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Relationships Between Social Vulnerability and Coronavirus Disease 2019 Vaccination Coverage and Vaccine Effectiveness

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

***Disclaimer*.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Abstract

Background.—Coronavirus disease 2019 (COVID-19) vaccination coverage remains lower in communities with higher social vulnerability. Factors such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure risk and access to healthcare are often correlated with social vulnerability and may therefore contribute to a relationship between vulnerability and observed vaccine effectiveness (VE). Understanding whether these factors impact VE could contribute to our understanding of real-world VE.

Methods.—We used electronic health record data from 7 health systems to assess vaccination coverage among patients with medically attended COVID-19-like illness. We then used a test-negative design to assess VE for 2- and 3-dose messenger RNA (mRNA) adult (≥18 years) vaccine recipients across Social Vulnerability Index (SVI) quartiles. SVI rankings were determined by geocoding patient addresses to census tracts; rankings were grouped into quartiles for analysis.

Results.—In July 2021, primary series vaccination coverage was higher in the least vulnerable quartile than in the most vulnerable quartile (56% vs 36%, respectively). In February 2022, booster dose coverage among persons who had completed a primary series was higher in the least vulnerable quartile than in the most vulnerable quartile (43% vs 30%). VE among 2-dose and 3-dose recipients during the Delta and Omicron BA.1 periods of predominance was similar across SVI quartiles.

Conclusions.—COVID-19 vaccination coverage varied substantially by SVI. Differences in VE estimates by SVI were minimal across groups after adjusting for baseline patient factors. However, lower vaccination coverage among more socially vulnerable groups means that the burden of illness is still disproportionately borne by the most socially vulnerable populations.

Keywords

COVID-19; Social Vulnerability Index; vaccination coverage; vaccine effectiveness

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The coronavirus disease 2019 (COVID-19) pandemic has led to over 1 million deaths and millions more medical visits and hospitalizations in the United States through August 2022 [1]. This burden has disproportionately affected socially vulnerable populations, and social and structural factors may differentially impact engagement in protective measures, risk of exposure, susceptibility to infection, and risk of adverse health outcomes [2]. Since first authorized in December 2020, COVID-19 vaccines have been a critical public health tool for protection against COVID-19, yet lower coverage within vulnerable populations may

result in increased disease incidence [3, 4], and it remains unclear whether we might also expect a relationship between social vulnerability and COVID-19 vaccine effectiveness (VE) estimates.

Previous studies have used the US Centers for Disease Control and Prevention (CDC) and Agency for Toxic Substances and Disease Registry (ATSDR) Social Vulnerability Index (SVI) to characterize COVID-19 disparities [3, 5–8]. SVI captures 15 attributes of social vulnerability across four themes: socioeconomic status, household composition and disability, minority status and language, and housing type and transportation [9]. These elements may be associated with vaccination coverage and may impact VE via mechanisms including: (1) Intensity and duration of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposure (eg, crowding, reliance on public transportation, occupational requirements); (2) Susceptibility to infection (eg, biological factors such as immune system response) [10, 11]; and (3) Access to healthcare or likelihood of seeking healthcare or testing in a hospital, emergency department, or urgent care clinic versus other settings (eg, insurance status, access to telemedicine and at-home testing). Although age, underlying medical conditions, and geographic region are identified in COVID-19 VE analyses as potential confounders [12–15], additional social and structural factors not routinely captured may also confound or modify the association. Understanding whether these factors impact VE could contribute to our understanding of how VE may vary, particularly in higher-risk communities.

The VISION Network is a multistate collaboration between CDC and health systems with integrated clinical, testing, and immunization records that assesses VE against laboratory-confirmed COVID-19-associated emergency department and urgent care (ED/UC events) and hospitalizations. In this analysis, we assessed vaccination coverage through July 2022 and estimated VE in 2- and 3-dose adult messenger RNA (mRNA) vaccine recipients. Our primary goals were to describe vaccination coverage across SVI quartiles among patients accessing medical services and to determine whether SVI influenced COVID-19 VE estimates in these settings.

METHODS

Setting and Participants

VISION is a research network that evaluates COVID-19 VE across diverse populations and geographic areas using a test-negative case-control study design, comparing the odds of antecedent vaccination between laboratory-confirmed COVID-19 case-patients and test-negative control-patients presenting with COVID-19-like illness (CLI) in ED/UC or hospital settings [13, 16, 17]. Seven partners with facilities in Colorado, Indiana, Minnesota, Oregon, Texas, Utah, Wisconsin, and Washington submitted data for this analysis.

For both vaccination coverage and VE analyses, eligible encounters occurred among adults aged ≥18 years with ≥1 CLI discharge code. CLI criteria were defined as a clinical diagnosis of acute respiratory illness (eg, pneumonia) or associated signs or symptoms (eg, cough, fever). Eligible hospital admissions required a length of stay ≥24 hours. Repeat encounters, defined as >1 ED/UC visit within 24 hours or hospital readmission within 30

days, were analyzed as a single encounter. SARS-CoV-2 infection status was determined by molecular testing performed within 14 days before or up to 72 hours after an encounter. The vaccination coverage analysis included ED/UC events or hospitalizations occurring between 1 January 2021 (2 weeks following the recommendation of the first available COVID-19 vaccine) [18] and 26 June to 8 July 2022 (varying by site), encompassing periods of the Delta and Omicron BA.1, BA.2/BA.2.12.1, and BA.4/BA.5 variant circulation.

Analysis of VE across SVI groups during specified time periods was limited to the Delta and early Omicron (BA.1) periods and was restricted to presumed immunocompetent patients with an event between 30 September 2021 (7 days after CDC recommended a first booster dose for some adults) and March 16–29, 2022 (when the SARS-CoV-2 BA.1 variant no longer accounted for ≥50% of cases at individual sites).

Vaccination Status

Vaccination status was determined from state and local immunization registries and electronic health records as of the encounter index date, defined as the earliest of either the date of molecular SARS-CoV-2 testing or the date of admission. For the vaccination coverage analysis, we considered Pfizer-BioNTech and Moderna (mRNA) and Johnson & Johnson/Janssen (J&J) vaccines. Patients who had received no vaccine doses by the index date were considered unvaccinated. We identified the date of first vaccination (any mRNA or J&J dose) and the date of primary series completion (second mRNA dose or first J&J dose). Date of booster dose was defined as the date of the third mRNA dose among those who received 2 mRNA doses as their primary series or the date of the second vaccine (either mRNA or J&J) among those who received J&J as their primary series. For the VE analysis, we considered mRNA vaccination and estimated VE for 2-dose (primary series) and 3-dose (primary series plus booster dose) recipients. Patients who received 2 doses were further divided into those who received the second dose 14–149 days or ≥150 days prior to the index date. Encounters were excluded from the VE analysis if the patient received only 1 dose, a second mRNA dose 1–13 days before the index date, a third dose 1–6 days before the index date, or ≥4 vaccine doses.

Social Vulnerability

Social vulnerability was measured using 2018 SVI data [9]. US census tracts are ranked across 15 SVI measures, generating percentiles ranging from 0 (least vulnerable) to 1 (most vulnerable). Each tract is ranked overall and for each of 4 SVI themes. Patient addresses from eligible encounters were geocoded to census tracts using various mapping tools (Supplementary Table 1), with corresponding SVI rankings reported to the nearest 5th percentile. Overall and thematic SVI rankings were grouped into quartiles. Encounters missing geocoded data to determine SVI were excluded.

