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Original article

SARS-CoV-2 transmission potential and rural-urban disease burden disparities across Alabama, Louisiana, and Mississippi, March 2020 — May 2021

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A R T I C L E I N F O

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Purpose: To quantify and compare SARS-CoV-2 transmission potential across Alabama, Louisiana, and Mississippi and selected counties.
Methods: To determine the time-varying reproduction number R_t of SARS-CoV-2, we applied the R package EpiEstim to the time series of daily incidence of confirmed cases (mid-March 2020 — May 17, 2021) shifted backward by 9 days. Median R_t percentage change when policies changed was determined. Linear regression was performed between $\log_{10}$-transformed cumulative incidence and $\log_{10}$-transformed population size at four time points.
Results: Stay-at-home orders, face mask mandates, and vaccinations were associated with the most significant reductions in SARS-CoV-2 transmission in the three southern states. R_t across the three states decreased significantly by $\geq$20% following stay-at-home orders. We observed varying degrees of reductions in R_t across states following other policies. Rural Alabama counties experienced higher per capita cumulative cases relative to urban ones as of June 17 and October 17, 2020. Meanwhile, Louisiana and Mississippi saw the disproportionate impact of SARS-CoV-2 in rural counties compared to urban ones throughout the study period.
Conclusion: State and county policies had an impact on local pandemic trajectories. The rural-urban disparities in case burden call for evidence-based approaches in tailoring health promotion interventions and vaccination campaigns to rural residents.

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Introduction

As of May 17, 2021, there were more than three million reported cases of coronavirus disease 2019 (COVID-19) in the United States (US), with over 30,000 new cases a day and almost 600,000 deaths [1]. Evidence suggests disparities in COVID-19 burden across US census regions; the Southern region reported the second-highest cases with the most significant percentage increase during the early months of the pandemic [2]. The southern US experienced surges in cases over the summer of 2020, partly driven

Abbreviations: CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus disease 2019; R_t, Time-varying reproduction number; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; US, United States.

Conflict of interests: The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Isaac C. H. Fung reports a relationship with Alphabet Inc that includes: equity or stocks. Sylvia K. Ofori reports a relationship with Ionis Pharmaceuticals Inc that includes: employment.

SKO reports that she is a paid intern at Ionis Pharmaceuticals, Inc. ICHF declares that he has invested in equity in Alphabet, Inc (GOOGL).

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by infection of younger adults [3], probably due to non-compliance to Centers for Disease Control and Prevention (CDC) guidelines [4]. Despite the intensity of COVID-19 transmission in this region, compliance with social distancing measures was reported to be low [5].

Alabama, Mississippi and Louisiana are three Southern Gulf states that have been heavily affected by the COVID-19 pandemic. These states are flanked by Florida to the east and Texas to the west (see Supplementary Figures S1 and S2). Mississippi reported their first case on March 11, 2020 [6], followed by Alabama on March 13, 2020 [7], and finally Louisiana on March 14, 2020 [8].

To curb the pandemic, reaching the herd immunity threshold through vaccination is key [9]. However, vaccine hesitancy presents a challenge in the South [10]. The three Gulf states studied here had the lowest vaccination rates; <40% of the population had received at least one dose as of June 7, 2021 [11].

Rural-urban disparities in COVID-19 burden have been established in the literature [12,13]. A study found that urban Louisianans had a significantly higher risk (Adjusted Relative Risk: 1.32, 95% CI, 1.22–1.43) of COVID-19 infection than rural Louisianans [14]. In Mississippi, studies suggested that approximately half of the COVID-19-attributed hospitalizations were in rural areas as of April 25, 2020 [15,16]. The disparity was also true for Alabama [17]. Therefore, the rural-urban disparity could have gone in either direction. All three states had a higher percentage of residents living in rural areas than the national percentage (i.e. 14%): 23.16% for Alabama, 15.97% for Louisiana, and 53.17% for Mississippi, as of 2019 [18–21]. Research suggested that approaches to managing COVID-19 should account for rural-urban disparities including behavioral differences [16,22].

Time-varying reproduction number (R_t) is the average number of secondary cases generated by a typical infectious individual in the presence of public health interventions, behavioral changes, and increase in population immunity level. Hence, R_t changes over time throughout an epidemic. R_t estimation informs policymakers about how implemented policies and behavioral changes at the state and county level impacted COVID-19 transmission. When $R_t > 1$, transmission is sustained, whereas when $R_t < 1$, the epidemic will eventually die out [23,24].

In this study, we explored the impact of different policies on SARS-CoV-2 transmission potential at the state level in Alabama, Louisiana, and Mississippi and evaluated rural-urban transmission differences using a representative set of counties with median, 75th, and 100th percentile population size. Counties with a population below the median were not analyzed due to the low case count in counties with small population size.

Methods

This study used retrospective data from the COVID-19 pandemic in Alabama, Louisiana, and Mississippi. The cumulative incidence data for each county in Alabama, Louisiana, and Mississippi were downloaded from the New York Times GitHub data repository up till May 17, 2021 [1]. The first COVID-19 cases were reported on March 13, 2020, in Alabama, March 9, 2020, in Louisiana, and March 11, 2020, in Mississippi. The daily number of new cases was obtained from the reported cumulative incidence by calculating the difference between consecutive cumulative case counts (Text S1). Executive orders of state administrations and timing for the implementation of policies were obtained from government and news sources. Data from every county in each state were included for the state level analysis.

