ORIGINAL RESEARCH ARTICLE

State-Level Variations and Factors Associated with Adult Vaccination Coverage: A Multilevel Modeling Approach

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Abstract

Background Adult vaccination rates in the USA are generally low and fall short of public health goals.

Objectives Our aim was to evaluate the effect of state-level characteristics on adult vaccination coverage in the USA.

Methods This study was a cross-sectional, retrospective analysis of 2015–2017 Behavioral Risk Factor Surveillance System data, conducted from March to October 2019 and including seasonal influenza; pneumococcal; tetanus, diphtheria, and acellular pertussis (Tdap); and herpes zoster (HZ) vaccines. Multilevel logistic regression models examined interstate vaccination coverage variability and assessed the impact of state-level characteristics, with model-adjusted coverage estimated.

Results Model-adjusted vaccination coverage varied by state, with 35.1–48.1% coverage for influenza (2017), 68.2–80.8% for pneumococcal (2017), 21.9–46.5% for Tdap (2016), and 30.5–50.9% for HZ (2017). Characteristics associated with vaccination included state-level insurance coverage, pharmacists' vaccination authority, vaccination exemptions, and adult immunization information systems participation, as well as individual-level measures of income and education. After adjusting for these factors, substantial interstate heterogeneity remained.

Conclusions Model-adjusted coverage was generally low and varied by state. A small number of state-level characteristics partially explained interstate coverage variability. This and future research assessing additional state characteristics may help determine policies most likely to increase adult vaccination.

Plain Language Summary

Adult vaccination rates in the USA are generally low and fall short of public health goals. Previous studies have indicated that adult vaccination rates vary between states and that individual characteristics affect vaccination coverage. We used modeling to evaluate the effects of both individual- and state-level factors on adult vaccination coverage. Health insurance coverage, the authority of pharmacists to vaccinate, existence of vaccination exemptions, and immunization information systems adult participation rates had a positive impact on vaccination coverage, although the impact varied by vaccine. These results provide policy decision makers at both state and federal levels with information to consider when expanding vaccination programs or preventive care efforts. However, additional data are needed to further explain the variations between states.

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1 Introduction

Adult vaccination rates in the USA are generally low and fall short of public health goals [1, 2]. The 'Healthy People 2020' framework of the Department of Health and Human Services set the goal for seasonal influenza vaccination uptake among noninstitutionalized adults at 70% [3]; however, actual coverage falls well behind, with only 44.8% vaccinated [1]. For pneumococcal vaccination, the goal was set at 90% [3], but the latest coverage estimate among adults aged > 65 years was only 63.6% [1]. Although the 30% goal for herpes zoster (HZ) vaccination among adults aged ≥ 60 years was met, nearly 70% of individuals in this age group remain unvaccinated [1].

Although national estimates provide a snapshot for progress in achieving vaccination goals, it is also necessary to examine vaccination coverage at a more granular level given the diversity of populations and public health decision making at state and local levels. Previous studies have documented heterogeneity in vaccination coverage across states [2, 4, 5]. Recently, data from the 2011–2014 Behavioral Risk Factor Surveillance System (BRFSS) surveys were used to estimate state-level adult vaccination coverage and evaluate how these estimates were influenced by individual characteristics such as demographics, health status, barriers to care, and healthcare utilization [5]. Even after adjusting for these individual-level variables, significant variability across state coverage rates remained [5]. However, the effect of multiple state-level characteristics on adult vaccination coverage has not been studied together, despite available guidance provided by the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America, on improving adult coverage through policy efforts [6, 7]. Only a limited set of state-level characteristics have been included in studies assessing adolescents' vaccination coverage barriers [8, 9].

Given the human and economic burden of vaccine-preventable diseases in the US adult population [10, 11], understanding the factors affecting the interstate heterogeneity of adult vaccination coverage is a critical step toward developing effective strategies to increase coverage. In this context, we used a multilevel modeling framework to evaluate the effects of both individual-level and state-level factors on adult vaccination coverage. We also estimated model-adjusted adult vaccination coverage and compliance with age-appropriate vaccination recommendations [12].

2 Methods

For this analysis, we considered the key adult vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) [5]. We consider key vaccines to be those with important epidemiological impact and low vaccination coverage among the general adult population. Therefore, we excluded from our analysis vaccines against measles, mumps, and rubella syndrome [13], hepatitis [14], and human papilloma virus [15]. This was a cross-sectional, retrospective study using data from the 2015–2017 BRFSS, conducted from 13 March to 29 October 2019 and including seasonal influenza; pneumococcal; tetanus, diphtheria, and acellular pertussis (Tdap); and HZ vaccines.

2.1 Study Data and Sources

Two sets of data were used: (1) the latest available 2015–2017 BRFSS anonymized individual-level data and

(2) a data set derived from various state-level sources aligning to the years of BRFSS data. State-level data were linked with the BRFSS data by state using the most recent year of state-level data that best aligned with the year of BRFSS data included in each analysis.