Statistical Analysis

Vaccination coverage was assessed by plotting SVI quartiles over time, including eligible CLI-associated ED/UC and hospital encounters through 8 July 2022. Vaccination status among patients with multiple encounters was determined using data from the latest encounter. Coverage was reported for each SVI quartile as the proportion receiving the

specified vaccine regimen (ie, primary series or booster) divided by the number of persons with ≥1 eligible encounter.

VE against a laboratory-confirmed COVID-19 ED/UC visit or hospitalization was estimated using a test-negative design (TND), which has been widely used in COVID-19 VE studies [13, 19–23]. The TND reduces confounding that may otherwise occur due to misclassification or differences in healthcare-seeking behavior between cases and controls [24]. VE was assessed by comparing the odds of being vaccinated between those with positive and negative SARS-CoV-2 test results. Weighted multivariable logistic regression was performed, adjusting for age, site-specific geographical cluster, calendar time, and local SARS-CoV-2 circulation using a 7-day moving average of percent positivity of reverse-transcription polymerase chain reaction (RT-PCR) SARS-CoV-2 tests. Covariates with a standardized mean difference (SMD) of ≥0.20 after weighting by the propensity score were included in VE models to minimize residual confounding. Weights were calculated for each model as the patients' inverse-propensity-to-be-vaccinated, with generalized boosted regression trees estimating propensity based on facility characteristics, demographics, and underlying medical conditions truncated at the 99th percentile. Results were stratified by receipt of 2 doses 14–149 days prior to the index date, 2 doses ≥150 days prior, and 3 doses, compared to an unvaccinated reference group (Supplemental Methods).

VE estimates were stratified by variant period (Delta and Omicron BA.1) and age (18–49, 50–64, ≥65 years) for the overall SVI score, and by variant period for each of the 4 SVI themes (Supplemental Methods). To directly compare VE across SVI quartiles, an interaction between SVI quartile and vaccination dose was included in the regression models. Models with and without the interaction term were compared using a likelihood ratio test; a significant *P* value ($P < .05$) suggested that a difference in VE existed across SVI quartiles. Analyses were performed using SAS version 9.4 and R version 4.1.2. This study was reviewed and approved by the institutional review boards (IRB) at participating sites or under a reliance agreement with Westat, Inc.

RESULTS

Participants in Vaccination Coverage Analysis

From 1 January 2021, through 8 July 2022, 605 220 adult CLI-associated ED/UC encounters and 216 667 adult hospitalizations were identified. Of those, 133 784 (22%) ED/UC encounters and 57 671 (27%) hospitalization encounters were excluded due to missing SVI information or inability to geocode the patient address (Tables 1 and 2). Demographic characteristics were largely similar between patients with and without SVI information. A larger proportion of encounters missing SVI was observed among patients with unknown race/ethnicity and unknown urban-rural classification. A total of 593 668 unique eligible patients were included in the analysis of vaccination coverage, including 257 119 (43%) unvaccinated patients, 209 217 (35%) patients who completed a primary series only, and 91 360 (15%) who completed a primary series and received a booster dose. Characteristics of encounters by SVI quartile are listed in Table 1 for ED/UC encounters and Table 2 for hospitalizations.

Vaccination Coverage

From 1 January to 28 February 2021, when only mRNA products (Pfizer-BioNTech, Moderna) were authorized for adults, 48 618 patients had completed a primary vaccination series. An absolute difference in initial vaccine uptake of 8% was observed between the first and fourth SVI quartiles (Q1 = 15%, Q4 = 7%). Starting in March 2021, following CDC recommendations for three vaccine products (Pfizer-BioNTech, Moderna, and J&J) [18, 25, 26], the proportion of adults completing a primary series further diverged by SVI quartile (Figure 1). By 1 July 2021, there was a 20% absolute difference in primary vaccination series completion between highest and lowest quartiles (Q1 = 56%, Q4 = 36%). Similar trends were observed among patients with a completed primary series who received a booster dose (3rd dose mRNA or 2nd dose following J&J) and widened over time (Q1 = 8% and Q4 = 4% on 1 October 2021; Q1 = 44% and Q4 = 32% on 1 June 2022) (Figure 2). Differences remained when stratified by age (Supplementary Figures 1–3).

Participants in VE Analysis

From 30 September 2021 to March 16–29, 2022, 168 384 adult patients with CLI-associated ED/UC encounters and 43 208 adult patients with CLI-associated hospitalizations were identified. In total, 191 085 ED/UC encounters (93 962 [49%] during the Delta period and 97 123 [51%] during BA.1) and 43 657 hospitalization encounters (21 948 [50%] during the Delta period and 21 709 [50%] during BA.1) were included in the VE analysis (Figures 3 and 4).

COVID-19 VE by Overall SVI

During the Delta period, VE against COVID-19-associated ED/UC encounters after 2-dose mRNA vaccination 14–149 days prior was similar across all SVI quartiles and without consistent differences across quartiles, ranging from 84% in SVI Q4 (95% confidence interval [CI]: 79–87) to 89% in Q3 (95% CI: 85–91) (Figure 3). VE for 2-dose mRNA vaccination 14–149 days prior during BA.1 was also similar across SVI quartiles, ranging from 42% in Q2 (95% CI: 33–49) to 54% in Q3 (95% CI: 47–61). Similar VE was seen across SVI quartiles for 2-dose mRNA vaccination ≥150 days prior, ranging from 74% in Q3 (95% CI: 71–77) to 81% in Q1 (95% CI: 79–82) during Delta and 27% in Q4 (95% CI: 20–33) to 37% in Q2 (95% CI: 32–41) during BA.1, although the interaction term for both suggested some difference across quartiles ($P < .05$). During Delta predominance, 3-dose VE was estimated between 93% in Q4 (95% CI: 89–95) and 96% in Q1 (95% CI: 95–96), with no significant differences across quartiles. Three-dose VE remained similar during BA.1, with VE between 76% in Q4 (95% CI: 72–80) and 80% in Q2 and Q3 (95% CI: 77–82).

VE against a COVID-19-associated hospitalization after 2-dose mRNA vaccination 14–149 days prior was similar across SVI quartiles, ranging from 90% in Q1 and Q4 (95% CI: 83–94) to 94% in Q3 (95% CI: 88–97) during the Delta era and 59% in Q1 (95% CI: 39–72) to 65% in Q2 (95% CI: 48–76) during BA.1 (Figure 4). Similar patterns across SVI quartiles were seen for 2-dose mRNA vaccination ≥150 days prior, ranging from 82% in Q3 (95% CI: 78–85) to 86% in Q2 (95% CI: 83–88) during Delta and 43% in Q4 (95% CI: 32–52) to 58% in Q1 (95% CI: 51–65) during BA.1, although the interaction term was significant

during BA.1 ($P = .03$). Similar values across SVI quartiles were observed in the Delta era for 3-dose VE, with estimates between 94% in Q3 and Q4 (95% CI: 88–97) and 98% in Q2 (95% CI: 96–99) ($P = .05$). During BA.1, 3-dose VE against a COVID-19-associated hospitalization was estimated between 82% in Q4 (95% CI: 76–86) and 89% in Q2 (95% CI: 87–92) ($P = .03$). Although the interaction term was statistically significant across SVI quartile groups during BA.1, absolute differences in VE were small and confidence intervals generally overlapped.

VE by SVI Theme and Age Group

VE estimates for COVID-19-associated ED/UC encounters were similar for each of the four SVI themes and each age group. Some VE estimates (eg, 2-dose ≥150 days group) for theme 1 (socioeconomic status) were statistically significantly different by quartile, but absolute differences were small (Supplementary Table 2). VE estimates for ED/UC encounters by age group were also statistically significant with similarly small absolute differences (Supplementary Table 3). VE against COVID-19-associated hospitalization by SVI theme and age group yielded similar results: VE estimates were similar across quartiles for each of the SVI themes and by age group. Where there were statistically significant differences in VE estimates, absolute differences remained small (Supplementary Tables 4 and 5).

