

Impact of healthcare capacity disparities on the COVID-19 vaccination coverage in the United States: a cross-sectional study



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Summary

Background The impact of the COVID-19 vaccination campaign in the US has been hampered by a substantial geographical heterogeneity of the vaccination coverage. Several studies have proposed vaccination hesitancy as a key driver of the vaccination uptake disparities. However, the impact of other important structural determinants such as local disparities in healthcare capacity is virtually unknown.

Methods In this cross-sectional study, we conducted causal inference and geospatial analyses to assess the impact of healthcare capacity on the vaccination coverage disparity in the US. We evaluated the causal relationship between the healthcare system capacity of 2417 US counties and their COVID-19 vaccination rate. We also conducted geospatial analyses using spatial scan statistics to identify areas with low vaccination rates.

Findings We found a causal effect of the constraints in the healthcare capacity of a county and its low-vaccination uptake. Counties with higher constraints in their healthcare capacity were more probable to have COVID-19 vaccination rates ≤ 50 , with 35% higher constraints in low-vaccinated areas (vaccination rates ≤ 50) compared to high-vaccinated areas (vaccination rates > 50). We also found that COVID-19 vaccination in the US exhibits a distinct spatial structure with defined “vaccination coldspots”.

Interpretation We found that the healthcare capacity of a county is an important determinant of low vaccine uptake. Our study highlights that even in high-income nations, internal disparities in healthcare capacity play an important role in the health outcomes of the nation. Therefore, strengthening the funding and infrastructure of the healthcare system, particularly in rural underserved areas, should be intensified to help vulnerable communities.

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Introduction

After more than 2 years into the pandemic, as of September 12, 2022, COVID-19 has caused 6,515,039 deaths worldwide, and the US has reported 1,050,426 of

these deaths.¹ Among high-income nations, the US has one of the highest COVID-19 mortality rates. One of the potential reasons for this is that the US has failed to achieve vaccination levels similar to those in other

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Research in context**Evidence before this study**

We searched PubMed and Web of Science for publications on COVID-19 vaccination in the US, published between May 1, 2021, and March 1, 2022. We used the keywords “COVID-19”, “determinants of COVID-19 vaccine uptake”, “COVID-19 vaccination campaign in the US”, and “COVID-19 vaccine disparities” and searched for articles in English. We found that most studies focused on assessing the impact of vaccine hesitancy and other social and behavioral determinants of vaccine uptake in the US. However, little is known about the impact of structural determinants such as the local healthcare capacity in the COVID-19 vaccination coverage in the country.

Added value of this study

To our knowledge, this is the first study that examines the impact of the healthcare capacity as a determinant of the COVID-19 vaccination coverage disparities in the US. Using COVID-19 vaccine data from 2417 US counties, we assessed the association between healthcare capacity and the vaccination coverage at the county level using causal inference and geospatial analyses.

Implications of all the available evidence

Although vaccination hesitancy has played an important role in driving the disparities in vaccination uptake in the US, our results suggest that healthcare system capacity plays an important and overlooked role as well. We found a positive association between the deficient healthcare capacity and the low vaccination uptake at the US county level. We also found that COVID-19 vaccination in the US exhibits a distinct spatial structure with defined clustered areas of population with a low percentage of vaccination. The COVID-19 pandemic has uncovered the impact of healthcare disparities in the country, and it has exposed the weakness in rural healthcare. In high-income nations like the US, disparities in access to healthcare and healthcare capacity are internal determinants that play a key role in the health outcomes of the whole country. Therefore, it is imperative that federal, state, and county decision-makers consider the importance of strengthening the healthcare structure in these vulnerable low-vaccinated areas to increase vaccination uptake and relieve the burden that the pandemic has brought to these vulnerable communities.

developed countries. As of September 2022, only 68% of the US population has been fully vaccinated against COVID-19, and this value is low compared to several high-income nations.¹ Although this percentage is very close to the 70% goal that the US government established, if vaccination coverage is examined at the state level, the differences are striking. Vaccination coverage in the US is geographically heterogeneous. While some areas of the US have achieved full vaccination in more than 80% of their population, other regions still lag behind with rates below 50%.² A successful long-term management of the pandemic can only be achieved if vaccination uptake is substantially increased to diminish this spatial heterogeneity. However, it is necessary first to understand the factors driving the disparities in vaccination coverage and uptake in the country.