2.1.1 Individual-Level Data

Individual-level data were obtained from the 2015, 2016, and 2017 BRFSS surveys [16]. Annual BRFSS surveys include interviews of more than 400,000 US adult residents aged ≥ 18 years, including information on sociodemographic characteristics, behavioral risk factors, chronic medical conditions, and use of preventive services. Questions on the receipt of influenza and pneumococcal vaccines are included in the BRFSS questionnaire in all years. Questions related to HZ vaccination were asked in eight states in 2015, in five states in 2016, and nationally in 2017. Questions related to Tdap vaccination were asked in nine states in 2015, nationally in 2016, and in nine states in 2017 (Table 1 in the electronic supplementary material [ESM] 1).

2.1.2 State-Level Data

Table 1 presents the derived state-level data used in the analysis with corresponding sources and year of data used (see ESM 2 for detailed descriptions of each source).

2.2 Outcomes

The study's outcome measures were based on the following age-appropriate adult vaccination recommendations from the ACIP during 2015–2017:

- *Influenza*: one dose annually for adults aged > 18 years [17].
- *Pneumococcal*: one dose of pneumococcal conjugate vaccine and one dose of pneumococcal polysaccharide vaccine administered in series for adults aged > 65 years [18].
- *Tdap*: a tetanus and diphtheria (Td) booster dose every 10 years for adults aged > 18 years, with a single dose of Tdap in place of a decennial Td booster dose as early as possible [19].
- *HZ:* one dose for adults aged > 60 years [20].

Specifically, the study included the following:

- Four measures related to the individual receipt of influenza, pneumococcal, Tdap, and HZ vaccinations.
- Three measures of "compliance" with all age-appropriate vaccine recommendations (i.e., receipt of influenza and Tdap vaccinations for individuals aged 18–59 years;

receipt of influenza, Tdap, and HZ vaccinations for individuals aged 60–64 years; and receipt of influenza, pneumococcal, Tdap, and HZ vaccinations for individuals aged > 65 years).

In the BRFSS questionnaire, individuals had the following options as answers to the vaccination-related questions: yes, no, don't know/not sure, or refused to answer. For each vaccine (influenza, pneumococcal, and HZ vaccines, respectively), crude vaccine coverage was calculated as the number of individuals who answered "yes" divided by the number of individuals who answered "yes" plus the number of individuals who answered "no." The percentage of adults who received all age-appropriate recommended vaccinations (i.e., crude percentage compliant with age-appropriate recommended vaccinations) was calculated as the number of respondents who answered "yes" to receiving all age-appropriate recommended vaccinations divided by the number of respondents who answered "yes" or "no" to receiving all age-appropriate recommended vaccinations. Individuals with unknown, missing, or refused answers to any of their age-appropriate recommended vaccination questions were not included in the numerator or the denominator of the calculations. For the Tdap vaccine, crude vaccine coverage was calculated as the number of individuals who had received a Tdap vaccination since 2005 divided by the number of individuals who had received a Tdap vaccination plus the number of individuals who had received a tetanus shot that was not Tdap plus the number of individuals who had not received a tetanus shot since 2005. Individuals who reported receiving a tetanus vaccine but were not sure whether it was the Tdap vaccine were excluded from the analyses.

2.3 Covariates

The study's multilevel models included both individual- and state-level covariates. The previously described [5] set of individual-level covariates included sociodemographic characteristics, health status information, potential barriers to care, and healthcare utilization (ESM 3). Candidate state-level characteristics for this exploratory analysis were selected based on a targeted review of publicly available data sources that included information on "actionable" variables (i.e., variables that could be influenced by local initiatives and policies; Table 1) that may affect adult immunization [13].

These variables were linked to the BRFSS data by state, and only those significantly associated with the outcome were retained in the final multilevel models.

2.4 Statistical Methods

We used multivariable logistic regression models to assess the impact of individual-level characteristics on vaccination coverage and compliance (ESM 4). For consistency across studies, we included the same individual-level covariates in the models that were previously selected using a systematic variable-selection process [5]. For models including more than 1 year of BRFSS data, additional control variables were included for year and the interaction of state and year [5]. National and state-level model-adjusted vaccination coverage rates were generated from the regression models using predicted marginal proportions, as described previously [5]. For vaccines that were not included in the BRFSS in every survey year (i.e., Tdap and HZ), rates were calculated only for the available years.

For the multilevel modeling of vaccination coverage and compliance, the individual-level variables were combined with state-level data to assess how their simultaneous contribution was associated with the study outcomes. For each vaccination coverage and compliance measure, the most recent year of data available in the BRFSS was used. The state-level variables were linked with the BRFSS data by state using the most recent year of state-level data that best aligned with the year of BRFSS data. For the multilevel models, individuals were treated as nested within their states of residence. At the first level, the log odds of vaccination or compliance was modeled using fixed effects for individual-level covariates along with a random intercept term. At the second level, the state-level intercepts were modeled as a function of state-level covariates and a state-specific random effect to account for within-state correlation. Continuous state-level variables were standardized by subtracting the mean and dividing by the standard deviation. The multilevel models took the following form:

$$\text{logit}(p_{ij}) = \beta_{0j} + \beta_1 x_{1ij} + \cdots + \beta_p x_{pij} \quad \text{(Level 1 model)}$$

$$\beta_{0j} = \beta_0 + \gamma_1 z_{1j} + \cdots + \gamma_q z_{qj} + u_j \quad \text{(Level 2 model)},$$

where,

- x_1 through x_p represent individual-level covariates.
- z_1 through z_q represent state-level covariates.
- the subscripts refer to patient i within state j.
- the random effects u_j were assumed to follow a normal distribution with mean 0 and variance σ_s^2, representing residual interstate variation after accounting for the state-level covariates.