DISCUSSION

As previously observed [3, 5, 6], COVID-19 vaccination coverage in the VISION Network population varied by SVI through July 2022, with adults in more vulnerable groups less frequently vaccinated. Among vaccinated individuals, those living in areas with greater social vulnerability were also vaccinated later. However, we did not find notable or consistent differences in VE by SVI (overall or within themes) after accounting for other patient-level factors. These findings suggest that differences in vaccine coverage, rather than VE, likely contribute to the disproportionate burden of COVID-19 illness observed within socially vulnerable communities.

The persistent differences in coverage by SVI over 1.5 years after COVID-19 vaccines were authorized suggests that vaccine hesitancy, in addition to barriers to access, is driving lower vaccination coverage within vulnerable communities. This highlights the need for more effective efforts to promote the benefits and safety of COVID-19 vaccines to mitigate disparities. The relationship between race and ethnicity and SVI has been well documented [27, 28], as have differences in vaccine hesitancy by some elements of SVI, including race and ethnicity, education, and income [29–32]. Considered in that context, the findings of this analysis make clear the importance of focusing efforts on identifying strategies to increase vaccination coverage among vulnerable groups with greater vaccine hesitancy to reduce disparities in disease burden and impact. Multipart, communication-based, and community-specific approaches tend to be most successful at reducing hesitancy and increasing vaccination uptake [33–35]. Educational initiatives, incorporating religious or community leaders, and embedding conversations around vaccination within routine healthcare settings have also been shown to be effective [33–37]. Social media has also

proven to be a promising tool; for example, when used to provide a platform for information and answers, or to emphasize acceptance of vaccination as a social norm [33, 34, 36].

Evidence of a relationship between social vulnerability and VE is limited. Although several adult and pediatric VE studies have considered SVI as a covariate [20, 38–40], to our knowledge ours is the first study to report COVID-19 VE across SVI quartiles and themes. Studies from other vaccine-preventable diseases have offered clues on the role of social vulnerability. Studies of childhood rotavirus immunizations in high-income countries found decreased VE in lower SES neighborhoods [41, 42]. Further evidence of reduced VE of live oral rotavirus vaccines in low-income countries suggests an interplay of multiple SES-related factors, including differential disease epidemiology, preexisting medical conditions, malnutrition, and immune response [43]. Serology studies from rotavirus and other infectious diseases have demonstrated differences in immunoglobin levels by SES, with malnutrition, psychosocial stressors, and underlying medical conditions diminishing the development of antibodies [44]. However, other studies have shown antibody response by SES to be dependent on pathogen-specific epidemiology, complicating efforts to establish causality [45]. Beyond SES, research on the impact of crowded housing and population density has found that VE remains high despite increased disease transmission, suggesting (as in our findings) the stronger role of vaccination coverage in disease prevention [46]. Other studies have demonstrated the relationship between increased exposure, such as what might occur in areas with greater crowding or population density, and reduced vaccine efficacy [47]. Findings from these studies provide additional evidence to suggest that COVID-19 vaccines are effective across diverse populations.

This analysis was subject to several limitations. First, it did not account for effects of prior infection, which may differ by SVI quartile and impact VE if previous infection reduces the risk of re-infection. Second, about one-quarter of encounters were missing SVI and excluded, which may impact generalizability. Third, findings may not be generalizable to the entire US population. Furthermore, this analysis only assessed SVI in patients presenting for medical care with CLI discharge codes, which may also limit generalizability. Fourth, other factors such as differences in early vaccine priority groups [48, 49] or timing of booster dose eligibility [50] may have differed across SVI groups and affected uptake and timing of primary vaccination or booster doses. However, differences in coverage persisted after vaccines were widely available for all adults, and <1% of patients who completed their primary series <150 days before 1 September 2021 (late adopters), went on to receive a booster dose, so it is unlikely that the timing or uptake of booster doses was impacted by the timing of the primary series. Similarly, there may be unmeasured differences between cases and controls. Finally, under-ascertainment of vaccination coverage may have differed by SVI group, although unlikely to be significant given robust vaccine verification methods.

In this multistate analysis, COVID-19 vaccination coverage varied markedly by SVI. Differences in estimated VE by SVI, however, were small after adjusting for other patient-level factors. Lower vaccination coverage in areas with greater social vulnerability means that the burden of a preventable illness is still disproportionately borne by more vulnerable populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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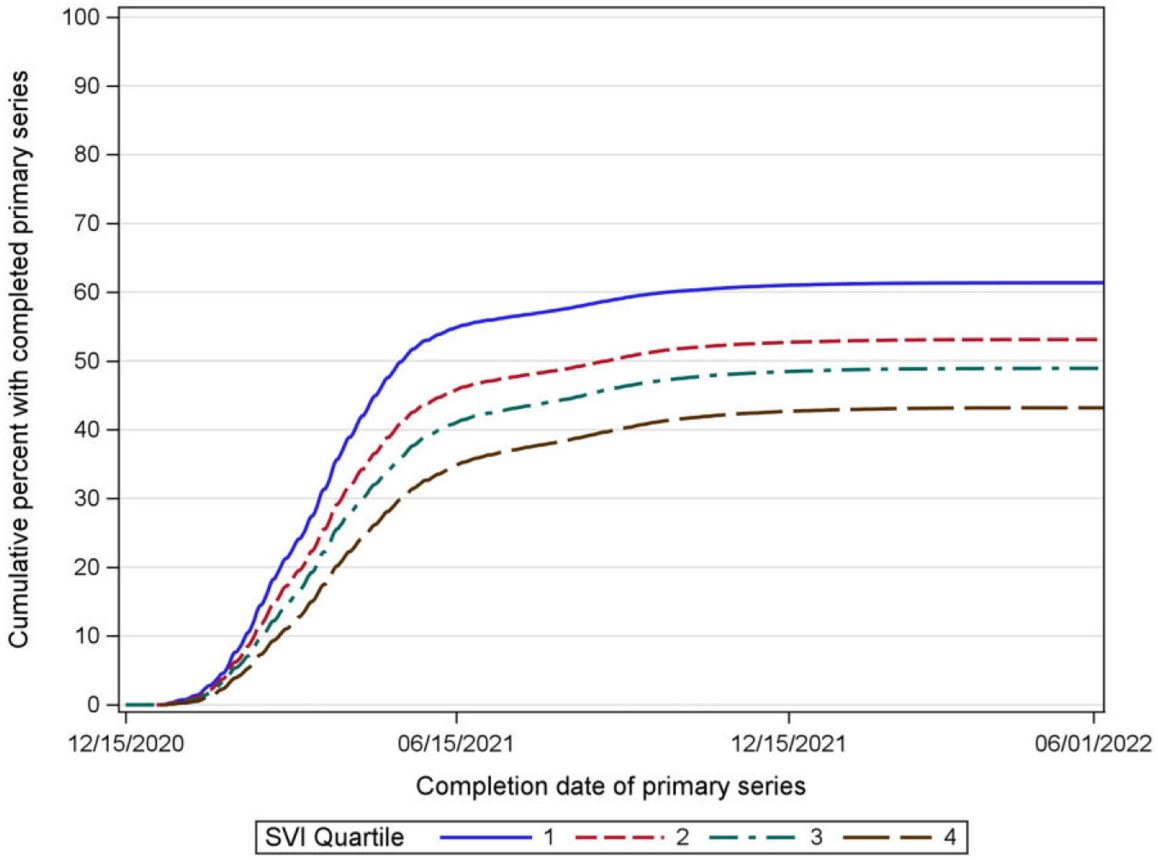


Figure 1.

