^2}{m_i} \) measures the local variability conditional on the values of neighboring random effects (Law & Haining, 2004).
2 USING BAYESIAN METHODS TO ESTIMATE COUNTY-LEVEL VACCINATION COVERAGE FOR HUMAN PAPILLOMAVIRUS VACCINE AMONG ADOLESCENTS AGED 13–17 YEARS IN SOUTHEASTERN UNITED STATES OF AMERICA

2.1 Background

The Centers for Disease Control and Prevention (CDC) has been analyzing data collected yearly on adolescents since 2006. In 2006 and 2007, the National Immunization Survey – Teen (NIS-Teen), was only capable of producing national-level vaccination coverage estimates. Beginning 2008, NIS-Teen started with collecting data from all the 50 states, District of Columbia (DC), and selected local areas allowing to produce state-level and selected local area-level vaccination coverage estimates. During the 2009 survey year and there-after, some US territories were also added to the survey.

The NIS-Teen survey uses a random-digit-dialed sample of landline frame and starting 2011 a cell-phone sample frame was added. Telephone interviews are conducted with the adolescents’ parents/guardians to collect information on the adolescent, maternal, and household sociodemographic characteristics and vaccination providers. With respondents’ consent, questionnaires are mailed to all identified vaccination providers to obtain the adolescents’ immunization history records.

The southeastern states in the US have high rates of HPV-related cancers and low HPV vaccination coverage rates, compared to other states in the US as indicated in chapter 1. Since one of the objectives of the NIS-Teen survey is to evaluate ongoing strategies to improve
vaccination coverage and to identify disparities in vaccination coverage by selected sociodemographic characteristics, in this chapter we will be exploring methods that will be more suitable to estimate county-level initiation of HPV vaccination coverage in the southeastern states where coverage is low. In recent years, there have been very high demand for county-level vaccination coverage including HPV vaccination by grantees and policy makers to enable the changes in strategies where needed most and for allocating more of the budgetary funds to improve overall vaccination coverage which may prevent HPV-related cancers in the future.

2.2 Methods

We used the 2016 NIS-Teen adequate provider data for this dissertation research. NIS-Teen defines an adolescent having adequate provider data as one having vaccination history data from one or more of the named vaccination providers or if the parent reported that the adolescent was completely unvaccinated. This data set is a complex sample survey among adolescents aged 13–17 years in the 50 states, District of Columbia (DC), selected local areas, and some US territories. The Council of American Survey Research Organization (CASRO) response rate was 55.5% for landline and 29.5% for cell-phone. Among those who completed the household survey and had adequate provider-reported vaccination histories, 4,684 were by landline (53.8%) and 15,791 were by cell-phone (47.4%) (Walker et al., 2017). We will be using only data from the 10 southeastern (SE) states in the US. These 10 states together have 925 counties: Alabama (67 counties), Florida (67 counties), Georgia (159 counties), Kentucky (120 counties), Mississippi (82 counties), North Carolina (100 counties), South Carolina (46 counties), Tennessee (95 counties), Virginia (134 counties), and West Virginia (55 counties). A map of all the 925 counties in the SE of US is shown in Figure 2-1 below.
Figure 2.1 Map of United States of America Indicating Counties in All 10 Southeastern States. (Alabama [67 counties]; Florida [67 counties]; Georgia [159 counties]; Kentucky [120 counties]; Mississippi [82 counties]; North Carolina [100 counties]; South Carolina [46 counties]; Tennessee [95 counties]; Virginia [134 counties]; and West Virginia [55 counties]).

The expensive nature of most surveys including the NIS-Teen survey makes it difficult to have observations from all the counties. The 2016 NIS-Teen data set from the SE states do not have observations from 277 counties. This implies that using direct estimation will not yield a reliable estimate due to inadequate sample size, hence we will be constructing Bayesian Hierarchical (BH) models to compute more reliable HPV vaccination initiation coverage for all the 925 counties in the SE states of the US. We will also explore spatial correlation using Conditional Autoregressive (CAR) model as part of the model building.

The variables of interest and definitions are as follows:
The outcome for this analysis is receipt of at least one HPV dose (initiation) (yes or no)

Age of Teen in years (13; 14; 15; 16; and 17) at year of interview

Sex of Teen (Male; Female)

Race/Ethnicity (White, non-Hispanic; Black, non-Hispanic; Hispanic; and Other non-Hispanic or Multiple Races)

Income to poverty ratio (<133% Federal Poverty Level [FPL]; 133% - <322% FPL; 322% - <503% FPL; and >503%FPL)

Mother’s Education (<High School; High School Graduate; Some College Education; and College Degree or Higher Education)

Mother’s Age in years (≤34 years; 35-44 years; and ≥45 years)

Health insurance status (Private Only; Medicaid/Children’s Health Insurance Program [CHIP]; Uninsured; Military; and Other Forms of Insurance Payments).

In the preliminary analysis, we have found that the teen’s age at interview, sex, race or ethnicity, using Medicaid or CHIP as their insurance payment source, and living in the State of Georgia or Mississippi were significant covariates for modeling the rate of HPV vaccination initiation.

2.3 Analysis

We started our analysis by aggregating the individual observations into county-level observations in the SE states of US and then regrouping the observations within each county-level by age at interview, sex, race or ethnicity, income-to-poverty ratio, mother’s education,
mother’s age, and insurance payment type. This reduced the initial individual level sample size of 3,521 (Alabama [n = 333], Florida [n = 376], Georgia [n = 367], Kentucky [n = 333], Mississippi [n = 377], North Carolina [n = 366], South Carolina [n = 314], Tennessee [n = 291], Virginia [n = 451], and West Virginia [n = 313]) to 3,352. Based on the covariates of interest, the overall possible group combination for all our variables of interest is supposed to be 9,600 per county.

The map (Figure 2-2) below shows all the counties with observations in gold and those without observation in brown in the SE states of US. There were 15 out of the 648 counties with 30 or more observations and the rest had less than 30 observations. The range of observations by county is from 1 to 143. Due to confidentiality constraints, we will not be able to name which counties had less than 30 observations.
Figure 2.2 Map of United States of America Indicating Counties in All 10 Southeastern States with or without Survey Data. Missing (no observed data for survey year 2016) or Non-Missing (observed data for survey year 2016) Data in Sample for Analysis.

We used the following procedures “PROC SQL”, “PROC FREQ”, “PROC IML”, and “PROC GLIMMIX” in SAS 9.4 to prepare the data for our analysis. We further used the package “R2WinBUGS” in RStudio 1.0.136 to call WINBUGS 14.1 to run the 16 different BH models with different combinations of random effects and spatial effects (CAR model). The most complex model included randomizing both the state and the county in which the individual lived as well as including spatial effects for both state and county. The simplest model did not include either the state or the county of the individual as random effects and/or spatial effects. Details of the 16 models are given in section 2.4.
The initial values for all the BH analyses were generated using a logistic regression model ("PROC GLIMMIX" in SAS 9.4) which included all the covariates that were used in the BH models. In section 2.4, we will describe in detail what the models entailed and present the results in section 2.5.

2.4 Models

Aggregating the individual binary outcome ("YES or "NO") indicating their HPV vaccination status into county-level outcomes will allow us to use the Binomial distribution for our outcome instead of the Bernoulli distribution.

In the binomial hierarchy model in which we observe vaccination status in the counties in the SE states of US, we will define the total number of groups in all considered counties as $m$ and the sample size of the $i^{th}$ group as $n_i$. We will denote the number of individuals who were vaccinated by $y_i$ which is often assumed to independently follow binomial distribution with a conditional probability, $p_i$:

$$ y_i \sim Bin(n_i, p_i) $$

where $p_i$ represents the probability that an individual in the $i^{th}$ group is vaccinated. The likelihood is given by

$$ \prod_{i=1}^{N} L(p_i | y_i, n_i) = \prod_{i=1}^{N} \binom{n_i}{y_i} p_i^{y_i} (1 - p_i)^{n_i - y_i}. $$

We apply a logistic link to the probability to relate the vaccination count with covariates of interest. We consider the necessity of including a random state effect and a random county effect to allow differences across states and counties, and spatial conditional autoregressive
models at both the state-level and county-levels to capture the spatial relationships. In all the models, the prior distribution for all intercepts, slope coefficients of covariates, and random state and county effects, were assumed to have a normal distribution. The hyper prior distributions for the variances were inverse-gamma distributions. Let $s_i$ and $c_i$ denote the state and the county that the $i^{th}$ group belongs to in our sample. The most complex model that we consider is given below.

\[ y_i \sim Bin(n_i, p_i) \]

\[ \text{logit}(p_i) = \beta_0 + \beta_{s,0} + \beta_{c,0} + \sum_{j=1}^{20} \beta_j x_{ij} + b_{s_i} + c_{c_i} \]

where $\beta_{s,0} \sim N(0, \sigma_s^2)$ and $\sigma_s^2 = \frac{1}{\tau_s}$ represents the random state effect,

$\beta_{c,0} \sim N(0, \sigma_c^2)$ and $\sigma_c^2 = \frac{1}{\tau_c}$ represents the random county effect,

$x_{ij}$ is the observed value of the $j^{th}$ covariate in the $i^{th}$ group,

$b_{s_i}$ captures the spatial effect at the state level and is assumed to have a CAR model:

\[ (b_1, \cdots, b_{N_s}) \sim CAR(W_s, \text{sigma.} b^2) \]

\[ \text{tau.} b \sim Gamma(0.5, 0.5) \]

\[ \text{sigma.} b < -\frac{1}{\sqrt{\text{tau.} b}} \]

where $N_s = 10$

$W_s$ is 0 – 1 contiguity matrix (10 x 10 matrix) with 1 indicating being neighbors

$\text{tau.} b$ is a scalar argument representing the precision (inverse variance) parameter of the CAR prior
and

\( c_{ci} \) captures the spatial effect at the county level and is also assumed to have a CAR model:

\[
(c_1, \ldots, c_{N_c}) \sim \text{CAR}(W_c, \text{sigma.c}^2)
\]

\[
\text{tau.c} \sim \text{Gamma}(0.5, 0.5)
\]

\[
\text{sigma.c} < -\frac{1}{\sqrt{\text{tau.c}}}
\]

where \( N_c = 648 \)

\( W_c \) is \( 0 \) – \( 1 \) contiguity matrix (648 x 648 matrix) with 1 indicating being neighbors

\( \text{tau.c} \) is a scalar argument representing the precision (inverse variance) parameter of the CAR prior.

We assume that

\( \beta_j \sim N(0, \sigma_j^2) \) and \( \sigma_j^2 = \frac{1}{\tau_j^2} \) independently,

and

\( \tau_j^2 \sim \text{Gamma}(0.525, 0.525) \) for \( j = 1, \ldots, 20 \).

We also assume the intercept to be

\( \beta_0 \sim N(0, \sigma_0^2) \) and \( \sigma_0^2 = \frac{1}{\tau_0^2} \) with \( \tau_0^2 \sim \text{Gamma}(0.525, 0.525) \).

