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Small area estimation of human papillomavirus vaccination coverage among school-age children in Alabama counties

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ABSTRACT

Objectives: This study estimated county-level human papillomavirus (HPV) vaccination initiation rates in Alabama and determined whether disparities existed between counties in the Mississippi Delta region (MDR) and Appalachian region (AR).
Study design: This study used an observational cross-sectional design.
Methods: We used small area estimation methodology to estimate rates of medical provider–verified HPV vaccine initiation among school-age children in Alabama. Data for the study were retrieved from the 2015 National Immunization Survey ($n = 22{,}205$) and the US Census Bureau.
Results: The predictive model results showed that older age (odds ratio [OR] = 1.22, 95% confidence interval [CI] = 1.16, 1.29) was positively associated with vaccination initiation and black (OR = 0.79, 95% CI = 0.71, 0.87), white (OR = 0.56, 95% CI = 0.52, 0.60), and 'other' race/ethnicities (OR = 0.78, 95% CI = 0.70, 0.86), compared with Hispanics, and was negatively associated with vaccination initiation. The median ($\tilde{x}$)-modeled HPV vaccination initiation rate for all Alabama counties was 50.83% (interquartile range = 5.00%). Modeled HPV vaccination initiation rates were lowest in AR counties ($\tilde{x} = 49.81\%$), followed by counties not in the AR or MDR ($\tilde{x} = 53.26\%$) and MDR counties ($\tilde{x} = 54.90\%$).
Conclusions: Culturally sensitive school-based HPV vaccine delivery programs are needed for children living in AR counties in Alabama.

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Introduction

Annually, approximately 17,500 women and 9300 men in the United States are diagnosed with human papillomavirus (HPV)-related cancers.[1,2] The HPV vaccination may protect against the acquisition of HPV infection and, perhaps, by extension, later development of HPV-related cancers, such as cervical, vaginal, and vulval cancer in women, penile cancer in men, and anal cancer in both genders.[3] The Centers for Disease Control and Prevention (CDC) recommends a series of two vaccinations, six to twelve months apart, for both male and female adolescents from ages 11 to 12 years.[1] For adolescents aged 15 to 18 years and young adults aged 19 to 26 years, the vaccination is recommended for a three-dose schedule at 0, 1–2, and 6 months.[3] In 2018, the Food and Drug Administration approved the 9-valent HPV vaccine for men and women between the ages of 27 and 45 years.[4] The HPV vaccine is best administered before becoming sexually active.[1] Although the vaccine is highly effective in preventing future HPV infection from infecting the body, the vaccine neither prevents sexually transmitted diseases nor treats pre-existing HPV infections.[3]

Owing to its effectiveness in preventing associated cancers, the HPV vaccination is strongly supported by public health officials and medical personnel.[5] The vaccination not only protects the individual getting vaccinated but also reduces the spread of HPV among the general population; therefore, vaccinated communities as a whole experience reduced risk of HPV infection.[5] Previous studies have shown that HPV vaccination rates in the United States are low. Specifically, less than 40% of suggested girls and less than 22% of suggested boys have received the entire series,[6] which is much lower than the Healthy People 2020 goal of 80% coverage.[7]

Understanding the barriers to vaccination uptake within communities can assist community officials in education and vaccination programs to maximize vaccination uptake.[8] This is especially true within communities that may have limited access to connect with the medical community or have limited knowledge of the vaccine and the possible consequences of not adhering to vaccination recommendations.[9]

Research has shown that the state of Alabama has historically had high rates of cancer related to the HPV.[10,11] Areas within the Mississippi Delta region (MDR) and Appalachian region (AR), including the counties in Alabama, have significantly higher rates of HPV-related cancers than other regions of the United States.[12,13] The residents of these areas have, in general, lower incomes, less education, and less access to resources that promote health.[12,13] Understanding HPV vaccination coverage within these counties and the reasons for non-compliance with vaccination guidelines could reduce the incidence of HPV infection and, perhaps, the incidence of HPV-related cancers.[14] The Deep South Network for Cancer Control (DSN) was established to help promote cancer awareness and prevention, such as HPV vaccination compliance, in these vulnerable communities.[14] Understanding vaccination coverage rates among school-age children in Alabama counties could help school health officials working with practitioners at the DSN to target counties with low vaccination coverage rates.