Date COVID-19 primary series vaccination (2 mRNA doses or 1 Johnson & Johnson/Janssen [J&J] dose) completed by SVI quartile among unique subjects, 1 January 2021–8 July 2022*. *In the states represented in this analysis, the Delta variant was predominant from 1 June–3 July 2021, through 15 December–28 December 2021, depending on site. The Omicron variant was predominant beginning December 16–29 2021, through the conclusion of the study period. Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SVI, Social Vulnerability Index.

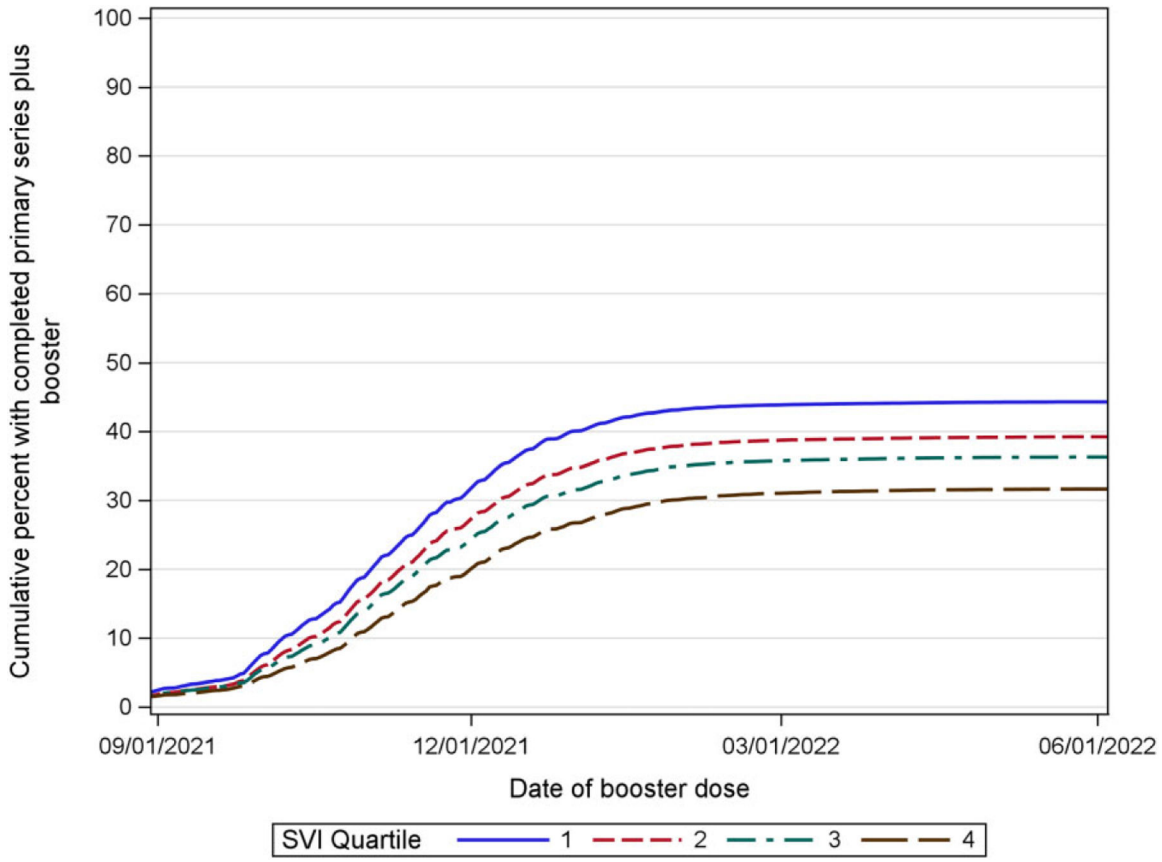
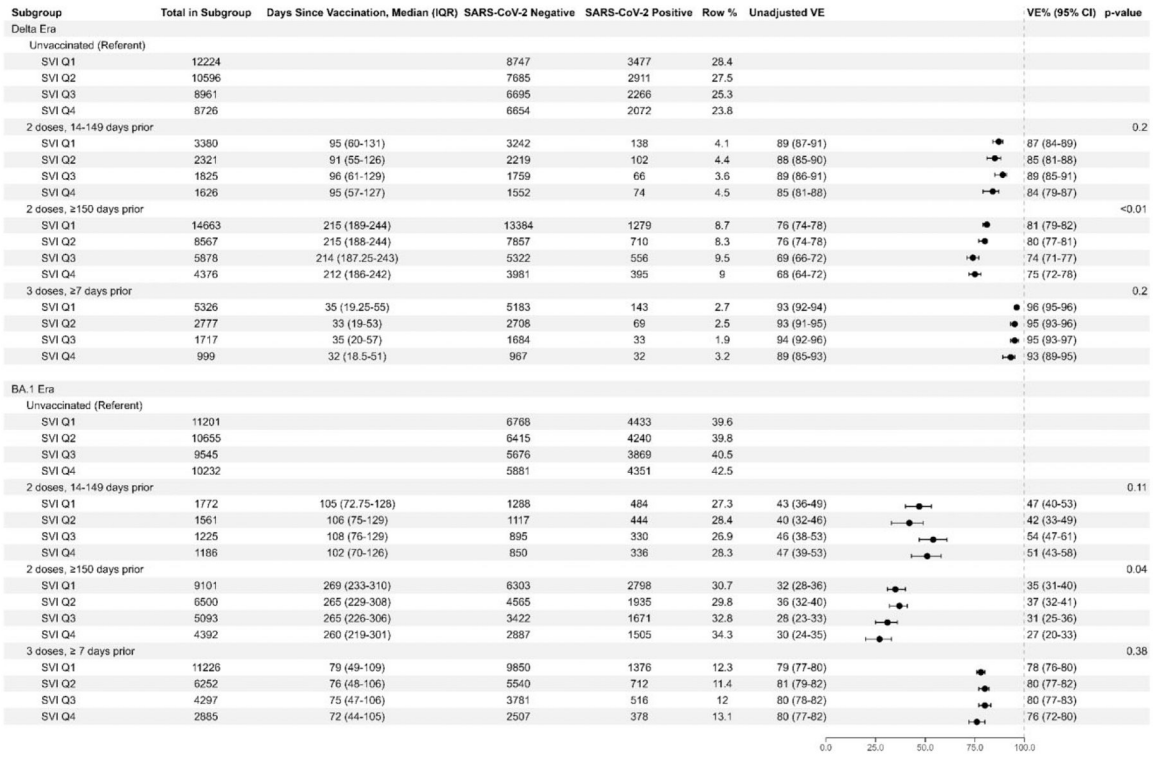


Figure 2.