Vaccination hesitancy has been broadly discussed as a key driver of the low vaccination uptake, especially in the US.³ However, COVID-19 hesitancy in the country has been estimated to be around 20%, a percentage far below the actual percentage of unvaccinated people,⁴ suggesting that additional unidentified key factors are behind the low vaccination rates observed in some areas of the US. It is known that the pandemic has disproportionately affected Americans living in socially vulnerable areas.^{5,6} In fact, areas with low vaccination in the US experienced the highest mortality rates during the recent Delta and Omicron waves.⁷ Social vulnerability arises from a combination of socio-economic factors that include limited healthcare resources and

barriers to accessing these resources.⁸ The impact of poor healthcare capacity on the vaccination coverage is a factor that has been proposed to play a major role in low-income countries, but not in high-income ones as the US.⁹ However, the COVID-19 pandemic has shown that the scenario is much more complex. High-income countries with better healthcare resources have had, in fact, a higher burden of COVID-19 cases, related hospitalisations and deaths than low-income countries with fewer healthcare resources.¹⁰ Although the US, as a nation, ranks number one in the Global Health Security Index that measures the capacity of a country to prepare for epidemics and pandemics (<https://www.ghsindex.org/country/united-states/>),^{11,12} at the local level the landscape is different. The healthcare system in the US is characterised by substantial variation in local infrastructure and capacity, with many underserved communities lacking adequate access to healthcare.^{5,13,14} These disparities include the number of healthcare workers and number of hospitals per capita, health insurance coverage, and healthcare funding, which have influenced the spatial structure of several health problems in the US, including chronic and mental health diseases.^{14,15} However, how much these healthcare capacity disparities have affected the management of the COVID-19 pandemic is unknown.

In this study, we conducted causal inference and geospatial analyses to assess the impact of the local healthcare capacity on vaccination coverage disparities in the US at the county level. Understanding the impact

of healthcare capacity on vaccination coverage disparities will help refine local strategies to increase vaccination coverage in areas with the highest health needs.

Methods

Variables and data sources

Institutional review board approval and informed consent were not necessary for this cross-sectional study because all data were deidentified and publicly available (Common Rule 45 CFR §46). This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. We used a causal inference analysis to evaluate the causal relationship between a *treatment* and an *outcome*, with the *treatment* defined as the healthcare system capacity at the county level measured by the Resource-Constrained Health System (RCHS) index, and the *outcome* defined as a COVID-19 vaccination rate less than or equal to 50% of the county's population. The RCHS index is a measure that integrates indicators of low healthcare system capacity with indicators of healthcare system weakness at the county level. These indicators include healthcare workforce per capita, healthcare infrastructure per capita, healthcare spending per capita, and care quality indicators (Table 1). A high RCHS index value indicates a weak healthcare system capacity, whereas a low value indicates a strong healthcare system of the county. The RCHS index is one of the five measures comprising the recently released Surgo COVID Vaccine Uptake Index (CVAC; <https://vaccine.precisionforcovid.org>).¹⁶ Vaccine coverage was measured as the proportion of the fully vaccinated population per US county, defined as the percentage of people who have received two doses of the mRNA Pfizer-BioNTech or Moderna vaccines, or a single dose of the Janssen/Johnson & Johnson vaccine. Data for cumulative full vaccination rates in the total population at a county level were obtained from the Centers for Disease Control and Prevention (CDC) COVID data tracker for the contiguous US (https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=all_states&data-type=CommunityLevels).¹⁷ We excluded the states of Colorado, Georgia, Texas, Virginia, and West Virginia due to incomplete or unreliable vaccination data. As a result, data from 2417 counties (77% out of the 3143 in the continental US) were included in the analysis. Counties were classified as rural or urban based on the 2013 National Center for Health Statistics.^{18,19} Cumulative vaccination rates were estimated as of March 31, 2022. For the causal inference analysis, counties were aggregated into low (vaccination rate county median $\leq 50\%$) and high ($>50\%$) vaccination coverage groups. Based on the literature review and on the US COVID-19 Vaccine Coverage Index, we incorporated the Social Vulnerability Index (SVI; <https://www.atcdr.cdc.gov/placeandhealth/svi/index.htm>)²⁰ and the