There are challenges in estimating HPV vaccination rates within small areas owing to the lack of a national registry.[15] Small area estimation (SAE), which assumes that different areas with the same characteristics have similar outcomes, permits researchers and practitioners to estimate disease rates and behavioral outcomes within small areas—such as counties—when sample sizes garnered in public health surveillance programs are limited for said areas.[16] Local health statistics and SAE can be used to understand HPV vaccination coverage rates in hard-to-reach counties, such as the 20 southwestern/southeastern counties in the MDR of Alabama and the 37 northernmost counties in the AR of Alabama, and help maximize public health resources for education and vaccination distribution.[16]

When sample sizes for counties from nationally representative surveys are low, especially in rural locations, SAE can be an effective way to gather data and understand HPV vaccination coverage in an effort to reduce cancer mortality.[17] SAE may also be an effective methodology for understanding HPV vaccination coverage among students when time and resources to conduct comprehensive surveys of students are not available to school administrators and school health personnel.

Studies have shown that there are several personhood characteristics that influence HPV vaccine uptake, including gender, age, and race/ethnicity (which are variables commonly used in studies involving SAE methodology, as in this study). Although limited data exist, some studies have shown that HPV vaccination uptake is much lower among males, often owing to a lack of education surrounding the importance of vaccinating male adolescents or the severity of HPV in males.[9] Age is often associated with HPV vaccination owing, in part, to parents' beliefs that their child is too young or not sexually active at the recommended ages of vaccination.[18] In one study, rates for the completed HPV vaccine series decreased among women aged 19–26 years.[19] Race and ethnicity have been shown to be associated with HPV vaccine uptake, with Hispanics generally exhibiting higher coverage rates than other races/ethnicities.[9,20] Most studies point to limited education about the vaccine, the effectiveness of the vaccine, and the dangers of HPV and HPV-related cancers as the main causes for racial disparities in HPV vaccination uptake.[9,20]

The purpose of the present study was to (1) estimate the geographic distribution, at the county level, of HPV vaccination initiation among school-age children in Alabama and (2) determine if differences in HPV vaccine initiation among school-age children existed in MDR counties, AR counties, and all other counties within Alabama. HPV vaccination initiation is a commonly studied outcome in studies involving data from nationally representative surveys.[21,22]

Methods

Study design

SAE using a fixed-effects, regression-based synthetic estimator approach, which is explicated in the studies by Gonzalez[23] and Hansen et al.,[24] was carried out to estimate HPV vaccination initiation (i.e., 'at least one HPV vaccination administration') among children in Alabama counties. Data

for the predictive model calculated in the present study were retrieved from the 2015 National Immunization Survey (NIS) of the CDC.[25] The NIS is a landline and cellular telephone–based survey of immunization coverage among children and teens conducted annually by the CDC with a nationally representative sample of parents and guardians. With parental or guardian consent, the questionnaire is mailed to each family's vaccination provider for verification.

Similar to the study by Zhang et al.,[26] the following variables—used as fixed-effects independent variables in the SAE predictive model—were obtained from the data set: age (10–14 years, code = 0; 15–19 years, code = 1), sex (male, code = 0; female, code = 1), and race/ethnicity (Hispanic, code = 1; non-Hispanic black, code= 2; non-Hispanic other race, code = 3; and non-Hispanic white, code = 4). The category codes for all fixed-effects variables in this study were selected as a means to match NIS data with variable codes in the Census Bureau crosstabulated population counts, explained in more detail momentarily. HPV vaccination initiation data for each participant were dichotomously coded so as to create the following dependent variable: whether or not a participant ($n = 22,205$) had received at least one HPV vaccine (not vaccinated, code= 0; at least one vaccination, code = 1). All data from parental/guardian surveys were verified by contacting each family's vaccination clinic or vaccination provider in an effort to ensure accuracy of results.

Table 1 – Demographic characteristics from the 2015 National Immunization Survey study sample and the 2015 census for Alabama.

Variable	2015 NIS ($n = 22,205$)	2015 census for 67 Alabama counties (total $n = 628,210$)
	n (%)	Mean,[a] n (SE)
Age (years)		
10–14	9179 (41.30)	4611.50 (99.81)
15–19	13,026 (58.70)	4764.70 (103.90)
Sex		
Male	11,504 (51.80)	4765.90 (102.38)
Female	10,701 (48.20)	4610.30 (100.90)
Race/ethnicity		
Hispanic	4951 (22.30)	516.61 (11.36)
Non-Hispanic black	2225 (10.00)	2808.60 (88.60)
Non-Hispanic other race	2202 (9.90)	409.30 (9.90)
Non-Hispanic white	12,205 (57.80)	5641.70 (106.45)
Observed HPV vaccination uptake (initiation)		
No	9445 (42.50)	
Yes	12,760 (57.50)	

NIS, National Immunization Survey; HPV, human papillomavirus; SE, standard error of the mean.
[a] Mean sample size across Alabama counties.

