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Data Availability Statement: The data underlying the results presented in the study are available from the U.S. Centers for Disease Control and Prevention at https://www.cdc.gov/nchs/nvss/vsrr/ covid19/excess_deaths.htm. **RESEARCH ARTICLE**

COVID-19 mortality in the United States: It's been two Americas from the start

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Abstract

During the summer of 2021, a narrative of "two Americas" emerged: one with high demand for the COVID-19 vaccine and the second with widespread vaccine hesitancy and opposition to masks and vaccines. We analyzed "excess mortality" rates (the difference between total deaths and what would have been expected based on earlier time periods) prepared by the CDC for the United States from January 3, 2020 to September 26, 2021. Between Jan. 3, 2020 and Sept. 26, 2021, there were 895,693 excess deaths associated with COVID-19, 26% more than reported as such. The proportion of deaths estimated by the excess mortality method that was reported as COVID-19 was highest in the Northeast (92%) and lowest in the West (72%) and South (76%). Of the estimated deaths, 43% occurred between Oct. 4, 2020 and Feb. 27, 2021. Before May 31, 2020, approximately 56% of deaths were in the Northeast, where 17% of the population resides. Subsequently, 48% of deaths were in the South, which makes up 38% of the population. Since May 31, 2020, the South experienced COVID-19 mortality 26% higher than the national rate, whereas the Northeast's rate was 42% lower. If each region had the same mortality rate as the Northeast, more than 316,234 COVID-19 deaths between May 31, 2020 and Sept. 26, 2021 were "avoidable." More than half (63%) of the avoidable deaths occurred between May 31, 2020 and February, 2021, and more than half (60%) were in the South. Regional differences in COVID-19 mortality have been strong throughout the pandemic. The South has had higher mortality rates than the rest of the U.S. since May 31, 2020, and experienced 62% of the avoidable deaths. A comprehensive COVID-19 policy, including population-based restrictions as well as vaccines, is needed to control the pandemic.

Introduction

During the summer of 2021, as vaccine uptake slowed, a narrative of "two Americas" emerged: one with a high demand for the COVID-19 vaccine and the second with high vaccine hesitancy, and later widespread opposition to mask and vaccine mandates. The second America was mostly concentrated in Southern states and rural areas, especially in counties that voted for Donald Trump. Through the summer, the number of cases, hospitalizations, and deaths **Funding:** The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

increased dramatically in the second America [1, 2]. This narrative shapes not only our understanding of what happened, but also what should, or could, be done to control the ongoing pandemic and future outbreaks.

However, this narrative is not quite true. In fact, our analysis of how COVID-19 mortality evolved over time shows that stark regional differences existed from the start of the pandemic, both in cases and deaths as well as testing and vaccine uptake. To see this, we analyzed "excess mortality," the difference between total deaths and what would have been expected based on earlier time periods. Reported cases, hospitalizations, and deaths are known to substantially underestimate actual infections and deaths by a variable fraction depending on testing availability, patient and physician awareness and attitudes, hospital resources, and other factors [3, 4]. Since COVID-19 awareness and concern [2, 5, 6], as well as test availability and use [7–9], vary markedly throughout the U.S., excess mortality estimates can help avoid potential bias due to systematic differences in reporting between areas with high and low prevalence areas.

Methods

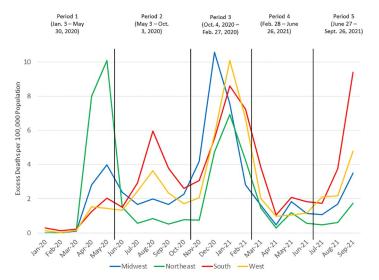
In order to identify when regional differences in the pandemic emerged, and their temporal association with vaccine uptake, we analyzed the evolution of COVID-19 mortality patterns. Our analysis is based on state-level weekly excess mortality calculations published by CDC [10]. Farrington surveillance algorithms, which use over-dispersed Poisson generalized linear models with spline terms to model trends in counts, accounting for seasonality, were implemented for each jurisdiction (states, plus the District of Columbia and New York City). These models generate a set of expected counts of deaths by week and jurisdiction, and excess mortality is simply the difference between observed and predicted deaths in each week and jurisdiction. Additional details, including weighting to adjust for potential underreporting in the most recent weeks, are provided by CDC [10].

