County-level vaccination coverage and rates of COVID-19 cases and deaths in the United States: An ecological analysis

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Summary

Background On Dec 14, 2020, the United States initiated a nationwide COVID-19 vaccination campaign. Demonstrating clear population-level impact following vaccine introduction helps to further elucidate and quantify the public-health benefits of vaccination.

Methods Using a negative binomial regression model we evaluated the ecological association between county-level COVID-19 vaccine uptake and rates of COVID-19 cases and deaths in the United States from April 1, 2021 through October 31, 2021 controlling for a broad set of county-level environmental, sociodemographic, economic, and health-status-related characteristics. County-level data were obtained from several publicly available databases that were merged for analysis.

Findings After adjustment for county-level characteristics, US counties with ≥ 80% of their residents ≥ 12 years of age fully vaccinated against COVID-19 had 30% (95% CI: 25–35; $P < .001$) and 46% (38–52; $P < .001$) lower rates of COVID-19 cases and deaths, respectively, versus those with <50% coverage (reference group). A dose response was observed: counties with 70–79% uptake had 20% (95% CI: 16–24; $P < .001$) and 35% (29–40; $P < .001$) lower rates of cases and deaths, respectively; counties with 60–69% uptake had 8% (5–11; $P < .001$) and 20% (15–24; $P < .001$) lower rates; and counties with 50–59% uptake had 2% (0–4; $P = .09$) and 8% (4–12; $P < .001$) lower rates. Restricting the analysis to the period when the Delta variant was predominant (June 1, 2021 – October 31, 2021) showed similar findings.

Interpretation Our results showed that US counties with higher proportions of persons ≥ 12 years of age fully vaccinated against COVID-19 had substantially lower rates of COVID-19 cases and deaths—a finding that showed dose response and persisted even in the period when Delta was predominant.

Funding Pfizer.

Keywords: COVID-19; SARS-CoV-2; Vaccination; Coverage; Impact; County; Transmission; United States

Introduction

The first administration of a COVID-19 vaccine in the United States occurred on December 14, 2020 during a large wave of COVID-19. By the end of February 2021, three vaccines had received emergency use authorization (EUA) and were recommended for use in the United States by the Advisory Committee on Immunization Practices (ACIP) based on safety and efficacy data from phase 3 randomized placebo-controlled trials:[1–3] (*i*) Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine (Dec 11, 2020), (*ii*) Moderna mRNA-1273 mRNA COVID-19 vaccine (Dec 18, 2020), and (*iii*) Janssen Ad26.COV2.S replication-incompetent adenovirus serotype 26 COVID-19 vaccine (Feb 27, 2021).[4] On August 23, 2021, BNT162b2 received full FDA authorization.[5] Both BNT162b2[1] and mRNA-1273[2] demonstrated efficacy > 94% after two doses against symptomatic COVID-19 and severe disease in randomized controlled trials. Ad26.COV2.S,[3] administered as a single dose, demonstrated at least 66% efficacy against moderate or severe COVID-19.

ACIP recommended a multi-tiered approach to vaccine distribution prioritizing high-risk adults.[6] By April 19, 2021, all 50 states and the District of Columbia expanded COVID-19 vaccine eligibility to all individuals ≥ 16 years

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Research in context

Evidence before this work

Since the start of the US nationwide COVID-19 vaccination campaign, we have been closely monitoring the scientific literature (PubMed and *medRxiv*) and press coverage to identify reports describing the community-level impact of COVID-19 vaccination in a real-world setting using the terms COVID-19, vaccin*, model, effective*, impact, and reduc* up to October 31, 2021. To our knowledge, only state-level analyses in the lay press linking vaccine uptake to COVID-19 disease rates have been published. However, more granular analyses that control for important, potentially-confounding community-level factors are urgently needed.

Added value of this work

To assess population-level impact of COVID-19 vaccination, we evaluated the association between county-level COVID-19 vaccine uptake and rates of COVID-19 cases and deaths in the United States controlling for a broad set of county-level environmental, sociodemographic, economic, and health-status-related characteristics. Demonstrating clear population-level impact following vaccine introduction helps to further elucidate and quantify the public-health benefits of vaccination and is critical information for policymakers and the public—many of whom remain skeptical of COVID-19 vaccination.

Implications of all the available evidence

Our results comprehensively showed that US counties with higher proportions of COVID-19 vaccine coverage among individuals ≥12 years of age lower rates of COVID-19 cases and deaths. These findings underscore the importance of continuing to prioritize improving COVID-19 vaccination rates, even in hard to reach communities. Compared to US counties with <50% of residents ≥12 years of age fully vaccinated, counties with at least 80% vaccine coverage had rates of COVID-19 cases and deaths that were 30% and 46% lower, respectively, after adjusting for important county-level differences. This finding showed dose response and persisted even in the period when Delta was predominant.

of age. BNT162b2 was made available for children 12–15 years of age in mid-May 2021.[7] Vaccination, however, has not occurred uniformly in the United States.[8,9] Public health experts are now starting to warn of the formation of “two Americas”— one segment in which vaccination uptake is high and disease remains relatively controlled, and another where vaccination rates remain low and COVID-19 outbreaks continue to occur.[10]