The hierarchy for the most complex model is diagrammatically displayed in Figure 2-3 below
Figure 2.3. The Most Complex Hierarchical Model. Logistic Regression where $Y(i)$ is the $i^{th}$ group binary response variable, $n(i)$ sample size of the $i^{th}$ group, $p(i)$ is the probability that an individual in the $i^{th}$ group has initiated or received at least one dose of HPV vaccination, and $X(i)$ is a set of covariates for the $i^{th}$ group. $S(i)$ is the $i^{th}$ group state random effect, with an independent normal random variable with mean zero and variance $\sigma_{st}^2$. $C(i)$ is the $i^{th}$ group county random effect, with an independent normal random variable with mean zero and variance $\sigma_{ct}^2$. $b(i)$ is the state spatial effect of the $i^{th}$ group, with $(b(1),...,b(10))$ jointly has a CAR model defined above where the variance parameter is $\sigma_b^2$ and controls the amount of variability in $\{b(i)\}$. $c(i)$ is the county spatial effect of the $i^{th}$ group, with $(c(1),...,c(925))$ jointly has a CAR model the variance parameter $\sigma_c^2$ controls the amount of variability in $\{c(i)\}$. 
Not including any random and/or spatial state or county effect, we have the least complex hierarchy model which is as given below:

\[ y_i \sim Bin(n_i, p_i) \]

\[ \logit(p_i) = \beta_0 + \sum_{j=1}^{20} \beta_j x_{ij} \]

The \( \beta_i' \)s have the same parameter distributions as that of the most complex models stated above.

We further diagrammatically display the hierarchy of the least complex model in Figure 2-4 below:

Figure 2.4. The Least Complex Hierarchical Model. Logistic Regression where \( Y(i) \) is the \( i^{th} \) group binary response variable, \( n(i) \) sample size of the \( i^{th} \) group, \( p(i) \) is the probability that an individual in the \( i^{th} \) group has initiated or received at least one dose of HPV vaccination, and \( X(i) \) is a set of covariates for the \( i^{th} \) group.

Considering whether including the random state effect, the random county effect, the state spatial effect and the county spatial effect, we explored 16 models in total. For each model, we run 100,000 MCMC iterations, took the first 10,000 as “burn-in”, and generate 90,000 samples per covariate. Convergence were attained in less than 1,000 simulations. The time
elapsed for the simulations of all 16 models ranged from a minimum of 2,738 seconds (≈ 46 minutes) to a maximum of 7,077 seconds (≈ 118 minutes) on a PC (16.0GB RAM, 3.4GHz CPU). A summary of the model diagnostics and statistics for all 16 models that we analyzed is presented in the Table 2-1 below:
<table>
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<tr>
<th>Model</th>
<th>Iterations</th>
<th>Sample</th>
<th>Time Elapsed (Seconds)</th>
<th>Random Intercept</th>
<th>CAR Model</th>
</tr>
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<td></td>
<td>STATES  COUNTIES</td>
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</tr>
<tr>
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<tr>
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<td>7</td>
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<td>YES   NO</td>
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<td>8</td>
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</tr>
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</table>

**Table 2.1. Deviance Summaries for all 16 Analyzed Models.**

Dbar: this is the posterior mean of the Deviance.
Dhat: this is a point estimate of the Deviance.
pD = Dbar - Dhat = var(Deviance) / 2.
DIC: Deviance Information Criterion (DIC) is an Estimate of Expected Predictive Error (Lower Deviance is Better) = Dbar + pD = Dhat + 2pD.
Deviance = -2 logp(y|θ).
Range of DIC = (4559.80 - 4615.86)
Note: * Means Model with the smallest DIC
All the models used the same number of covariates (as stated in Section 2.2) and they only differed from whether states and/or counties were included in the models as random effects and/or spatial effects. In the NIS-Teen 2016 survey year, there were 648 counties out of the 925 counties from the 10 SE states in the data set. This means we will be estimating HPV vaccination coverage for an additional 277 counties with no covariate information based on the final selected model.

Model 4 (the model with both randomized states and counties) has the smallest Deviance Information Criterion (DIC = 4559.8000) and is the selected model. The calculation of the DIC considers both model fit (measured by Dbar) and model complexity (measured by pD) in comparing models. In using the DIC criterion for model selection, differences in DIC greater than 10 is considered a substantial change, which helps to rule out models with higher DIC; differences in DIC between 5 and 10 are considered substantial and should be reviewed carefully taking into consideration other factors for model selection; but, if the difference in DIC is < 5, because it could be misleading just to report the model with the lowest DIC, other factors should also be taken into consideration before selecting the final model (Spiegelhalter, Best, Carlin, & Van Der Linde).

More specifically, the selected model is given below:

\[ y_i \sim Bin(n_i, p_i) \]

\[ \text{logit}(p_i) = \beta_0 + \beta_{s,i,0} + \beta_{c,i,0} + \sum_{j=1}^{20} \beta_j x_{ij} \]

where \( \beta_0 \sim N(0, \sigma_0^2) \) and \( \sigma_0^2 = \frac{1}{\tau_0} \) with \( \tau_0^{2} \sim \text{Gamma}(0.525, 0.525) \).
\[ \beta_{s_t,0} \sim N(0, \sigma^2_s) \text{ and } \sigma^2_s = \frac{1}{\tau^2_s} \text{ represents the random state effect, } s_t = 1, \ldots, 10, \]

\[ \beta_{c_t,0} \sim N(0, \sigma^2_c) \text{ and } \sigma^2_c = \frac{1}{\tau^2_c} \text{ represents the random county effect, } c_t = 1, \ldots, 648, \]

\( x_{ij} \) is the observed value of the \( j^{th} \) covariate in the \( i^{th} \) group.

\[ \beta_j \sim N(0, \sigma^2_j) \text{ and } \sigma^2_j = \frac{1}{\tau^2_j} \text{ independent covariates with } \tau^2_j \sim \text{Gamma}(0.525, 0.525) \text{ for } j = 1, \ldots, 20. \]

The hierarchy structure of the selected model is diagrammatically displayed in Figure 2-5 below:

---

**Figure 2.5. The Selected Hierarchical Model.** Logistic Regression where \( Y(i) \) is the \( i^{th} \) group binary response variable, \( n(i) \) sample size of the \( i^{th} \) group, \( p(i) \) is the probability that an individual in the \( i^{th} \) group has initiated or received at least one dose of HPV vaccination, and \( X(i) \) is a set of covariates for the \( i^{th} \) group. \( St(i) \) is the \( i^{th} \) group state random effect, with an independent normal random variable with mean zero and variance \( \sigma^2_{St} \). \( Ct(i) \) is the \( i^{th} \) group county
random effect, with an independent normal random variable with mean zero and variance $\sigma^2_{ct}$.

Our selected model did not include the CAR model (spatial effect). This implies that neighboring states or counties do not provide additional improvement in modeling the vaccination rate of a county given the information of existing covariates and random state and county effects.

The summary of posterior means and 95% credible intervals of covariates estimated from WinBUGS using data from 648 counties are shown in the Table 2-2 below:

**Table 2.2. Posterior Summaries for Regression Coefficients in the Selected Model.**

<table>
<thead>
<tr>
<th>Label</th>
<th>Mean</th>
<th>2.50%</th>
<th>Median</th>
<th>97.50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.1324</td>
<td>-0.6402</td>
<td>-0.1290</td>
<td>0.3647</td>
</tr>
<tr>
<td>Age at interview of teen 14 Years*</td>
<td>0.3086</td>
<td>0.08769</td>
<td>0.3081</td>
<td>0.5301</td>
</tr>
<tr>
<td>Age at interview of teen 15 Years*</td>
<td>0.4180</td>
<td>0.1941</td>
<td>0.4180</td>
<td>0.6427</td>
</tr>
<tr>
<td>Age at interview of teen 16 Years*</td>
<td>0.6609</td>
<td>0.4402</td>
<td>0.6607</td>
<td>0.8821</td>
</tr>
<tr>
<td>Age at interview of teen 17 Years*</td>
<td>0.4139</td>
<td>0.1785</td>
<td>0.4135</td>
<td>0.6486</td>
</tr>
<tr>
<td>Sex of teen Male*</td>
<td>-0.3436</td>
<td>-0.4863</td>
<td>-0.3434</td>
<td>-0.2012</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Non-Hispanic Black*</td>
<td>0.2645</td>
<td>0.0547</td>
<td>0.2641</td>
<td>0.4745</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Hispanic*</td>
<td>0.4095</td>
<td>0.1258</td>
<td>0.4091</td>
<td>0.6966</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Other*</td>
<td>0.2725</td>
<td>0.01189</td>
<td>0.2722</td>
<td>0.5319</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥133% and &lt; 322%</td>
<td>-0.1246</td>
<td>-0.3405</td>
<td>-0.1246</td>
<td>0.09146</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥322% and &lt; 503%</td>
<td>-0.2152</td>
<td>-0.4873</td>
<td>-0.2154</td>
<td>0.0572</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥503%</td>
<td>0.0615</td>
<td>-0.2148</td>
<td>0.0611</td>
<td>0.3404</td>
</tr>
<tr>
<td>Teen's Mother's Education Level High School Graduate</td>
<td>-0.0735</td>
<td>-0.3527</td>
<td>-0.0734</td>
<td>0.2082</td>
</tr>
<tr>
<td>Teen's Mother's Education Level More than High School Graduate</td>
<td>-0.1204</td>
<td>-0.3954</td>
<td>-0.1202</td>
<td>0.1563</td>
</tr>
<tr>
<td>Teen's Mother's Education Level College Graduate</td>
<td>0.0586</td>
<td>-0.2306</td>
<td>0.0586</td>
<td>0.3465</td>
</tr>
<tr>
<td>Teen's Mother's Age Group 35 to 44 Years</td>
<td>-0.1409</td>
<td>-0.4011</td>
<td>-0.1405</td>
<td>0.1163</td>
</tr>
<tr>
<td>Teen's Mother's Age Group ≥ 45 Years</td>
<td>-0.1531</td>
<td>-0.4282</td>
<td>-0.1519</td>
<td>0.1181</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Medicaid or CHIP*</td>
<td>0.4424</td>
<td>0.2275</td>
<td>0.4415</td>
<td>0.6588</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Uninsured</td>
<td>-0.1866</td>
<td>-0.6</td>
<td>-0.1864</td>
<td>0.2223</td>
</tr>
</tbody>
</table>
Our 95% posterior credible intervals from the Table 2-3 above shows that factors associated with higher likelihood of HPV vaccination initiation in the 10 southeastern states in US are as follows: age at interview from 14 through 17 years old; being of any race or ethnicity other than non-Hispanic white; having Medicaid and or CHIP as your health insurance status; and living in the State of Georgia among the 10 southeastern states. These had positive means and nonzero regression coefficients at the 95% credible intervals.

Factors that were associated with lower likelihood of HPV vaccination initiation in the 10 southeastern states in US were being an adolescent male and living in the State of Mississippi among the 10 southeastern states. These had negative means and nonzero regression coefficients at the 95% credible intervals.
For our selected model and its binomial distribution, our objective is to estimate the posterior distribution for the rate of HPV vaccination initiation for each county.