Data analysis

The R Project for Statistical Computing (version 3.4.1) was used for all analyses. An assumption of the SAE approach taken in the present study is that the characteristics of the sample match the characteristics of the population. Because, as shown in Table 1, the race/ethnicity composition of the 2015 NIS sample was proportionally different from the study population (i.e., school-age children in Alabama counties), frequency weights were developed and used in all analyses to (1) reduce bias in our estimators and (2) ensure that the sample race/ethnicity composition matched the race/ethnicity composition of the population.

A multiple logistic regression model was calculated to determine the relationship between HPV vaccination initiation and the three demographic independent variables: age, sex, and race/ethnicity. Previous studies have shown that age, sex, and race/ethnicity are (1) predictors of HPV vaccine initiation[27] and (2) commonly used as independent variables in SAE studies.[26] Beta coefficients in the model were bootstrapped with 10,000 resamples,[28] and bias-corrected 95% confidence intervals (CIs) were generated for each estimate.[29] Beta coefficients from the logistic regression model were used to calculate the probability of HPV vaccine initiation for each study participant.

Linking the model with census data

To estimate HPV vaccination initiation among children in the 67 Alabama counties, population count data were obtained from the US Census Bureau for 2015 at the county level.[30] The data set obtained from the Census Bureau consisted of aggregate population counts for each Alabama county, stratified by age (10–14 or 15–19 years), sex (male or female), and race/ethnicity (Hispanic, non-Hispanic black, non-Hispanic other race, or non-Hispanic white), resulting in 16 possible demographic categories. Categories were selected to match the data from the 2015 NIS.

The aggregate Census Bureau data were converted into individual demographic profiles based on the independent variables from the multiple logistic regression model. As the data from the Census Bureau were stratified along three dimensions, each cell was converted into the appropriate number of individuals with the three-dimensional profile of the cell. For example, aggregate data from the Census Bureau for Autauga County showed that 1449 individuals met the following stratification: 10–14 years old, male, and non-Hispanic white. While this population count is in the aggregate, the summary statistic can be converted into 1449 individuals matching the aforementioned demographic profile. Altogether, the 67 counties in Alabama yielded 628,210 individual profiles in 2015. The predicted HPV vaccination initiation rate in a given Alabama county was calculated as the sum of the probable counts of HPV vaccination initiation in each demographic combination divided by the total population of individuals between the ages of 10 and 19 years in the county.

Regional comparisons

After estimation of HPV vaccination initiation rates in Alabama counties, aggregation of county rates was conducted according to the following schema: MDR counties ($n = 20$), AR counties ($n = 37$), and other counties (i.e., counties neither in the MDR nor in the AR, $n = 13$). Given that the MDR and AR are federally designated areas of socio-economic disadvantage,[31,32] we hypothesized that the average HPV vaccination initiation rate would be lower in MDR and AR counties than other counties. To evaluate this hypothesis, Mann–Whitney U

tests[33] were used for analyzing differences in the average HPV vaccination initiation rate by regions.

Results

Demographic characteristics of the NIS study sample are shown in Table 1. Average Alabama county sample sizes—with accompanying standard errors—for demographic categories, based on 2015 Census Bureau population data, are also given in Table 1. The unadjusted, direct, observed rate of HPV vaccination initiation in the entire sample was 57.50%. The following bivariate analyses are not shown in a table. HPV vaccination initiation was more common among 15- to 19-year-olds (59.40%) than 10- to 14-year-olds (54.80%). In addition, HPV vaccination initiation was similar among females (57.60%) and males (57.30%). Furthermore, HPV vaccination initiation was most common among Hispanics (66.50%), followed by non-Hispanic blacks (61.10%), non-Hispanic other race (60.60%), and non-Hispanic whites (52.80%).