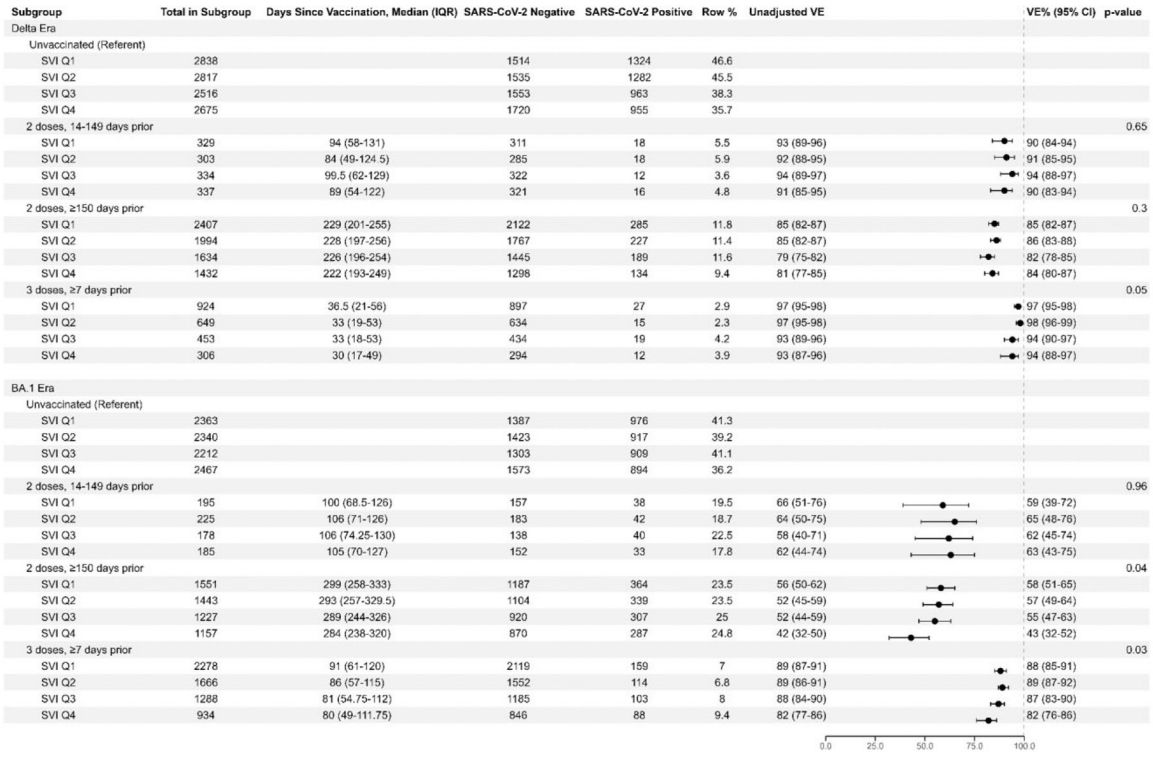
Date COVID-19 booster dose completed by SVI quartile among unique subjects with a completed primary series (3 mRNA doses or 1 Johnson & Johnson/Janssen [J&J] dose plus additional vaccine dose), 1 September 2021 to 8 July 2022*. *In the states represented in this analysis, the Delta variant was predominant from 1 June–3 July 2021, through 15 December–28 December 2021, depending on site. The Omicron variant was predominant beginning December 16–29 2021, through the conclusion of the study period. Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SVI, Social Vulnerability Index.



Subgroup	Total in Subgroup	Days Since Vaccination, Median (IQR)	SARS-CoV-2 Negative	SARS-CoV-2 Positive	Row %	Unadjusted VE	VE% (95% CI)	p-value
Delta Era								
Unvaccinated (Referent)								
SVI Q1	12224		8747	3477	28.4			
SVI Q2	10596		7685	2911	27.5			
SVI Q3	8961		6695	2266	25.3			
SVI Q4	8726		6654	2072	23.8			
2 doses, 14-149 days prior								0.2
SVI Q1	3380	95 (60-131)	3242	138	4.1	89 (87-91)	87 (84-89)	
SVI Q2	2321	91 (55-126)	2219	102	4.4	88 (85-90)	85 (81-88)	
SVI Q3	1825	96 (61-129)	1759	66	3.6	89 (86-91)	89 (85-91)	
SVI Q4	1626	95 (57-127)	1552	74	4.5	85 (81-88)	84 (79-87)	
2 doses, ≥150 days prior								<0.01
SVI Q1	14663	215 (189-244)	13384	1279	8.7	76 (74-78)	81 (79-82)	
SVI Q2	8567	215 (188-244)	7857	710	8.3	76 (74-78)	80 (77-81)	
SVI Q3	5878	214 (187.25-243)	5322	556	9.5	69 (66-72)	74 (71-77)	
SVI Q4	4376	212 (186-242)	3981	395	9	68 (64-72)	75 (72-78)	
3 doses, ≥7 days prior								0.2
SVI Q1	5326	35 (19.25-55)	5183	143	2.7	93 (92-94)	96 (95-96)	
SVI Q2	2777	33 (19-53)	2708	69	2.5	93 (91-95)	95 (93-96)	
SVI Q3	1717	35 (20-57)	1684	33	1.9	94 (92-96)	95 (93-97)	
SVI Q4	999	32 (18.5-51)	967	32	3.2	89 (85-93)	93 (89-95)	
BA.1 Era								
Unvaccinated (Referent)								
SVI Q1	11201		6768	4433	39.6			
SVI Q2	10655		6415	4240	39.8			
SVI Q3	9545		5676	3869	40.5			
SVI Q4	10232		5881	4351	42.5			
2 doses, 14-149 days prior								0.11
SVI Q1	1772	105 (72.75-128)	1288	484	27.3	43 (36-49)	47 (40-53)	
SVI Q2	1561	106 (75-129)	1117	444	28.4	40 (32-46)	42 (33-49)	
SVI Q3	1225	108 (76-129)	895	330	26.9	46 (38-53)	54 (47-61)	
SVI Q4	1186	102 (70-126)	850	336	28.3	47 (39-53)	51 (43-58)	
2 doses, ≥150 days prior								0.04
SVI Q1	9101	269 (233-310)	6303	2798	30.7	32 (28-36)	35 (31-40)	
SVI Q2	6500	265 (229-308)	4565	1935	29.8	36 (32-40)	37 (32-41)	
SVI Q3	5093	265 (226-306)	3422	1671	32.8	28 (23-33)	31 (25-36)	
SVI Q4	4392	260 (219-301)	2887	1505	34.3	30 (24-35)	27 (20-33)	
3 doses, ≥ 7 days prior								0.38
SVI Q1	11226	79 (49-109)	9850	1376	12.3	79 (77-80)	78 (76-80)	
SVI Q2	6252	76 (48-106)	5540	712	11.4	81 (79-82)	80 (77-82)	
SVI Q3	4297	75 (47-106)	3781	516	12	80 (78-82)	80 (77-83)	
SVI Q4	2885	72 (44-105)	2507	378	13.1	80 (77-82)	76 (72-80)	

Figure 3.

mRNA COVID-19 vaccine effectiveness against laboratory-confirmed COVID-19-associated emergency department or urgent care event by SVI quartile, vaccine doses and timing, and SARS-CoV-2 subvariant era. Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SVI, Social Vulnerability Index.