Given

\[
\text{logit}(p_i) = \beta_0 + \beta_{s_i,0} + \beta_{c_i,0} + \sum_{j=1}^{20} \beta_j x_{ij}
\]

let

\[
\theta_i = \beta_0 + \beta_{s_i,0} + \beta_{c_i,0} + \sum_{j=1}^{20} \beta_j x_{ij}
\]

Then

\[
\text{logit}(p_i) = \theta_i
\]

We estimate the posterior proportion of HPV vaccination initiation of adolescents in each group and each county, by plugging in the sampled values of \( \beta \)'s and the corresponding values of \( x' \)s followed by a transformation back from logit to proportion as follows:

\[
\hat{p}_i = \left( \frac{e^{\hat{\theta}_i}}{1 + e^{\hat{\theta}_i}} \right)
\]

For each of the 925 counties in the 10 SE states, we estimated 9,600 groups of posterior proportion estimates which will result in 8.88 million rates of HPV vaccination initiation of adolescents.
To estimate the corresponding overall rate of HPV vaccination initiation of adolescents in the $c_i$th county, $\bar{\mu}_{c_i}$, based on the rule of total probability, we use the following:

$$\bar{\mu}_{c_i} = \sum_{i=1}^{9600} p_{ic_i} \cdot W_{c_i}$$

where $W_{c_i}$ is the proportion that the $c_i$th county individuals belong to the $i^{th}$ group.

We get a value of $\bar{\mu}_{c_i}$ for each MCMC sample unit. From all 90,000 MCMC samples, we simulate the posterior distribution of $\bar{\mu}_{c_i}$, from which we get the posterior mean and 95% credible interval of HPV vaccination initiation rate for each county. We will present some of our results in section 2.5 below.

To estimate the HPV vaccination initiation rates for the 277 missing counties, we first simulate their random effects from $\beta_{c_i,0} \sim N(0, \sigma_c^2)$ and $\sigma_c^2 = \frac{1}{\tau_c^2}$, where the value of $\tau_c^2$ is taken from the 90,000 MCMC samples simulated for our known counties random effect. Then using the same way as before, we estimate the HPV vaccination initiation rate for each of the missing counties. Table 2-3 shows the estimate of missing counties in red.

2.5 Results

We used “PROC UNIVARITE” in SAS 9.4 to calculate our HPV vaccination initiation coverage estimates after using “PROC IML” in SAS 9.4 to perform the above-stated calculations and including the survey weights produced with the data sets. We added 1% of the smallest survey weights to all 9,600 groups to compensate for the weights in any missing group due to the group missing in the survey data set.
The HPV vaccination initiation coverage estimates and 95% credible intervals are presented overall (males and females) and by sex for all 925 counties in the southeastern states in US in Appendix B. The estimates for the 277 counties with missing survey data information are highlighted in red font.

Overall, the HPV vaccination initiation coverage among adolescent in all the 925 counties ranges from 32.8% (Jackson County, MS) to 70.5% (Arlington County, VA). The narrowest 95% credible interval is 15.5% while the widest is 52.3%. For the 925 counties studied, the overall HPV vaccination initiation coverage among adolescent in the southeastern was 52.9% (95% credible interval: 40.2% - 65.7%). The 648 counties had data on the HPV vaccination while 277 counties were missing these data. The overall HPV vaccination initiation coverage among adolescent in the 648 counties with non-missing information was 51.5% (95% credible interval: 39.8% - 66.8%). The HPV vaccination initiation coverage among adolescent in the 277 counties with missing data was estimated to be 55.2% (95% credible interval: 41.3% - 64.0%).

Among adolescent females the HPV vaccination initiation coverage in all the 925 counties ranges from 22.5% (Issaquena, Tallahatchie, Tunica, and Wayne Counties, in MS) to 73.3% (Arlington County, VA). For adolescent females, the narrowest 95% credible interval is 15.2%; the widest was 52.3%. For adolescent females in all the 925 counties studied, the overall HPV vaccination initiation coverage among adolescent in the SE of the US was 54.1% (95% credible interval: 26.1% - 69.0%). The overall adolescent female HPV vaccination initiation coverage among adolescents in the 648 counties with non-missing information was 55.5% (95%
credible interval: 43.1% - 69.6%). The HPV vaccination initiation coverage among adolescent females in the 277 counties with missing information was estimated to be 33.7% (95% credible interval: 24.5% - 67.3%).

Among adolescent males the HPV vaccination initiation coverage in all the 925 counties ranges from 18.7% (Issaquena, Tallahatchie, Tunica, and Wayne Counties, in MS) to 69.5% (Douglas County, GA). For adolescent males, the narrowest 95% credible interval is 16.2%; the widest was 52.6%. For adolescent males in all the 925 counties studied, the overall HPV vaccination initiation coverage in the SE of the US was 46.5% (95% credible interval: 22.2% - 62.6%). The overall adolescent male HPV vaccination initiation coverage among adolescents in the 648 counties with non-missing information was 47.7% (95% credible interval: 35.7% - 63.2%). The HPV vaccination initiation coverage among adolescent males in the 277 counties with missing information was estimated to be 30.0% (95% credible interval: 20.6% - 61.0%).

The following maps in Figure 2-6 to Figure 2-14 show the disparities in HPV vaccination initiation among the counties in the southeastern states in the US.
Figure 2.6. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Overall (Males and Females) Aged 13–17 Years During 2016 in all 925 Counties in Southeastern States in US Using Bayesian Methods.
Figure 2.7. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Overall (Males and Females) Aged 13–17 Years During 2016 in all 648 Counties with Survey Data in Southeastern States in US Using Bayesian Methods.
Figure 2.8. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Overall (Males and Females) Aged 13–17 Years During 2016 in all 277 Counties without Survey Data in Southeastern States in US Using Bayesian Methods.
Figure 2.9. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Females Aged 13–17 Years During 2016 in all 925 Counties in Southeastern States in US Using Bayesian Methods.
Figure 2.10. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Females Aged 13–17 Years During 2016 in all 648 Counties with Survey Data in Southeastern States in US Using Bayesian Methods.
Figure 2.11. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Females Aged 13–17 Years During 2016 in all 277 Counties without Survey Data in Southeastern States in US Using Bayesian Methods.
Figure 2.12. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Males Aged 13–17 Years During 2016 in all 925 Counties in Southeastern States in US Using Bayesian Methods.
Figure 2.13. Figure 2.14. Estimated ≥1 Dose HPV Vaccination Coverage Among Adolescents Males Aged 13–17 Years During 2016 in all 648 Counties with Survey Data in Southeastern States in US Using Bayesian Methods.
2.6 Discussion of Research Findings

In this dissertation our aim is to estimate county-level HPV vaccination initiation coverage among adolescents aged 13 – 17 years in southeastern states of the US. Overall HPV initiation rates for all 925 counties in the studied 10 southeastern states ranged from 32.8% – 70.5% with an average initiation rate of 52.9% (95% credible interval: 40.2-65.7) which was below the national initiation rates for HPV vaccination in 2016. National HPV vaccination coverage for ≥1-dose among teens was 60.4% in 2016 (Walker et al., 2017). For females, HPV initiation rates for all 925 counties studied ranged from 35.9% – 73.3%. For males, HPV initiation rates for all 925 counties studied ranged from 28.9% – 69.5%. These rates are also
lower than the national 2016 averages of 65.1% for females and 56.0% for males (Walker et al., 2017).

Females generally express a higher intent to receive HPV vaccination compared to males.

Jones, M. et al., conducted a study that assessed intention to vaccinate against HPV among 340 college students consisting 138 males and 202 females (Jones & Cook, 2008). Among other indicators of HPV initiation, these students completed questionnaires on their likelihood to accept HPV vaccination that prevented infection with cervical cancer and genital warts. Even though the students reported intent beyond 75% to receive an HPV vaccine, the female students had a significantly higher rate (88.6%) of intention to vaccinate compared to males (77.5%; p < .01). An observation in the study by Jones, M., and colleagues was that, these rates were driven by the diseases that males perceived HPV vaccine would prevent. Males showed an increased motivation to initiate HPV vaccination if the vaccine would prevent cervical cancer and warts (77.5%) compared to preventing cervical cancer alone (34.1%).

It is apparent that males generally associate HPV vaccination with only cervical cancer. Since males have no cervix, they probably find cervical cancer as less of a risk to them and are thus less motivated to initiate HPV vaccination. This is still evident in the research by Jones, M., et al which showed higher intention to vaccinate among males, if they reported multiple partners. HPV vaccines protect against several oro-genital cancers, and the gender disparity in intent to vaccinate against HPV and HPV vaccination rates must be addressed through education. Education on the benefits of HPV vaccination beyond sexual and reproductive health
will most likely improve intention and initiation rates for HPV vaccination among both males and females and reduce the disparities in HPV vaccine uptake.

Beyond a low prevalence of HPV vaccine initiation among males compared to females, factors significantly associated with lower likelihood of HPV vaccination initiation in the 10 southeastern states in U.S. were: Male adolescence and Living in the State of Mississippi. High incidence and prevalence rates of cancers including cervical cancers have been estimated in the rural southern part of U.S., especially Mississippi Delta. Determinants attributed to the high cervical cancer rates in the Mississippi Delta include limited economic and healthcare resources as well as decreased access to healthcare (H. I. Hall, Jamison, & Coughlin, 2004). The impact of these determinants is further strengthened by other social and cultural barriers that have been demonstrated to be associated with low HPV vaccine uptake (H. Hall, Jamison, & Coughlin, 2002). A path to increasing HPV vaccination rates and cervical cancer in the southeastern states should include programs that address barriers to vaccination described in the southern part of US. This implies implementing education programs as well as processes that will make healthcare available and increase access to healthcare and screening services. The American Cancer Society recognizes the critical need for education of parents, adolescents, about cervical cancer prevention as well as screening, to allow early detection, and even regular screening even after vaccination to assess effectiveness of vaccination programs in communities (Saslow et al., 2007).

Factors associated with higher likelihood of HPV vaccination initiation in the 10 southeastern states in U.S. are: Age at interview from 14 through 17 years, Race / ethnicity
other than non-Hispanic White, Use of Medicaid / CHIP as vaccination payment source and Living in the State of Georgia among the southeastern states. These factors are also prevalent nationally and dictate HPV vaccination initiation rates. Thus, the disparities created in vaccination rates between the Southeastern States and all other States in U.S. is worth investigating.

The Bible belt describes parts of U.S. characterized by a population that predominantly Christians or have religious characteristics that make them firmly grounded in practices of values associated with their believes (Barton, 2010; Heatwole, 1978; Heyrman, 2013). Bible belt is chiefly associated with the southern part of the United States even though some phenomena of the Bible belt is also traced to Middle Western parts of the US. Populations of the Bible belt tend to believe in abstinence, frown against “uncommon” sexual practices and hence are more likely to consider themselves at less risk for sexually transmitted infections including HPV (Barton, 2010; Heatwole, 1978). It is possible, that the perception of being at less risk for sexually transmitted infection is a factor driving the low rates of HPV initiation in the Southeastern States compared to other States in the US. This needs to be investigated and factors that are found to negatively impact HPV vaccination rates addressed accordingly.