Preliminary real-world effectiveness estimates from the United States,[11−14] Israel,[15,16] the United Kingdom,[17−23] and other locations[24−27] have been published since the introduction of COVID-19 vaccines globally. To our knowledge, however, no studies have evaluated the community-level impact of improving vaccination coverage in any country. In the United States, only crude state-level analyses in the lay press linking vaccine uptake to COVID-19 disease rates have been published.[28−30] The US Centers for Disease Control and Prevention (CDC) has tracked county-level vaccine uptake and COVID-19 cases over time,[31] however, more granular analyses that control for potentially-confounding community-level factors are urgently needed. Demonstrating clear population-level impact following vaccine introduction helps elucidate and quantify the public-health benefits of vaccination and is critical information for policymakers and the public—many of whom remain skeptical of COVID-19 vaccination. To assess population-level impact of COVID-19 vaccination, we evaluated the association between US county-level COVID-19 vaccine uptake and rates of COVID-19 cases and deaths controlling for a broad set of county-level environmental, sociodemographic, economic, and health-status-related characteristics.

Methods

Outcomes

We obtained county-level cumulative numbers of reported and confirmed COVID-19 cases and COVID-19-related deaths from the Johns Hopkins University Coronavirus Resource Center[32] available April 1, 2021 – October 31, 2021. The start of the study period corresponds to the end of a large US COVID-19 wave and when meaningful proportion of individuals ≥ 12 years of age became fully vaccinated (Figure 1). Cumulative county-level rates of COVID-19 cases and deaths through October 31, 2021 were expressed per 100,000 residents.

Exposure

Vaccine coverage data were obtained from CDC’s publicly-available COVID data tracker database[33] where *fully vaccinated* is defined as having received 2 doses of BNT162b2 or mRNA-1273 or one dose of Ad26.COV2.S. Similar to our previous analysis examining county-level predictors of COVID-19 rates prior to the rollout of vaccines,[34] county-level environmental, sociodemographic, economic, and health-status characteristics potentially associated with vaccine uptake, transmission or mortality of COVID-19, or both, were obtained from several publicly-available databases (Supplementary e Table 1). These variables were used as covariates when examining the relationship between COVID-19 vaccine uptake and rates of COVID-19 cases and deaths. Environmental factors included urbanicity (urban *vs* rural), population density, residential crowding (housing with > 1 person per room[35]), and air pollution (particles per

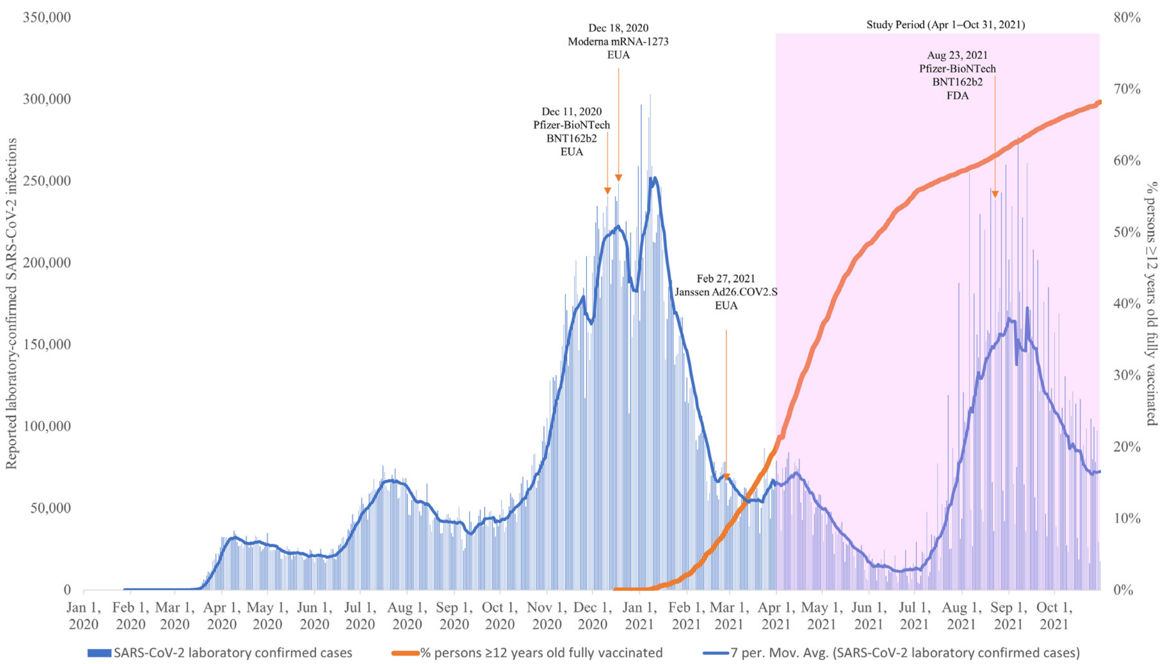

Figure 1. Daily laboratory-confirmed COVID-19 cases in the United States and percent of persons ≥12 years of age fully vaccinated, January 1, 2020 – October 31, 2021.

