Peer Review File

Article information: http://dx.doi.org/10.21037/jphe-20-96

Comment 1: The authors should devote a portion of the discussion to specifically detailing the limitations, weaknesses, and potential misinterpretations of their study, and how they have dealt with them. Aside from the formal ecological fallacy (the danger of applying aggregated results on an individual level to make inferences about socioeconomic characteristics) particular they should address:

1. Potential for systematic differences between states (or counties) in recording COVID-19 cases/death frequency.
2. Potential for systematic differences between states in the measurement socioeconomic parameters.
3. The potential for confounding factors which have not been considered in the study (either known, or unknown) for which there may or may not be data.

Reply 1: We agree with the reviewer. This is a limited in scope and data availability study that provides useful insights for future targeted studies

Changes in the text: The following section is added in the manuscript: "This study had some limitations. Daily COVID-19 cases and deaths were reported by state, county of city health departments based on data provided to them by health care and related facilities. Although government agencies operate and comply with the same set of federal regulations, it was possible that raw daily counts may have been irregularly reported. However, given that original data were continuously updated and screened, we expect that the potential for systematic error on COVID-19 reports to be small. It is also possible that deaths may have been misclassified, particularly in regions with many daily deaths; however, there is no evidence of substantial under or over-reporting COVID-19 deaths in the literature. The spatial scale of the analysis may also be challenging, given the vast differences in the distribution of COVID-19 cases, deaths and population characteristics within states. Analysis at a finer scale would have been incomplete for the study period, due to relatively low COVID-19 cases and deaths in sparsely populated rural counties (because of the relatively widespread of statewide policies on school closures and gathering restrictions). Given that minorities disproportionally reside in heavily populated urban areas that experienced the highest COVID-19 cases and deaths rates, we anticipate that the use of state-level population characteristics, that includes rural areas with predominantly white residents, may underestimate the effect of race and ethnicity on COVID-19 mortality. Other individual and community-level parameters may also affect COVID-19 spread and mortality. These may include pre-existing medical conditions, smoking, housing, living conditions, time spent indoors or outdoors, environmental factors (temperature, humidity, solar radiation, air quality) affecting the survival of SARS-CoV-2 virus, personal hygiene and activities, and businesses practices. Understanding their effect on COVID-19 spread and mortality require a combination of field, laboratory, biomedical and health-related studies."

Comment 2: As entities, the states are highly heterogeneous. This is particularly evident in the four most populous states which the authors choose as a case study in Figure 1, all of which have a particularly stark rural/urban divide. For example, upstate New York, or rural Texas has vastly different demographic and socioeconomic parameters to New York City or Texan metropolitan

areas such as Houston, DFW, or Austin. This is true in all of the parameters which the authors choose to study (table 2). Repeating the analysis at a smaller aggregation level (such as county level) would provide much greater confidence in the results of the analysis, and in particular I believe the benefits would greatly outweigh the downsides (e.g., minor difficulties between county of residency and county of hospitalization as alluded to by the authors). This is amplified by the fact that many of the policy responses were devolved from state level down to county or metropolitan level.
Reply 2: Conceptually this may be true, but practically it was challenging for the following reasons. As already mentioned, matching COVID-19 cases and deaths reported in a county for residents living in another county may disproportionally affect rural communities. In addition, the majority of COVID-19 cases and deaths were observed within and around urban areas, whereas the progression of both cases and deaths in rural counties (the majority of US counties) was very slow (1-2 cases per day, 0-1 deaths every other day). As a result, the outputs of Boltzmann sigmoidal fitting would have been more uncertain (and in some cases would not resemble a sigmoidal curve). Considering the distribution of COVID-19 cases, deaths and population characteristics between urban (higher percentage of minorities) and rural (higher percentage of white residents) communities, we anticipate that the potential effect of race on COVID-19 may be somewhat underestimated, but it was in agreement with previous studies. It is possible that as the virus becomes endemic within the US, county-level analysis may be feasible for the second (summer 2020) and subsequent waves of the pandemic.
Changes in the text: See Response to Comment #1.

Comment 3: Numerical reporting could be much clearer throughout, including reporting specific p-values in tables or in the text where significance is implied.
Reply 3: The manuscript was revised for consistency and in response to specific comments.
Changes in the text: See Response to Comments #14-18.