Healthcare Access Barriers Index (HABI; <https://vaccine.precisionforcovid.org/>)¹⁶ as common causes that influence the *treatment* and *outcome* in the causal analysis. Vaccine hesitancy data from the CDC at the county level (<https://data.cdc.gov/stories/s/Vaccine-Hesitancy-for-COVID-19/cnd2-a6zw/>).²¹ was included as a modifier of the *outcome*. A detailed description of the indexes and data sources used for this study is presented in Table 1. Vaccination level area comparisons relative to healthcare capacity were conducted using the average number of medical doctors per 1000 people (<https://www.ruralhealthinfo.org/data-explorer?id=197>),²² the average number of intensive care unit (ICU) beds per 1000 people (<https://www.kaggle.com/datasets/jaimeblasco/icu-beds-by-county-in-the-us>),²³ and the other health-related indices including RCHS, SVI, and HABI. Statistical comparisons between the two vaccination level groups for these variables were conducted using generalized linear mixed-effects models with the state as a random variable to adjust for the variability merging at the state level generated by factors such as healthcare policies and spending.

Causal inference analysis

Randomised controlled trials offer the most plausible unbiased estimates of the effect of a given treatment on a specific health outcome.²⁴ However, epidemiological experiments of that type are not possible due to ethical, feasibility, or time limitations.²⁵ Causal inference approaches using epidemiological observational data are perhaps the best alternative to estimate the causal association between a *treatment* and a health *outcome* in an epidemiological context.^{26,27} In this study, we implemented a causal inference approach to assess, in an unbiased manner, the average effect of the constraints in the healthcare system capacity of a US county, measured by the RCHS index, over the county's COVID-19 vaccination rate.

We designed a Directed Acyclic Graph (DAG), as illustrated in Fig. 1. This non-parametric graphical model visualization represents the assumed causal relationships between the established variables of interest. We included in the DAG the SVI and the HABI as two important confounders that could have a causal effect on both, the *treatment*, the RCHS index, and the *outcome*, low vaccination rate ($\leq 50\%$) estimated as of March 31, 2022. Another variable included in the DAG was vaccination hesitancy, which was classified as a modifier affected by the RCHS index and affecting the vaccination outcome. An unobserved variable, *U*, was also included in the causal analysis to account for the unmeasured variables that can be potential confounders. We implemented a correlation analysis to test the conditional independences assumed in the DAG in the dataset, and also assuming a linear relationship between

Variable	Description	Source
Vaccination rate	Cumulative full vaccination rates in the total population at a county level	CDC COVID data tracker for the contiguous US https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=all_states&data-type=CommunityLevels
Resource-Constrained Health System Index (RCHS)	This index is composed by two subthemes using the following indicators: 1) <u>Low Healthcare System Capacity</u> - Provider workforce per capita (Total active federal and non-federal Medical Doctors, Doctors of Osteopathy, Advanced Practice Registered Nurses, Physician Assistants, and Pharmacists) - Infrastructure for vaccine administration per capita (Hospitals, Urgent Care Facilities, Veterans Health Administration Medical Facilities, Federally Qualified Health Centers and look-alike, Pharmacies) 2) <u>Weak Healthcare System</u> - AHRQ Prevention quality indicator - Health spending per capita - Total healthcare funding (CDC COVID Funding, Public Health Emergency Preparedness (PHEP) funding, CDC grant funding for Immunization and respiratory Diseases and Vaccines for children, State Public Health Funding)	Surgo Ventures - The US COVID-19 vaccine coverage index Original source for each indicator can be found at https://cvi-data-output.s3.amazonaws.com/assets/CVAC_Methodology_Feb2021.pdf
Healthcare Accessibility Barriers Index (HABI)	This index is composed by two subthemes using the following indicators: 1) <u>Barriers due to Cost</u> - Proportion of individuals without health insurance coverage - Proportion of adults who reported that there was a time in the past 12 months when they needed to see a doctor but could not because of cost. 2) <u>Barriers due to Transportation</u> - Households without a vehicle - Transit Connectivity Index	
Social Vulnerability Index (SVI)	SVI indicates the relative vulnerability of every county ranking 15 social factors, including high poverty, unemployment, education, crowded housing, minority status, and disability	https://www.atsdr.cdc.gov/placeandhealth/svi/documentation/pdf/SVI2018Documentation_01192022_1.pdf
Vaccine Hesitancy	Percentage of the population in each county that may be vaccine hesitant or unsure about vaccination	Assistant Secretary for Planning and Evaluation (ASPE), U.S. Census Bureau's Household Pulse Survey (HPS) https://data.cdc.gov/stories/s/Vaccine-Hesitancy-for-COVID-19/cnd2-a6zw/

Table 1: Summary of the variables included in the analysis.