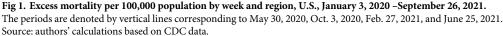
Estimates from other sources might be slightly different, but the differences are not so great as to affect the overall conclusions. In order to avoid reporting lags that potentially vary by region (especially during the summer of 2021 when some states experienced far greater caseloads than others), we concluded the analysis on September 26, 2021. In addition, baseline forecasts, and hence estimated excess mortality, become less reliable further from the pre-pandemic period.

We grouped the states into the four standard Census regions. Other *ad hoc* groupings could exaggerate or minimize differences. The on-line appendix includes figures comparing the percapita weekly rates of excess mortality to demonstrate the similarity of patterns within each region. This is especially true in the Northeast and South, but there is more internal variation in the West, where California is somewhat of an outlier. Based on a preliminary analysis of the data, we designated five periods with substantially different patterns of excess mortality. To account for differences in population sizes and length of the time periods, calculations were done by week and state, and aggregated into regional and period.

To calculate "avoidable mortality," we subtracted from the observed excess deaths the excess deaths that would have been experienced in each region and period if every region had the lowest excess mortality rate experienced by any region in that period. We did not include the first period in these calculations for the reason described below, but performed a sensitivity analysis in which we estimated the numbers of deaths that could have been avoided in Period 1 as one-half of the difference between the actual rates and those in the region with the lowest excess mortality rate in that period.

Vaccine coverage rates were calculated by Eva Rest of Georgetown University based on a data set compiled by Tiu and colleagues [11].





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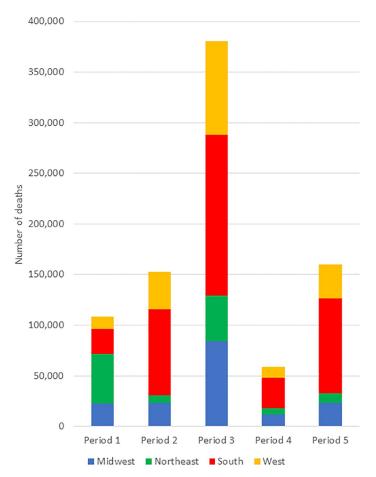
Results

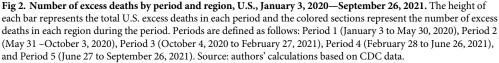
Between Jan. 3, 2020 and Sept. 26, 2021, the excess mortality associated with COVID-19 in the U.S. totaled 895,693, a per capita rate of 270 per 100,000 population. During the same period, 710,999 COVID-19 deaths were reported, amounting to 79% of the estimated excess mortality. In other words, during this period the U.S. experienced 26% more COVID-19 deaths than reported as such.

As can be seen in Fig 1, over time there are clear differences among the regions, especially between the Northeast and South. Fig 2 shows 43% of the excess deaths occurred between Oct. 4, 2020 and Feb. 27, 2021. Before May 31, 2020 (period 1), approximately 56% of deaths were in the Northeast; subsequently, 48% were in the South.

Controlling for the different sizes of the regions and lengths of the periods, <u>Table 1</u> displays excess mortality by region per 100,000 population per day. Before May 31, 2020, the daily mortality rate in the Northeast (0.881 per 100,000) was 3.3 times the national rate while the rate for the South (0.132 per 100,000) was 48% of the national rate. Subsequently, the South experienced COVID-19 mortality 26% higher than the national rate, whereas the Northeast's rate was 42% lower.

Table 1 also shows that the ratio of estimated to reported COVID-19 deaths varies over time and among the regions. The proportion is lowest in the West (71.8%) and South (76.2%). The proportions were similar in all regions (approximately 82%) in Period 1, but vary markedly afterward, dropping to less than 60% in the West in some periods. The overall proportion is highest in the Northeast (92%), and is greater than 100% in the third and fourth period (109% and 121% respectively. This is probably because some people who died of another primary cause had a positive COVID-19 test and were included in the reported counts [12], as called for by the National Center for Health Statistics [13]. A recent analysis attributed the more accurate coding of COVID-19 deaths in the New England states (which are in the Northeast region) to well-run and funded public health departments, excellent hospitals, and state medical examiners who ensure death certificate information is both accurate and timely





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[14]. The report also noted that some states in the region had large increases in deaths from overdoses rather than COVID-19, indicating a weakness of the excess mortality approach.