County selection

Three counties were selected for each state based on population sizes and >10 daily new cases since ≤10 daily counts lead to unreliable R_t estimates [25]. Counties at the median, approximately 75th, and 100th percentiles as defined by the 2019 county-level population data from the US Census Bureau were selected [26]: Chambers (median), Cullman (75th percentile), and Jefferson (100th percentile; County Seat: Birmingham) in Alabama; Evangeline (median), Iberia (75th percentile), and East Baton Rouge (100th percentile; Parish Seat: Baton Rouge) in Louisiana; and Leake (median), Marshall (75th percentile), and Hinds (100th percentile; County Seats: Raymond and Jackson) in Mississippi. Counties with population below the median were not analyzed here, as preliminary analysis found that the low case count in counties with small population size rendered the R_t estimates generated by the EpiEstim package very uncertain.

Statistical analysis

R_t was estimated using the instantaneous reproduction number method [23]. The EpiEstim package version 2.2–4 in R version 4.1.0 was used for the analysis [27]. The serial interval distribution was parametrically defined (mean = 4.60 days; standard deviation = 5.55 days) [28]. The time series was shifted by 9 days to approximate the onset of infection by assuming a mean incubation period of 6 days and a median testing delay of 3 days [25,29–31].

Two sets of time window arrangements were used. First, the 7-day sliding window was used to minimize the fluctuations observed with smaller time steps by taking the average of R_t estimates over a week. Secondly, the non-overlapping time window method between which a bundle of interventions was implemented was used to estimate the average R_t over a given period (Table S1).

To assess the extent of change in the R_t after policies were implemented, the percentage change was calculated for the non-overlapping time window R_t using the formula: $\frac{R_{t2}-R_{t1}}{R_{t1}} \times 100$. R_{t2} refers to the R_t estimate of the time window after a new policy was implemented and R_{t1} refers to the previous window. The “sample from the posterior R distribution” function (sample_posterior_R) was used to sample 1000 estimates of R_t for each interval in the EpiEstim package and the associated 95% Credible interval (CrI) of the percentage change was calculated using bootstrapping.

We explored the power-law relationship between the population size of counties and per capita cumulative case count using linear regression between the $\log_{10}$-transformed per capita cumulative case count and the $\log_{10}$-transformed population size. A negative slope indicates that counties with lower population size were associated with higher case burden while a positive slope means the opposite (Text S1) [32,33]. Time variability was assessed by regressing data at four time points (Date of report: June 17, 2020, October 17, 2020, February 17, 2021, and May 17, 2021).

Additional analyses of New York Times mask-wearing survey data (July 2020) and of Google mobility data were described in Text S1.

Ethics

The Georgia Southern University Institutional Review Board made a non-human subject determination for this project (H20364) under the G8 exemption category according to the Code of Federal Regulations Title 45 Part 46.

Results

The daily number of new cases peaked twice in July and December 2020 in Alabama and Mississippi while the epidemic curve peaked thrice in April, July, and December 2020 in Louisiana (Fig. 1). The cumulative case count per 10,000 population and the