First, multilevel models were fit for each outcome including all 12 actionable state-level factors (full model). Then, state-level variables that were significant at the $p < 0.1$ level

Table 1 Candidate state-level variables, descriptive statistics

State-level variable	Source	Data year[a]	Category or statistic[b]	
Healthcare expenditures per capita ($)	Kaiser Family Foundation State Health Facts [43]	2014	*N*	51
			Mean ± SD	8332.16 ± 1256.75
			Median (IQR)	8107.00 (7372.00–9258.00)
			Minimum; maximum	5982.00; 11,944.00
HMO penetration rate (%)	Kaiser Family Foundation State Health Facts [43]	2016	*N*	51
			Mean ± SD, %	24.8 ± 13.68
			Median (IQR)	25.7 (14.2–34.2)
			Minimum; maximum	0.2; 59.2
Percentage of residents on Medicaid (%)	Kaiser Family Foundation State Health Facts [43]	2016	*N*	51
			Mean ± SD, %	20.0 ± 4.83
			Median (IQR)	19.4 (17.5–23.3)
			Minimum; maximum	11.1; 32.5
		2017	*N*	51
			Mean ± SD	19.9 ± 5.05
			Median (IQR)	19.0 (17.3–22.9)
			Minimum; maximum	10.7; 33.6
Percentage of residents uninsured (%)	Kaiser Family Foundation State Health Facts [43]	2016	*N*	51
			Mean ± SD	7.9 ± 3.05
			Median (IQR)	7.9 (5.6–9.9)
			Minimum; maximum	2.5; 16.6
		2017	*N*	51
			Mean ± SD	8.1 ± 3.12
			Median (IQR)	7.8 (5.6–9.5)
			Minimum; maximum	2.8; 17.4
Percentage of adults without a usual place of medical care (%)	Kaiser Family Foundation State Health Facts [43]	2014	*N*	51
			Mean ± SD	16.3 ± 5.18
			Median (IQR)	16.1 (12.4–19.7)
			Minimum; maximum	2.8; 26.7
Percentage of residents on Medicare (%)	Kaiser Family Foundation State Health Facts [43]	2016	*N*	51
			Mean ± SD	17.7 ± 2.43
			Median (IQR)	17.8 (16.6–19.4)
			Minimum; maximum	11.4; 23.4
		2017	*N*	51
			Mean ± SD	18.1 ± 2.48
			Median (IQR)	18.1 (17.0–19.8)
			Minimum; maximum	11.8; 23.9
Percentage of private sector establishments that offer health insurance to employees (%)	Kaiser Family Foundation State Health Facts [43]	2016	*N*	51
			Mean ± SD	46.0 ± 7.78
			Median (IQR)	44.8 (41.7–50.7)
			Minimum; maximum	28.3; 78.1
		2017	*N*	51
			Mean ± SD, %	47.8 ± 8.25
			Median (IQR)	48.0 (42.6–51.0)
			Minimum; maximum	32.5; 81.8
Number of professionally active primary care physicians, per 1000 residents	Kaiser Family Foundation State Health Facts [43]	2019	N	51
			Mean ± SD, %	1.5 ± 0.53
			Median (IQR)	1.4 (1.2–1.7)
			Minimum; maximum	0.9; 4.5
Vaccination exemptions permitted for personal reasons[c] (%)	Immunization Action Coalition [44]	2018	Yes	19 (37.3)
			No	32 (62.7)

Table 1 (continued)

State-level variable	Source	Data year[a]	Category or statistic[b]	
Percentage of adults participating in IIS (%)	CDC [45]	2016	*N*	50[d]
			Mean ± SD	50.1 ± 24.52
			Median (IQR)	53.1 (36.4–65.6)
Pharmacist level of autonomy to vaccinate, *n* (%)	American Pharmacists Association [46]	2016	By protocol only	5 (9.8)
			By protocol or prescription	29 (56.9)
			No protocol or prescription required	17 (33.3)
Percentage of state funding allocated to immunization program (%)	CDC [47]	2016	*N*	51
			Mean ± SD	2.6 ± 1.03
			Median (IQR)	2.9 (1.8–3.4)
			Minimum; maximum	0.6; 5.2
		2017	*N*	51
			Mean ± SD	1.6 ± 0.85
			Median (IQR)	1.3 (0.9–2.2)
			Minimum; maximum	0.2; 3.9

BRFSS Behavioral Risk Factor Surveillance System, *CDC* Centers for Disease Control and Prevention, *HMO* health maintenance organization, *IIS* immunization information systems, *IQR* interquartile range, *SD* standard deviation

[a]State-level data were linked with the BRFSS data by state using the most recent year of state-level data that best aligned with the year of BRFSS data included in each analysis

[b]Numbers include all states and Washington, D.C. unless noted

[c]Thought to be a proxy for general attitudes and behaviors toward vaccination

[d]Does not include Washington, D.C.

were retained in a reduced model. Using a likelihood ratio test, the reduced model was compared with the full model to look for significant differences between the two models. The reduced model was retained as the final multilevel model because no significant differences were found between the reduced and full models. Fitting the full model with all 12 state-level variables was not feasible for the two compliance measures that only included nine states (i.e., compliance measures for individuals aged 60–64 years and individuals aged ≥ 65 years). Therefore, for these two compliance measures, the final set of state-level variables selected for the compliance measure for individuals aged 18–59 years was used to fit the full model. The final multilevel models were used to estimate the adjusted impact of each individual-level and state-level factor on the likelihood of vaccination or compliance. Weighted odds ratios (ORs) and 95% confidence intervals (CIs) for each individual-level and state-level factor were estimated for consistency and comparison with previous literature [5].