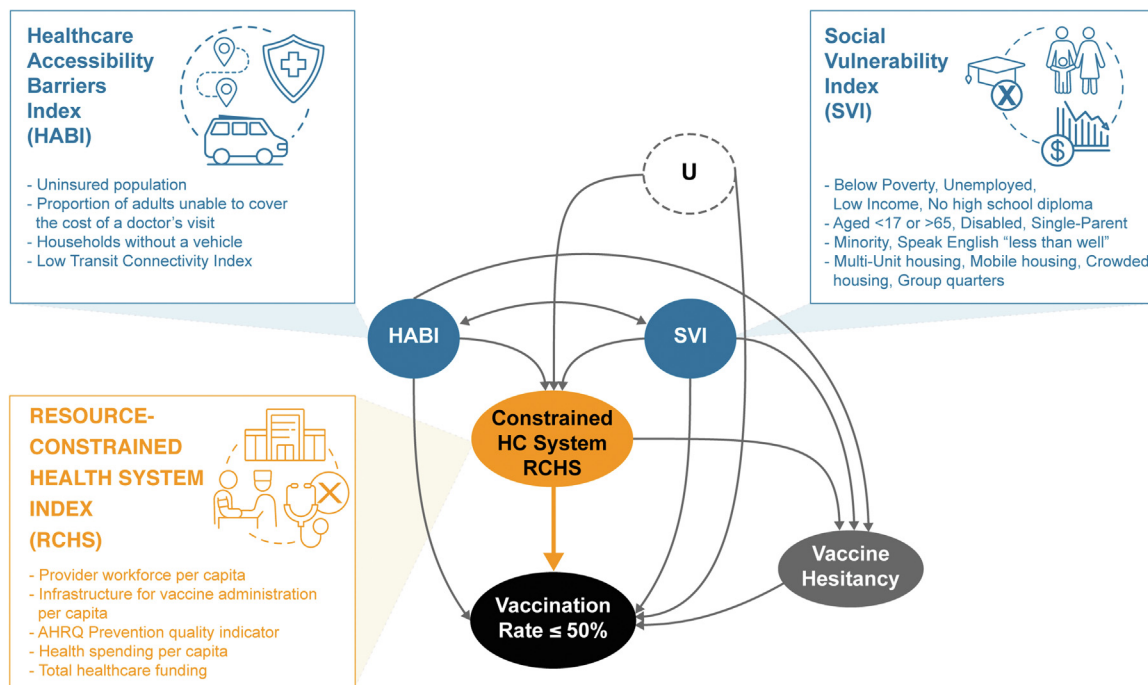


Fig. 1: Directed Acyclic Graph (DAG) used to estimate the causal effect of the resource-constrained health system index (RCHSI) on the low-vaccination coverage $\leq 50\%$ of a county. The orange arrow represents the causal association of interest. Variables considered as common causes that affect the treatment and the outcome simultaneously are shown in blue (*healthcare accessibility barriers index (HABI)* and *social vulnerability index (SVI)*). Vaccine Hesitancy was classified as a modifier affected by the RCHS index and affecting the vaccination outcome. The U variable represents unmeasured variables that can be potential confounders. Inset boxes detail the indicators used for calculating each of the indexes.

the treatment and the outcome since the treatment is a continuous variable and the outcome is a binary variable in our analysis. We conducted the analysis using the package DAGitty of R version 0.3-1.²⁸ No conditional independences were identified in the DAG.