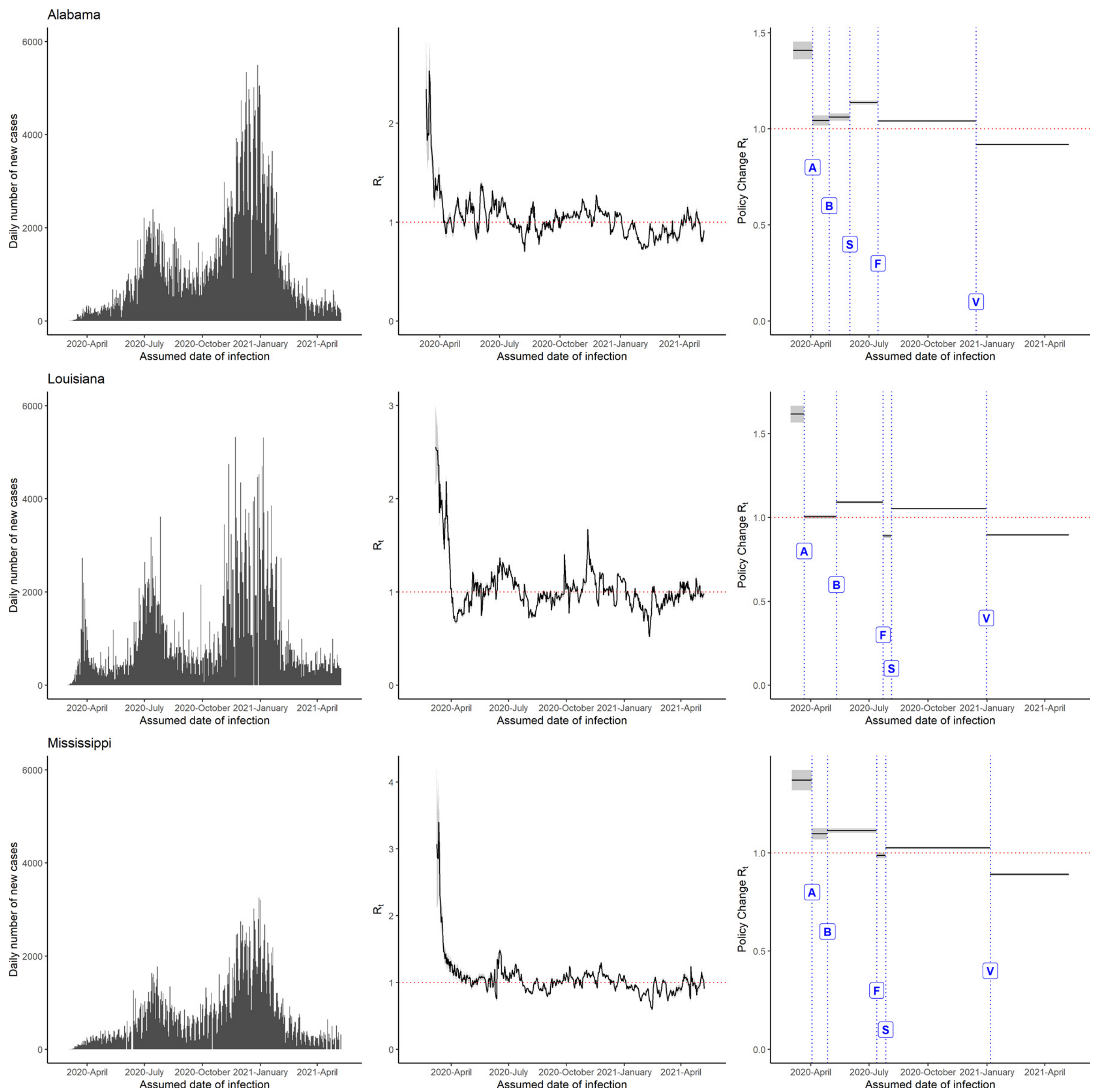

Fig. 1. The daily number of new cases (left panel), 7-day sliding window Rt, (middle panel), and non-overlapping window Rt for policy change (right panel) for Alabama, Louisiana, and Mississippi. The government policies represented by the alphabets in the figure are: *A* = Stay at home order directive, *B* = Shelter in place/safer at home, *S* = School reopening, *F* = Face mask mandate and *V* = Rollout of vaccination began. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

cumulative case count of each county of the three states are presented in maps (Figures S1 and S2). Detailed results can be found in Text S2.

7-day sliding window r_t estimates at the state level

The 7-day sliding window R_t for all three states was >1 in April 2020 but dropped to <1 between April and May for Louisiana before increasing again in late May. Alabama maintained a value >1 before dropping <1 in late May then fluctuated around 1 until December. Mississippi experienced similar fluctuations until December 2020. In all three states, the R_t was <1 between February and April 2021 but experienced a surge in May 2021 (Fig. 1).

7-day sliding window r_t estimates at the county level

In Alabama, the R_t for Jefferson decreased to <1 in March 2020 and then fluctuated around 1 until May 2021; the R_t for Cullman and Chambers followed a similar trajectory. In Louisiana, all three selected parishes had peaks of R_t >3 in March, June, and November 2020; R_t decreased to <1 in April 2020 and generally fluctuated around 1 until May 2021. The selected counties in Mississippi followed a trend similar to the counties in Alabama and Louisiana (Figures S3, S4 and S5, and Text S2).

Policy impacts at the state level

The impact of policy changes on the transmission potential of SARS-CoV-2 as represented by the non-overlapping time window R_t are summarized in Figures 1,2, and Table S2. Alabama, Louisiana, and Mississippi followed a similar trajectory in the changes in R_t as state orders were executed. The Stay-at-Home orders (represented as the letter A: enacted on April 4, 2020, in Alabama, on March 22, 2020, in Louisiana, and on April 3, 2020, in Mississippi) were associated with a minimum of 20% decline in R_t in all three states, probably due to the early intervention.

When the stay-at-home order was relaxed (represented as B), the R_t elevated in Louisiana by 8.69% (95% CrI: 7.19%, 10.09%),

Fig. 2. Median percentage change (95% credible intervals, CrI) of policy change R_t estimates for Alabama, Louisiana, and Mississippi grouped by social and public health interventions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

but the change was statistically insignificant in Alabama (1.56%, 95% CrI: −1.19%, 4.75%) and Mississippi (1.49%, 95% CrI: −1.41%, 4.27%). On the contrary, when facemask mandates (represented as F) were enacted, there was a decline in the R_t by 8.55% (95% CrI: 7.68%, 9.41%), 18.51% (95% CrI: 1.75%, 17.16%), and 11.34% (95% CrI: 9.71%, 13.04%) in Alabama, Louisiana and Mississippi, respectively. Louisiana recorded the highest surge in transmission post-school reopening (represented by S) on July 23, 2020, with R_t increasing by 18.29% (95% CrI: 16.55%, 19.99%), followed by Alabama (7.19%, 95% CrI: 5.01%, 9.06%) and Mississippi (3.87%, 95% CrI: 2.22%, 5.59%). Our findings also suggested that the vaccination rollout (represented by V) against COVID-19 in all three states was associated with the median R_t values reduced to <1.