Comment 4: Spelling, punctuation, and grammar could be improved throughout the manuscript. In some cases this leads to difficult comprehension. This occurs throughout the paper, examples line 69, “may have experiencing”; line 71, “who they represent”; or the sentence beginning on line 72.
Reply 4: The manuscript has been proofread
Changes in the text: Statements are modified as follows: “There are preliminary indications that minorities have been disproportionally affected by COVID-19 (12, 13). In fact, more than 50% of deaths in Wisconsin and Chicago, Illinois were African–Americans, despite that African-Americans account for less than 30% of the population (14). Assessing racial and socioeconomic disparities of COVID-19 in the midst of pandemic are challenging because of poor and irregular tracking of race and socioeconomic characteristics.“

Comment 5: Given the public interest in COVID-19 research, the authors should consider making their data and statistics (tables, shapefiles etc.) available either as supplementary information or in a publicly available repository such as GitHub.
Reply 5: This study is part of a dissertation. The data will be released as soon as the dissertation is completed in accordance with CUNY policies.
Changes in the text: None

Comment 6: Line 79 – The authors state that COVID-19 cases and deaths were consistently reported for all states. There is multiple anecdotal evidence that suggests this was not the case. The authors should justify this statement and support it with references.
Reply 6: We agree with the reviewer. It is expected that COVID-19 mortality rates may be accurately counted upon thorough review of death certificates over the next couple years.
Changes in the text: We revised the statement as follows: "For this analysis, statewide COVID-19 cases and deaths as reported by state, county and city health departments." Further analysis of reporting issues is described in the Response to Comment #1.

Comment 7: Line 83 – The authors state that social distancing policies were implemented across each state. In many states, the COVID-19 response policy was devolved down to a county or even a metropolitan level. Even where there was a statewide policy response, many counties or cities either imposed additional measures or had vastly different enforcement levels. See for example https://doi.org/10.26633/RPSP.2020.90. This supports the argument presented above of repeating the analysis with a lower aggregation level.
Reply 7: We agree with the reviewer that as the disease progressed, localities implemented measures differently, particularly regarding the enforcement. Many social distancing policies were decided and implemented on a state level (closure of educational activities, gatherings restrictions) while other may have been loosely followed (closure of non-essential businesses). The dates of policy implementation are available by state. For the reasons outlines in Comment #2, this analysis may only be limited on state level.
Changes in the text: The statement is modified as follows: "state-wide social distancing policies and measures were initially implemented such as the closure of educational facilities and gathering restrictions and trends were representative of state outcomes. It is noteworthy that the implementation of policies such as the closure of non-essential business may have not be consistent across the US due to lack of enforcements by local agencies."

Comment 8: Line 103 – "Higher than (e-1)" – the authors should clarify this and if necessary use inliine math formatting.
Reply 8: During the first wave of the pandemic, healthcare and associated facilities were crippling to take care and track patients, included deaths. For this reason, it was possible that daily death counts may have been reported irregularly, such as deaths occurring over a period of a few days being reported as a lump sum at the end of the period. To identify these cases, COVID-19 counts and deaths that were higher than (e-1) of previous days COVID-19 counts and deaths were flagged and monitored to determine the cause and any trend changes.
Changes in the text: The text was modified as follows: "Daily COVID-19 cases of deaths higher than (e-1) times the previous day COVID-19 counts or deaths were flagged and assessed. They were attributed to the introduction of new testing technologies at the beginning of the pandemic in the US that increased the number of positive tests and cumulative reports of deaths at home or non-clinical facilities (e.g. nursing homes), respectively."

Comment 9: Line 104 – the authors should specify what is meant my "irregular increases".
Reply 9: See response in Comment #8
Changes in the text: See response in Comment #8

Comment 10: Equation 1 – there appears to be a typo in this equation as there is an open parenthesis on the denominator with no close parenthesis. You should also explicitly define i and x.
Reply 10: It is corrected. The "*i*" indicator was explained (*i*-th day). Fr consstency, we also replaced the factor "*x*" that corresponds to the date, with the indicator "*i*", in the equation.
Changes in the text: The equation is modified as follows $Y_{i,k} = \frac{Y_{0,k} - Y_{max,k}}{\left(1+e^{\left(\frac{i-c_k}{a_k}\right)}\right)} + Y_{max,k}$. The following statement was added: "…, where $Y_{i,k}$ was COVID-19 cases or deaths on *i*-day in *k*-th state"