Using the individual-level and state-level variables selected into the final models as fixed effects, multivariable regression models examining vaccination coverage and compliance were estimated (ESM 4). Continuous state-level variables included in the final multilevel models were dichotomized into categories of above or below the national average. For each state-level variable, predicted marginal

proportions were used, as described previously [5], to estimate model-adjusted rates at each of the two levels.

Finally, the variance partition coefficient (VPC) and median odds ratio (MOR) were computed to quantify the effect of state on the variation in likelihood of vaccination coverage or compliance (ESM 4) [21]. The VPC represents the proportion of the total observed individual variation in vaccination coverage or compliance that can be attributed to interstate variation. The MOR is defined as the median value of the ORs obtained when comparing two individuals with the same covariates who are randomly chosen from two different states [21]. Here, the MOR represents how much the likelihood of vaccination coverage or compliance (in median) would increase for an individual moving to a state with higher vaccination coverage or compliance.

Because this study was exploratory in nature, we did not adjust for multiple statistical comparisons. Nonresponse at the unit level resulting in missing data was accounted for in the BRFSS weighting methodology. Analysis weights provided by the BRFSS using their raking weighting methodology were used in all analyses to produce estimates representative of the overall US population [22]. For multilevel modeling, survey weights were rescaled so that the new weights summed to the cluster sample size [23].

All programming was conducted using SAS version 9.4 statistical software (SAS Institute Inc.; Cary, NC, USA;

2011) with SUDAAN 11 as a callable add-on (RTI International; Research Triangle Park, NC, USA; 2012).

3 Results

Table 2 shows the national model-adjusted vaccination coverage rates in the most recent year, adjusted for individual-level characteristics. Compliance with age-appropriate vaccination recommendations ranged nationally from 9.6 to 16.2% (Table 2). However, significant interstate variability remained, even after adjusting for individual characteristics (Fig. 1). Table 2 shows the state-level model-adjusted vaccination coverage ranges for influenza (2017), pneumococcal (2017), Tdap (2016), and HZ (2017) vaccines; across states, compliance measures ranged from 5.3 to 25.4% (Table 2; Tables 2–8 in ESM 1).

3.1 Multilevel Model Results: Individual-Level Variables

Higher income and education were associated with a higher likelihood of receiving the vaccines and following the age-appropriate vaccination recommendations (Table 9 in ESM 1). Being Black, leaving long periods between medical checkups, and the absence of a designated health provider were associated with lower such likelihoods. The impact of age varied by vaccine: the likelihood of influenza vaccination was lower below the age of 55 years, the likelihood of receiving the pneumococcal or HZ vaccine increased with age, and the likelihood of Tdap vaccination decreased with age (Table 9 in ESM 1).

3.2 Multilevel Model Results: State-Level Variables

Seven of the 12 candidate state-level variables were retained in the final five reduced models, although the specific variables retained varied for each model (Table 3). For example, states with higher health maintenance organization penetration rates had a lower likelihood of influenza vaccination, although this variable was not retained or significantly associated with the other vaccination coverage and compliance outcomes (Table 3).

In states permitting vaccination exemptions, individuals were more likely to receive the pneumococcal and Tdap vaccines (Table 3). Accordingly, the model-adjusted vaccination coverage estimates were slightly higher in these states both for pneumococcal (77 vs. 75%) and for Tdap (36 vs. 32%) vaccination.

In states with higher immunization information systems (IIS) adult participation rates, individuals were more likely to receive the Tdap and HZ vaccines, and individuals aged 18–59 years were more likely to be compliant with age-appropriate influenza and Tdap vaccinations (OR 1.12, 1.11, and 1.08, respectively; Table 3). Consistently, these states had slightly higher model-adjusted vaccination coverage estimates for Tdap (35 vs. 31%) and HZ (42 vs. 36%) vaccines.

In states allowing pharmacists greater authority to vaccinate, the likelihood of receiving the HZ vaccine was higher (Table 3). States allowing pharmacists to vaccinate only by protocol had the lowest model-adjusted estimates of HZ vaccination coverage (36 vs. 40% for states allowing pharmacists to vaccinate by protocol, prescription, or without restrictions).

In states with a higher percentage of uninsured residents, individuals had a statistically significantly reduced likelihood of being vaccinated for HZ and of being compliant with age-appropriate influenza and Tdap vaccinations (Table 3). However, the magnitude of the effect was limited; states with percentages of uninsured residents above the national average had similar model-adjusted vaccination coverage estimates for HZ when compared with states at or below the national average (both around 40%).

Lastly, a higher percentage of private sector establishments offering health insurance to employees was associated with a decreased likelihood of receiving age-appropriate recommended influenza and Tdap vaccinations among individuals aged 18–59 years (Table 3).