Table 1
The slope (and 95% Confidence Intervals) of the linear regression line between $\log_{10}$-transformed per capita cumulative case number and $\log_{10}$-transformed population size, by state, Alabama, Louisiana, and Mississippi, on June 17, 2020, October 17, 2020, February 17, 2021, and May 17, 2021 (date of report).

State	June 17, 2020	October 17, 2020	February 17, 2021	May 17, 2021
Alabama	−0.3229 (−0.4964, −0.1495)	−0.0820 (−0.1404, −0.0236)	0.0041 (−0.0418, 0.0499)	0.0117 (−0.0318, 0.0553)
Louisiana	−0.0273 (−0.1812, 0.1266)	−0.0760 (−0.1332, −0.0189)	−0.0523 (−0.0901, −0.0146)	−0.0383 (−0.0742, −0.0024)
Mississippi	−0.2006 (−0.3837, −0.0175)	−0.1382 (−0.2013, −0.0749)	−0.0554 (−0.0945, −0.0164)	−0.0448 (−0.0808, −0.0089)

Policy impacts at the county level

Following the enactment of the stay-at-home order in Alabama, Cullman County (75th percentile) observed the highest percentage decrease in R_t by 53.55% (95% CrI: 21.79%, 71.73%) (Table S3). When the stay-at-home order was relaxed, Chambers (50th percentile) and Cullman (75th percentile), observed an increase in R_t by 59.33% (95% CrI: 20.45%, 111.44%) and 67.89% (95% CrI: 14.07%, 161.52%) respectively. Interestingly, re-opening of schools and face mask mandates were not associated with a statistically significant change in R_t in all counties except Jefferson (100th percentile). Vaccination was associated with a dwindle in R_t in Cullman (−17.41%, 95% CrI: −21.14%, −13.58%) and Jefferson counties (−15.07%, 95% CrI: −16.31%, −13.73%).

Louisiana had the lowest median R_t of 1.37 (95% CrI: 1.32, 1.42) among the three states before the implementation of the Stay-at-home order after the pandemic hit (Table S4). After the stay-at-home order was enacted, Iberia (75th percentile) observed the highest decline by 59.04% (95% CrI: 36.77%, 74.33%), then East Baton Rouge (100th percentile) by 34.84% (95% CrI: 24.53%, 43.91%). The relaxation of the stay-at-home order was not associated with significant changes in R_t in any of the selected counties. In contrast, the face mask mandate was associated with an apparent decline in R_t in Iberia (−18.94%, 95% CrI: −27.07%, −10.40%) and East Baton Rouge (−17.26%, 95% CrI: −21.11%, −12.86%). School reopening was associated with an increase in R_t in Iberia (18.84%, 95% CrI: 7.98%, 31.42%) and East Baton Rouge (16.31%, 95% CrI: 11.06%, 21.68%). Vaccination rollout was associated with a reduction in R_t by 9%−14% in all three parishes.

In Mississippi, the stay-at-home order had the least impact in Hinds (100th percentile) with a 19.69% (95% CrI: 4.88%, 33.08%) R_t reduction (Table S5). The facemask mandate was not found to be associated with a change in R_t in Marshall (75th percentile) and Leake (50th percentile) counties. School reopening was followed by a surge in R_t in Hinds by 6.66% (95% CrI: 1.48%, 12.92%). Vaccination rollouts were associated with a statistically significant decline in R_t across all counties. Details of county-level policy impacts are presented in Tables S3, S4, and S5.

Power-law relationship between cumulative case number and population size for all the counties in each of the three states

Figure 3 and Table 1 present the results of the linear regression analysis between the $\log_{10}$-transformed per-capita cumulative incidence and the $\log_{10}$-transformed population size for all the counties in each of the three states. The negative slopes for Alabama on June 17 (−0.3229, 95% CI: −0.4964, −0.1495) and October 17, 2020 (−0.0820, 95% CI: −0.1404, −0.0236), suggested that in 2020, rural counties were experiencing a higher case burden than urban counties, whereas such disparity was not observed in the first half of 2021. The negative slopes for Louisiana and Mississippi at all four assessed dates suggested that low-population counties experienced a higher case burden throughout the study period.

Masking-wearing survey data and Google mobility data

The New York Times mask-wearing survey data (July 2020) of Alabama, Louisiana and Mississippi are presented in a map (Figure S6) and described in Text S2. The 7-day moving average of Google mobility data in these three states and their correlation with incident case count and Rt were described in Text S2 and Tables S6-S8.

Discussion

Overall, facemask mandates, stay-at-home orders, and vaccination rollout were the executive orders that were statistically significantly associated with decreased R_t values across all three states analyzed herein. School reopening was found to be associated with slightly increased transmission statewide, in Hinds county (100th percentile) in Mississippi, and in Iberia and East Baton Rouge parishes (75th and 100th percentile) in Louisiana. Meanwhile, the stay-at-home orders were associated with a decline in R_t in a majority of the selected counties. Our findings also suggest that counties with smaller population sizes were associated with a higher case burden throughout the study period for Louisiana and Mississippi and in the selected time points in 2020 for Alabama. Transmission appeared to be in decline after vaccines became available in the selected counties for each state except Chambers, Alabama. Counties with 100th percentile population size observed a significant decline in R_t following the stay-at-home order and face mask mandates.