Because the rates of excess mortality vary so markedly, one can calculate how many deaths could have been avoided if each region had the same rates as the lowest region in each time period. We assume that no deaths were avoidable in the first period, before much was known about treating or preventing COVID-19. Subsequently, we counted as "avoidable" the difference between the rates seen and those in the Northeast, which were the lowest in each period. According to this calculation, 316,234 COVID-19 deaths between May 31, 2020 and Sept. 26, 2021 were "avoidable." Fig 3 shows that more than half of the avoidable deaths (62%) were in the South. More than half (63%) of the avoidable deaths occurred between May 31, 2020 and February, 2021, and an additional 36% between June 27 and Sept. 26, 2021.

Discussion

The theme of "two Americas" arose in the summer of 2021, regarding at first vaccine refusal, and later opposition to vaccine and mask mandates and more generally, Covid denialism [15].

Using the proportion voting for Donald Trump as a proxy for party affiliation, journalistic analyses found consistently lower vaccination rates and higher COVID-19 mortality in Southern states, which are predominantly Republican, and the opposite in the Northeastern states, which are predominantly Democratic [2, 5, 6]. But there are other geographic differences, including age distribution and education levels, that can be confounding factors [16].

Our analysis of excess mortality demonstrates that large disparities have existed since the beginning of the pandemic in the U.S. The starkest contrast is between the Northeast (which is heavily Democratic) and South (predominantly Republican). As first noted by Woolf and colleagues [17] for 2020, the first wave of the pandemic was highly concentrated in the Northeast, and particularly in the New York metropolitan area. Since May 31, 2020, however, approximately 48% all excess deaths were in the South, which makes up 38% of the population. The disparity was most apparent in the summer of 2020 (May 31–Oct. 3), when the daily excess mortality rates were 0.539 per 100,000 in the South, 0.369 per 100,000 nationally, and 0.111 per 100,000 in the Northeast. Similarly, of the 316,234 avoidable COVID-19 deaths between May 31, 2020 and Sept. 26, 2021, the majority (62%) were in the South.

As a sensitivity analysis, we estimated the numbers of deaths that could have been avoided in Period 1 as one-half of the difference between the actual rates and those in the West (which had the lowest excess mortality rate in that period). This increases the number of avoidable deaths to 402,700 an increase of 86,466. With this assumption the proportion of avoidable deaths in the South was still high, 56%.

The regional level of analysis is simple enough for disparities to be clearly apparent, but masks more extreme disparities at the state and local levels. A *Washington Post* analysis, for instance, demonstrates a strong relationship between the proportion who voted for Donald Trump in 2020 and COVID-19 mortality at the county-level [18]. A second analysis shows a strong correlation at the state level between vaccine uptake and the Trump vote [18]. Thus, the disparities in this analysis are likely underestimates of actual differences at finer levels of geography.

Strong resistance to vaccine and mask mandates emerged during the summer of 2021, especially in the South and in states with Republican governors [19, 20]. Consistent with this, excess mortality in the summer of 2021 was correlated with vaccine uptake. As seen in Table 1, the Northeast had the lowest COVID-19 mortality rates and the highest vaccination coverage: 52% of the population was fully vaccinated on June 27, 2021 and 60% on September 26, 2021. The South, at the other extreme, had the highest COVID-19 mortality rates and lowest vaccine coverage (40% and 49% on the same dates).