million [PPM]). Sociodemographic and economic variables included gender, age, race/ethnicity, a residential housing segregation index (0−100 scale, with 100 being most-segregated counties between whites and non-whites[36]), high school education status, unemployment status, median household income, and income inequality (ratio of household incomes at 80th *vs* 20th percentiles[37]). Health-status-related variables included prevalence of diabetes, obesity, and smoking, and, as a potential indicator of risky close-contact behavior, rates of sexually transmitted infections (STI).[38]

To account for levels of natural immunity and prior risk of infection and disease transmission, we also included data about disease activity prior to the study period during two periods corresponding to prior COVID-19 waves: (*i*) January 22, 2020 through October 31, 2020 and (*ii*) September 1, 2020 through March 31, 2021. Finally, as a proxy for adherence to stay-at-home orders and recommendations to minimize travel,[39] we obtained Google Community Mobility Reports describing percent change in county-level travel to non-residential locations during the same periods of the pandemic mentioned above and for our outcome period.[40]

Statistical analysis

We followed Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines for our ecological study. County-level characteristics were summarized with descriptive statistics. Missing county-level characteristics (in < 1% of the US population) were imputed using state-level values (Supplementary eTable 1). Google mobility data, when missing from the least-populous counties due to privacy concerns, were not imputed (Supplementary eTable 1). Using the *menbreg* command in Stata version 14.0 (StataCorp LLC, College Station, Texas), we fit negative binomial regression models (which allow for overdispersion)[41] to estimate the relationship between county-level vaccine coverage and cumulative rates of COVID-19 cases and deaths controlling for differences in county-level environmental, sociodemographic, economic, and health-status-related characteristics. We modeled cumulative rates of cases and deaths by county utilizing the offset command to account for (the natural log of) county population size. We calculated crude and adjusted incidence rate ratios (IRR) for the primary exposure of interest (i.e., county-level percentage of persons ≥ 12 years of age who were fully vaccinated categorized as < 50% [reference], 50−59%, 60−69%, 70−79%, and ≥ 80%). For all models, we included state (n=51; 50 states and the District of Columbia) as a group-level random intercept to account for potential correlation in counties within the same state. We constructed univariate and multivariable models based on a priori selection of covariates likely to confound the relationship between county-level vaccine coverage and COVID-19 case and death rates.[34] We assessed multicollinearity using variance inflation factors (VIF). Finally, we limited our analysis to counties that reported vaccination uptake completeness of ≥ 90% (i.e., that the proportion of fully vaccinated people whose Federal Information Processing Standards

(FIPS) code for identifying county of residence was reported and matched a valid county FIPS code in the jurisdiction was ≥ 90%). In sensitivity analyses we evaluated the impact of (*i*) including counties with ≥ 80% vaccine uptake completeness (*vs* ≥90%) and (*ii*) restricting the outcome period to the time when the Delta variant was predominant (June 1, 2021 to October 31, 2021).

Role of the funding source

The funder of the study approved the study design, and participated in data analysis, interpretation, writing of the report, and decision to publish.

Results

County characteristics

Of the 3142 US counties, 83% (2617/3142) had CDC COVID-19 vaccine uptake reporting completeness of ≥90% (i.e., our study population), accounting for 90% of the US population. Generally, environmental, sociodemographic, economic, and health-status related characteristics of all US counties closely resembled that of counties for which COVID-19 vaccine coverage reporting completeness was ≥ 90%. However, counties with < 90% reporting completeness had, on average, smaller population size, more uninsured individuals, and more Hispanics (Supplementary eTable 2). Google mobility data were not available for 286/2617 (11%) of counties included in our analysis, which accounted for < 1% of the US population.

Among 2617 counties in our study population, county-level percentage of persons ≥12 years of age that were fully vaccinated through October 31, 2021 ranged from < 1% to > 99% with median uptake of 53%. Fifty-nine percent (1564/2671) of counties had ≥ 50% of their vaccine-eligible population fully vaccinated, corresponding to 89% of the US population for whom COVID-19 vaccine coverage reporting completeness was ≥ 90%. Table 1 summarizes county characteristics by percentage of persons ≥ 12 years of age who were fully vaccinated. On average, counties with a lower percentage fully vaccinated had lower median population size (P < 001), were less densely populated (P<.001), were less urban (P < 001), had lower median annual household incomes (P < 001) and higher percentage of uninsured residents (P < 001), and had a higher prevalence of comorbidities such as diabetes, obesity, and current smokers (all P < 001). Counties with higher percentages of fully vaccinated were predominantly in populous areas and large cities along the east and west coast, while areas in the South had few counties with ≥ 80% fully vaccinated (Figure 2).

During the study period, the numbers of laboratory-confirmed COVID-19 cases and deaths in the United States were 15,209,214 and 168,129, respectively. Cases across 2671 counties included in our analysis ranged from 0 to 273,556, with Los Angeles, CA having the most (2% of all US cases). Only 1% (25/2671) reported no cases. No deaths were reported in 4% (101/2671), however, these counties made up < 1% of the US population. The most deaths, 3493, occurred in Los Angeles County, CA.