Subgroup	Total in Subgroup	Days Since Vaccination, Median (IQR)	SARS-CoV-2 Negative	SARS-CoV-2 Positive	Row %	Unadjusted VE	VE% (95% CI)	p-value
Delta Era								
Unvaccinated (Referent)								
SVI Q1	2838		1514	1324	46.6			
SVI Q2	2817		1535	1282	45.5			
SVI Q3	2516		1553	963	38.3			
SVI Q4	2675		1720	955	35.7			
2 doses, 14-149 days prior								0.65
SVI Q1	329	94 (58-131)	311	18	5.5	93 (89-96)	90 (84-94)	
SVI Q2	303	84 (49-124.5)	285	18	5.9	92 (88-95)	91 (85-95)	
SVI Q3	334	99.5 (62-129)	322	12	3.6	94 (89-97)	94 (88-97)	
SVI Q4	337	89 (54-122)	321	16	4.8	91 (85-95)	90 (83-94)	
2 doses, ≥150 days prior								0.3
SVI Q1	2407	229 (201-255)	2122	285	11.8	85 (82-87)	85 (82-87)	
SVI Q2	1994	228 (197-256)	1767	227	11.4	85 (82-87)	86 (83-88)	
SVI Q3	1634	226 (196-254)	1445	189	11.6	79 (75-82)	82 (78-85)	
SVI Q4	1432	222 (193-249)	1298	134	9.4	81 (77-85)	84 (80-87)	
3 doses, ≥7 days prior								0.05
SVI Q1	924	36.5 (21-56)	897	27	2.9	97 (95-98)	97 (95-98)	
SVI Q2	649	33 (19-53)	634	15	2.3	97 (95-98)	98 (96-99)	
SVI Q3	453	33 (18-53)	434	19	4.2	93 (89-96)	94 (90-97)	
SVI Q4	306	30 (17-49)	294	12	3.9	93 (87-96)	94 (88-97)	
BA.1 Era								
Unvaccinated (Referent)								
SVI Q1	2363		1387	976	41.3			
SVI Q2	2340		1423	917	39.2			
SVI Q3	2212		1303	909	41.1			
SVI Q4	2467		1573	894	36.2			
2 doses, 14-149 days prior								0.96
SVI Q1	195	100 (68.5-126)	157	38	19.5	66 (51-76)	59 (39-72)	
SVI Q2	225	106 (71-126)	183	42	18.7	64 (50-75)	65 (48-76)	
SVI Q3	178	106 (74.25-130)	138	40	22.5	58 (40-71)	62 (45-74)	
SVI Q4	185	105 (70-127)	152	33	17.8	62 (44-74)	63 (43-75)	
2 doses, ≥150 days prior								0.04
SVI Q1	1551	299 (258-333)	1187	364	23.5	56 (50-62)	58 (51-65)	
SVI Q2	1443	293 (257-329.5)	1104	339	23.5	52 (45-59)	57 (49-64)	
SVI Q3	1227	289 (244-326)	920	307	25	52 (44-59)	55 (47-63)	
SVI Q4	1157	284 (238-320)	870	287	24.8	42 (32-50)	43 (32-52)	
3 doses, ≥7 days prior								0.03
SVI Q1	2278	91 (61-120)	2119	159	7	89 (87-91)	88 (85-91)	
SVI Q2	1666	86 (57-115)	1552	114	6.8	89 (86-91)	89 (87-92)	
SVI Q3	1288	81 (54.75-112)	1185	103	8	88 (84-90)	87 (83-90)	
SVI Q4	934	80 (49-111.75)	846	88	9.4	82 (77-86)	82 (76-86)	

Figure 4.

mRNA COVID-19 vaccine effectiveness against laboratory-confirmed COVID-19-associated hospitalization by SVI quartile, vaccine doses and timing, and SARS-CoV-2 subvariant era. Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SVI, Social Vulnerability Index.

Table 1.

Characteristics of Emergency Department and Urgent Care Encounters Among Adults With COVID-19–Like Illness by Social Vulnerability Index (SVI) Quartile, 1 January 2021 to 8 July 2022

			SVI Quartile				
Characteristic	**Overall (Col %)**	**SMD[a]**	**SVI Q1 (Row %)**	**SVI Q2 (Row %)**	**SVI Q3 (Row %)**	**SVI Q4 (Row %)**	**Unable to Geocode or Missing[b] (Row %)**
Total	605 220	…	169 392	123 142	96 313	82 589	133 784
Subvariant predominance era							
Pre-Delta	59 737 (10.0)	0.066	15 842 (26.5)	13 109 (21.9)	9335 (15.6)	7880 (13.2)	13 571 (22.7)
Delta	271 795 (45.4)	…	78 031 (28.7)	55 280 (20.3)	42 539 (15.7)	34 495 (12.7)	61 450 (22.6)
BA.1	155 860 (26.0)	…	41 235 (26.5)	31 359 (20.1)	25 862 (16.6)	24 000 (15.4)	33 404 (21.4)
BA.2[c]	111 263 (18.6)	…	32 008 (28.8)	22 089 (19.9)	17 608 (15.8)	15 441 (13.9)	24 117 (21.7)
Site							
BSWH[d]	104 474 (17.3)	0.741	22 149 (21.2)	19 907 (19.1)	21 255 (20.3)	26 948 (25.8)	14 215 (13.6)
HP[e]	110 670 (18.3)	…	53 327 (48.2)	25 666 (23.2)	13 693 (12.4)	14 610 (13.2)	3374 (3.0)
IH[f]	164 061 (27.1)	…	57 513 (35.1)	36 323 (22.1)	27 994 (17.1)	12 233 (7.5)	29 998 (18.3)
KPNW[g]	61 437 (10.2)	…	10 518 (17.1)	15 222 (24.8)	12 254 (19.9)	8722 (14.2)	14 721 (24.0)
PHIX[h]	9740 (1.6)	…	276 (2.8)	741 (7.6)	1061 (10.9)	2601 (26.7)	5061 (52.0)
RGN[i]	104 707 (17.3)	…	16 148 (15.4)	20 763 (19.8)	17 929 (17.1)	15 452 (14.8)	34 415 (32.9)
UCO[j]	50 131 (8.3)	…	9461 (18.9)	4520 (9.0)	2127 (4.2)	2023 (4.0)	32 000 (63.8)
Age group							
18–49 y	314 953 (52.0)	0.102	83 092 (26.4)	62 192 (19.7)	49 439 (15.7)	44 352 (14.1)	75 878 (24.1)
50–64 y	124 176 (20.5)	…	34 682 (27.9)	24 919 (20.1)	20 418 (16.4)	18 509 (14.9)	25 648 (20.7)
≥65 y	166 085 (27.4)	…	51 617 (31.1)	36 031 (21.7)	26 454 (15.9)	19 728 (11.9)	32 255 (19.4)
Sex							
Male	244 463 (40.4)	0.021	69 566 (28.5)	49 783 (20.4)	38 378 (15.7)	32 458 (13.3)	54 278 (22.2)
Female	360 757 (59.6)	…	99 826 (27.7)	73 359 (20.3)	57 935 (16.1)	50 131 (13.9)	79 506 (22.0)
Race/Ethnicity							
Non-Hispanic White	411 302 (68.0)	0.505	137 529 (33.4)	91 462 (22.2)	62 318 (15.2)	38 248 (9.3)	81 745 (19.9)
Non-Hispanic Black	59 521 (9.8)	…	8561 (14.4)	9938 (16.7)	11 148 (18.7)	20 376 (34.2)	9498 (16.0)