The statistical estimand of the causal analysis, defined as the numerical value of the effect of the RCHS index over the occurrence of a county in the low-vaccination group (vaccination rate $\leq 50\%$) was tested in a set of four variations of the double machine learning algorithm²⁹ using the Python modules DoWhy version 0.6³⁰ and EconML version 0.13.³¹ We assessed the effect of the RCHS index on the low vaccination coverage ($\leq 50\%$) at the county level using an Average Treatment Effect (ATE). Additionally, we estimated the effect of the RCHS index, conditioned by Hesitancy, using the Conditional Average Treatment Effect (CATE). A detailed description of the calculations and testing of the estimand can be found in the [Supplementary Material](#). We implemented five sensitivity tests to validate the causal association between the RCHS index and low vaccination rate ($\leq 50\%$), including the addition of a random common cause, the addition of an unobserved common cause, the replacement of a random subset, running the estimate on a random sample of the data containing measurement error in the confounders

(Bootstrap refutation), and adding a placebo treatment. The dataset and the Python and R scripts used for this study are available at: https://github.com/juandavidgutier/healthcare_capacity_disparities.

Geospatial analysis

Spatial analyses were conducted to identify and map the geographical locations of areas with low COVID-19 vaccination coverage in the US. The spatial structure of vaccination uptake was analysed using a spatial scan statistical analysis of cumulative vaccination at the county level as of March 31, 2022, implemented in the SaTScan software.^{32,33} This methodology has become the most widely used test for clustering detection in epidemiology,³² and its efficiency and accuracy are well documented.^{34,35} We used scan statistics to identify geographical locations where the number of fully vaccinated individuals was lower than expected under the null hypothesis of a random spatial distribution of the vaccinated individuals across the country.³³ Then, we evaluated their statistical significance by gradually scanning a circular window that spans the study region. We analysed vaccination uptake using the SaTScan Poisson model with the size of the population at risk by location (county) included as an offset. Briefly, the

identification of coldspots (areas with low vaccination rates) using the Poisson model implemented in SaTScan is achieved by testing each potential cluster against the null hypothesis that the distribution of cases (fully vaccinated individuals was proportional to the population size [no clustering] using likelihood ratio and t-tests).³² An associated *p*-value of the statistics was then determined through Monte Carlo simulations and used to evaluate whether fully vaccinated individuals are randomly distributed in space. A coldspot was identified if the *p*-value was less than 0.05. After a cluster was identified, the strength of the clustering was estimated using the relative risk (RR) within the cluster versus outside the cluster. Furthermore, temporal trends of vaccination rates were analysed by aggregating the counties within vaccination coldspots and counties outside the coldspots. Retrospective temporal vaccination rates within and outside the coldspots were estimated for each month from April 2021 to March 2022. All geographic information system (GIS) analyses and cartographic displays were performed with ArcGIS Pro version 2.9³⁶ software. Plots were built using GraphPad Prism 9.

Role of the funding source

No funding to declare.

Results

As of March 31, 2022, 166,239,504 (63.1%) of 263,365,882 residents living in the counties included in the analyses were fully vaccinated. We estimated that 1160 (48.0%) out of the 2417 counties included in the study had a vaccination rate equal to, or lower than 50%, with 36,074,972 individuals residing in these low-vaccination counties. The average RCHS index was 0.50 (95% confidence interval [CI] 0.48–0.52) in lower-vaccinated and 0.37 (95% CI 0.35–0.38) in higher-vaccinated counties (Table 2). Likewise, SVI was 0.53 (95% CI 0.25–0.56) in low-vaccinated and 0.44 (95% CI 0.42–0.46) in high-vaccinated counties. Moreover, the average number of medical doctors per 1000 in low-vaccinated counties was 0.19 (95% CI 0.18–0.20)

compared to 0.81 (0.76–0.85) in high-vaccinated ones. Similarly, the average number of ICU beds per 1000 in low-vaccinated counties was 0.12 (0.11–0.14) compared to 0.18 (95% CI 0.17–0.19) ICU beds in high-vaccinated ones.