The results of the multiple logistic regression model predicting HPV vaccination initiation based on age, sex, and race/ethnicity are shown in Table 2. The model was able to correctly specify HPV vaccination initiation in 90.00% of cases, chi-squared (5) = 353.46, $P < 0.001$. The results showed that 15- to 19-year-olds were more likely than 10- to 14-year-olds to have initiated HPV vaccination (odds ratio [OR] = 1.22, 95% CI = 1.16, 1.29). Black (OR = 0.79, 95% CI = 0.71, 0.87), 'other' race/ethnicities (OR = 0.78, 95% CI = 0.70, 0.86), and white individuals (OR = 0.56, 95% CI = 0.52, 0.60) were less likely than Hispanics to have initiated HPV vaccination. Differences in HPV vaccination initiation between males and females were not statistically significant.

Small area estimates of HPV vaccination initiation among children in Alabama counties are shown in Fig. 1. The Jenks optimization method,[34] which is a commonly selected classification technique that maximizes variation between categories and minimizes variation within categories, for specifying breaks in the choropleth map (Fig. 1) was used. For 2015, predicted HPV vaccination initiation rates ranged from 46.74% in Winston County, Alabama, to 60.15% in Macon County, Alabama. The median HPV vaccination initiation rate for all Alabama counties was 50.83%, with an interquartile range (i.e., the middle 50% of HPV vaccination initiation rates) of 5.00%. A Mann–Whitney U test comparing HPV vaccination initiation rates in AR counties (median = 49.81%)—which are the 37 northernmost counties in Alabama—and all other counties (median = 53.26%) was statistically significant, U = 36.00, $P < 0.001$. A Mann–Whitney U test comparing HPV vaccination initiation rates in MDR counties (median = 54.90%)—which are 20 counties located in the southwestern and east central areas of Alabama—and all other counties (median = 49.85%) was also statistically significant, U = 36.00, $P < 0.001$.

Table 2 – Beta coefficients and odds ratios from the logistic regression model used for small area estimation of HPV vaccination coverage in Alabama counties ($n = 22,205$).

Variable	β	[β 95% CI]	P	OR	[OR 95% CI]
Intercept	0.56	[0.49, 0.64]	*	1.76	[1.63, 1.89]
Age (years)					
10–14	Ref				
15–19	0.20	[0.15, 0.25]	*	1.22	[1.16, 1.29]
Sex					
Male	Ref				
Female	0.01	[−0.04, 0.07]		1.01	[0.96, 1.07]
Race/ethnicity					
Hispanic	Ref				
Black	− 0.24	[−0.34, −0.13]	*	0.79	[0.71, 0.87]
Other race	− 0.25	[−0.36, −0.15]	*	0.78	[0.70, 0.86]
White	− 0.58	[−0.65, −0.51]	*	0.56	[0.52, 0.60]

CI, confidence interval; OR, odds ratio; HPV, human papillomavirus; Ref, reference category for categorical independent variables; *, statistically significant coefficient based on P-value < 0.05.

Discussion

This study used nationally representative data from 2015 on medical provider–verified HPV vaccination initiation among children between the ages of 10 and 19 years to construct a predictive model capable of estimating county-level HPV vaccination initiation rates in Alabama counties. By pairing probabilities for all demographic combinations from the predictive model with crosstabulated census population counts of children by age, race/ethnicity, and sex in each Alabama county, we were able to calculate the prevalence of HPV vaccination initiation for each county and, further, aggregate county rates into Alabama regions to make comparisons.

Modeled rates of HPV vaccination initiation estimated in this study are similar to other recently published reports about HPV vaccination initiation among adolescents in the United States.[35] In this study, HPV vaccine initiation rates among children were the lowest in the AR in Alabama, which is consistent with previous studies.[36] To our best knowledge, the present study is the first and only study to focus on HPV vaccine initiation rates among children in Alabama. We found that the HPV vaccine initiation rates (46.74%) among children in the AR were much lower than among those in non-Appalachian counties (60.15%). Other published studies of HPV vaccination initiation have shown geographic disparities.[36]

Among all the subregions in the AR across different states, Reagan-Steiner et al.[37] indicated that Southern Appalachian counties had the lowest HPV vaccine initiation rates, which included all counties in Alabama. Among the Appalachian counties in Alabama, the vaccine initiation rates varied from 46.74% to 53.44%, which was lower than those of the non-ARs, which varied from 53.44% to 60.15%. In other words, the highest HPV vaccine initiation rates among children in Appalachian counties were the lowest in non-Appalachian counties in Alabama. Therefore, the present study indicated significant disparities and geographic variation in HPV initiation rates between Appalachian counties and non-Appalachian counties among children in Alabama. More interestingly, previous studies also found that lower HPV vaccine initiation rates were associated with higher rates of cervical cancer in the AR in the United States.[36–38]