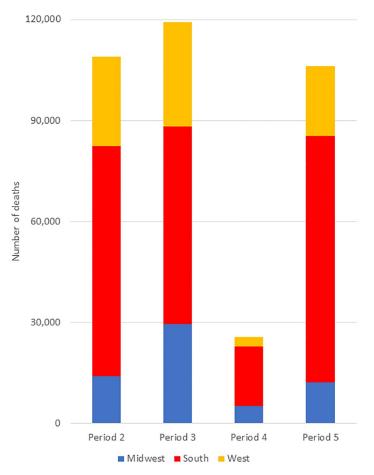
Nationally, vaccines have already saved many lives [21] and boosters have the potential to save many more [22]. However, our analysis suggests that major differences in COVID-19 mortality emerged in the summer of 2020, well before vaccines became available. Indeed, 63% of the avoidable deaths occurred by the end of February, 2021, when the vaccine rollout was just beginning. These avoidable deaths occurred before the Delta variant became dominant in the United States, so Delta is not part of the explanation. Similarly, because the South has had dramatically higher COVID-19 mortality than the Northeast (since June, 2020) during all seasons of the year, weather is not a likely explanation. Northeasters may have carried some natural immunity into the summer of 2020 [23], but by July, 2020, Anand and colleagues estimate substantially higher seroprevalence rates in the South (37.9%) than in the Northeast (17.5%), so natural immunity cannot explain the large differences starting in the summer of 2020 [24]. Excess COVID-19 mortality in the South and other areas of the country, therefore, is likely to be due at least in part to higher transmission resulting from differences in mask use, school attendance, social distancing, and other behaviors.