A systematic review of 55 original research articles that investigated barriers to HPV vaccine initiation and completion among U.S. adolescents reported that health care recommendation were the most important factors for HPV vaccination listed by parents (Holman et al., 2014). Most parents do not know about HPV and its impact on the general population and are not aware of vaccination to prevent the possible health consequences of HPV
infection. In the review by Holman et al., financial concerns and parental attitudes/concerns were the predominant factors listed by healthcare professionals as barriers to HPV vaccine initiation (Holman et al., 2014).

Inability to pay for vaccination is an important barrier to HPV vaccination. This is especially pronounced among populations who lack health insurance of any type.

Factors delineated among parental attitudes/concerns include the effect of HPV vaccination on sexual behavior. Parents express the fear, that their children may become confident that they are protected from HPV infection after vaccination and thus start sexual engagement. This fear of sexual confidence following HPV vaccination has also been attributed to the content of information in the press/published material on HPV vaccination and how parents assimilate this information (A. Forster, Wardle, Stephenson, & Waller, 2010).

Rysavy, M., and researchers conducted a cross-sectional survey of 223 young women aged 13 to 24 years to compare sexual attitudes and behaviors of young women who have either been vaccinated against HPV or not (Rysavy et al., 2014). Neither the mean age at initial sexual engagement (16.8 vs 17.0) nor the average number of sexual partners (6 for both groups) were significantly different between the young women who were vaccinated or were not vaccinated. They concluded that sexual behaviors and high-risk behaviors were comparable in both the vaccinated and unvaccinated groups. The absence of significance in differences of sexual behavior and risk among HPV vaccinated females and HPV vaccination naïve females has also
been demonstrated in other studies (A. S. Forster, Marlow, Stephenson, Wardle, & Waller, 2012; Kumakech et al., 2017; Ruiz-Sternberg & Pinzón-Rondón, 2014).

Results from selective review of behavioral and social science literature on HPV vaccine attitudes and uptake conducted by Zimet, D., and colleagues also showed no evidence of increased sexual risk after HPV vaccination (Zimet, Rosberger, Fisher, Perez, & Stupiansky, 2013). Zimet and colleagues conclude that the general behavioral and social concerns raised in relation to HPV vaccination are based on misconceptions or myths which need to be clarified during HPV prevention educational programs. They explain that effective communication on the indication and benefits of HPV vaccination is key to improving HPV vaccine uptake rates.

Aside the unfounded fear of post HPV vaccination sexual “promiscuity” among young females, research also report that some parents hold the belief that their children have a very low risk of getting infected with HPV and consequently do not see the need to vaccinate their children (Oldach, B. R., & Katz, M. L., 2012; Thompson, V. L. S., et al., 2012). This holds especially for males among whom they perceive no direct benefit and may be a dominant issue in the Bible belt as discussed earlier.

Generally psychosocial predictors of HPV vaccination uptake and acceptance include factors that increase positive attitudes to HPV vaccines (Perez et al., 2017). This includes that knowledge and believe that vaccines including HPV vaccines are safe (Kester, Zimet, Fortenberry, Kahn, & Shew, 2013)and do not carry undue adverse effects (Perez et al., 2017). Also imparting knowledge that explains the benefits of vaccination in relation to preventing
related cancers that are also common to all genders increases the likelihood of vaccine initiation and uptake. Healthcare providers play an important role in achieving this aim.

Clinical studies confirm that HPV vaccines are generally safe and well-tolerated with very rare reports of serious adverse effects. The common adverse effects are related to site injection symptoms and pain. Bonanni and colleagues explain that complex regional pain syndrome which is a fear of possible adverse effects following vaccination is an important determinant of vaccine uptake hesitancy which should be addressed well by healthcare providers and vaccination education programs (Bonanni et al., 2017). Good communication strategies, multicomponent and dialogue based interventions involving culturally adapted messages that uses adequate language that is understood and appreciated by targeted populations are most effective for this purpose (Bonanni et al., 2017).

It is important to implement and support efforts and programs that address the importance of HPV vaccination for adolescents especially before their sexual debut. This should be a strong collaboration between healthcare professionals, educators and parents. This can also improve missed opportunities for HPV vaccination especially among high risk groups. Healthcare systems should examine and address HPV vaccination barriers and health beliefs that are specific to different populations. Brewer and colleagues explain that missed opportunities to HPV vaccination include both absence of provider recommendations and anticipated regrets by parents (Brewer et al., 2011).
3 BAYESIAN MODELING OF THE TEMPORAL TREND OF HUMAN PAPILLOMAVIRUS VACCINATION COVERAGE ESTIMATES AMONG ADOLESCENTS AGED 13–17 YEARS IN SOUTHEASTERN STATES OF THE UNITED STATES OF AMERICA

3.1 Background

In this chapter our interest will be to analyze human papillomavirus (HPV) vaccination initiation over time (quarter of survey year) and space (in the 10 southeastern states in US) among adolescent males and females aged 13–17 years. The graph in Figure 3-1 below shows the rate of HPV vaccination initiation among these adolescents in the southeastern (SE) states of the US. The quarterly coverage rates for the adolescents ranged from 24.4% in 2011 (Quarter 1) to 55.7% in 2016 (Quarter 4). The quarterly coverage rates in the SE states of the US consistently lag the national quarterly coverage rates that ranged from 28.1% in 2011 (Quarter 1) to 62.4% in 2016 (Quarter 4) with exception of the 3rd quarter in 2014 (49.0% versus 44.1%), as shown in Figure 3-1 below. The average HPV vaccination coverage rate increases quarterly at 1.37% and 1.49% for SE states in the US and nationally respectively.

These trend analyses will help inform us about the trajectories of the HPV vaccination programs in the SE states in US. Also, when there are dips in vaccination coverage there can be investigations and exploration of events that can take place to identify corrective measures that can be taken to improve the outreach of vaccination programs. We can also gauge HPV vaccination initiation coverage rate change over time, which can also help in judicial purchase and effective distribution of the HPV vaccine.
Figure 3.1. Quarterly ≥1 Dose HPV Vaccination Coverage, NIS-Teen 2011–2016.

3.2 Methods

We used the National Immunization Survey–Teen (NIS-Teen) data set from 2011 to 2016 survey years that constitute interviews from landline and cellar telephone households for
this research (Jain, Singleton, Montgomery, & Skalland, 2009; Centers for Disease Control and Prevention, 2014). The NIS-Teen is an ongoing cross-sectional survey conducted by the Centers for Disease Control and Prevention (CDC), using random-digit-dial telephone interviews with parents/guardians to obtain demographic and vaccination information for their adolescents aged 13–17 years. NIS-Teen also includes a mailed survey to all vaccination providers identified by the parent and for which consent was granted to contact for vaccination history (Jain, Singleton, Montgomery, & Skalland, 2009; Centers for Disease Control and Prevention, 2014). The NIS-Teen uses a national probability sample of households in the US, which includes all 50 states, the District of Columbia, and some select local areas. The NIS-Teen is conducted using the sampling frame of telephone numbers selected for the NIS-Child (Centers for Disease Control and Prevention, 2014). The Council of American Survey Research Organizations (CASRO) landline response rates from 2011 to 2016 ranged from 51.1% to 60.3%. The yearly CASRO response rate for the cell phone sample from 2011 to 2016 ranged from 22.4% to 31.2% (Centers for Disease Control and Prevention, 2017). Among those who completed the household survey and had adequate provider-reported vaccination histories from 2011 to 2016, the annual number of sampled adolescents ranged from 6,039 to 20,848 by landline (59.5% to 61.5%) and 2,716 to 17,091 by cell-phone (47.4% - 56.4%) (Centers for Disease Control and Prevention, 2017). We will be using only data from the 10 southeastern (SE) states in the US. These 10 states are as follows: Alabama (AL), Florida (FL), Georgia (GA), Kentucky (KY), Mississippi (MS), North Carolina (NC), South Carolina (SC), Tennessee (TN), Virginia (VA), and West Virginia (WV). A map of all the 10 SE of US is shown in Figure 2-1 above.

Our variables of interest and definitions are as follows:
▪ The outcome for this analysis is receipt of at least one HPV dose (initiation) (YES; NO)
▪ Quarter of Survey Year (2011Q1; 2011Q2; 2011Q3; 2011Q4; 2012Q1; 2012Q2; 2012Q3; 2012Q4; 2013Q1; 2013Q2; 2013Q3; 2013Q4; 2014Q1; 2014Q2; 2014Q3; 2014Q4; 2015Q1; 2015Q2; 2015Q3; 2015Q4; 2016Q1; 2016Q2; 2016Q3; and 2016Q4)
▪ State in which Teen lives (AL; FL; GA; KY; MS; NC; SC; TN; VA; and WV)
▪ Age of Teen in years (13; 14; 15; 16; and 17) at year of interview
▪ Sex of Teen (Male; and Female)
▪ Race/Ethnicity (White, non-Hispanic; Black, non-Hispanic; Hispanic; and Other non-Hispanic or Multiple Races)
▪ Income to poverty ratio (<133% Federal Poverty Level [FPL]; 133% - < 322% FPL; 322% - <503% FPL; and >503% FPL)
▪ Mother’s Education (<High School; High School Graduate; Some College Education; and College Degree or Higher Education)
▪ Mother’s Age in years (≤34 years; 35-44 years; and ≥45 years)
▪ Health insurance status (Private Only; Medicaid/Children’s Health Insurance Program [CHIP]; Uninsured; Military; and Other Forms of Insurance Payments).

3.3 Analysis

We started our analysis by aggregating the individual observations into quarter of survey year (QSY) for all the observations in the SE states of the US and then regrouping the observations within each QSY by the state in which they lived, age at interview, sex, race or
ethnicity, income-to-poverty ratio, mother’s education, mother’s age, and insurance payment type. The total sample size of 20,862 reduced to 19,229 after the regrouping mentioned earlier on. Based on the covariates of interest, the overall possible group combinations for all our variables of interest is supposed to be 9,600 per state within each of the 24 QSYs. This will add up to 2,304,000 subgroups in the data set for our analysis.

We used the following procedures “PROC SQL”, “PROC FREQ”, “PROC IML”, and “PROC GLIMMIX” in SAS 9.4 to prepare the data for the analysis. We further used “R2WinBUGS” in RStudio 1.0.136 to call WINBUGS 14.1 to run the three different Bayesian Hierarchical (BH) models with or without spatial effects (Conditional Autoregressive [CAR] model). As we stated earlier in section 3.1 the QSYs are time component in all our models.

The most complex model included randomizing the state in which the individual lived (state as random effect) as well as including spatial effects for state (state as spatial effect). The simplest model neither included the state of the individual as random effects nor included any spatial effects.