Moreover, the present study indicated that race/ethnicity was another significant factor associated with HPV vaccine

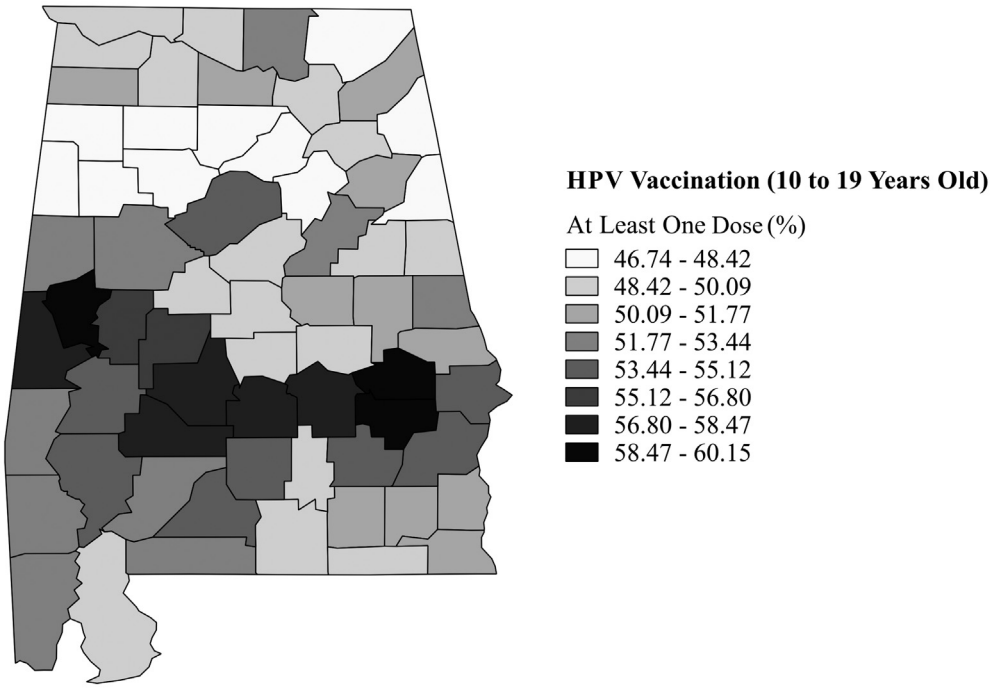

Fig. 1 – Model-based estimations of HPV vaccination initiation among children aged 10–19 years in Alabama counties in 2015. HPV, human papillomavirus.

initiation among children. In light of the present findings, Hispanic and non-Hispanic black children showed a higher level of HPV vaccine initiation than white children, but children in the 'other' ethnic group had a lower level of HPV vaccine initiation than white children, which mirrors the result of a previous study.[35] Hence, to achieve HPV vaccination equity, healthcare professionals and other social services should tailor their interventions to meet the unique needs among children with different racial/ethnic backgrounds and also consider geographic location.

Overall, several challenges might prevent children in the AR from getting an HPV vaccine. First, geographic accessibility to healthcare facilities and healthcare providers' recommendations for the HPV vaccine play an essential role in HPV vaccine initiation.[36] Reiter et al.[38] suggested that compared with Northern Appalachian counties, Southern Appalachian counties lacked geographic accessibility to healthcare facilities and had healthcare provider shortages.[38] A lack of healthcare facilities and providers may contribute to this HPV vaccine initiation disparity.[36] Second, specific cultural beliefs and attitudes in Appalachia toward the HPV vaccine may contribute to disparities. Katz et al.[39] indicated that most communities in Appalachia were church centered and highly conservative. This suggested that parents in Appalachia might be less likely to talk to their children about sexual activity than parents in non-Appalachian counties.[36] Furthermore, specific cultural beliefs in Appalachia may also prevent media coverage from advocating for knowledge of the HPV vaccine.[40,41] In sum, school-based interventions to improve HPV vaccine initiation rates among children in Alabama should be tailored to Appalachian culture.