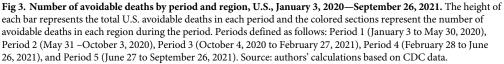
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U.S. 134,312 153,055 386,490 60,849 160,987 885,69 Excess mortality per capita by region and period (per 100,000 population) per day	South	24,667	85,031	158,350	30,270	93,712	392,030
Excess mortality per capita by region and period (per 100,000 population) per day Northeast 0.219 0.227 0.823 0.119 0.229 0.38 Northeast 0.881 0.111 0.609 0.112 0.202 0.42 South 0.132 0.539 0.859 0.203 0.816 0.49 West 0.105 0.375 0.810 0.117 0.466 0.37 U.S. 0.274 0.388 0.799 0.156 0.534 0.431 Excess mortality as a proportion of reported COVID-19 deaths Excess mortality as a proportion of reported COVID-19 deaths 81.7% 61.7% 83.49 Northeast 82.7% 98.8% 108.7% 51.1% 56.6% 92.39 South 78.8% 67.1% 84.6% 56.0% 76.2% 76.2% Vest 74.9% 57.0% 84.7% 54.1% 56.7% 71.8% U.S. 81.7% 65.4% 90.1% 69.5% 68.7% 70.49 Avoidable excess mortality by region and period	West	12,177	36,869	92,891	10,824	33,358	186,119
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Midwest 85.1% 61.0% 95.0% 84.7% 61.7% 83.49 Northeast 82.7% 98.8% 108.7% 121.3% 55.6% 92.39 South 78.8% 67.1% 84.6% 56.0% 76.2% 76.29 West 74.9% 57.0% 84.7% 54.1% 56.7% 71.89 U.S. 81.7% 65.4% 90.1% 69.5% 68.7% 79.49 Avoidable excess mortality by region and period 65.2% 70.49 50.05 Northeast 0 0 0 0 0 0 South 0 67.528 46.131 13,584 70.541 197.78 West 0 25.975 23,046 439 18,936 68.39 U.S. 0 107,108 91,915 17,048 100,162 316,23 Proportion fully vaccinated by region at the end of the period (% of the entire population) 100,162 316,23 100,162 316,23 Northeast	U.S.	0.274	0.368	0.799	0.156	0.534	0.430
Northeast 82.7% 98.8% 108.7% 121.3% 55.6% 92.3% South 78.8% 67.1% 84.6% 56.0% 76.2% 76.2% West 74.9% 57.0% 84.7% 54.1% 56.7% 71.8% U.S. 81.7% 65.4% 90.1% 69.5% 68.7% 79.4% Avoidable excess mortality by region $priod$ 00.1% 69.5% 68.7% 79.4% Northeast0 $13,606$ $22,738$ $3,026$ $10,685$ $50,051$ Northeast0000 0 0 0 South0 $67,528$ $46,131$ $13,584$ $70,541$ $197,78$ West0 $25,975$ $23,046$ 439 $18,936$ $68,39$ U.S.0 $107,108$ $91,915$ $17,048$ $100,162$ $316,23$ Proportion fully vaccinated by region at the end of the period ($\%$ of the entire population) $13,44,4\%$ 52.9% $50,0\%$ Northeast0 7.3% 44.4% 52.9% $49,8\%$ Northeast0 7.5% 42.9% $49,8\%$ West0 7.3% 39.8% 48.9%	Excess mor	tality as a proportion of rep	oorted COVID-19 deaths				
South78.8%67.1%84.6%56.0%76.2%76.2%West74.9%57.0%84.7%54.1%56.7%71.8%U.S.81.7%65.4%90.1%69.5%68.7%79.4%Avoidable excess mortality by region and period90.1%69.5%68.7%50.05%Northeast013,60622,7383,02610,68550,05%Northeast0000000South067,52846,13113,58470,541197,78%West025,97523,04643918,93668,39%U.S.0107,10891,91517,048100,162316,23Proportion fully vaccinated by region at the end of the period (% et the entire population)7.3%44.4%52.9%100,168Midwest6.8%51.9%60.3%50.0%100,168100,168100,168Northeast6.8%51.9%60.3%100,168100,168100,168South6.8%51.9%60.3%100,168100,168100,168Northeast6.8%51.9%60.3%100,168100,168100,168South6.8%51.9%60.3%100,168100,168100,168Northeast6.8%51.9%60.3%100,168100,168100,168South6.8%51.9%60.3%100,168100,168100,168Northeast6.8%51.9%60.3%100,168100,1	Midwest	85.1%	61.0%	95.0%	84.7%	61.7%	83.4%
West74.9%57.0%84.7%54.1%56.7%71.8%U.S. 81.7% 65.4% 90.1% 69.5% 68.7% 79.4% Avoidable excess mortality by region and periodMidwest0 $13,606$ $22,738$ $3,026$ $10,685$ $50,055$ Northeast0000000South0 $67,528$ $46,131$ $13,584$ $70,541$ $197,786$ West0 $25,975$ $23,046$ 439 $18,936$ $68,399$ U.S.0 $107,108$ $91,915$ $17,048$ $100,162$ $316,236$ Proportion fully vaccinated by region at the end of the period (% of the entire population) 7.3% 44.4% 52.9% Northeast 6.8% 51.9% 60.3% 50.0% South 7.5% 42.9% 49.8% West 7.3% 39.8% 48.9%	Northeast	82.7%	98.8%	108.7%	121.3%	55.6%	92.3%
U.S. 81.7% 65.4% 90.1% 69.5% 68.7% 79.4% Avoidable excess mortality by region and period $13,606$ $22,738$ $3,026$ $10,685$ $50,055$ Midwest 0 <	South	78.8%	67.1%	84.6%	56.0%	76.2%	76.2%
Avoidable excess mortality by region and period Midwest 0 13,606 22,738 3,026 10,685 50,055 Northeast 0 0 0 0 0 0 0 0 South 0 67,528 46,131 13,584 70,541 197,78 West 0 25,975 23,046 439 18,936 68,39 U.S. 0 107,108 91,915 17,048 100,162 316,23 Proportion fully vaccinated by region at the end of the period (% of the entire population) 7.3% 44.4% 52.9% 50.3% Northeast 0 7.3% 44.2% 50.3% 60.3% <	West	74.9%	57.0%	84.7%	54.1%	56.7%	71.8%
Midwest 0 13,606 22,738 3,026 10,685 50,053 Northeast 0	U.S.	81.7%	65.4%	90.1%	69.5%	68.7%	79.4%
Northeast 0 0 0 0 0 0 0 South 0 67,528 46,131 13,584 70,541 197,78 West 0 25,975 23,046 439 18,936 68,39 U.S. 0 107,108 91,915 17,048 100,162 316,23 Proportion Fully vaccinated by region at the end of the period (% of the entire population) 7.3% 44.4% 52.9% 60.3% Northeast 6.88% 51.9% 60.3%<	Avoidable e	excess mortality by region a	and period				
South 0 67,528 46,131 13,584 70,541 197,783 West 0 25,975 23,046 439 18,936 68,393 U.S. 0 107,108 91,915 17,048 100,162 316,233 Proportion Fully vaccinated by region at the end of the period (% of the entire population) 7.3% 44.4% 52.9% 60.3% Northeast 0 6.88% 51.9% 60.3% <	Midwest	0	13,606	22,738	3,026	10,685	50,055
West 0 25,975 23,046 439 18,936 68,39 U.S. 0 107,108 91,915 17,048 100,162 316,23 Proportion fully vaccinated by region at the end of the period (% of the entire population) 316,23 Midwest 7.3% 44.4% 52.9% Northeast 68.8% 51.9% 60.3% South 6.8% 51.9% 49.8% West 0 7.3% 39.8% 48.9%	Northeast	0	0	0	0	0	0
U.S. 0 107,108 91,915 17,048 100,162 316,23 Proportion fully vaccinated by region at the end of the period (% of the entire population) 316,23 Midwest Contrast Contrast Contrast 66.8% 51.9% 60.3% South Contrast Contrast Contrast 39.8% 48.9% 48.9%	South	0	67,528	46,131	13,584	70,541	197,783
Proportion fully vaccinated by region at the end of the period (% of the entire population) 11,110	West	0	25,975	23,046	439	18,936	68,395
Midwest 7.3% 44.4% 52.9% Northeast 6.8% 51.9% 60.3% South 7.5% 42.9% 49.8% West 7.3% 39.8% 48.9%	U.S.	0	107,108	91,915	17,048	100,162	316,234
Northeast Image: Montheast Image: Montheast	Proportion	fully vaccinated by region	at the end of the period (% o	of the entire population)			
South Control Control <thcontrol< th=""> <thcontrol< th=""> <thcon< td=""><td>Midwest</td><td></td><td></td><td>7.3%</td><td>44.4%</td><td>52.9%</td><td></td></thcon<></thcontrol<></thcontrol<>	Midwest			7.3%	44.4%	52.9%	
West 7.3% 39.8% 48.9%	Northeast			6.8%	51.9%	60.3%	
	South			7.5%	42.9%	49.8%	
U.S. 7.5% 47.7% 56.5%	West			7.3%	39.8%	48.9%	
	U.S.			7.5%	47.7%	56.5%	