3.3 Multilevel Model Results: Interstate Heterogeneity

The VPC ranged from 0.5 to 2.8%, and the MOR ranged from 1.14 to 1.34 (Table 4). For context, the VPC results indicated that less than 3% of the total observed individual variation in vaccination coverage or compliance could be attributed to interstate variation. Additionally, a MOR value of 1.14, as seen for the influenza vaccination coverage model, means that if randomly selected individuals were to move to another state with higher influenza vaccination coverage, their likelihood of receiving the influenza vaccine, in median, would increase by 14%. The MOR was > 1 for all the multilevel models, suggesting interstate differences in the likelihood of vaccination coverage and compliance.

4 Discussion

Model-adjusted vaccination coverage for influenza, pneumococcal, Tdap, and HZ vaccines, as well as compliance with age-appropriate vaccination recommendations were relatively low and varied substantially across states. The associations found between individual characteristics and vaccination coverage followed the same pattern as previously described [5]. To our knowledge, this is the first study

Table 2 Model-adjusted vaccination coverage and compliance with age-appropriate vaccination recommendations in the USA, 2015–2017

Vaccine type	Year of BRFSS survey	Model-adjusted estimates of vaccination coverage (%)	
		National	State range
Vaccination coverage			
Influenza	2015	40.5	30.7–53.8
	2016	38.3	34.1–48.9
	2017	40.0	35.1–48.1
Pneumococcal	2015	72.4	65.6–79.3
	2016	72.6	65.7–80.1
	2017	75.0	68.2–80.8
Tdap	2016	33.5	21.9–46.5
HZ	2017	40.0	30.5–50.9
Compliance with age-appropriate vaccination recommendations			
Influenza and Tdap for individuals aged 18–59 years	2016	16.2	10.8–25.4
Influenza, Tdap, and HZ for individuals aged 60–64 years[a]	2017	9.6	5.3–11.6
Influenza, pneumococcal, Tdap, and HZ for individuals aged ≥ 65 years[a]	2017	13.6	6.7–18.1

Model-adjusted estimate is adjusted for age, sex, race/ethnicity, education, income, health status, presence of chronic conditions, ability to pay for care, having a regular care provider, time since last checkup, and state. Model-adjusted estimate generated by taking the average of the predicted probability of vaccination for everyone as if they were all from the same state and period (while retaining all other characteristics). Across all years of data for each measure, the percentages of observations that were dropped from the analyses due to missing data were 8.3% for influenza, 9.7% for pneumococcal, 38.4% for Tdap, and 9.1% for HZ vaccination coverage. Missing data were most prevalent for Tdap vaccination coverage because individuals who reported receiving a tetanus vaccine but were not sure whether it was the Tdap vaccine were excluded from the analyses

BRFSS Behavioral Risk Factor Surveillance System, *HZ* herpes zoster, *Tdap* tetanus, diphtheria, acellular pertussis

[a]These estimates are not representative at the national level because they are based on the 2017 BRFSS data obtained from the nine states that included questions about all the corresponding vaccines

evaluating the effect of multiple actionable state-level characteristics on adult vaccination coverage and compliance. Health insurance coverage, the level of pharmacists' authority to vaccinate, vaccination exemptions, and percentage of adults participating in IIS had a significant impact on the uptake of certain vaccines, although much of the heterogeneity across states remained unexplained.

4.1 Health Insurance Coverage

Individuals in states with a higher proportion of uninsured population had a lower likelihood of receiving the HZ vaccine and age-appropriate recommended influenza and Tdap vaccinations; the association was not statistically significant for Tdap vaccination coverage. Indeed, the latest CDC analysis on adult vaccination coverage reported that uninsured adults were less frequently vaccinated than their insured counterparts [1]. Those with private insurance had higher vaccination coverage than those with public insurance [1]. However, private insurance might act as a proxy variable for higher income, which was shown here and previously [5] to increase the likelihood of vaccination. A recent study using National Health Interview Survey data (2010–2016) found that adults with health insurance were 39% more likely to

have received the influenza vaccination than were uninsured adults (prevalence ratio 1.39; 95% CI 1.27–1.53) [24]. These findings deserve close inspection given that 27.5 million people in the USA did not have health insurance in 2018, an increase from 25.6 million in 2017 [25]. Although the Affordable Care Act [26] alleviated the financial barriers for many preventive services, including vaccines, individuals remaining uninsured have limited options for accessing free or low-cost vaccines, such as at local health departments.