Casual inference analysis

We found nonconditional independences between the variables used in the DAG implemented to estimate the effect of the RCHS index on the low vaccination coverage of a county (vaccination rate county median ≤ 50%). The machine learning algorithm with the largest RScorer was double machine learning (RScorer = -0.0025). The average ATE of the RCHS index on having a vaccination rate (≤50%) was 0.37 (95% CI: 0.23–0.50). The RCHS index is a continuous treatment variable ranging from 0 to 1, where 0 indicates no resource-constrained healthcare system. Taking this into account, the ATE needs to be interpreted as a linear effect on the risk scale. Thus, our results indicate that an increase of 0.01 in the RCHS index increases by 0.37% the probability of a county to be included in the low vaccination coverage group (vaccination rate county median ≤ 50%). The estimation of the CATE of the RCHS index on the low vaccination coverage conditioned by Vaccine Hesitancy showed no change in magnitude for different values of hesitancy rate (Supplementary Fig. S1 in Supplementary Materials), indicating that Vaccine Hesitancy does not modify the effect of the RCHS index on the low vaccination of a county. Further results from the causal inference analysis are summarized in Supplementary Materials.

Geospatial analysis

SatScan identified 38 clusters with low vaccination rates (vaccination coldspots) with an RR ranging from 0.66 to 0.98. These coldspots were distributed across the entire country, comprising 1300 out of the 2417 counties included in the study, with 930 (71.5%) of these counties being rural, compared to 612 (54.8%) of rural counties located outside the vaccination coldspots. As of March 31, 2022, the vaccination rate within the

Index	Low vaccination coverage (95% confidence interval)	High vaccination coverage (95% confidence interval)	<i>p</i> value
Resource-Constrained Health System	0.50 (0.48–0.52)	0.37 (0.35–0.38)	<0.001
Healthcare Access Barriers	0.55 (0.53–0.57)	0.39 (0.38–0.41)	<0.001
Social Vulnerability	0.53 (0.52–0.56)	0.44 (0.42–0.46)	<0.001
Vaccine hesitancy	0.22 (0.21–0.23)	0.17 (0.16–0.18)	<0.001
Medical doctors per 1000 people	0.19 (0.18–0.20)	0.81 (0.76–0.85)	<0.001
Intensive care unit beds per 1000 people	0.12 (0.11–0.14)	0.18 (0.17–0.19)	<0.001

Table 2: Healthcare capacity comparisons between low-vaccination (vaccination rate county median ≤ 50%) and high-vaccination (>50%) areas.

coldspots was 52.1% compared to 68.1% outside these areas. Coldspots with a RR between 0.66 and 0.73 (the lowest RR range), were located in the states of Nevada, Montana, North and South Dakota, and Nebraska, with most of them grouped in the Rocky Mountain region. Vaccination coldspots with an RR between 0.74 and 0.78 were located in Idaho and in several states located in the Gulf Coast and Lower Atlantic regions, including Oklahoma, Arkansas, Mississippi, Alabama, and New Mexico. Coldspots with an RR between 0.79 and 0.83 were in the Midwest and South regions, in the states of Kansas, Indiana, Ohio, Kentucky, Tennessee, and Louisiana (map in Fig. 2).

The vaccination rate was 24.9% within the low vaccination clusters, compared to 34.5% outside the coldspots at the early stage of the vaccination rollout campaign in April 2021 (area plot in Fig. 2). A slower rise in the vaccination rates within the coldspots was observed during the months of May and June 2021, with 6.4% and 3.7% increments, compared to 11.5% and 6.0% increments during the same period outside the vaccination coldspots. The percentage of the vaccinated population surpassed 50% in July 2021 in counties outside the vaccination coldspots, while the same rate was reached 6 months later (January 2022) in counties within the coldspots (bar chart in Fig. 2).

Discussion

Being one of the wealthiest nations in the world, it could be assumed that the capacity of the US healthcare

system is not a limiting factor in shaping the national heterogeneous vaccination COVID-19 uptake observed in the US. In this ecological study, we found that that is not the case. Our causal and geographical analyses unveiled a striking association between the disparities in the healthcare system capacity and the disparities in COVID-19 vaccination coverage. After controlling for other factors including vaccine hesitancy, health access barriers, and social vulnerability, we estimated that an increase of 0.01 (1%) in the Resource-Constrained Health System (RCHS) index increases the probability of a county to be in the group of low vaccinated counties ($\leq 50\%$ vaccination rate) by 0.37%. Likewise, low-vaccination areas had an average county RCHS index of 0.5, 35% higher compared to high-vaccination areas (RCHS = 0.37). In other words, our analysis showed that low-vaccination areas in the US were characterised by having a smaller health provider workforce per capita, a smaller healthcare infrastructure per capita, lower preventive care, and lower healthcare funding. Likewise, these low-vaccination areas were also characterized by having a higher average Social Vulnerability Index, and a higher average Healthcare Access Barrier Index, lower numbers of medical doctors and ICU beds per 1000 people compared to high-vaccination ones.