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Compared to estimates based on epidemiologic models, the excess mortality methods and assumptions are simple and straightforward. While they cannot explain <u>why</u> some regions had different mortality rates, excess mortality estimates can accurately document when and where COVID-19 occurred. Indeed, Woolf argues that state mortality differentials during the pandemic simply continue a decades-long trend in political differences between Republican and Democratic dominated states [25]. However, although causal patterns are complex and difficult to ascertain, differential implementation of and adherence to stay-at-home orders, mask use, and other non-pharmaceutical interventions seem to be at least a partial explanation for the regional differences in COVID-19 mortality. Thus, our analysis demonstrates the potential impact of population-based restrictions as well as vaccines, indicating that a comprehensive COVID-19 policy is needed to control future pandemics.

This analysis demonstrates the benefits of the excess mortality approach [26]. This method provides objective estimates of COVID-19's impact on mortality that do not rely on test availability, clinical decisions, and reporting processes that can lead to under—and over-counting. The ratio of estimated to reported COVID-19 deaths ranged from 121% (Northeast in period





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4) to 54% in the West and 56% in the South in the same period. An analysis of reported COVID-19 deaths, therefore would have shown both fewer avoidable deaths and regional disparities. The presence of reporting delays, which can be greater in some areas than others, means that excess mortality estimates and differentials are not reliable for a period of weeks, so excess mortality estimates are limited as real-time surveillance tools. And the reliability of these methods will decline as we go further beyond the base period. However, over the period studied, they can be quite informative.

Although the causes are not fully understood, COVID-19 clearly has played out differently across the country over the nearly two years since it emerged. The analysis therefore illustrates how the importance of going beyond cumulative case counts for the U.S. as a whole that dominates the news cycle. Beyond the regional differences that are the focus of this paper, there are substantial differences between rural and urban areas with states and among socio-demographic groups. Because they are less sensitive to differences in reporting patterns than case counts, excess mortality methods can be especially useful in understanding these patterns [27].