Multivariable modeling

Univariate and multivariable results were similar (Table 2). In fully-adjusted models, counties with ≥80% coverage had 30% (95%CI: 25−35; P < 001) lower rates of COVID-19 cases and 46% (38−52; P < 001) lower rates of COVID-19-related deaths compared to counties with <50% coverage (Table 2; Figure 3). Multivariable models revealed a dose-response: counties with 70−79% uptake had 20% (95% CI: 16−24; P < .001) and 35% (29−40; P < 001) lower rates of cases and deaths, respectively; counties with 60−69% uptake had 8% (5−11; P < .001) and 20% (15−24; P < 001) lower rates; and counties with 50−59% uptake had 2% (0−4; P =.09) and 8% (4−12; P < .001) lower rates (Figure 3). Sensitivity analyses including counties with reported completeness of ≥80% (instead of ≥ 90%) yielded similar results (Supplementary eTable 3). Results were also similar when restricting the analysis to when the Delta variant was predominant (June 1, 2021 – October 31, 2021) (Supplementary eTable 4). VIFs for variables included in multivariable models (for both cases and deaths) were all < 5 with mean < 2, suggesting no evidence of multicollinearity.

Discussion

US counties with higher proportions of persons ≥12 years of age fully vaccinated against COVID-19 had lower rates of COVID-19 cases and deaths in a period that included the introduction and widespread dissemination of the Delta variant. Between April 1, 2021 and October 31 of 2021, counties with ≥80% of vaccine-eligible persons fully vaccinated had 30% (95%CI: 25−35) lower rates of COVID-19 cases and 46% (38−52) lower rates of COVID-19-related deaths compared to counties with <50% coverage after adjusting for important county-level differences. A strong dose-response was observed for counties with 70−79%, 60−69%, and 50−59% vaccine coverage. To our knowledge, apart from crude analyses in the lay press linking vaccine uptake to COVID-19 disease rates,[28−30] our results are the first to comprehensively show a relationship between community-level vaccine coverage and reductions in rates of COVID-19 cases and deaths. These findings persisted after adjustment for county-level environmental, sociodemographic, economic, and health-status-related characteristics. Further, if the analysis was restricted to the period when the Delta variant

	Percentage of persons ≥12 years of age fully vaccinated against COVID-19					P-value
	<50% Median (IQR) per US county	50–59%	60–69%	70–79%	≥80%	
Number of counties	1053	808	486	203	67	
Outcome Variables (April 1, 2021 – October 31, 2021)						
Laboratory-confirmed COVID-19 cases	1145 (454 – 2410)	1466 (585 – 3753)	3062 (947 – 9004)	5639 (1738 – 18,832)	2566 (653 – 14,266)	<0.001
Rate of laboratory-confirmed COVID-19 cases per 100,000	5966 (4669 – 7143)	5501 (4608 – 6557)	4750 (3998 – 5731)	3828 (3068 – 4826)	3379 (2463 – 4131)	<0.001
Laboratory-confirmed COVID-19 deaths	17 (6 – 34)	19 (7 – 49)	28 (10 – 90)	44 (12 – 154)	26 (5 – 134)	<0.001
Rate of laboratory-confirmed COVID-19 deaths per 100,000	86 (56 – 125)	66 (45 – 96)	46 (30 – 66)	32 (22 – 45)	23 (16 – 45)	<0.001
Environmental exposure variables						
Population size	19,035 (8545 – 38,280)	26,513 (11,344 – 65,209)	64,550 (19,646 – 192,843)	151,391 (37,181 – 490,161)	64,633 (17,582 – 546,695)	<0.001
Population density (persons per square mile of land)	31 (11 – 63)	43 (18 – 105)	92 (25 – 325)	242 (35 – 831)	82 (13 – 1069)	<0.001
Percent urban	27 (– 48)	43 (17 – 64)	63 (36 – 83)	80 (50 – 94)	73 (32 – 95)	<0.001
Percent living in crowded housing (>1 person per room)	2 (1 – 3)	2 (1 – 3)	2 (1 – 3)	2 (1 – 4)	3 (1 – 6)	<0.001
Air pollution (parts per million)	8 (6 – 9)	8 (7 – 9)	8 (6 – 9)	7 (6 – 9)	7 (5 – 8)	<0.001
Sociodemographic and economic exposure variables						
Percent female	50 (49 – 51)	50 (49 – 51)	50 (50 – 51)	51 (50 – 51)	51 (50 – 51)	<0.001
Percent aged 0–19 years	25 (23 – 26)	25 (23 – 26)	24 (22 – 26)	24 (22 – 26)	23 (20 – 29)	0.015
Percent aged 20–29 years	12 (10 – 13)	12 (10 – 13)	12 (11 – 14)	13 (11 – 14)	12 (11 – 14)	<0.001
Percent aged 30–49 years	23 (22 – 24)	23 (21 – 24)	24 (22 – 25)	24 (23 – 26)	25 (22 – 28)	<0.001
Percent aged 50–64 years	20 (19 – 22)	21 (19 – 22)	20 (19 – 22)	20 (18 – 22)	20 (18 – 23)	0.364
Percent aged 65–79 years	15 (13 – 17)	15 (13 – 16)	14 (12 – 16)	13 (11 – 16)	12 (11 – 16)	<0.001
Percent aged ≥80 years	5 (4 – 6)	5 (4 – 6)	4 (4 – 5)	4 (3 – 5)	4 (3 – 5)	<0.001
Percent Non-Hispanic White	85 (69 – 93)	86 (65 – 92)	81 (63 – 90)	73 (55 – 85)	58 (26 – 84)	<0.001
Percent Non-Hispanic Black	2 (1 – 8)	2 (1 – 8)	2 (1 – 9)	3 (1 – 9)	1 (1 – 5)	<0.001
Percent Asian	1 (– 1)	1 (– 1)	1 (1 – 3)	3 (1 – 6)	2 (1 – 6)	<.0001
Percent other race	1 (– 2)	1 (– 1)	1 (– 2)	1 (– 2)	1 (1 – 2)	<0.001
Percent Hispanic	4 (2 – 9)	4 (2 – 8)	6 (3 – 12)	8 (4 – 20)	12 (5 – 26)	<0.001
Residential housing segregation scale (0–100, with 100 being most segregated between Whites and non-Whites	32 (22 – 41)	32 (23 – 41)	34 (26 – 42)	35 (27 – 44)	35 (25 – 45)	<0.001
Percent without high school degree	10 (7 – 15)	12 (8 – 16)	13 (8 – 17)	13 (9 – 17)	12 (10 – 19)	<0.001
Percent unemployed	6 (5 – 8)	7 (5 – 8)	7 (6 – 8)	8 (6 – 9)	8 (6 – 10)	<0.001
Median household income (in 2019 dollars)	49,377 (43,492 – 55,619)	53,836 (47,752 – 60,174)	59,714 (52,715 – 67,229)	67,390 (57,048 – 85,357)	69,113 (50,524 – 98,837)	<0.001
Percentage of median state household income	84 (75 – 94)	88 (78 – 98)	93 (81 – 105)	96 (84 – 116)	104 (82 – 128)	<0.001