The initial values for all the BH analyses were generated using a logistic regression model (“PROC GLIMMIX” in SAS 9.4) which included all the covariates that were used in the BH models. In section 3.4, we will describe in detail what the models entailed and present the results in section 3.5.
3.4 Models

We aggregated the individual binary outcome ("YES or "NO") indicating their HPV vaccination status into the QSY outcomes, which will allow us to use the Binomial distribution for our outcome instead of the Bernoulli distribution.

In the binomial hierarchy model in which we observe vaccination status in the SE states of US, we will define the total number of groups in all considered QSYs as \( N \) and the sample size of the \( i^{th} \) group as \( n_i \). We will denote the number of individuals who were vaccinated by \( y_i \), which it is often assumed to independently follow binomial distribution with a conditional probability.

\[
i.e., \quad y_i \sim \text{Bin}(n_i, p_i).
\]

The likelihood is given by

\[
\prod_{i=1}^{N} L(p_i | y_i, n_i) = \prod_{i=1}^{N} \binom{n_i}{y_i} p_i^{y_i} (1 - p_i)^{n_i - y_i}.
\]

We apply a logistic link to the probability to relate the vaccination count with covariates of interest. We consider the necessity of including a random state effect to allow differences across states, and spatial CAR models at the state-level to capture the spatial relationships. In all the models, the prior distribution for all intercepts, slope coefficients of covariates, random state effect, and quarter of survey year were assumed to have a normal distribution. The hyper prior distributions for the variances were inverse-gamma distributions. Let \( s_i \) and \( q_i \) denote the state and the QSY that the \( i^{th} \) group belongs to in our sample.

The most complex model that we consider is below.
\[ \begin{align*}
    y_i & \sim Bin (n_i, p_i) \\
    \logit(p_i) &= \beta_0 + \beta_{s_i,0} + \beta_{Q, i} q_i + \sum_{j=1}^{20} \beta_j x_{ij} + b_{s_i}
\end{align*} \]

where $\beta_{s_i,0} \sim N(0, \sigma_s^2)$ represents the random state effect and $\sigma_s^2 = \frac{1}{\tau_s^2}$

$\beta_{Q, i} \sim N(0, \sigma_q^2)$ represents the slope coefficient of time of survey (QSY)

and $\sigma_q^2 = \frac{1}{\tau_q^2}$

$q_i$ = the observed quarter of survey in the $i^{th}$ group

$x_{ij}$ is the observed value of the $j^{th}$ covariate in the $i^{th}$ group,

$b_{s_i}$ captures the spatial effect at the state level and is assumed to have a CAR model:

\[ (b_1, \cdots b_{N_s}) \sim CAR(W_s, \text{sigma.} b^2) \]

\[ tau.b \sim Gamma(0.5, 0.5) \]

\[ \text{sigma.} b < -\frac{1}{\sqrt{\text{tau.} b}} \]

where $N_s = 10$

$W_s$ is 0–1 contiguity matrix (10 x 10 matrix) with 1 indicating being neighbors

$tau. b$ is a scalar argument representing the precision (inverse variance) parameter of the CAR prior.

We assume that

\[ \beta_j \sim N(0, \sigma_j^2) \text{ and } \sigma_j^2 = \frac{1}{\tau_j^2} \text{ independently,} \]

and
\( \tau_j^2 \sim \text{Gamma}(0.05, 0.05) \) for \( j = 1, \ldots, 20 \).

We also assume our intercept to be
\[
\beta_0 \sim N(0, \sigma_0^2) \text{ and } \sigma_0^2 = \frac{1}{\tau_0^2} \text{ with } \tau_0^2 \sim \text{Gamma}(0.05, 0.05).
\]

The hierarchy for our most complex model is diagrammatically displayed in Figure 3-2.

---

**Figure 3.2. The Most Complex Hierarchical Temporal Trend Model.** Logistic Regression where \( Y(i) \) is the \( i \)th group binary response variable, \( n(i) \) sample size of the \( i \)th group, \( p(i) \) is the probability that an individual in the \( i \)th group has initiated or received at least one dose of HPV vaccination, and \( X(i) \) is a set of covariates for the \( i \)th group. \( Q(i) \) is the quarter in which an individual in the group was surveyed. \( S(i) \) is the \( i \)th group state random effect, with an independent normal random variable with mean zero and variance \( \sigma_{st}^2 \). \( b(i) \) is the state spatial effect of the \( i \)th group, with \( (b(1), \ldots, b(10)) \) jointly has a CAR model defined in above where the variance parameter is \( \sigma_b^2 \) and controls the amount of variability in \( \{b(i)\} \).

The least complex hierarchy model that we considered is:

\[
y_i \sim \text{Bin}(n_i, p_i)
\]

\[
\text{logit}(p_i) = \beta_0 + \beta_{Q_i}Q_i + \sum_{j=1}^{20} \beta_j x_{ij}
\]
where \( \beta_{q_t} \sim N(0, \sigma_q^2) \) represents the slope coefficient of time of survey (QSY).

and \( \sigma_q^2 = \frac{1}{\tau_q^2} \).

\( q_t \) = the observed quarter of survey in the \( i^{th} \) group

\( x_{ij} \) is the observed value of the \( j^{th} \) covariate in the \( i^{th} \) group

We assume that

\( \beta_j \sim N(0, \sigma_j^2) \) and \( \sigma_j^2 = \frac{1}{\tau_j^2} \) independently,

and

\( \tau_j^2 \sim Gamma(0.05, 0.05) \) for \( j = 1, \ldots, 20 \).

We also assume the intercept to be

\( \beta_0 \sim N(0, \sigma_0^2) \) and \( \sigma_0^2 = \frac{1}{\tau_0^2} \) with \( \tau_0^2 \sim Gamma(0.05, 0.05) \).

Here the \( \beta_i's \) have the same parameter distributions as that of the most complex models stated above. We further diagrammatically display the hierarchy of the least complex model in Figure 3-3 below:
Figure 3.3. The Least Complex of All Three Models Considered. Logistic Regression
where \( Y(i) \) is the \( i \)th group binary response variable, \( n(i) \) sample size of the \( i \)th group, \( p(i) \) is the probability that an individual in the \( i \)th group has initiated or received at least one dose of HPV vaccination, and \( X(i) \) is a set of covariates for the \( i \)th group. \( Q(i) \) is the quarter of which an individual in the group was surveyed.

We considered three models based on our possible combinations of including the random state effect and the state spatial effect. For each model, we run 100,000 MCMC iterations, took the first 10,000 as “burn-in”, and generate 90,000 samples per covariate. Convergence were attained in about 1,000 simulations. The time elapsed for all the three models ranged from a minimum of 17,425 seconds (\( \approx 4.84 \) hours) to a maximum of 22,622 seconds (\( \approx 6.28 \) hours) on a PC (16.0GB RAM, 3.4GHz CPU). A summary of the model diagnostics and statistics for all the three models that were analyzed is presented in Table 3-1 below:

<table>
<thead>
<tr>
<th>STATES</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iterations</td>
<td>100,000</td>
<td>100,000</td>
<td>100,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample</td>
<td>90,000</td>
<td>90,000</td>
<td>90,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Elapsed</td>
<td>22,622</td>
<td>19,797</td>
<td>17,425</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random Intercept</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAR Component</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dbar</td>
<td>24104.6000</td>
<td>24104.4000</td>
<td>24289.5000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dhat</td>
<td>24073.8000</td>
<td>24073.5000</td>
<td>24267.6000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pD</td>
<td>30.7970</td>
<td>30.8470</td>
<td>21.9470</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIC</td>
<td>24135.3000</td>
<td>24135.2000</td>
<td>24311.5000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: The 3rd model has a posterior discrepancy (pD) of 21.9470, which is the lowest among the three models, indicating better fit.
Dbar: this is the posterior mean of the Deviance.
Dhat: this is a point estimate of the Deviance.
\[ pD = Dbar - Dhat = \text{var(Deviance)} / 2. \]
DIC: Deviance Information Criterion (DIC) is an Estimate of Expected Predictive Error (Lower Deviance is Better)
\[ = Dbar + pD = Dhat + 2pD. \]
Deviance = \(-2 \log p(y|\theta)\).
Range of DIC = (24135.2 - 24311.5)
Note: * Means Selected Model

All three models used the same number of covariates (as stated in Section 3.2) and they only differed by whether state was included in the model as a random effect and/or a spatial effect.

Model 1 has the smallest Deviance Information Criterion (DIC = 24135.2000) compared to Models 2 and 3, but it is only 0.10 less than the DIC for Model 2 (DIC = 24135.3000). The calculation of the DIC considers both model fit (measured by Dbar) and model complexity (measured by pD) in comparing models. In using the DIC criterion for model selection, differences in DIC greater than 10 is considered a substantial change, which helps to rule out models with higher DIC; differences in DIC between 5 and 10 are considered substantial and should be reviewed carefully taking into consideration other factors for model selection; but, if the difference in DIC is < 5, because it could be misleading just to report the model with the lowest DIC, other factors should also be taken into consideration before selecting the final model (Spiegelhalter, Best, Carlin, & Van Der Linde). We selected Model 2 because the time elapsed for the completion of this model was 19,797 seconds which was much less than the time elapsed for Model 1 which was 22,622 seconds. Table 3-1 above have a summary of our results.

The following distributions define the above-selected hierarchy complex model:
\[ y_i \sim Bin(n_i, p_i) \]
\[ \text{logit}(p_i) = \beta_0 + \beta_{s_i,0} + \beta_{Q_i}q_i + \sum_{j=1}^{20} \beta_j x_{ij} \]

where \( \beta_{s_i,0} \sim N(0, \sigma_s^2) \) and \( \sigma_s^2 = \frac{1}{\tau_s^2} \) represents the random state effect,

\( \beta_{Q_i} \sim N(0, \sigma_q^2) \) represents the slope coefficient of time of survey (QSY)

and \( \sigma_q^2 = \frac{1}{\tau_q^2} \),

\( q_i = \) the observed quarter of survey in the \( i^{th} \) group

\( x_{ij} \) is the observed value of the \( j^{th} \) covariate in the \( i^{th} \) group.

We assume that

\( \beta_j \sim N(0, \sigma_j^2) \) and \( \sigma_j^2 = \frac{1}{\tau_j^2} \) independently,

and

\( \tau_j^2 \sim Gamma(0.05, 0.05) \) for \( j = 1, ..., 20 \).

We also assume our intercept to be

\( \beta_0 \sim N(0, \sigma_0^2) \) and \( \sigma_0^2 = \frac{1}{\tau_0^2} \) with \( \tau_0^2 \sim Gamma(0.05, 0.05) \).

The hierarchy structure of the selected model is diagrammatically displayed in Figure 3-4 below:
Figure 3.4. Selected Model Among All Three Models Considered. Logistic Regression where $Y(i)$ is the $i^{th}$ group binary response variable, $n(i)$ sample size of the $i^{th}$ group, $p(i)$ is the probability that an individual in the $i^{th}$ group has initiated or received at least one dose of HPV vaccination, and $X(i)$ is a set of covariates for the $i^{th}$ group. $Q_d(i)$ is the quarter in which an individual in the group was surveyed. $S_t(i)$ is the $i^{th}$ group state random effect, with an independent normal random variable with mean zero and variance $\sigma^2_{St}$.