Stay-at-home orders were issued in 43 of 50 states, when COVID-19 pandemic first hit the US in Spring 2020 [34]. These were primarily intended to reduce interpersonal contact and thus SARS-CoV-2 transmission, as demonstrated in prior studies [35,36]. The reason for the insignificant elevation of R_t when the stay-at-home orders were relaxed in Alabama and Mississippi is subject to interpretation. A possible reason was that the stay-at-home order was implemented in a rather relaxed manner, and its relaxation did not make a substantial behavioral change in human contact. Other southern states like Georgia also experienced a significant decline in R_t to a value of <1 following the stay-at-home order [30]. Another study to assess the effectiveness of stay-at-home orders in the US also found that such orders significantly reduced infection rates in Alabama, Louisiana, and Mississippi [36]. In our study, Louisiana recorded the highest decline in R_t after this order probably due to the early implementation as confirmed in other studies [37,38]. The relaxation of the order, therefore, led to an increase in R_t at the state level, and in Louisiana the increase was statistically significant. Underlying factors explaining the insignificant changes in transmission in Alabama and Mississippi should be explored in further studies.

School reopening has been reported by several studies to increase transmission of SARS-CoV-2 [39–41]. In our study, the Policy Change R_t increase after school reopening was statistically significant in Iberia and East Baton Rouge parishes, Louisiana (75th and 100th percentile population size) and Hinds, Mississippi (100th percentile size). A mathematical modeling study on school reopen-

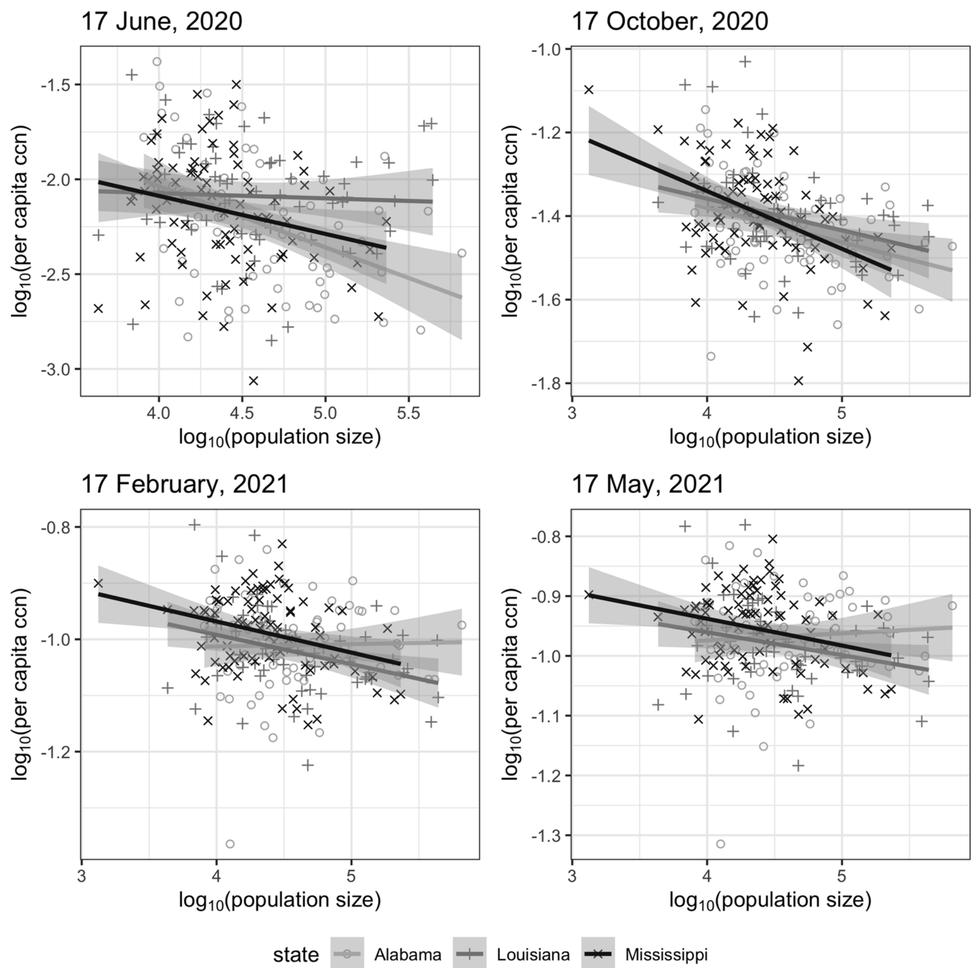

Fig. 3. Linear regression plots of the relationship between $\log_{10}$-transformed per capita cumulative case number (ccn), and the $\log_{10}$-transformed population size for Alabama (light gray circle), Louisiana (gray cross), and Mississippi (black diagonal cross) by date of report on June 17, 2020, October 17, 2020, February 17, 2021 and May 17, 2021.

ing reported that it was associated with increased risk in urban regions [42]. On the contrary, a study on COVID-19 in middle and high schools observed that counties with smaller population size in Florida were more likely to have an increased risk of transmission due to early reopening and a lack of mask mandates [43]. Other studies in Michigan and Washington states also concluded the impact of school re-opening on SARS-CoV-2 depended on the community transmission potential [44]. This is a probable explanation for the insignificant changes in Policy Change R_t in the five of the six selected counties with median and 75th percentile population sizes in our study.