Table 1 *(Continued)*

	Percentage of persons ≥12 years of age fully vaccinated against COVID-19					P-value
	<50% Median (IQR) per US county	50−59%	60−69%	70−79%	≥80%	
Income inequality ratio (comparing 80th percentile of house-hold income vs 20th percentile	4 (4 − 5)	4 (4 − 5)	4 (4 − 5)	4 (4 − 5)	5 (4 − 5)	<0.001
Percent uninsured	13 (9 − 16)	9 (7 − 13)	8 (6 − 12)	8 (6 − 12)	9 (5 − 14)	<0.001
Health status to related variables						
Percent with diabetes	13 (10 − 15)	12 (10 − 15)	11 (9 − 13)	10 (8 − 11)	9 (7 − 11)	<0.001
Percent obese	35 (30 − 38)	35 (31 − 38)	33 (30 − 36)	29 (26 − 32)	26 (21 − 31)	<0.001
Percent current smokers	23 (20 − 26)	21 (19 − 24)	20 (18 − 21)	17 (15 − 20)	16 (12 − 19)	<0.001
Rate of sexually transmitted infections per 1000 persons	3 (2 − 5)	3 (2 − 5)	4 (3 − 5)	4 (3 − 6)	4 (3 − 6)	<0.001
Travel outside the home during pandemic						
Percent change in travel outside the home between Feb 15, 2020 to Oct 31, 2020 compared with prepandemic baseline	-7 (-13 − -4)	-8 (-14 − -4)	-8 (-14 − -2)	-9 (-15 − -1)	-19 (-25 − -8)	<0.001
Percent change in travel outside the home between Sep 1, 2020 to Mar 31, 2021 compared with prepandemic baseline	-14 (-20 − -7)	-13 (-18 − -7)	-13 (-18 − -8)	-16 (-23 − -9)	-23 (-31 − -16)	<0.001
Percent change in travel outside the home between Apr 1, 2021 to October 31, 2021 compared with prepandemic baseline	-4 (-17 − 5)	-2 (-14 − 7)	2 (-9 − 11)	1 (-9 − 12)	-11 (-22 − 3)	<0.001
Prior COVID-19 activity						
Laboratory-confirmed COVID-19 cases between Jan 22, 2020 to Oct 31, 2020	201 (60 − 599)	283 (94 − 905)	617 (178 − 2222)	1734 (207 − 7949)	847 (91 − 8351)	<0.001
Laboratory-confirmed COVID-19 cases between Sep 1, 2020 to Mar 31, 2021	1544 (664 − 3124)	2168 (945 − 5034)	4614 (1403 − 14,709)	10,033 (2235 − 33,395)	6494 (898 − 30,543)	<0.001
Laboratory-confirmed COVID-19 deaths between Jan 22, 2020 to Oct 31, 2020	3 (− 11)	4 (1 − 21)	12 (2 − 54)	43 (3 − 220)	20 (1 − 202)	<0.001
Laboratory-confirmed COVID-19 deaths between Sep 1, 2020 to Mar 31, 2021	31 (13 − 62)	40 (18 − 88)	65 (25 − 205)	110 (32 − 392)	111 (11 − 391)	<0.001
COVID-19 Vaccination Uptake						
Percent of persons ≥12 years of age fully vaccinated against COVID-19 as of October 31, 2021	44 (39 − 47)	55 (52 − 58)	64 (62 − 67)	74 (72 − 77)	84 (82 − 89)	<0.001

***Table 1*: US county characteristics by percentage of residents ≥ 12 years of age who were fully vaccinated against COVID-19 (*n*=2263).**
Analysis was conducted among counties with COVID-19 vaccine coverage reporting completeness of ≥90%. *P* value is from a Wilcoxon Rank Sum test comparing medians.