The selected model did not include the CAR model (spatial effect). This implies that neighboring states do not provide additional improvement in modeling the vaccination rate during the quarter of which the survey was done, given the information on existing covariates and random state effects. The initial covariate values for the WinBUGS simulation were obtained after analyzing the data using “PROC GLIMMIX” in SAS version 9.4.

The summary of posterior means and 95% credible intervals of covariates estimated from WinBUGS for the selected model are shown in the Table 3-2 below:
### Table 3.2. Posterior Summaries for Regression Coefficients in the Selected Temporal Trend Model

<table>
<thead>
<tr>
<th>Label</th>
<th>Mean</th>
<th>2.5%</th>
<th>Median</th>
<th>97.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept*</td>
<td>-0.9668</td>
<td>-1.2110</td>
<td>-0.9680</td>
<td>-0.7146</td>
</tr>
<tr>
<td>Quarter of Survey Interview*</td>
<td>0.0692</td>
<td>0.0648</td>
<td>0.0692</td>
<td>0.0736</td>
</tr>
<tr>
<td>Age at interview of teen 14 Years*</td>
<td>0.2441</td>
<td>0.1501</td>
<td>0.2442</td>
<td>0.3386</td>
</tr>
<tr>
<td>Age at interview of teen 15 Years*</td>
<td>0.4058</td>
<td>0.3105</td>
<td>0.4057</td>
<td>0.5011</td>
</tr>
<tr>
<td>Age at interview of teen 16 Years*</td>
<td>0.4279</td>
<td>0.3330</td>
<td>0.4279</td>
<td>0.5230</td>
</tr>
<tr>
<td>Age at interview of teen 17 Years*</td>
<td>0.4371</td>
<td>0.3386</td>
<td>0.4369</td>
<td>0.5364</td>
</tr>
<tr>
<td>Sex of teen Male*</td>
<td>-1.1258</td>
<td>-1.1860</td>
<td>-1.1260</td>
<td>-1.0650</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Non-Hispanic Black*</td>
<td>0.2306</td>
<td>0.1451</td>
<td>0.2303</td>
<td>0.3178</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Hispanic*</td>
<td>0.4194</td>
<td>0.3006</td>
<td>0.4195</td>
<td>0.5383</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Other</td>
<td>0.0711</td>
<td>-0.0477</td>
<td>0.0711</td>
<td>0.1901</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥133% and &lt; 322%*</td>
<td>-0.1729</td>
<td>-0.2646</td>
<td>-0.1728</td>
<td>-0.0811</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥322% and &lt; 503%</td>
<td>-0.1106</td>
<td>-0.2254</td>
<td>-0.1107</td>
<td>0.0043</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥503%*</td>
<td>0.1507</td>
<td>0.0323</td>
<td>0.1506</td>
<td>0.2682</td>
</tr>
<tr>
<td>Teen's Mother's Education Level High School Graduate*</td>
<td>-0.1273</td>
<td>-0.2437</td>
<td>-0.1273</td>
<td>-0.0102</td>
</tr>
<tr>
<td>Teen's Mother's Education Level More than High School Graduate</td>
<td>-0.0793</td>
<td>-0.1924</td>
<td>-0.0793</td>
<td>0.0347</td>
</tr>
<tr>
<td>Teen's Parent's Education Level College Graduate</td>
<td>-0.0009</td>
<td>-0.1210</td>
<td>-0.0010</td>
<td>0.1204</td>
</tr>
<tr>
<td>Teen's Parent's Age Group 35 to 44 Years*</td>
<td>-0.1829</td>
<td>-0.2925</td>
<td>-0.1830</td>
<td>-0.0732</td>
</tr>
<tr>
<td>Teen's Parent's Age Group ≥ 45 Years*</td>
<td>-0.2112</td>
<td>-0.3266</td>
<td>-0.2114</td>
<td>-0.0967</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Medicaid or CHIP*</td>
<td>0.4193</td>
<td>0.3256</td>
<td>0.4192</td>
<td>0.5140</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Uninsured*</td>
<td>-0.2367</td>
<td>-0.4015</td>
<td>-0.2365</td>
<td>-0.0729</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Military</td>
<td>-0.0501</td>
<td>-0.1909</td>
<td>-0.0501</td>
<td>0.0901</td>
</tr>
<tr>
<td>Teen's Insurance Payment Source Other*</td>
<td>-0.1400</td>
<td>-0.2507</td>
<td>-0.1396</td>
<td>-0.0298</td>
</tr>
<tr>
<td>Precision of Quarter of Survey Interview*</td>
<td>1.6949</td>
<td>0.0000</td>
<td>0.0120</td>
<td>16.8607</td>
</tr>
<tr>
<td>State of Alabama Random Effect Parameter</td>
<td>-0.1384</td>
<td>-0.3365</td>
<td>-0.1366</td>
<td>0.0501</td>
</tr>
<tr>
<td>State of Florida Random Effect Parameter</td>
<td>0.0635</td>
<td>-0.1307</td>
<td>0.0645</td>
<td>0.2551</td>
</tr>
<tr>
<td>State of Georgia Random Effect Parameter</td>
<td>0.2910</td>
<td>0.0989</td>
<td>0.2911</td>
<td>0.4839</td>
</tr>
<tr>
<td>State of Kentucky Random Effect Parameter</td>
<td>-0.1401</td>
<td>-0.3387</td>
<td>-0.1383</td>
<td>0.0492</td>
</tr>
<tr>
<td>State of Mississippi Random Effect Parameter</td>
<td>-0.3947</td>
<td>-0.5969</td>
<td>-0.3923</td>
<td>-0.2052</td>
</tr>
<tr>
<td>State of North Carolina Random Effect Parameter</td>
<td>0.1833</td>
<td>-0.0101</td>
<td>0.1842</td>
<td>0.3759</td>
</tr>
<tr>
<td>State of South Carolina Random Effect Parameter</td>
<td>-0.2499</td>
<td>-0.4496</td>
<td>-0.2476</td>
<td>-0.0611</td>
</tr>
<tr>
<td>State of Tennessee Random Effect Parameter</td>
<td>-0.0075</td>
<td>-0.2037</td>
<td>-0.0060</td>
<td>0.1837</td>
</tr>
<tr>
<td>State of Virginia Random Effect Parameter</td>
<td>0.1760</td>
<td>-0.0175</td>
<td>0.1767</td>
<td>0.3672</td>
</tr>
<tr>
<td>State of West Virginia Random Effect Parameter</td>
<td>0.1657</td>
<td>-0.0286</td>
<td>0.1667</td>
<td>0.3590</td>
</tr>
</tbody>
</table>

Note: * Posterior Credible Interval Does Not Includes 0 (Zero).

The 95% posterior credible intervals from the Table 3-2 above shows that factors associated with higher likelihood of HPV vaccination initiation in the 10 southeastern states in
US are as follows: age at interview from 14 through 17 years old; being a non-Hispanic black or Hispanic race or ethnicity; having household Income to Poverty Ratio \(\geq 503\%\); having Medicaid and or CHIP as your health insurance status; and living in the State of Georgia among the 10 southeastern states. These had positive means and nonzero regression coefficients at the 95% credible intervals.

Factors that were associated with lower likelihood of HPV vaccination initiation in the 10 southeastern states in US were being an adolescent male; having household income to poverty ratio from 133\% to less than 503\%; teen's mother's being a College Graduate; teen's mother's being \(\geq 45\) years old; teen being uninsured or using other insurance for vaccination payment purposes; and living in the State of Mississippi or South Carolina among the 10 southeastern states. These had negative means and nonzero regression coefficients at the 95% credible intervals.

For the selected model and its binomial distribution, the objective is to estimate the posterior distribution for the rate of HPV vaccination initiation for each quarter of survey year interviewed.

Given

\[
\text{logit}(p_i) = \beta_0 + \beta_{s_i,0} + \beta_{Q,t} q_i + \sum_{j=1}^{20} \beta_j x_{ij}
\]

let

\[
\theta_i = \beta_0 + \beta_{s_i,0} + \beta_{Q,t} q_i + \sum_{j=1}^{20} \beta_j x_{ij}
\]
Then

\[ \text{logit}(p_i) = \theta_i \]

We estimate the posterior proportion of HPV vaccination initiation of adolescents in each group and in each QSY, by plugging in the sampled values of \( \beta \)'s and the corresponding values of \( x' \) s followed by a transformation back from logit to a proportion as follows:

\[
p_{\hat{i}} = \left( \frac{e^{\theta_{i}}}{1 + e^{\theta_{i}}} \right)
\]

For each of the 24 QSYs in the 10 SE states, we estimated 9,600 groups of posterior proportion estimates which will result in 2.304 million rates of HPV vaccination initiation of adolescents.

To estimate the corresponding overall rate of HPV vaccination initiation of adolescents in the \( Q_1 \) th QSY, \( \mu_{Q_t} \), based on the rule of total probability, we use the following:

\[
\mu_{Q_t} = \sum_{i=1}^{9600} p_{tQ_t} \times Wt_{Q_t}
\]

where \( Wt_{Q_t} \) is the proportion that the \( Q_1 \) th QSY individuals belong to the \( i^{th} \) group. We get a value of \( \mu_{Q_t} \) for each MCMC sample unit. From all 90,000 MCMC samples, we simulate the posterior distribution of \( \mu_{Q_t} \), from which we get the posterior mean and 95% credible interval of HPV vaccination initiation rate for each QSY. We will present some of our results in section 3.5 below.
3.5 Results

We used “PROC UNIVARITE” in SAS 9.4 to calculate the HPV vaccination initiation coverage estimates after using “PROC IML” in SAS 9.4 to perform the above-stated calculations and including the survey weights produced with the data sets. We added 1% of the smallest survey weights to all 9,600 groups in each QSY within each state to compensate for the weights in any missing group in the survey data set.

In Table 3-3 and Figure 3-5 below, we present the overall quarterly HPV vaccination initiation coverage estimates and their corresponding 95% credible intervals from 2011 to 2016 after adjusting for all the covariates mentioned in section 3.2 above in the Bayesian modeling of the SE states in US. The Bayesian method estimates that in the 1st quarter of 2011, the rate of HPV vaccination initiation coverage was 25.5% with a 95% credible interval of (24.4% - 26.7%) for the SE states in the US. Also, in the 4th quarter of 2016, the rate of HPV vaccination initiation coverage was 61.1% with a 95% credible interval (59.8% - 62.4%). This showed a quarterly overall rate increase of $\approx 1.6\%$ point. The 95% credible intervals for all the estimated rates are very narrow which means there is very small uncertainty in the estimates derived. The estimated coverage rates indicated a small dip from the 2nd quarter of 2013 compared to the 3rd quarter of 2013, even though there was an increase in the unadjusted coverage rates during that same period.
Table 3.3. Quarterly ≥1 Dose HPV Vaccination Coverage in Southeastern States in United States, NIS-Teen 2011–2016 Using Bayesian Methods.