4.2 Pharmacist Authority to Vaccinate

Individuals in states allowing pharmacists greater authority to vaccinate were more likely to receive the HZ vaccine; no significant association was found for the other vaccines. Pharmacists' authority to vaccinate may particularly affect HZ vaccination because it is currently reimbursed under Medicare Part D for the majority of adults aged ≥ 65 years in the USA. Many physician offices do not have the infrastructure in place to bill Part D claims and will instead refer patients to the pharmacy for vaccination [27]. A national survey reported that 80.8% of the 1999 participating community pharmacies provided immunization services, most commonly for influenza (96%), HZ (91%), pneumococcal
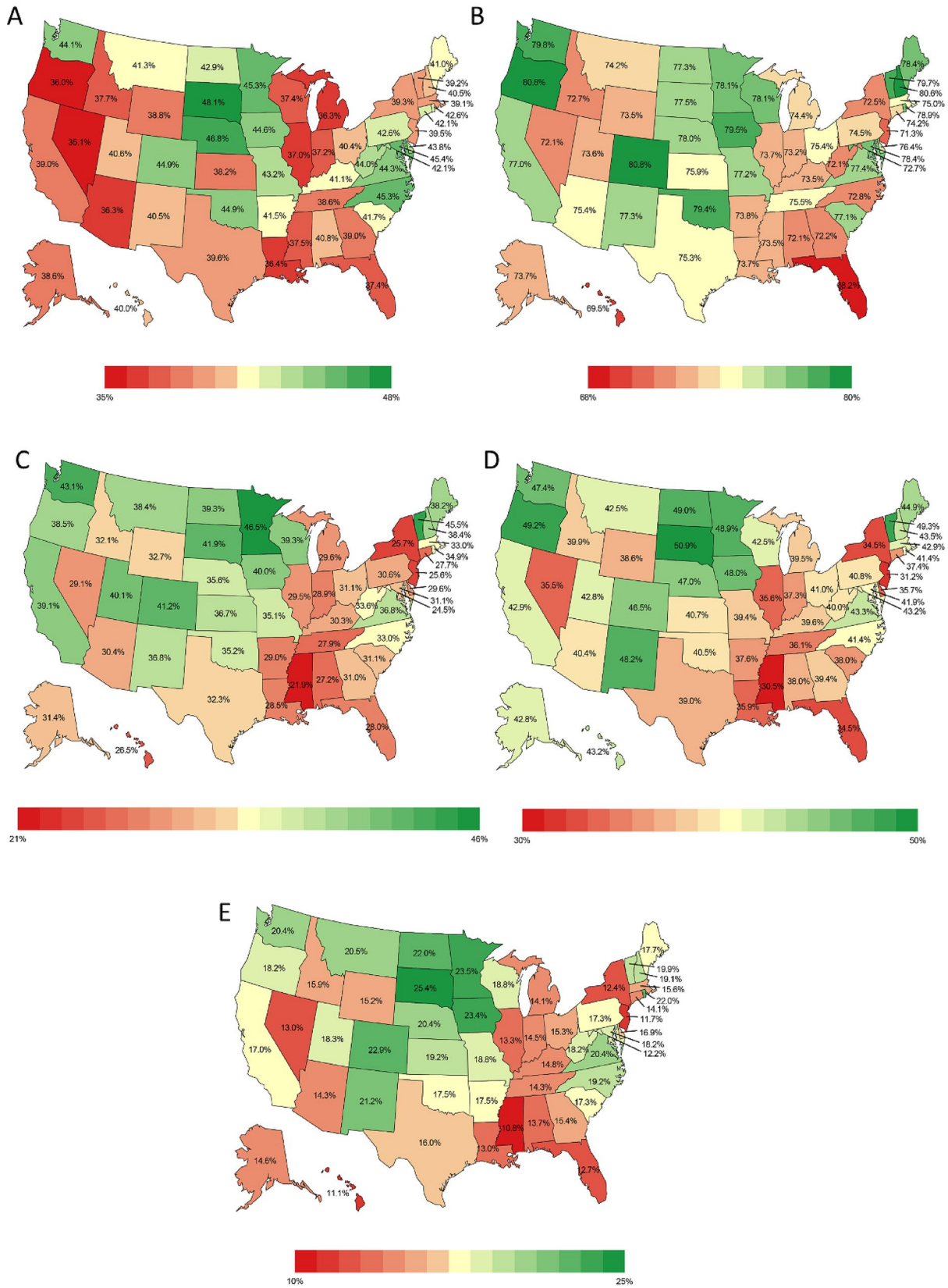
◄**Fig. 1** Model-adjusted vaccination coverage and compliance across the USA for **a** influenza vaccination coverage, ages > 18 years (2017 BRFSS data); **b** pneumococcal vaccination coverage, ages > 65 years (2017 BRFSS data); **c** Tdap vaccination coverage, ages > 18 years (2016 BRFSS data); **d** HZ vaccination coverage, ages > 60 years (2017 BRFSS data); **e** compliance with age-appropriate influenza and Tdap vaccination recommendations, ages 18–59 years (2016 BRFSS data). [1]Heat maps were not generated for the outcomes related to vaccination compliance with age-appropriate recommended vaccinations that had data for only a subset of states. The heat maps use a color scheme of red, yellow, and green to graphically illustrate differences across states and assist with identifying geographic trends (e.g., low vaccination coverage in southern states). Since the ranges of model-adjusted coverage and compliance varied considerably, each map used a different scale based on the results for the corresponding measure (i.e., each map used the low and high value for each measure individually instead of using a fixed scale for all measures). **a** Influenza vaccination coverage ranged from 35.1% in Nevada to 48.1% in South Dakota. **b** Pneumococcal vaccination coverage rates ranged from 68.2% in Florida to 80.8% in both Colorado and Oregon. **c** Tdap vaccination coverage rates ranged from 21.9% in Mississippi to 46.5% in Minnesota. **d** HZ vaccination coverage rates ranged from 30.5% in Mississippi to 50.9% in South Dakota. **e** Compliance with age-appropriate influenza and Tdap vaccination coverage vaccination recommendations for adults aged 18–59 years ranged from 10.8% in Mississippi to 25.4% in South Dakota. *BRFSS* Behavioral Risk Factor Surveillance System, *HZ* herpes zoster, *Tdap* tetanus, diphtheria, acellular pertussis