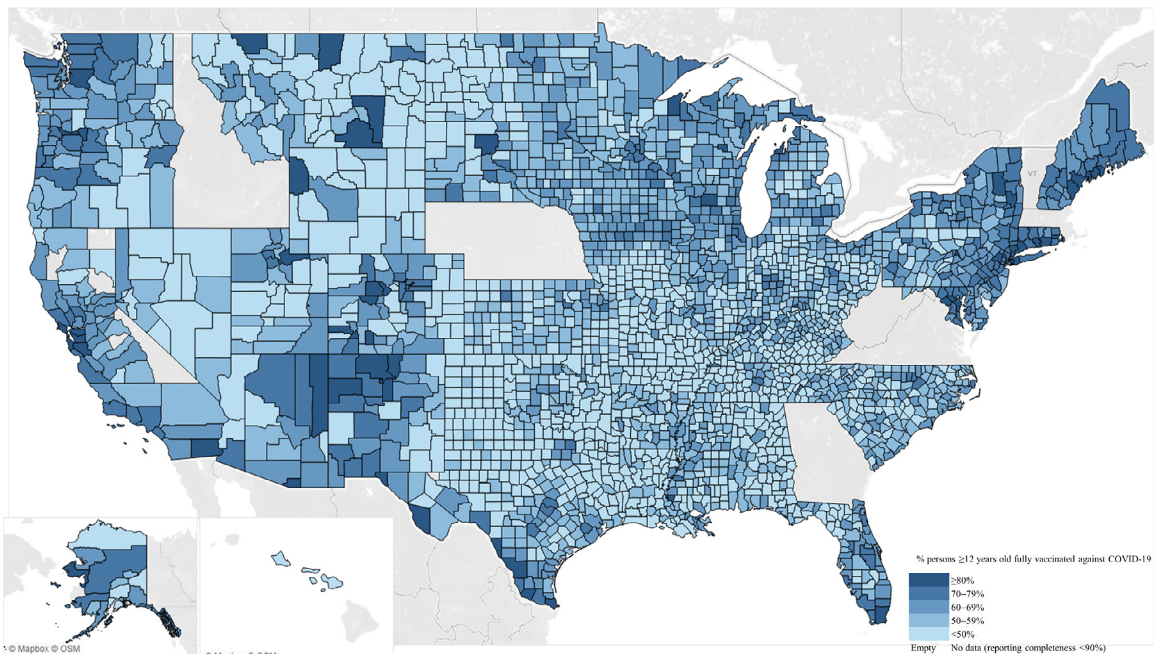

Figure 2. Percent of persons ≥ 12 years of age fully vaccinated against COVID-19 through October 31, 2021. Gray areas are areas where vaccine coverage data were not available or vaccine coverage reporting completeness was < 90%.

was predominant (after June 1, 2021), results were similar.

Exact herd-immunity thresholds for interrupting SARS-CoV-2 transmission are not known, but most experts have suggested that at least 60–70% of the population would need to be being immune via either natural infection or immunization. Interestingly, our results support this, showing that counties that achieve at least 60–70% of vaccine-eligible individuals being fully vaccinated had significantly lower rates of both COVID-19 cases and deaths. Even with highly efficacious vaccines, herd-immunity thresholds may be difficult to reach given significant vaccine hesitancy still exists in many segments of the US population who are vaccine eligible. This is especially concerning with the rapid spread of the highly transmissible Delta and Omicron variants—which will likely drive herd immunity thresholds higher.

Most US communities are still far from reaching ≥70% of individuals ≥12 year of age being fully vaccinated and vaccination rates have started to stagnate.[33] Through October 31, 2021, only 9% of all US counties (accounting for an estimated 36% of the total US population) achieved ≥70% of vaccine-eligible individuals being fully vaccinated. Those that did, tended to be larger in population size, more densely populated, more urban, have higher household income, and a lower percentage of residents who were uninsured or had underlying health conditions or behaviors that increase the risk of developing severe COVID-19. Areas along both the east and west coast had a large share of counties with ≥70% fully vaccinated, while areas in the Southern and Midwestern United States had almost no counties reaching this level of uptake. These findings likely reflect health access issues in poor rural US communities that are driven by healthcare provider shortages, insufficient broadband Internet availability, and longer travel distances–all of which can make getting vaccinated more difficult.[42] These areas also face additional challenges including a lack of trust in the government and heightened concern about the safety of COVID-19 vaccines.[9] Thus, new approaches to reduce vaccine hesitancy and to incentivize vaccination should be explored and will likely require partnership across private and public sectors. This also highlights the potential utility of expanding vaccination to children and ensuring the appropriate utilization of boosters—to help inch closer to and maintain community immunity threshold levels.