In 2020, rural counties in Alabama, Louisiana and Mississippi had higher case burden than urban counties, similar to what was found in Georgia [30]. To the contrary, the opposite was true in the non-Appalachian region of Kentucky. Meanwhile, rural-urban disparities was generally not observed in the Appalachian region of Kentucky and both Delta and non-Delta regions of Arkansas over much of 2020 [33]. In a study of 5 Western states [41], North Dakota was the only state where densely populated counties consistently had a higher per-capita cumulative incidence throughout 2020. Rural counties in Louisiana and Mississippi continued to experience a higher burden in the first half of 2021. This may be due to the low vaccination rates in these counties, poor compliance to public health measures, hospital closures, increased likelihood of unemployment, and delay in seeking care due to lack of insurance [45,46]. This reiterates the need for public health outreach and the development of programs and policies to address the disparity.

Limitations

First, the R package EpiEstim solely takes into account case data and is not able to account for other data sources, such as changes in testing rate and contact patterns over time. Second, the uncertainty associated with data accuracy and quality was a critical issue to consider. Data quality can be affected by testing policies of each state and the efficiency of the states' case reporting systems. Third, the original dataset contained the dates of the case report and not the dates of infection or symptoms onset. Therefore, the epidemic curve was shifted backward by 9 days to account for the incubation period (mean, 6 days) and delay to testing (median, 3 days). This method was considered "tolerable" by Gostic et al. [25]. We acknowledge that we did not use deconvolution [47], which was more computationally demanding, to approximate the date of infection. Fourth, this is an ecological study that identifies association but cannot demonstrate causality between public health policy and changes in R_t. We were not able to conduct individual-level analysis due to the lack of demographic information of each case in aggregated data; hence, we could not investigate demographic risk factors for COVID-19 infection. Likewise, public health policies were implemented at a population level. Individuals' compliance to policies might vary. Fifth, the comparison between three different states, in the same manner, may not be very accurate as test reporting could vary from state to state. Sixth, for county-level analysis, we did not choose county with population size below the median for comparison. Hence, our results are restricted to relatively larger communities. The impact of the different policies might not have a monotonic relationship with population size, and this might be partially related to the limit in range.

Conclusions

Among all the policies implemented, the stay-at-home orders, face mask mandates, and vaccinations were associated with the most significant reductions in SARS-CoV-2 transmission in Alabama, Louisiana and Mississippi. The current study provides further evidence that state and county mandates and policy changes could have an impact on the trajectories of the pandemic in their jurisdictions. The rural-urban disparities in COVID-19 case burden reported here call for better evidence-based approaches in tailoring health promotion interventions and vaccination campaigns to rural residents and identifying the pertinent factors underlying the rural-urban disparities in the southern US.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.annepidem.2022.04.006.