<table>
<thead>
<tr>
<th>Quarter of Interview</th>
<th>Unadjusted Estimates</th>
<th>Bayesian Adjusted Estimates for Southeastern US States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>National % (95% C.I.)</td>
<td>Southeastern (SE) % (95% C.I.) States in US</td>
</tr>
<tr>
<td></td>
<td>Mean % (2.5% - 97.5%)</td>
<td>Mean % (2.5% - 97.5%)</td>
</tr>
<tr>
<td>2011Q1</td>
<td>28.1 (25.9-30.4)</td>
<td>27.9 (24.1-32.1)</td>
</tr>
<tr>
<td>2011Q2</td>
<td>28.7 (26.6-30.8)</td>
<td>28.9 (24.1-32.1)</td>
</tr>
<tr>
<td>2011Q4</td>
<td>31.7 (29.5-34.1)*</td>
<td>31.3 (26.8-36.0)</td>
</tr>
<tr>
<td>2012Q1</td>
<td>32.6 (30.6-34.7)*</td>
<td>32.2 (27.8-36.8)</td>
</tr>
<tr>
<td>2012Q2</td>
<td>36.7 (33.8-39.7)*</td>
<td>36.2 (31.8-39.0)</td>
</tr>
<tr>
<td>2012Q3</td>
<td>38.3 (35.6-41.1)*</td>
<td>38.0 (33.5-42.6)</td>
</tr>
<tr>
<td>2012Q4</td>
<td>38.8 (36.6-41.0)*</td>
<td>38.5 (34.1-42.6)</td>
</tr>
<tr>
<td>2013Q1</td>
<td>43.6 (40.9-46.4)*</td>
<td>38.9 (33.4-44.8)</td>
</tr>
<tr>
<td>2013Q2</td>
<td>43.8 (41.1-46.5)*</td>
<td>38.7 (33.4-44.2)</td>
</tr>
<tr>
<td>2013Q3</td>
<td>46.5 (44.1-48.9)*</td>
<td>40.2 (36.0-44.6)</td>
</tr>
<tr>
<td>2013Q4</td>
<td>49.0 (45.8-52.2)*</td>
<td>44.1 (37.7-50.6)</td>
</tr>
<tr>
<td>2014Q1</td>
<td>47.8 (45.3-50.4)*</td>
<td>46.0 (41.0-51.0)</td>
</tr>
<tr>
<td>2014Q2</td>
<td>50.2 (47.7-52.7)*</td>
<td>45.0 (40.0-50.1)</td>
</tr>
<tr>
<td>2014Q3</td>
<td>50.9 (48.4-53.5)*</td>
<td>52.6 (47.4-57.7)</td>
</tr>
<tr>
<td>2014Q4</td>
<td>53.5 (50.6-56.4)*</td>
<td>46.4 (40.9-52.0)</td>
</tr>
<tr>
<td>2015Q1</td>
<td>54.3 (51.9-56.8)*</td>
<td>51.0 (46.3-55.6)</td>
</tr>
<tr>
<td>2015Q2</td>
<td>54.5 (51.9-57.0)*</td>
<td>47.0 (42.0-52.1)</td>
</tr>
<tr>
<td>2015Q3</td>
<td>59.5 (56.8-62.0)*</td>
<td>56.8 (51.7-61.7)</td>
</tr>
<tr>
<td>2015Q4</td>
<td>56.9 (54.4-59.4)</td>
<td>50.6 (45.1-56.1)</td>
</tr>
<tr>
<td>2016Q1</td>
<td>59.2 (56.8-61.5)*</td>
<td>50.4 (45.9-55.0)</td>
</tr>
<tr>
<td>2016Q2</td>
<td>58.9 (56.1-61.7)</td>
<td>57.3 (51.6-62.8)</td>
</tr>
<tr>
<td>2016Q3</td>
<td>61.5 (59.4-63.5)*</td>
<td>59.3 (55.1-63.5)</td>
</tr>
<tr>
<td>2016Q4</td>
<td>62.4 (59.5-65.3)*</td>
<td>55.7 (49.6-61.6)</td>
</tr>
</tbody>
</table>

% Indicates Percent Vaccination Coverage; C.I. = Confidence Interval.
* Significantly Higher Compared to Bayesian Mean Estimates in Southeastern States in the US
3.6 Discussion of Research Findings

In this part of the dissertation our aim is to model the quarterly trends in HPV vaccination coverage estimates in the southeastern US states using Bayesian methods. We were
able to estimate HPV vaccination from first quarter of 2011 to fourth quarter of 2016. The HPV vaccination coverage ranged from 25.2% with 95% credible interval of (24.4% - 26.7%) to 61.1% with a 95% credible interval of (59.8% - 62.4%). There was an overall quarterly increase of approximately 1.6%. The 95% credible intervals estimated were all narrow indicating a very small uncertainty in the estimates which we derived.

Factors that were associated with higher likelihood of HPV vaccination initiation in the 10 southeastern US states were age at interview from 14 years through 17 years using age 13 as reference, non-Hispanic blacks or Hispanic race or ethnicity using non-Hispanic whites as reference, using Medicaid of CHIP for vaccination payment source compared to using private insurance and living in the State of Georgia among all 10 southeastern states.

Factors that were associated with lower likelihood of HPV vaccination initiation in the 10 southeastern US states were being a male adolescent in the southeastern US, family’s household income to poverty ration from 133% to less than 503%, the adolescents mother being a college graduate and or being 45 years old or older, the adolescent being uninsured or using other insurance payment source for vaccination purposes or living in the state of Mississippi or South Carolina among the 10 southeastern US states.
4 SUMMARY

4.1 Study Strengths and Limitations

The strength of this study can be attributed to the fact that Bayesian methods provides a natural and principle way of combining prior information with data within a solid decision-theoretical framework. Moreover, all inferences are based on the posterior distribution which follows the Bayes’ Theorem. Inference generated are always conditional on the data and are exact because they do not rely on either the “plug-in” principle or the asymptotic approximation. There are generally no differences in inferences between small or large samples because of the use of similar processes. Bayesian methods conform to the likelihood principle and can also be used to answer specific scientific questions directly. The use of MCMC and other algorithms in Bayesian methods makes computations tractable for virtually all parametric models making it convenient for a wide range of models including hierarchical models and missing data problems. The inclusion of CAR model in Bayesian methods adds to its strength because of “borrow strength” from neighboring counties or areas for estimation.

The NIS-Teen data has a provider-verified vaccination data component which makes it unique in terms of actual vaccination count. The NIS-Teen is a dual frame landline and cell-phone sampling frame which makes it a good representation of the population. Although the NIS-Teen 2016 data set had 277 counties with missing data among our study population, using Bayesian methods, we were able to calculate estimates at the county levels.

Bayesian methods however, do not mention how to select your prior results. Skills are needed to translate subject prior beliefs into mathematically formulated prior information. This can lead to generating misleading results if caution is not taken. Also, posterior distributions that are heavily influenced by the prior information can be easily generated.
Models with large number of parameters especially often comes with a very high computational cost. If random seed is not used, simulations will usually provide slightly different results each time.

4.2 Conclusion

Using Bayesian models, we were able to estimate HPV vaccination rates for small areas which did not have data for direct estimation and can be used for estimation rates of health indicators. Our study points out that Bayesian methods can provide means of assessing disease burden in areas where resource for data collection is lacking. Statisticians may consider the use of Bayesian methods to address data related needs. Also, it will be important to conduct comparative studies in varied populations to estimate the validity of Bayesian methods in assessing disease and indicator rates. Factors hypothesized to be appropriate predictors of validity will be of interest in research.

Our finding and consistency with literature that HPV initiation rates vary by gender, with females being more likely to initiate HPV vaccination compared to males is worth mentioning. Beyond consistency with results, we wish to call to attention that efforts must be put in place to address the gender disparity in HPV initiation, coverage and completion. Also challenges with HPV vaccination in the Southeastern states of US especially the State of Mississippi needs to be addressed. It is important to have policies and resources aimed at improving the HPV prevention interventions in these areas. We find for example that Medicaid availability is one of the important factors for increasing HPV initiation rates in the Southeastern areas.
Racial disparity in HPV vaccination also needs to be addressed. Research into factors that hinder HPV initiation among non-Hispanic Whites in the Southeastern areas could also provide clues concerning challenges in uptake of vaccines in the other US States. This is because the race/ethnicity factor is common to all states. Georgia has a comparatively better rate of HPV initiation and coverage. Assessing and evaluating prevention programs in Georgia could also provide lessons on how they overcome certain barriers and lessons of success in relation to their HPV vaccination programs.

Since adolescent age is an important factor for HPV initiation, it would be of interest to develop and test age-specific educational materials in relation to HPV uptake. Involving adolescents in the decision-making process concerning HPV vaccination in these areas could also help improve the rates of HPV coverage and reduce the associated burden.

4.3 Future Research

For our county-level HPV vaccination initiation coverage we used only the NIS-Teen 2016 data set which had 277 counties with missing vaccination information. To improve on that, our future research is to combine about 3 survey years of the NIS-Teen data sets and to reduce our covariates in our models to using age at interview, sex of the adolescent, and race/ethnicity. This will increase the number of subgroups within each county for our analysis. We also aggregated only individual level data to county-level data in our analysis, hence we plan to include state and/or county-level factors that are associated with vaccination to observe if “borrowing strength” from spatial effect (Car model) will be a better modeling tool to estimate county-level HPV vaccination coverage. We furthermore plan to use our best model to estimate other adolescent recommended vaccines.
For our temporal trend model, our future research plan is to also reduce our covariates to the three covariates mentioned earlier and to add county-level factors or covariates that are known to be associated with vaccination. We will then use our best model to predict quarterly HPV vaccination coverage estimates. We also plan to model temporal trends for the other adolescent recommended vaccines and find out which covariates have higher association of adolescent recommended vaccination in general and to determine if there any seasonality in the quarter of vaccination. Our future research also includes considering temporal models at the county level and exploring other CAR models. We plan to also consider the sensitivity of the models in choosing our prior distributions. This will be valuable to vaccination programs and policy decision makers to ensure the prudent utilization of funds for adolescent vaccines.
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doi:10.1016/j.ijg.2014.03.033

doi:10.1016/j.jpag.2013.08.009


APPENDICES

Appendix A: CAR Model Information

Appendix A.1: Prior Values Used in the Selected Model Excluding those for County Random Effects Obtained From the Logistics Regression Model Using “PROC GLIMMIX” In SAS.