Characteristic	Overall (Col %)	SMD[a]	SVI Quartile				Unable to Geocode or Missing[b] (Row %)
			SVI Q1 (Row %)	SVI Q2 (Row %)	SVI Q3 (Row %)	SVI Q4 (Row %)	
Hispanic	66 945 (11.1)	…	10 560 (15.8)	12 041 (18.0)	14 560 (21.7)	16 866 (25.2)	12 918 (19.3)
Non-Hispanic Other	36 713 (6.1)	…	9793 (26.7)	6973 (19.0)	5726 (15.6)	5122 (14.0)	9099 (24.8)
Unknown	30 739 (5.1)	…	2949 (9.6)	2728 (8.9)	2561 (8.3)	1977 (6.4)	20 524 (66.8)
Medicaid insurance							
No	471 396 (77.9)	0.326	146 169 (31.0)	96 818 (20.5)	71 129 (15.1)	53 261 (11.3)	104 019 (22.1)
Yes	123 383 (20.4)	…	22 019 (17.8)	24 577 (19.9)	23 541 (19.1)	28 072 (22.8)	25 174 (20.4)
Missing/Unknown	10 441 (1.7)	…	1204 (11.5)	1747 (16.7)	1643 (15.7)	1256 (12.0)	4591 (44.0)
Urban-rural classification of facility							
Large central metro	215 203 (35.6)	0.377	72 208 (33.6)	43 005 (20.0)	36 814 (17.1)	40 840 (19.0)	22 336 (10.4)
Large fringe metro	126 890 (21.0)	…	37 784 (29.8)	26 669 (21.0)	17 722 (14.0)	10 700 (8.4)	34 015 (26.8)
Medium metro	130 405 (21.5)	…	33 769 (25.9)	24 778 (19.0)	18 115 (13.9)	14 450 (11.1)	39 293 (30.1)
Small metro	49 407 (8.2)	…	10 623 (21.5)	9854 (19.9)	11 563 (23.4)	7204 (14.6)	10 163 (20.6)
Micropolitan	27 404 (4.5)	…	6935 (25.3)	8196 (29.9)	4071 (14.9)	2481 (9.1)	5721 (20.9)
Non-core	15 867 (2.6)	…	2044 (12.9)	4598 (29.0)	3436 (21.7)	1943 (12.2)	3846 (24.2)
Unknown	40 044 (6.6)	…	6029 (15.1)	6042 (15.1)	4592 (11.5)	4971 (12.4)	18 410 (46.0)
Underlying respiratory condition at discharge							
No	493 424 (81.5)	0.113	142 921 (29.0)	99 690 (20.2)	75 580 (15.3)	63 858 (12.9)	111 375 (22.6)
Yes	111 796 (18.5)	…	26 471 (23.7)	23 452 (21.0)	20 733 (18.5)	18 731 (16.8)	22 409 (20.0)
Underlying nonrespiratory condition at discharge							
No	426 794 (70.5)	0.142	126 364 (29.6)	85 221 (20.0)	62 724 (14.7)	52 585 (12.3)	99 900 (23.4)
Yes	178 426 (29.5)	…	43 028 (24.1)	37 921 (21.3)	33 589 (18.8)	30 004 (16.8)	33 884 (19.0)
Any likely immunocompromised status							
No	574 942 (95.0)	0.046	161 577 (28.1)	116 659 (20.3)	90 558 (15.8)	77 661 (13.5)	128 487 (22.3)
Yes	30 278 (5.0)	…	7815 (25.8)	6483 (21.4)	5755 (19.0)	4928 (16.3)	5297 (17.5)
Immunization status and days since last dose							
Unvaccinated (referent)	254 731 (42.1)	0.299	55 083 (21.6)	50 008 (19.6)	42 764 (16.8)	41 386 (16.2)	65 490 (25.7)
2-dose mRNA <150 d since last dose	70 419 (11.6)	…	21 968 (31.2)	15 161 (21.5)	10 792 (15.3)	8392 (11.9)	14 106 (20.0)
2-dose mRNA ≥150 d since last dose	129 612 (21.4)	…	41 057 (31.7)	26 499 (20.4)	19 947 (15.4)	15 765 (12.2)	26 344 (20.3)
3-dose mRNA <120 d since last dose	51 283 (8.5)	…	18 669 (36.4)	10 816 (21.1)	7517 (14.7)	5078 (9.9)	9203 (17.9)
3-dose mRNA ≥120 d since last dose	35 190 (5.8)	…	13 587 (38.6)	7343 (20.9)	4840 (13.8)	3365 (9.6)	6055 (17.2)

Characteristic	Overall (Col %)	SMD[a]	SVI Quartile				Unable to Geocode or Missing[b] (Row %)
			SVI Q1 (Row %)	SVI Q2 (Row %)	SVI Q3 (Row %)	SVI Q4 (Row %)	
Other Immunization combination	63 985 (10.6)	…	19 028 (29.7)	13 315 (20.8)	10 453 (16.3)	8603 (13.4)	12 586 (19.7)
SARS-CoV-2 test result							
Positive	107 993 (17.8)	0.06	27 497 (25.5)	21 304 (19.7)	17 526 (16.2)	15 920 (14.7)	25 746 (23.8)
Negative	497 227 (82.2)	…	141 895 (28.5)	101 838 (20.5)	78 787 (15.8)	66 669 (13.4)	108 038 (21.7)
Known historical positive SARS-CoV-2 test result							
Yes	64 256 (10.6)	0.069	15 624 (24.3)	13 369 (20.8)	11 315 (17.6)	10 507 (16.4)	13 441 (20.9)
No	540 964 (89.4)	…	153 768 (28.4)	109 773 (20.3)	84 998 (15.7)	72 082 (13.3)	120 343 (22.2)

Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SARS-Cov-2, severe acute respiratory syndrome coronavirus 2; SMD, standardized mean difference.

[a] An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between emergency department and urgent care visits for different Social Vulnerability Index Groups. A single SMD was calculated by averaging the absolute SMDs obtained from pairwise comparisons of each SVI quartile category, excluding encounters without SVI due to missing geocoded data.

[b] Unable to geocode or missing includes any patient encounters where the address was not provided or could not be geocoded.

[c] Data from the BA.2 era (defined as the day after the BA.1 predominance period ended at each site (16–29 March 2022) through the last date of data collection at each site (26 June to 8 July 2022) was used for vaccination coverage only and was not included in VE analyses.

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[h] Paso Del Norte Health Information Exchange (Texas).

[i] Regenstrief Institute (Indiana).

[j] University of Colorado (Colorado).

Table 2.

Characteristics of Hospitalizations Among Adults With COVID-19–Like Illness by Social Vulnerability Index (SVI) Quartile, 1 January 2021 to 8 July 2022