References

[1] New York Times. covid-19 data. 2021. https://github.com/nytimes/covid-19-data [Accessed 17 May 2021].
[2] Wang Y, Liu Y, Struthers J, Lian M. Spatiotemporal characteristics of the COVID-19 epidemic in the United States. Clin Infect Dis 2021;72(4):643–51. doi:10.1093/cid/ciaa934.
[3] Boehmer TK, DeVies J, Caruso E, van Santen KL, Tang S, Black CL, et al. Changing age distribution of the COVID-19 pandemic—United States, May–August 2020. MMWR Morb Mortal Wkly Rep 2020;69(39):1404–9. doi:10.15585/mmwr.mm6939e1.
[4] Alexander M, Unruh L, Koval A, Belanger W. United States response to the COVID-19 pandemic, January–November 2020. Health Econ Policy Law 2022;17(1):62–75. doi:10.1017/S1744133121000116.
[5] Yamamoto N, Jiang B, Wang H. Quantifying compliance with COVID-19 mitigation policies in the US: a mathematical modeling study. Infect Dis Model 2021;6:503–13. doi:10.1016/j.idm.2021.02.004.
[6] Mississippi State of Department of Health. Mississippi reports first positive case of coronavirus. March 11, 2020. https://msdh.ms.gov/msdhsite/_static/23,21819,341.html. [Accessed 6 May 2022].
[7] Alabama Emergency Management Agency. First Alabama resident confirmed as positive for COVID-19. 13 March 2020. https://ema.alabama.gov/2020/03/13/first-alabama-resident-confirmed-as-positive-for-covid-19/ [Accessed 6 May 2022].
[8] Louisiana Department of Health. State of Louisiana reports first COVID-19 related death. 14 March 2021. Available at: https://ldh.la.gov/index.cfm/newsroom/detail/5479. [Accessed 6 May 2022].
[9] Omer SB, Yildirim I, Forman HP. Herd immunity and implications for SARS–CoV-2 control. JAMA Network Open 2020;324(20):2095–6.
[10] Chandler K. Vaccine Hesitancy a Problem in Effort to Return to 'Normal'. *U.S. News and World Report*. https://www.usnews.com/news/best-states/alabama/articles/2021-04-30/vaccine-hesitancy-a-problem-in-effort-to-return-to-normal [Accessed 6 May 2022].
[11] Jiménez J., Gamio L., Walker A.S. The American South could see a summer Covid surge as vaccinations lag. The New York Times. June 7, 2021. https://www.nytimes.com/2021/06/07/world/us-south-covid-vaccine.html [Accessed 6 May 2022].
[12] Iyanda AE, Boakye KA, Lu Y, Oppong JR. Racial/ethnic heterogeneity and rural-urban disparity of COVID-19 case fatality ratio in the USA: a negative binomial and GIS-based analysis. J Racial Ethn Health Disparities 2021;9:708–21 2021/02/26. doi:10.1007/s40615-021-01006-7.
[13] Cuadros DF, Branscum AJ, Mukandavire Z, Miller FD, MacKinnon N. Dynamics of the COVID-19 epidemic in urban and rural areas in the United States. Ann Epidemiol 2021;59:16–20. doi:10.1016/j.annepidem.2021.04.007.
[14] Madhav KC, Oral E, Straif-Bourgeois S, Rung AL, Peters ES. The effect of area deprivation on COVID-19 risk in Louisiana. PLoS ONE 2020;15(12) e0243028-e0243028. doi:10.1371/journal.pone.0243028.
[15] Lucar J, Wingler MJB, Cretella DA, Ward LM, Sims Gomillia CE, Chamberlain N, et al. Epidemiology, clinical features, and outcomes of hospitalized adults with COVID-19: early experience from an academic medical center in Mississippi. South Med J. 2021;114(3):144–9. doi:10.14423/SMJ.0000000000001222.
[16] Kaufman BG, Whitaker R, Pink G, Holmes GM. Half of rural residents at high risk of serious illness due to COVID-19, creating stress on rural hospitals. J Rural Health 2020;36(4):584–90.
[17] Scarinci IC, Pandya VN, Kim Y-I, et al. Factors associated with perceived susceptibility to covid-19 among urban and rural adults in Alabama. J Community Health 2021:1–10. doi:10.1007/s10900-021-00976-3.
[18] Rural Health Information Hub. Mississippi. https://www.ruralhealthinfo.org/states/mississippi. [Accessed 6 May 2022].
[19] Rural Health Information Hub. Louisiana. https://www.ruralhealthinfo.org/states/louisiana. [Accessed 6 May 2022].
[20] Rural Health Information Hub. Alabama. https://www.ruralhealthinfo.org/states/alabama. [Accessed 6 May 2022].
[21] Nonmetro population change has remained near zero in recent years. Accessed 08/31/ 2021. https://www.ers.usda.gov/data-products/charts-of-note/charts-of-note/?topicId=4e8a0642-e40d-4299-906e-906bbaaf9e4d.
[22] Park M, Lim JT, Wang L, Cook AR, Dickens BL. Urban-rural disparities for COVID-19: Evidence from 10 countries and areas in the Western Pacific. Health Data Science 2021;2021:9790275. doi:10.34133/2021/9790275.
[23] Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. Am. J. Epidemiol. 2013;178(9):1505–12. doi:10.1093/aje/kwt133.
[24] Thompson RN, Stockwin JE, van Gaalen RD, Polonsky JA, Kamvar ZN, Demarsh PA, et al. Improved inference of time-varying reproduction numbers during infectious disease outbreaks. Epidemics 2019;29:100356. doi:10.1016/j.epidem.2019.100356.
[25] Gostic KM, McGough L, Baskerville EB, Abbott S, Joshi K, Tedijanto C, et al. Practical considerations for measuring the effective reproductive number, R_t. PLoS Comput. Biol. 2020;16(12):e1008409. doi:10.1371/journal.pcbi.1008409.
[26] United States Census Bureau. County population totals: 2010-2019. 2021. https://www.census.gov/data/tables/time-series/demo/popest/2010s-counties-total.html. [Accessed 6 May 2022.]
[27] R Core Team. R: a language and environment for statistical computing. https://www.R-project.org/ [Accessed 6 May 2022].
[28] You C, Deng Y, Hu W, Sun J, Lin Q, Zhou F, et al. Estimation of the time-varying reproduction number of COVID-19 outbreak in China. Int J Hyg Environ Health 2020;228:113555. doi:10.1016/j.ijheh.2020.113555.
[29] Fung IC, Hung YW, Ofori SK, Muniz-Rodriguez K, Lai PY, Chowell G. SARS-CoV-2 Transmission in Alberta, British Columbia, and Ontario, Canada, December 25, 2019, to December 1, 2020. Disaster Med Public Health Prep 2021:1–10 In press. doi:10.1017/dmp.2021.78.
[30] Ogwara CA, Mallhi AK, Hua X, Muniz-Rodriguez K, Schwind JS, Zhou X, et al. Spatially refined time-varying reproduction numbers of COVID-19 by health district in Georgia, USA, March–December 2020. Epidemiologia 2021;2(2):179–97. doi:10.3390/epidemiologia2020014.
[31] Muniz-Rodriguez K, Chowell G, Schwind JS, Ford R, Ofori SK, Ogwara CA, et al. Time-varying Reproduction Numbers of COVID-19 in Georgia, USA, March 2, 2020 to November 20, 2020. Perm J. 2021;25:20.232. https://thepermanentejournal.org/issues/2021/spring/7627-time-varying-reproduction-numbers-of-covid-19-in-georgia,-usa,-march-2,-2020-to-november-20,-2020.html [Accessed 6 May 2022].
[32] Fung IC-H, Zhou X, Cheung C-N, Ofori SK, Muniz-Rodriguez K, Cheung C-H, et al. Assessing early heterogeneity in doubling times of the COVID-19 epidemic across prefectures in mainland China, January–February 2020. Epidemiologia 2021;2(1):95–113. doi:10.3390/epidemiologia2010009.
[33] Politis MD, Hua X, Ogwara CA, Davies MR, Adebile TM, Sherman MP, et al. Spatially refined time-varying reproduction numbers of SARS-CoV-2 in Arkansas and Kentucky and their relationship to population size and public health policy, March-November 2020. Ann Epidemiol. 2022;68:37–44. doi:10.1016/j.annepidem.2021.12.012.
[34] Padalabalanarayanan S, Hanumanthu VS, Sen B. Association of state stay-at-home orders and state-level African American population with COVID-19 case rates. JAMA Network Open 2020;3(10):e2026010 e2026010-e2026010. doi:10.1001/jamanetworkopen.2020.26010.
[35] Fowler JH, Hill SJ, Levin R, Obradovich N. Stay-at-home orders associate with subsequent decreases in COVID-19 cases and fatalities in the United States. PLoS ONE 2021;16(6):e0248849. doi:10.1371/journal.pone.0248849.
[36] Castillo RC, Staguhn ED, Weston-Farber E. The effect of state-level stay-at-home orders on COVID-19 infection rates. Am J Infect Control 2020;48(8):958–60. doi:10.1016/j.ajic.2020.05.017.
[37] Lasry A, Kidder D, Hast M, Poovey J, Sunshine G, Winglee K, et al. Timing of community mitigation and changes in reported covid-19 and community mobility - Four U.S. metropolitan areas, February 26-April 1, 2020. MMWR Morb Mortal Wkly Rep 2020;69(15):451–7. doi:10.15585/mmwr.mm6915e2.
[38] Moreland A, Herlihy C, Tynan MA, Sunshine G, McCord RF, Hilton C, et al. Timing of state and territorial COVID-19 stay-at-home orders and changes in population movement - United States, March 1-May 31, 2020. MMWR Morb Mortal Wkly Rep 2020;69(35):1198–203. doi:10.15585/mmwr.mm6935a2.
[39] Fantini MP, Reno C, Biserni GB, Savoia E, Lanari M. COVID-19 and the re-opening of schools: a policy maker's dilemma. Ital J Pediatr 2020;46(1):79 2020/06/09. doi:10.1186/s13052-020-00844-1.
[40] Davies MR, Hua X, Jacobs TD, Wiggill GI, Lai P-Y, Du Z, et al. SARS-CoV-2 transmission potential and policy changes in South Carolina, February 2020 – January 2021. medRxiv 2021. doi:10.1101/2021.09.25.21263798.
[41] Hua X, Kehoe ARD, Tome J, Motaghi M, Ofori SK, Lai P-Y, et al. Late surges in COVID-19 cases and varying transmission potential partially due to public health policy changes in 5 Western states, March 10, 2020-January 10, 2021. medRxiv 2021. doi:10.1101/2021.07.04.21259992.