<table>
<thead>
<tr>
<th>Label</th>
<th>Estimates</th>
<th>STD Error</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.1200</td>
<td>0.2232</td>
<td>0.6038</td>
</tr>
<tr>
<td>Age at interview of teen 14 Years*</td>
<td>0.2935</td>
<td>0.1106</td>
<td>0.0080</td>
</tr>
<tr>
<td>Age at interview of teen 15 Years*</td>
<td>0.3991</td>
<td>0.1115</td>
<td>0.0004</td>
</tr>
<tr>
<td>Age at interview of teen 16 Years*</td>
<td>0.6293</td>
<td>0.1109</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Age at interview of teen 17 Years*</td>
<td>0.3938</td>
<td>0.1175</td>
<td>0.0008</td>
</tr>
<tr>
<td>Sex of teen Male*</td>
<td>-0.3324</td>
<td>0.0710</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Non-Hispanic Black*</td>
<td>0.2686</td>
<td>0.1037</td>
<td>0.0096</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Hispanic*</td>
<td>0.4177</td>
<td>0.1416</td>
<td>0.0032</td>
</tr>
<tr>
<td>Race / Ethnicity of teen Other*</td>
<td>0.2720</td>
<td>0.1296</td>
<td>0.0359</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥133% and &lt; 322%</td>
<td>-0.1128</td>
<td>0.1074</td>
<td>0.2935</td>
</tr>
<tr>
<td>Teen's Household Income to Poverty Ratio ≥322% and &lt; 503%</td>
<td>-0.1993</td>
<td>0.1359</td>
<td>0.1426</td>
</tr>
<tr>
<td>Teen’s Household Income to Poverty Ratio ≥503%</td>
<td>0.0838</td>
<td>0.1386</td>
<td>0.5452</td>
</tr>
<tr>
<td>Teen's Mother's Education Level High School Graduate</td>
<td>-0.0685</td>
<td>0.1409</td>
<td>0.6271</td>
</tr>
<tr>
<td>Teen’s Mother's Education Level More than High School Graduate</td>
<td>-0.1142</td>
<td>0.1386</td>
<td>0.4098</td>
</tr>
<tr>
<td>Teen’s Mother's Education Level College Graduate</td>
<td>0.0638</td>
<td>0.1458</td>
<td>0.6617</td>
</tr>
<tr>
<td>Teen’s Mother's Age Group 35 to 44 Years</td>
<td>-0.1437</td>
<td>0.1302</td>
<td>0.2699</td>
</tr>
<tr>
<td>Teen’s Mother's Age Group ≥ 45 Years</td>
<td>-0.1492</td>
<td>0.1378</td>
<td>0.2787</td>
</tr>
<tr>
<td>Teen’s Insurance Payment Source Medicaid or CHIP*</td>
<td>0.4237</td>
<td>0.1082</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Teen’s Insurance Payment Source Uninsured</td>
<td>-0.1657</td>
<td>0.2039</td>
<td>0.4164</td>
</tr>
<tr>
<td>Teen’s Insurance Payment Source Military</td>
<td>-0.2309</td>
<td>0.1586</td>
<td>0.1454</td>
</tr>
<tr>
<td>Teen’s Insurance Payment Source Other</td>
<td>-0.1704</td>
<td>0.1323</td>
<td>0.1979</td>
</tr>
<tr>
<td>State of Alabama Random Effect Parameter</td>
<td>-0.1066</td>
<td>0.1389</td>
<td>0.4429</td>
</tr>
<tr>
<td>State of Florida Random Effect Parameter</td>
<td>0.0833</td>
<td>0.1354</td>
<td>0.5383</td>
</tr>
<tr>
<td>State of Georgia Random Effect Parameter*</td>
<td>0.4662</td>
<td>0.1363</td>
<td>0.0006</td>
</tr>
<tr>
<td>State of Kentucky Random Effect Parameter</td>
<td>-0.2244</td>
<td>0.1381</td>
<td>0.1043</td>
</tr>
<tr>
<td>State of Mississippi Random Effect Parameter*</td>
<td>-0.4114</td>
<td>0.1344</td>
<td>0.0022</td>
</tr>
<tr>
<td>State of North Carolina Random Effect Parameter</td>
<td>0.0652</td>
<td>0.1354</td>
<td>0.6299</td>
</tr>
<tr>
<td>State of South Carolina Random Effect Parameter</td>
<td>-0.2146</td>
<td>0.1409</td>
<td>0.1279</td>
</tr>
<tr>
<td>State of Tennessee Random Effect Parameter</td>
<td>0.0259</td>
<td>0.1435</td>
<td>0.8567</td>
</tr>
<tr>
<td>State of Virginia Random Effect Parameter</td>
<td>0.1888</td>
<td>0.1428</td>
<td>0.1864</td>
</tr>
<tr>
<td>State of West Virginia Random Effect Parameter</td>
<td>0.1275</td>
<td>0.1403</td>
<td>0.3633</td>
</tr>
</tbody>
</table>

Note: * P-value < 0.05
Appendix A.2: CAR Model Information Used for the 10 Southeastern States in United States in the Analysis

\[(b_1, \ldots, b_{N_s}) \sim \text{car.normal}(\text{adj}[], \text{weights}[], \text{num}[], \text{tau}.b)\]

\[
\text{for}(k \text{ in } 1: \text{sumNumNeigh})\{
\text{weights}[k] < -1
\}
\]

\[\text{tau}.b \sim \text{Gamma}(0.5, 0.5)\]

\[\text{sigma}.b < -\frac{1}{\sqrt{\text{tau}.b}}\]

\[\text{num} = c(4, 2, 5, 3, 2, 4, 6, 4, 2)\]

\[\text{adj} = c(2, 3, 5, 8, 1, 3, 1, 2, 6, 7, 8, 8, 9, 10, 1, 8, 3, 7, 8, 9, 3, 6, 1, 3, 4, 5, 6, 9, 4, 6, 8, 10, 4, 9)\]

\[\text{sumNumNeigh} = 34\]

Appendix A.3: CAR Model Information Used for the 648 Counties in Southeastern States in United States in Analysis

\[(c_1, \ldots, c_{N_c}) \sim \text{car.normal}(\text{adjc}[], \text{weightsc}[], \text{numc}[], \text{tau}.c)\]

\[
\text{for}(l \text{ in } 1: \text{sumNumNeighc})\{
\text{weightsc}[l] < -1
\}
\]
\( \tau_c \sim \text{Gamma}(0.5, 0.5) \)

\[ \sigma_c < -\frac{1}{\sqrt{\tau_c}} \]

\[ \text{numc} = c(4, 5, 5, 6, 4, 2, 5, 3, 6, 6, 4, 6, 4, 4, 4, 6, 6, 4, 7, 4, 6, 6, 4, 6, 5, 3, 4, 4, 5, 5, 4, 6, 7, 4, 5, 5, 4, 7, 7, 5, 3, 4, 5, 4, 5, 3, 4, 6, 5, 5, 4, 7, 4, 5, 6, 2, 5, 3, 3, 3, 4, 4, 4, 3, 3, 0, 4, 2, 4, 4, 4, 6, 2, 2, 3, 3, 3, 6, 3, 2, 3, 4, 7, 6, 7, 3, 4, 2, 8, 6, 4, 3, 3, 2, 4, 3, 2, 7, 5, 2, 2, 1, 6, 6, 4, 6, 4, 4, 6, 4, 7, 4, 4, 2, 4, 6, 4, 5, 5, 3, 2, 2, 5, 4, 5, 3, 4, 5, 3, 4, 5, 4, 10, 4, 3, 8, 3, 7, 5, 3, 4, 3, 5, 3, 0, 5, 3, 3, 4, 1, 2, 1, 3, 3, 1, 4, 4, 4, 6, 3, 4, 4, 5, 3, 4, 3, 2, 5, 5, 5, 5, 1, 3, 1, 1, 4, 3, 8, 5, 3, 3, 1, 5, 4, 5, 6, 2, 5, 5, 5, 3, 7, 4, 5, 3, 5, 4, 6, 4, 3, 2, 3, 5, 7, 6, 6, 2, 4, 5, 5, 5, 2, 5, 2, 5, 6, 5, 6, 3, 3, 8, 5, 6, 6, 2, 3, 4, 5, 3, 3, 4, 3, 5, 5, 3, 3, 4, 4, 5, 2, 6, 4, 5, 5, 2, 2, 6, 4, 3, 6, 5, 7, 6, 4, 7, 3, 5, 4, 5, 6, 6, 5, 4, 6, 5, 5, 4, 5, 3, 6, 2, 4, 5, 3, 4, 8, 3, 3, 5, 4, 6, 4, 5, 3, 6, 3, 5, 5, 4, 3, 4, 6, 6, 5, 6, 4, 5, 4, 3, 5, 7, 3, 6, 5, 6, 6, 4, 7, 5, 7, 4, 6, 7, 3, 7, 4, 5, 4, 6, 5, 3, 5, 6, 2, 5, 6, 4, 7, 5, 4, 4, 6, 7, 4, 2, 3, 5, 3, 6, 3, 6, 3, 1, 5, 4, 5, 4, 6, 5, 5, 5, 2, 6, 6, 8, 0, 0, 5, 5, 4, 6, 2, 1, 6, 5, 5, 5, 7, 7, 4, 7, 6, 6, 7, 7, 4, 2, 4, 8, 7, 3, 3, 6, 4, 5, 5, 7, 7, 7, 2, 4, 2, 2, 5, 0, 6, 5, 6, 5, 7, 7, 5, 6, 4, 6, 6, 5, 7, 5, 4, 7, 6, 2, 3, 4, 5, 4, 4, 4, 6, 4, 2, 6, 5, 4, 4, 6, 6, 5, 4, 5, 6, 5, 7, 5, 5, 7, 7, 5, 6, 4, 5, 7, 6, 7, 4, 6, 5, 3, 6, 6, 5, 6, 3, 2, 5, 6, 4, 6, 5, 3, 3, 4, 6, 3, 6, 5, 2, 4, 5, 5, 4, 5, 6, 4, 3, 4, 5, 3, 4, 4, 7, 3, 3, 5, 3, 6, 5, 3, 5, 5, 5, 1, 3, 5, 3, 5, 3, 4, 5, 6, 3, 4, 4, 4, 4, 7, 6, 1, 5, 3, 1, 4, 4, 5, 4, 4, 6, 3, 5, 3, 7, 2, 5, 8, 1, 5, 6, 3, 4, 5, 2, 3, 1, 0, 5, 4, 3, 3, 1, 3, 5, 7, 3, 1, 4, 3, 3, 4, 5, 6, 5, 4, 4, 4, 5, 5, 5, 3, 3, 2, 3, 1, 2, 2, 5, 4, 5, 5, 2, 4, 5, 6, 3, 6, 5, 5, 1, 7, 6, 5, 4, 9, 5, 7, 4, 5, 4, 2, 3, 6, 3, 7, 4, 4, 3, 6, 2, 5, 3, 4, 5, 6, 5, 4, 3, 5, 5, 3, 5, 6, 5, 3, 6)

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**Appendix B: Using Bayesian Hierarchical Model to Estimate \(\geq 1\) Dose HPV Vaccination Coverage Among Adolescent Aged 13–17 Years, National Immunization Survey-Teen 2016 Survey Data.**

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<th>MALES % (95% C. L.)</th>
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