Regarding the spatial structure of COVID-19 vaccination, we found that the US exhibits defined clustered low-vaccination areas (coldspots) distributed mainly among 17 states (NV, MT, WY, ND, SD, NE, NM, OK, MS, AL, AR, LA, TN, KY, KS, IN, and OH). Interestingly, all of these 17 states are at the bottom of the

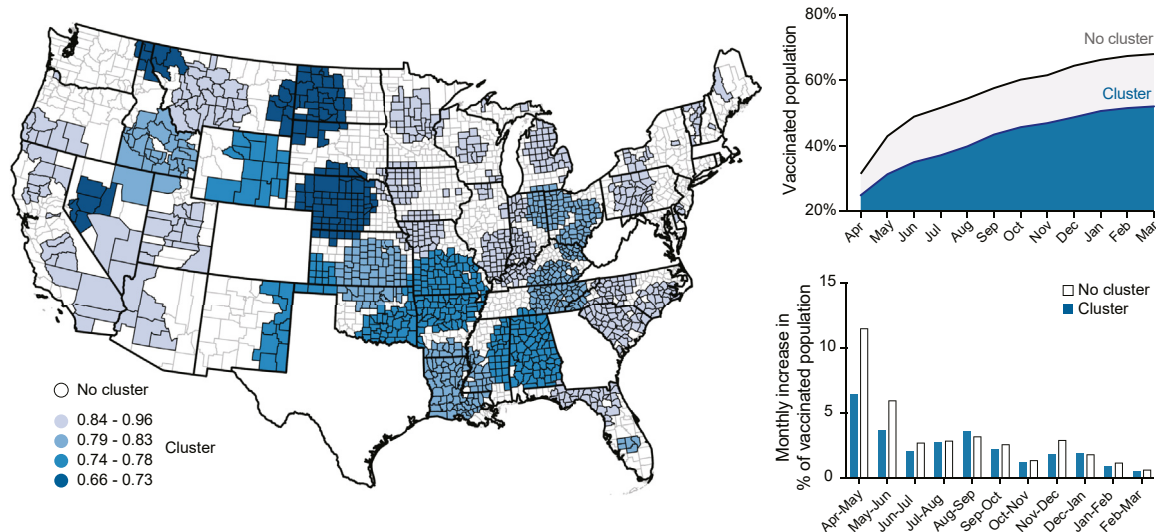


Fig. 2: Spatial structure of COVID-19 vaccine coverage in the US. The map on the left illustrates the geospatial location of the COVID-19 vaccine coldspots. The strength of the coldspot (relative risk of being vaccinated) is illustrated in a blue colors scale, with the lowest relative risk for being vaccinated illustrated in dark blue, and the highest relative risk for being vaccinated among the coldspots illustrated in light blue. The plot in the upper right corner illustrates the vaccination time trend within the clusters (blue) and outside the clusters (light grey). The plot in the lower right corner illustrates the monthly increase in the percentage of the vaccinated population within the clusters (blue bars) and outside the clusters (light grey bars) from April 2021 to March 2022.

ranking for healthcare access, healthcare quality, and public health in the US.³⁷ In addition, 12 of these states fall below the US average poverty rates with 12%–20% of their population living in poverty.³⁸ Adding all these factors, it is not surprising that many of these states have been at the epicenter of the different epidemic waves in the country.^{5,7} At the county level, we found that more than 71% of the counties inside coldspots were rural counties. These counties were mainly located inside geographically distinct regions including the Rocky Mountains, the Gulf Coast, the lower Atlantic region, and the Midwest. Challenges imposed by the local geography of these regions could be an important limiting factor for the deployment of vaccines and for the access of residents to rural clinics.⁵ Collectively, these findings show the economic and health vulnerability of primarily rural communities residing in the low-vaccinated areas in the US. Rural communities within the states identified in this study may be facing challenges that exacerbate the lower rates of COVID-19 vaccination. These challenges include but might not be limited to, restricted access to testing, vaccine and treatment supplies, and number of healthcare workers.³⁹