[42] Massad E, Amaku M, Tadeu Covas D, Fernandes Lopez L, Coutinho FAB. Estimating the effects of reopening of schools on the course of the epidemic of COVID-19. Epidemiol Infect 2021;149:e86. doi:10.1017/S0950268821000686.
[43] Doyle T, Kendrick K, Troelstrup T, Gumke M, Edwards J, Chapman S, et al. COVID-19 in primary and secondary school settings during the first semester of school reopening—Florida, August–December 2020. MMWR Morb Mortal Wkly Rep. 2021;70(12):437–41. doi:10.15585/mmwr.mm7012e2.
[44] National Center for Immunization and Respiratory Diseases (NCIRD) Division of Viral DiseasesScience Brief: Transmission of SARS-CoV-2 in K-12 Schools and Early Care and Education Programs – Updated. CDC COVID-19 Sci Briefs [Internet] 2021 Centers for Disease Control and Prevention (US). https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/transmission_k_12_schools.html. [Accessed 6 May 2022].
[45] Brown CC, Young SG, Pro GC. COVID-19 vaccination rates vary by community vulnerability: a county-level analysis. Vaccine 2021;39(31):4245–9. doi:10.1016/j.vaccine.2021.06.038.
[46] Melvin SC, Wiggins C, Burse N, Thompson E, Monger M. The role of public health in COVID-19 emergency response efforts from a rural health perspective. Prev Chronic Dis 2020;17:E70. doi:10.5888/pcd17.200256.
[47] Goldstein E, Dushoff J, Ma J, Plotkin JB, Earn DJ, Lipsitch M. Reconstructing influenza incidence by deconvolution of daily mortality time series. Proc Natl Acad Sci U S A 2009;106(51):21825–9. doi:10.1073/pnas.0902958106.