Our study has limitations. We did not have vaccine coverage data for all counties. However, we had coverage data (i.e., ≥ 90% reporting completeness) for 83% of all US counties which represented 90% of the US population. Moreover, results were similar if the analysis was expanded to include counties with ≥ 80% vaccine uptake reporting completeness. Another limitation is that our study was ecological and the potential for unmeasured confounding exists. For example, we did not have county-level data about non-pharmaceutical interventions (e.g., mask mandates, business closures, occupancy restrictions). However, we included county-level data describing mobility during the pandemic—which is a proxy for social-distancing measures.[43] Further, we controlled for a wealth of county-level variables and found similar results between crude and adjusted

Model*	Counties (3142)	US Population (328,239,523)	% Total US Population	Percentage of persons ≥12 years of age fully vaccinated against COVID-19							
				50−59%		60−69%		70−79%		≥80%	
				IRR	*P*-value	IRR	*P*-value	IRR	*P*-value	IRR	*P*-value
Cases											
Crude*	2617	295,680,341	90%	0.98 (0.94 − 1.01)	.162	0.91 (0.87 − 0.95)	<.001	0.78 (0.74 − 0.83)	<.001	0.70 (0.64 − 0.77)	<0.001
Environmental	2617	295,680,341	90%	0.97 (0.93 − 1.00)	.05	0.90 (0.86 − 0.94)	<.001	0.76 (0.71 − 0.81)	<.001	0.67 (0.61 − 0.74)	<0.001
Environmental, mobility	2331	294,698,989	90%	0.96 (0.93 − 1.00)	.038	0.90 (0.86 − 0.94)	<.001	0.77 (0.72 − 0.82)	<.001	0.67 (0.61 − 0.74)	<0.001
Environmental, mobility, prior disease activity	2331	294,698,989	90%	0.96 (0.93 − 1.00)	.039	0.90 (0.86 − 0.94)	<.001	0.77 (0.72 − 0.82)	<.001	0.67 (0.61 − 0.74)	<0.001
Environmental, mobility, prior disease activity, sociodemographic and economic	2307	291,505,705	89%	0.97 (0.95 − 1.00)	.019	0.90 (0.88 − 0.93)	<.001	0.78 (0.74 − 0.82)	<.001	0.69 (0.64 − 0.74)	<0.001
Environmental, mobility, prior disease activity, sociodemographic and economic, health-status-related	2307	291,505,705	89%	0.98 (0.96 − 1.00)	.09	0.92 (0.89 − 0.95)	<.001	0.80 (0.76 − 0.84)	<.001	0.70 (0.65 − 0.75)	<0.001
Deaths											
Crude*	2617	295,680,341	90%	0.88 (0.84 − 0.92)	<.001	0.69 (0.65 − 0.72)	<.001	0.51 (0.47 − 0.55)	<.001	0.41 (0.37 − 0.47)	<0.001
Environmental	2617	295,680,341	90%	0.91 (0.87 − 0.95)	<.001	0.74 (0.70 − 0.78)	<.001	0.55 (0.50 − 0.59)	<.001	0.42 (0.37 − 0.48)	<0.001
Environmental, mobility	2331	294,698,989	90%	0.91 (0.87 − 0.95)	<.001	0.75 (0.71 − 0.80)	<.001	0.57 (0.52 − 0.62)	<.001	0.45 (0.40 − 0.51)	<0.001
Environmental, mobility, prior disease activity	2331	294,698,989	90%	0.91 (0.87 − 0.95)	<.001	0.75 (0.71 − 0.80)	<.001	0.57 (0.52 − 0.61)	<.001	0.43 (0.38 − 0.49)	<.001
Environmental, mobility, prior disease activity, sociodemographic and economic	2307	291,505,705	89%	0.91 (0.87 − 0.95)	<.001	0.78 (0.74 − 0.82)	<.001	0.62 (0.57 − 0.67)	<.001	0.52 (0.46 − 0.59)	<.001
Environmental, mobility, prior disease activity, sociodemographic and economic, health-status-related	2307	291,505,705	89%	0.92 (0.88 − 0.96)	<.001	0.80 (0.76 − 0.85)	<.001	0.65 (0.60 − 0.71)	<.001	0.54 (0.48 − 0.62)	<.001

***Table 2*: Univariate and multivariable models describing the relationship between rates of COVID-19 cases and deaths and the percentage of residents ≥12 years of age who were fully vaccinated against COVID-19 (n=2263)*.**

CI = confidence interval. IRR = incidence rate ratio. Analysis was conducted among counties with COVID-19 vaccine coverage reporting completeness of ≥90%. Table S1 in the *Supplementary Appendix* describes each variable included in the model in detail.

* Negative binomial regression models were used. All models, including the crude model, include the county population size and include state (n=51 including the District of Columbia) as a random effect. Counties with ≥12 years of age COVID-19 vaccine coverage < 50% served as the reference group in all comparisons.[†]Environmental variables include urbanicity.