In light of these findings, school-based delivery programs—which have the opportunity to reach the greatest number of children in a population—should facilitate the accessibility of the HPV vaccine among children living within the AR of Alabama, that is, the northernmost 37 counties in Alabama, which are primarily enveloped by the 6th, 7th, and 8th Alabama school districts.[42] Research has shown that school-based delivery programs are efficacious approaches for promoting the HPV vaccine. These approaches have been implemented successfully in the United States, including California, North Carolina, South Carolina, Colorado, Illinois, and Kentuky.[43] Gallagher et al.[44] indicated that a school-based delivery program for low-income children achieved high coverage of HPV vaccination, cooperating with the specific mobilization of out-of-school children and those who refused to accept the HPV vaccine initially. Given the relatively low socio-economic status of children living in the AR, compared with children living in other areas of Alabama, school-based delivery systems may be contextually appropriate for Appalachian school districts.

Moreover, the present study also highlighted that a culturally tailored school-based educational program should be considered among Appalachian counties in Alabama. Owing to the highly conservative culture in Appalachia, parental attitudes toward the HPV vaccine may be the most significant barrier to HPV vaccine initiation among children in Appalachia.[45] Therefore, school-based interventions should target non-Hispanic parents of school-age children in Alabama's 6th, 7th, and 8th school districts to improve HPV vaccine awareness and receipt. School teachers, administrators, social workers, and healthcare providers should carefully develop HPV educational programs to improve communication

between parents and children and to reinforce the importance of the HPV vaccine.

An alternative approach to increase HPV vaccination rates in the Appalachian counties of Alabama would involve legislative action. Since 2006, 25 states have enacted legislation that requires the HPV vaccine, funds the distribution of the vaccine, or ensures education about the vaccine is provided to school-age children and parents. Alabama, as of the writing of this manuscript, had not enacted legislation regarding the HPV vaccine.[46] School administrators in Alabama, particularly those in the 6th, 7th, and 8th school districts, should advocate for the drafting of legislation that would either mandate the HPV vaccination, fund its distribution, or provide culturally sensitive education to children and parents about the HPV vaccine.

While the present study was contextualized in Alabama, future research would be benefitted from the application of SAE techniques to data from other regions of the United States, especially urban areas outside of the MDR and AR. Other studies could additionally model geographic variation in the uptake of other vaccine types, such as the influenza vaccine or the hepatitis B vaccine, as these measures are available in the NIS.

Limitations

There are several limitations that should be considered in the present study. First, this study was a cross-sectional study, which does not permit causal inferences. Second, the present study only focused on HPV vaccine initiation rates among children in Alabama. Thus, this specific population may not be generalizable to the general population. Third, the present study only accounted for demographic characteristics with HPV vaccine initiation rates among children. Moreover, there were no geographic identifiers in the public use data set, making the estimation of a mixed-effects model with a county random effect impossible. Fourth, this study did not draw hypotheses from an existing theory. The independent variables in our predictive model were selected based on the work of previous researchers using SAE methodology.

Fifth, this study used synthetic regression SAE methodology to develop rates of HPV vaccination initiation. Therefore, the county-level rates presented in this study should be interpreted as probable rates and not as observed/direct rates. However, because representative surveys of HPV vaccination coverage among school-age children in all Alabama counties would be time and resource intensive, modeled rates via SAE provide a useful alternative for need assessment and program planning purposes.

Sixth, our 'other' race category included several race/ethnicities, such as Native Hawaiian, Pacific Islander, Asian, and American Indian, to ensure model stability as these race/ethnicity categories were less represented in the survey. Seventh, we did not examine HPV vaccination completion rates. Eighth, about 2.50% of households with children do not have a cellular or landline telephone.[47] Given that the NIS is a telephone-based survey, it is possible that a segment of the US population was systematically excluded from this study. Despite these limitations, the present study provided valuable insight into disparities and geographic variation in HPV initiation rates.

Conclusions

In summary, owing to limited knowledge about the geographic variation in HPV vaccination initiation among school-age children in Alabama counties, we used synthetic regression SAE methodology to fill a gap in the literature. Using data from the 2015 NIS, we estimated rates of HPV vaccination among school-age children in Alabama counties and showed disparities between various regions in Alabama. Specifically, our analysis revealed that children living in Appalachian counties in Alabama likely had lower HPV vaccination initiation rates in 2015 than children living in other counties in the state. Interventions aimed at increasing HPV vaccination initiation among school-age children in Alabama's Appalachian counties are needed.

Author statements

Ethical approval

This study used publicly available, de-identified secondary data. Therefore, the study was exempt from institutional review board approval.

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Competing interests

The authors declare there is no conflict of interest.

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