Characteristic	Overall (Col %)	SMD[a]	SVI Quartile				Unable to Geocode or Missing[b] (Row %)
			SVI Q1 (Row %)	SVI Q2 (Row %)	SVI Q3 (Row %)	SVI Q4 (Row %)	
Total	216 667	…	48 690	42 129	35 593	32 584	57 671
Subvariant predominance era							
Pre-Delta	39 097 (18.1)	0.062	8603 (22.0)	7700 (19.7)	5930 (15.2)	5159 (13.2)	11 705 (29.9)
Delta	92 619 (42.9)	…	20 320 (21.9)	17 773 (19.2)	15 075 (16.3)	13 743 (14.8)	25 708 (27.8)
BA.1	50 767 (23.5)	…	11 394 (22.4)	9955 (19.6)	8642 (17.0)	8282 (16.3)	12 494 (24.6)
BA.2[c]	33 408 (15.5)	…	8101 (24.2)	6526 (19.5)	5843 (17.5)	5295 (15.8)	7643 (22.9)
Site							
BSWH[d]	43 055 (19.9)	0.547	9654 (22.4)	8389 (19.5)	8914 (20.7)	10 680 (24.8)	5418 (12.6)
HP[e]	17 751 (8.2)	…	7971 (44.9)	4270 (24.1)	2308 (13.0)	2640 (14.9)	562 (3.2)
IH[f]	24 203 (11.2)	…	7525 (31.1)	5412 (22.4)	4738 (19.6)	2058 (8.5)	4470 (18.5)
KPNW[g]	15 457 (7.1)	…	2817 (18.2)	3991 (25.8)	3034 (19.6)	2019 (13.1)	3596 (23.3)
PHIX[h]	1364 (0.6)	…	16 (1.2)	69 (5.1)	113 (8.3)	592 (43.4)	574 (42.1)
RGN[i]	82 301 (38.0)	…	15 422 (18.7)	16 900 (20.5)	14 624 (17.8)	12 636 (15.4)	22 719 (27.6)
UCO[j]	32 536 (15.0)	…	5285 (16.2)	3098 (9.5)	1862 (5.7)	1959 (6.0)	20 332 (62.5)
Age group							
18–49 y	42 130 (19.4)	0.185	8057 (19.1)	7507 (17.8)	7266 (17.2)	7770 (18.4)	11 530 (27.4)
50–64 y	52 772 (24.4)	…	10 092 (19.1)	9859 (18.7)	9330 (17.7)	9639 (18.3)	13 852 (26.2)
≥65 y	121 765 (56.2)	…	30 541 (25.1)	24 763 (20.3)	18 997 (15.6)	15 175 (12.5)	32 289 (26.5)
Sex							
Male	103 584 (47.8)	0.038	23 863 (23.0)	19 952 (19.3)	16 564 (16.0)	14 889 (14.4)	28 316 (27.3)
Female	113 083 (52.2)	…	24 827 (22.0)	22 177 (19.6)	19 029 (16.8)	17 695 (15.6)	29 355 (26.0)
Race/Ethnicity							
Non-Hispanic White	154 725 (71.4)	0.483	41 473 (26.8)	34 024 (22.0)	25 060 (16.2)	16 620 (10.7)	37 548 (24.3)
Non-Hispanic Black	23 201 (10.7)	…	2095 (9.0)	2864 (12.3)	4399 (19.0)	8633 (37.2)	5210 (22.5)

Characteristic	Overall (Col %)	SMD[a]	SVI Quartile				Unable to Geocode or Missing[b] (Row %)
			SVI Q1 (Row %)	SVI Q2 (Row %)	SVI Q3 (Row %)	SVI Q4 (Row %)	
Hispanic	13 224 (6.1)	…	1645 (12.4)	2129 (16.1)	3043 (23.0)	4142 (31.3)	2265 (17.1)
Non-Hispanic Other	10 576 (4.9)	…	2037 (19.3)	1621 (15.3)	1551 (14.7)	1661 (15.7)	3706 (35.0)
Unknown	14 941 (6.9)	…	1440 (9.6)	1491 (10.0)	1540 (10.3)	1528 (10.2)	8942 (59.8)
Medicaid insurance							
No	173 313 (80.0)	0.296	43 048 (24.8)	35 111 (20.3)	28 084 (16.2)	23 012 (13.3)	44 058 (25.4)
Yes	40 076 (18.5)	…	5154 (12.9)	6329 (15.8)	6952 (17.3)	9193 (22.9)	12 448 (31.1)
Missing/Unknown	3278 (1.5)	…	488 (14.9)	689 (21.0)	557 (17.0)	379 (11.6)	1165 (35.5)
Urban-rural classification of facility							
Large central metro	87 541 (40.4)	0.338	25 701 (29.4)	17 394 (19.9)	15 655 (17.9)	16 957 (19.4)	11 834 (13.5)
Large fringe metro	50 557 (23.3)	…	8790 (17.4)	8474 (16.8)	6147 (12.2)	5362 (10.6)	21 784 (43.1)
Medium metro	39 746 (18.3)	…	7077 (17.8)	7165 (18.0)	5589 (14.1)	4655 (11.7)	15 260 (38.4)
Small metro	20 747 (9.6)	…	3803 (18.3)	4739 (22.8)	4742 (22.9)	3305 (15.9)	4158 (20.0)
Micropolitan	3887 (1.8)	…	629 (16.2)	1064 (27.4)	857 (22.0)	421 (10.8)	916 (23.6)
Non-core	2913 (1.3)	…	403 (13.8)	827 (28.4)	639 (21.9)	341 (11.7)	703 (24.1)
Unknown	11 276 (5.2)	…	2287 (20.3)	2466 (21.9)	1964 (17.4)	1543 (13.7)	3016 (26.7)
Underlying respiratory condition at discharge							
No	96 142 (44.4)	0.033	22 136 (23.0)	18 274 (19.0)	15 126 (15.7)	14 327 (14.9)	26 279 (27.3)
Yes	120 525 (55.6)	…	26 554 (22.0)	23 855 (19.8)	20 467 (17.0)	18 257 (15.1)	31 392 (26.0)
Underlying nonrespiratory condition at discharge							
No	32 296 (14.9)	0.075	6227 (19.3)	6238 (19.3)	5180 (16.0)	5186 (16.1)	9465 (29.3)
Yes	184 371 (85.1)	…	42 463 (23.0)	35 891 (19.5)	30 413 (16.5)	27 398 (14.9)	48 206 (26.1)
Any likely immunocompromised status							
No	170 552 (78.7)	0.067	37 369 (21.9)	33 138 (19.4)	28 345 (16.6)	26 484 (15.5)	45 216 (26.5)
Yes	46 115 (21.3)	…	11 321 (24.5)	8991 (19.5)	7248 (15.7)	6100 (13.2)	12 455 (27.0)
Immunization status and days since last dose							
Unvaccinated (referent)	94 136 (43.4)	0.245	17 089 (18.2)	17 334 (18.4)	15 768 (16.8)	16 035 (17.0)	27 910 (29.6)
2-dose mRNA <150 d since last dose	26 208 (12.1)	…	6447 (24.6)	5163 (19.7)	4010 (15.3)	3394 (13.0)	7194 (27.4)
2-dose mRNA ≥150 d since last dose	43 821 (20.2)	…	10 884 (24.8)	8944 (20.4)	7330 (16.7)	6356 (14.5)	10 307 (23.5)
3-dose mRNA <120 d since last dose	17 605 (8.1)	…	5086 (28.9)	3711 (21.1)	2806 (15.9)	2089 (11.9)	3913 (22.2)
3-dose mRNA ≥120 d since last dose	12 754 (5.9)	…	4043 (31.7)	2710 (21.2)	1934 (15.2)	1390 (10.9)	2677 (21.0)

Characteristic	Overall (Col %)	SMD[a]	SVI Quartile				Unable to Geocode or Missing[b] (Row %)
			SVI Q1 (Row %)	SVI Q2 (Row %)	SVI Q3 (Row %)	SVI Q4 (Row %)	
Other Immunization combination	22 143 (10.2)	…	5141 (23.2)	4267 (19.3)	3745 (16.9)	3320 (15.0)	5670 (25.6)
SARS-CoV-2 test result							
Positive	37 703 (17.4)	0.028	8096 (21.5)	7571 (20.1)	6359 (16.9)	5753 (15.3)	9924 (26.3)
Negative	178 964 (82.6)	…	40 594 (22.7)	34 558 (19.3)	29 234 (16.3)	26 831 (15.0)	47 747 (26.7)
Known historical positive SARS-CoV-2 test result							
Yes	20 252 (9.3)	0.062	3999 (19.7)	4111 (20.3)	3903 (19.3)	3589 (17.7)	4650 (23.0)
No	196 415 (90.7)	…	44 691 (22.8)	38 018 (19.4)	31 690 (16.1)	28 995 (14.8)	53 021 (27.0)

Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SMD, standardized mean difference.

[a] An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between emergency department and urgent care visits for different Social Vulnerability Index Groups. A single SMD was calculated by averaging the absolute SMDs obtained from pairwise comparisons of each SVI quartile category, excluding encounters without SVI due to missing geocoded data.

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