(90%), and Tdap (87%) vaccines [28]. Community pharmacists are convenient vaccination providers for the typical working adult, as shown in a retrospective analysis of over 6 million vaccinations administered in > 7500 pharmacies across the USA; 30% of which were provided during off-clinic hours [29]. The authors suggested that expanding pharmacists' authority to vaccinate would increase immunization rates [29]. This suggestion is corroborated by data showing that from 2003 to 2013, as more states were granting vaccination authorities to pharmacists, seasonal influenza immunization increased over time [30].

4.3 Vaccination Exemptions

Perhaps surprisingly, individuals living in states that permit vaccination exemptions for personal reasons had a slightly higher likelihood of receiving pneumococcal and Tdap vaccinations. We performed a post-hoc univariate analysis to examine whether the same trend was seen in unadjusted results. Indeed, states permitting personal exemptions had higher pneumococcal and Tdap vaccination coverage rates than states that did not permit personal exemptions (77 vs. 75% for pneumococcal, $p = 0.0306$; 36 vs. 32% for Tdap, $p = 0.0514$). Several studies have shown an inverse association between rates of nonmedical and personal belief vaccination exemptions and vaccination coverage rates among children [31–34], although to our knowledge, previous studies have not evaluated the relationship between vaccination exemptions and adult vaccination coverage.

An analysis of all states with vaccination exemptions in the years 2016–2017 showed that the incidence of vaccine-preventable diseases was lower in states in which personal vaccination exemptions were banned [33]. Vaccination exemptions are often clustered within the states and occur in relatively small percentages of children [35]. Large cities with higher numbers of vaccine-exempt children, and geographic clusters with higher numbers of exemptors contribute the most to the risk of outbreaks [33, 34, 36, 37]. Because several states with personal belief exemptions demonstrated the highest vaccination coverage with Tdap vaccines (Minnesota) and pneumococcal vaccines (Oregon and Colorado), additional research should be conducted to determine whether clinicians, local health departments, and/or policy makers are using interventions to counteract nonmedical exemptions and promote increased vaccination rates within the state.

4.4 Immunization Information Systems Participation

Individuals in states with a higher percentage of adults participating in IIS had a higher likelihood of being vaccinated with Tdap and HZ vaccines and a higher likelihood of compliance with age-appropriate influenza and Tdap vaccination recommendations. Year 2016 data indicated that the percentage of adults participating in IIS varied substantially across states, ranging from 0 to ≥ 95% [38]. Although immunization history data contained in IIS may be a powerful tool to target individuals for vaccination, results from recent studies are mixed [39–41]. In two recent studies, automated phone messages informing people of pending vaccinations based on IIS data did not succeed in increasing vaccination rates [40, 41]. However, when the IIS information was used by pharmacists to engage in conversation with their customers on specific pending vaccinations, one-third of the targeted individuals had all pending vaccinations completed within the next 6 months [39]. However, our study did not include information on whether the states had used such interventions based on IIS data to increase vaccination uptake; this could be a potential factor to investigate in future studies.

4.5 Interstate Heterogeneity

The results of the multilevel modeling were mixed with respect to which state-level factors were important determinants of vaccination coverage and compliance with age-appropriate vaccine recommendations, with different state-level variables associated with likelihood of vaccination for each of the vaccines. Continued interstate variation regarding the likelihood of vaccination is a key finding of this analysis, with much of the variability remaining unexplained by the models. All estimated MORs were > 1,

Table 3 Multilevel logistic regression results: state-level characteristics associated with an individual's likelihood of vaccination in the USA

State-level characteristic	Model 1: Received seasonal influenza vaccine, 2017	Model 2: Received pneumococcal vaccine, 2017	Model 3: Received Tdap vaccine, 2016	Model 4: Received HZ vaccine, 2017	Model 5: Received age-appropriate recommended influenza and Tdap vaccinations among individuals aged 18–59 years, 2016
HMO penetration rate, SD units	0.96 (0.93–1.00); 0.0263	–	–	–	0.93 (0.86–1.00); 0.0519
Percentage of residents on Medicaid, SD units	0.98 (0.94–1.01); 0.1883	–	–	–	–
Vaccination exemptions permitted for personal reasons [no]	–	1.12 (1.02–1.23); 0.0204	1.15 (1.00–1.32); 0.0467	–	–
Pharmacist vaccination authority [protocol]					
Protocol or prescription	–	–	0.92 (0.75–1.12); 0.3884	1.10 (0.95–1.27); 0.2193	–
Protocol, prescription, or no restrictions	–	–	1.06 (0.87–1.30); 0.5501	1.19 (1.03–1.39); 0.0194	–
Percentage of residents uninsured, SD units	–	–	0.95 (0.88–1.01); 0.1212	0.95 (0.90–1.00); 0.0450	0.92 (0.85–0.99); 0.0290
IIS adult participation rate, SD units	–	–	1.12 (1.05–1.21); 0.0018	1.11 (1.05–1.19); 0.0008	1.08 (1.01–1.16); 0.0274
Percentage of private sector establishments offering health insurance to employees	–	–	–	–	0.94 (0.88–1.00); 0.0497