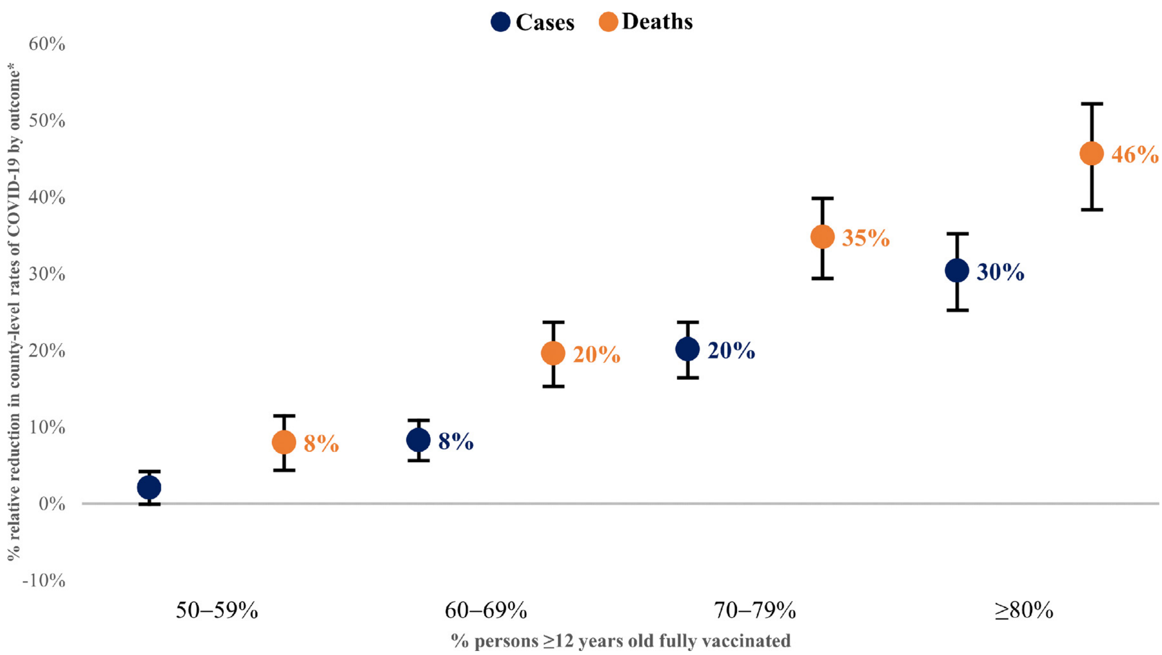

Figure 3. Percent relative reduction and 95% confidence intervals in *US* county-level rates of COVID-19 cases and deaths corresponding to the percentage of persons ≥ 12 years of age who are fully vaccinated against COVID-19. Results are from fully-adjusted multivariable models comparing counties with < 50% versus 50–59%, 60–69%, 70–79%, and ≥ 80% of persons ≥ 12 years of age fully vaccinated against COVID-19. Analysis excludes counties where vaccine coverage reporting completeness was < 90%.

models. Another limitation is that our data—apart from our outcome variables (rates of COVID-19 cases and deaths), primary exposure of interest (COVID-19 vaccine coverage), and mobility data—were historical. Thus, data about unemployment and health insurance status, household income, and other sociodemographic and environmental factors did not necessarily reflect the situation during our study period. Additionally, not all exposure data came from the same year. However, we obtained the most-recent estimates from all data sources and most of the data describing county-level characteristics were based on estimates from the last two years. Four percent of counties reported no deaths. These counties, however, accounted for <1% of the US population. Moreover, negative binomial regression models, which we used in our analysis, allow for overdispersion (which can result from excess zeros) and straightforward interpretation, and have been shown to model count data with zeros as well as other zero-inflated Poisson models.[44] Our findings are not vaccine-specific. Based on CDC data through June 2021, of the roughly 374 million COVID-19 vaccine doses distributed in the United States, 53% were BNT162b2, 44% were mRNA-1273, and only 3% were Ad26.COV2.S.[4] Thus our results largely reflect the impact of being fully vaccinated with mRNA vaccine. Finally, we did not have data describing county-level SARS-CoV-2 testing practices. If there was a correlation between county-level vaccination coverage and testing rates, this could have biased our results. In addition to rates of COVID-19 cases, however, we also included county-level COVID-19-related death rates which are less sensitive to testing practices.

Conclusions

Our results showed that US counties with higher proportions of persons ≥ 12 years of age fully vaccinated against COVID-19 had substantially lower rates of COVID-19 cases and deaths. Results were similar if the analysis was restricted to the period when Delta was predominant (i.e., after June 2021). Thus, communities should continue to prioritize improving COVID-19 vaccination rates, even in hard-to-reach places. Without sustained public-health interventions, the gap in rates of COVID-19 cases and deaths between well-vaccinated and poorly-vaccinated communities is likely to widen as we enter the winter viral season. Finally, similar analyses will be needed in the future to understand the impact of booster doses, especially against novel variants of concern like Omicron.

Contributors

JMM and DLS conceived the study. JMM, FK, and SP wrote the first draft of the protocol and manuscript. FK and JMM cleaned and analyzed the data and conducted the analysis. All authors contributed to study design, drafting the protocol, revising the manuscript for important intellectual content, were responsible for the decision to submit for publication, and approved the final submitted version of the manuscript. All authors accessed and verified the data underlying the study and take responsibility for the data.

Data sharing statement

All data utilized in this analysis are publicly available with sources disclosed in the Supplement.

Editorial disclaimer

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Declaration of interests

At the time of writing, all authors were employees of and hold stock and/or stock options in Pfizer Inc. The participated in data analysis, interpretation, writing of the report, and decision to publish.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2022.100191.

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