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References

- Baumgaertner E. Here's how the most- and least-vaccinated states fared against the Delta variant. Los Angeles Times [Internet]. 2021 Sep 20 [cited 2022 Jan 9]; Available from: https://www.latimes.com/ world-nation/story/2021-09-20/heres-how-the-most-and-least-vaccinated-states-fared-against-thedelta-variant
- Leonhardt D. U.S. Covid Deaths Get Even Redder. The New York Times [Internet]. 2021 Nov 8 [cited 2022 Jan 9]; Available from: <u>https://www.nytimes.com/2021/11/08/briefing/covid-death-toll-red-america.html</u>
- National Academies of Sciences, Engineering, and Medicine. Evaluating Data Types: A Guide for Decision Makers using Data to Understand the Extent and Spread of COVID-19 [Internet]. Washington, DC: The National Academies Press; 2020 [cited 2022 Jan 9]. 15 p. https://www.nap.edu/catalog/25826/evaluating-data-types-a-guide-for-decision-makers-using-data
- Fricker RD Jr. Covid-19: One year on.... Significance. 2021; 18(1):12–5. https://doi.org/10.1111/1740-9713.01485 PMID: 33821159
- Bump P. Those least likely to worry about getting covid (Republicans) have been those most likely to get covid. Washington Post [Internet]. 2022 Jan 20 [cited 2022 Mar 12]; Available from: https://www. washingtonpost.com/politics/2022/01/20/those-least-likely-worry-about-getting-covid-republicanshave-been-those-most-likely-get-covid/
- Wood D, Brumfiel G. Pro-Trump counties now have far higher COVID death rates. Misinformation is to blame. NPR [Internet]. 2021 Dec 5 [cited 2022 Mar 12]; Available from: https://www.npr.org/sections/ health-shots/2021/12/05/1059828993/data-vaccine-misinformation-trump-counties-covid-death-rate
- Tingley K. Counting Covid-19 Cases Doesn't Capture the Pandemic's Impact. The New York Times [Internet]. 2022 Jan 26 [cited 2022 Mar 12]; Available from: https://www.nytimes.com/2022/01/26/ magazine/covid-19-data-public-health.html
- Kasakove S. As At-Home Tests Surge, Doubts Rise About Accuracy of Public Covid Counts. The New York Times [Internet]. 2021 Dec 30 [cited 2022 Mar 12]; Available from: https://www.nytimes.com/2021/ 12/30/us/at-home-rapid-covid-tests-cases.html
- 9. CDC. COVID Data Tracker [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2022 Mar 12]. https://covid.cdc.gov/covid-data-tracker
- 10. Excess Deaths Associated with COVID-19 [Internet]. Centers for Disease Control and Prevention. 2022 [cited 2022 Jan 9]. https://www.cdc.gov/nchs/nvss/vsrr/covid19/excess_deaths.htm
- 11. Tiu A, Susswein Z, Merritt A, Bansal S. Characterizing the spatiotemporal heterogeneity of the COVID-19 vaccination landscape. MedRxiv: 2021.10.04.21263345 [Preprint]. 2021 [cited 2022 Jan 9]. https:// www.medrxiv.org/content/10.1101/2021.10.04.21263345v2
- Ackley CA, Lundberg DJ, Elo IT, Preston SH, Stokes AC. County-Level Estimates of Excess Mortality Associated with COVID-19 in the United States. MedRxiv [Preprint]. 2021 medRxiv 2021.04.23.21255564 [posted 2021 Apr 25; revised 2021 May 5; cited 2022 Jan 9]. https://www. medrxiv.org/content/10.1101/2021.04.23.21255564v3