Data are presented as odds ratio (95% confidence interval); p-value. Referent categories used in the logistic models are displayed in brackets for all categorical variables. In addition to the included variables, all models included individual-level sociodemographic, health status, potential barriers to care, and healthcare utilization variables as fixed effects, with state of residence as a random effect. Results of the multilevel models for compliance with age-appropriate recommended influenza, Tdap, and HZ vaccinations among individuals aged 60–64 years and compliance with age-appropriate recommended influenza, Tdap, HZ, and pneumococcal vaccinations among individuals aged > 65 years are not shown because the models did not include any state-level factors (i.e., none were significant at the $p < 0.1$ level)

HMO health maintenance organization, *HZ* herpes zoster, *IIS* immunization information systems, *SD* standard deviation, *Tdap* tetanus, diphtheria, acellular pertussis, – indicates that corresponding variables were not retained in the final models

Table 4 Measures of heterogeneity in vaccination coverage and compliance with age-appropriate recommended vaccinations among states within the USA

Vaccination coverage or compliance measure	Variance partition coefficient	Median odds ratio
Influenza	0.005	1.14
Pneumococcal	0.008	1.16
Tdap	0.015	1.23
HZ	0.009	1.17
Influenza and Tdap for individuals aged 18–59 years	0.013	1.22
Influenza, Tdap, and HZ for individuals aged 60–64 years	0.005	1.14
Influenza, Tdap, HZ, and pneumococcal for individuals aged > 65 years	0.028	1.34

HZ herpes zoster, *Tdap* tetanus, diphtheria, acellular pertussis

indicating that state of residence may affect an individual's likelihood of vaccination. Nevertheless, the low values for both the VPC and the MOR suggest the presence of residual variation unexplained by the individual-level and state-level factors that were included in the models.

4.6 Limitations

Although the BRFSS provides nationally representative data on a wide range of preventive services and behavioral risk factors, the survey data are self-reported and therefore subject to recall bias. Pierannunzi et al. [42] conducted a systematic review of the validity and reliability of the various sections of the BRFSS from 2004 to 2011. BRFSS prevalence estimates in all assessed areas were generally in line with results from comparable self-reported surveys but less similar to data captured using physical measures [42]. Our analysis used data only up until 2017. We assumed that all individuals were eligible for the recommended vaccines in their age group because the BRFSS data do not provide information on ineligibility due to contraindications or other reasons. The state-level variables included were limited to those obtained from publicly available data sources and variables that were considered actionable and were not inclusive of all state-level factors potentially affecting vaccination coverage. For example, state-level programs to increase uptake (such as those implementing patient and provider reminder programs in conjunction with IIS) and the level of care coordination between state and local agencies may potentially play a larger role in increasing coverage. Finally, state-level variables may not provide enough detailed information to demonstrate variations in the likelihood of vaccination at a more granular level in local communities, neighborhoods, or social groups. Additional local factors such as local health department funding, measures of social capital, and attitudes toward vaccination may be important concepts to consider for future research.

5 Conclusions

Given the low adult coverage for influenza, pneumococcal, Tdap, and HZ vaccines, as well as the substantial human and economic burden of these four vaccine-preventable diseases in the US adult population [10, 11], understanding the factors affecting the heterogeneity of adult vaccination coverage is a critical step toward developing effective strategies for increasing coverage. This study showed that the likelihood of adult vaccination uptake in the USA varied considerably between states. Moreover, it showed that—beyond certain individual characteristics—state characteristics such as percentage of adults participating in IIS, health insurance coverage, and vaccination exemptions also affect adult vaccination, although this varied by individual vaccine. After adjusting for these characteristics, substantial heterogeneity across states remained, indicating that other factors, such as local vaccination attitudes and beliefs, and/or local vaccination programs and policies, may be affecting adult vaccination coverage and compliance. Future research is needed to examine the impact of a more comprehensive set of state and local factors on vaccination rates. Nevertheless, results from this study will provide government officials and other vaccination policy decision makers, both at state and federal levels, with information to consider when expanding vaccination programs or preventive care efforts.

Declarations

Conflicts of interest EL, SP, and CH are employed by and hold shares in the GSK group of companies. DG and SH are employees of RTI Health Solutions, which was contracted by the GSK group of companies to design and implement the present study. The authors declare no other financial and nonfinancial relationships and activities.

Ethics approval Not applicable as this study did not include human subjects.

Consent to participate Not applicable as this study did not include human subjects.

Consent for publication Not applicable as this study did not include human subjects.

Data availability The datasets generated and/or analyzed during the current study were derived from a public dataset, namely the BRFSS (available at https://www.cdc.gov/brfss/annual_data/annual_data.htm) and others listed in ESM 2.

Code availability Not applicable.

Author contributions DG, SH, EL, SP, and CH contributed to the conception and design of the study and manuscript. DG, SH, and CH contributed to the data acquisition. DG, SH, and EL participated in the data analysis, and all authors participated in data interpretation. All authors revised the article critically for important intellectual content and provided final approval of the submitted version.

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