With COVID-19 incidence and mortality increasing throughout 2020, the beginning of the immunisation campaign faced unprecedented challenges that went beyond those of standard vaccination programs. Our analysis shows a clear difference between the vaccination rates in those counties that would become vaccination coldspots one year later by the end of 2021. Strikingly, the rate at which vaccination uptake increased within these coldspots was much slower than the rate in the counties outside of these low-vaccinated areas, particularly at the early stage of the vaccination rollout. Whereas the percentage of the vaccinated population outside the vaccination coldspots increased from 31.5% in April 2021 to 43.0% in May and reached more than 50% of the vaccination rate by July 2021, the vaccinated population within the coldspots was only 25% in April 2021, increased to 31.4% in May, and reached more than 50% vaccination rate only by January 2022. The slower vaccination uptake inside the coldspots was evident during the first 3 months of the period analysed. It was relatively similar both outside of, and within the coldspots after July 2021. This suggests that pre-existent barriers in these coldspots counties played, from the beginning, an essential role in limiting the number of people who were vaccinated. Our results showed that counties inside the coldspots face a more resource-constrained health system, suggesting that critical healthcare capacity and infrastructure, and barriers to access to adequate healthcare were essential determinants of vaccination uptake. The influence of these determinants was strongly relevant during the early stages of the vaccination campaigns, a period in which vaccination availability, distribution, and prioritization needed a strong healthcare structure to

aversively deliver the maximum number of doses in the shortest time. However, further studies need to be conducted to completely understand these COVID-19 vaccination disparities during the early stage of the vaccination rollout in the US.

Our study had limitations worth noting. An ecological study like the one presented here is an approach for examining the association between factors and diseases, performing population analyses in specific areas, and they do not correspond to individual risk and associations. It is difficult to adjust for all potential confounding factors due to the lack of individual data in ecological studies, and thus our results need to be interpreted with caution. Moreover, we recognize that the assumption about the linearity in the relationship between the treatment and the outcome is another limitation of our study. Further research on this topic could implement causal frames of the type of dose–response curve to analyse the treatment and outcome as continuous variables.⁴⁰ Implementing new developments based on a Gaussian process to estimate the causal effects of a continuous exposure could help to assess the effect of the linearity assumptions. Furthermore, several factors that could play an important role in the vaccination uptake disparities such as religious beliefs and political preferences were not included in our analysis, and while these factors might be measured by vaccine hesitancy, a variable included in our analysis, further analyses might focus on estimating the actual impact of these variables in the vaccination uptake in the country. Additionally, vaccination coverage was estimated using the definition of fully vaccinated individuals, and we did not include data for boosted vaccination. Lastly, data from five states were not included due to incomplete or unreliable vaccination data, and thus our results might not represent the current health structure and vaccination scenario in these states. However, we analysed data from more than 70% of the counties from the entire continental US that provide reliable results to depict the national-level associations discussed in our study.

Now that SARS-CoV-2 is projected to become endemic, the control of the surge of potentially dangerous new variants and seasonal epidemic outbreaks depends on the design of effective long-term immunisation programs. COVID-19 vaccines have proven to be the most effective intervention to reduce SARS-CoV-2 transmission, severity, and death. It is key that federal, state, and county decision-makers consider the importance of strengthening the healthcare structure in these vulnerable low-vaccinated areas to increase vaccination uptake and relieve the burden that the pandemic has brought to these vulnerable communities. Healthcare disparities and differential vaccination coverage may continue to influence the pandemic trajectory and delay efforts for epidemic control. In addition, the consequences of long-term COVID-19 will become a new challenge for the local healthcare

capacity, increasing the probability of long-term health disparities in these areas.

Contributors

Concept and design: All authors. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: D.F.C., C.M.M. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: D.F.C., J.G. Access to data and verified the data: D.F.C., J.G.

Data sharing statement

All data are available in public repositories: <https://vaccine.precisionforcovid.org/>; https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=all_states&data-type=CommunityLevels; <https://www.ruralhealthinfo.org/data-explorer?id=197>; <https://www.kaggle.com/datasets/jaimeblasco/icu-beds-by-county-in-the-us>; <https://www.atsdr.cdc.gov/placeandhealth/svi/index.html>.

Editor note

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Declaration of interests

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lana.2022.100409>.

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