- National Vital Statistics System. Guidance for Certifying Deaths Due to Coronavirus Disease 2019 (COVID–19). Vital Stat Report Guid [Internet]. 2020 Apr; 3. Available from: https://www.cdc.gov/nchs/ data/nvss/vsrg/vsrg03-508.pdf
- Barndollar H. How New England caught the COVID deaths much of the country missed. The Providence Journal [Internet]. 2022 Feb 24 [cited 2022 Mar 12]; Available from: https://www.providencejournal.com/story/news/2022/02/24/covid-death-toll-cause-accurate-new-england-medicalexaminer-nursing-homes/9132115002/
- 15. Rubin J. We're becoming two Americas: One healthy, one deliberately at risk. Washington Post [Internet]. 2021 Jul 19 [cited 2022 Jan 9]; Available from: https://www.washingtonpost.com/opinions/2021/ 07/19/two-americans-one-healthy-one-deliberately-risk/
- Shamus K, Tanner K. Age, education, voting for Trump associated with higher COVID-19 death rates in Michigan. Detroit Free Press [Internet]. 2022 Feb 23 [cited 2022 Mar 12]; Available from: https://www.freep.com/story/news/health/2022/03/11/michigan-covid-19-death-rates-county-education-age-trump/6924307001/
- 17. Woolf SH, Chapman DA, Sabo RT, Zimmerman EB. Excess Deaths From COVID-19 and Other Causes in the US, March 1, 2020, to January 2, 2021. JAMA. 2021 Apr 2.
- Bump P. What if, actually, vaccine advocates want people *not* to die? Washington Post [Internet]. 2021 Sep 20 [cited 2022 Jan 9]; Available from: https://www.washingtonpost.com/politics/2021/09/20/ what-if-actually-vaccine-advocates-want-people-not-die/
- Krugman P. How Covid Became a Red-State Crisis. The New York Times [Internet]. 2021 Jul 29 [cited 2022 Jan 9]; Available from: https://www.nytimes.com/2021/07/29/opinion/covid-vaccinationsrepublicans.html
- Jarvie J. One nation, divisible—over vaccines. Los Angeles Times [Internet]. 2021 [cited 2022 Jan 9]; https://enewspaper.latimes.com/infinity/article_share.aspx?guid=34b29cc1-f8bf-4da9-82b8-282102286176
- Schneider E, Shah A, Sah P, Moghadas S, Vilches T, Galvani A. The U.S. COVID-19 Vaccination Program at One Year: How Many Deaths and Hospitalizations Were Averted? [Internet]. The Commonwealth Fund. 2021 [cited 2022 Jan 9]. https://www.commonwealthfund.org/publications/issue-briefs/ 2021/dec/us-covid-19-vaccination-program-one-year-how-many-deaths-and
- Schneider E, Shah A, Sah P, Moghadas S, Vilches T, Galvani A. Responding to Omicron: Aggressively Increasing Booster Vaccinations Now Could Prevent Many Hospitalizations and Deaths [Internet]. Commonwealth Fund. [cited 2022 Jan 9]. https://www.commonwealthfund.org/blog/2022/respondingomicron
- Havers FP, Reed C, Lim T, Montgomery JM, Klena JD, Hall AJ, et al. Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. JAMA Intern Med. 2020 Jul 21; https://doi.org/10.1001/jamainternmed.2020.4130 PMID: 32692365
- Anand S, Montez-Rath M, Han J, Bozeman J, Kerschmann R, Beyer P, et al. Prevalence of SARS-CoV-2 antibodies in a large nationwide sample of patients on dialysis in the USA: a cross-sectional study. Lancet Lond Engl. 2020 Oct 24; 396(10259):1335–44.
- 25. Woolf SH. The Growing Influence of State Governments on Population Health in the United States. JAMA. 2022 Mar 3. https://doi.org/10.1001/jama.2022.3785 PMID: 35275203
- Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, et al. Coronavirus Pandemic (COVID-19). Our World Data [Internet]. 2020 Mar 5 [cited 2022 Jan 9]; Available from: https://ourworldindata.org/coronavirus
- 27. Stoto MA, Rothwell C, Lichtveld M, Wynia MK. A National Framework to Improve Mortality, Morbidity, and Disparities Data for COVID-19 and Other Large-Scale Disasters. Am J Public Health. 2021 Jul 1; 111(S2):S93–100. https://doi.org/10.2105/AJPH.2021.306334 PMID: 34314219