Comment 11: Line 129 – The US census is a decadal event. There was no census in 2019, the most recent being 2010 (or the 2020 census which is currently being conducted). Did the authors use the 2010 figures? If so they should comment on the accuracy of using 10 year old data. If they used more recent figures then presumably they actually used the data from the American Communities Survey 2019. As this is a sample survey there is inherent inaccuracy in the ACS figures. In this case they should consider using the ACS 2014-2018 5-year estimates which while slightly older have greater accuracy than the ACS 2019 estimates due to the larger sample size. The data are publicly available.
Reply 11: We used the ACS 2019 estimates.
Changes in the text: The statement is modifies as follows: "The characteristics of population in each state for 2019 were obtained from U.S. Census American Community Survey"

Comment 12: Line 130 – Age – why do the authors choose 45 years old as the cut off age? This choice should be justified as opposed to say 65+ or 18+. Young and old populations have very different mixing patterns, would it also make sense to look at percentage of young dependents?
Reply 12: Based on previous studies, those older than 45 years were most likely to experience severe symptoms of the disease and those older than 65+ years had disproportionally high COVID-19 mortality rate. In our analysis, we consider the relationship between COVID-19 mortality (dependent) and cases (independent), we chose to include the 45 years or older age bracket to account for the susceptibility of the aged population on COVID-19.
Changes in the text: The following statement was added: "The percent of people older than 45 years were selected to account for the increased COVID-19 susceptibility (both severe cases and/or mortality) of older population."

Comment 13: Line 131 – Race – Multiple studies have shown differing COVID-19 transmission characteristics and outcomes between racial groups. The authors should consider repeating the analysis including multiple racial groups (for example White, Black, Asian, Hispanic, and other) rather than just a white/non-white dichotomy.
Reply 13: More detailed representation of racial/ethnic groups may provide, in principle, a better representation of disparities, however, the uncertainty of regression outputs is increased due to the decreased the degrees of freedom and variability. For some racial groups, there are substantial differences in the percentage of racial groups (e.g. Asian and Hispanic). The is only one state with more than 10% of Asian population in the US (40 states with less than 5%), and 5 states with more than 25% of Hispanics (38 states less than 12.5%)
Changes in the text: No changes.

Comment 14: Line 143 – The authors use ANOVA to assess difference between groups. They should confirm that assumptions required for ANOVA are met (in particular the F-test is

susceptible to violations of homogeneity). Further, it is not clear if they are using adjustments (Tukey/Bonferroni etc.) in any post-hoc analysis (in part the reporting in the results lines 225–235 could clarify this).
Reply 14: The ANOVA analysis was repeated using Bonferroni adjustments.
Changes in the text: The statement is added (Data analysis): "Tests were conducted using Bonferroni adjusted alpha levels of .0125 per test (0.05/4)." The statement is modified in Results as follows: "The rate of the exponential increase period was significantly higher for the most densely populated urban areas (Q4) as compared to areas with the first three quintiles ($p < 0.001$). The pairwise comparison of the exponential increase period for areas within Q1, Q2 and Q3 by urban population density was non-significant. The rate of the exponential increase period was significantly lower for states with the higher percentage of males (Q3 and Q4) as compared to the states with the lowest male population (Q1) ($p = 0.010$). There was no difference on both the duration and mean rate for states grouped based on population older than 45 years, uninsured, non-Whites, Hispanics and living below poverty level."

Comment 15: Line 147 – The authors use a 0.10 confidence level. A more usual choice in similar ecological studies would be 0.05 or even 0.01, particularly given limitations in ecological analysis. The authors should consider using a 0.05 confidence level at a minimum, or provide a power analysis to support their choice of confidence level.
Reply 15: We revised it to have the same confidence levels for all statistical tests in this analysis. We also revised text in Results and Discussion to reflect the actual p-values (see Response to Comment #17 below).
Changes in the text: The statement is modified as follows: "Significance of the regression coefficient was determined by rejecting the null hypothesis at the 0.05 level."

Comment 16: Line 155 – How was spatial autocorrelation assessed? If a test was used (e.g. Moran's I) then this should be reported along with the associated p-value.
Reply 16: Yes.
Changes in the text: The statement is modified as follows: "Spatial autocorrelation of the regression residual was assessed using GeoDa software; however, no differences were observed (Moran's I=-0.003, p:0.040) (23)."

Comment 17: Exact p-values should be reported for all of the variables. Especially with alpha = 0.10. In an ecological analysis there is a large difference in confidence between say $p = 0.09$ and $p = 0.0001$. This should be done at least in the text, but ideally incorporated into table 2 in order to see the difference between significant and non-significant variables.
Reply 17: It is corrected. Table 2 is modified. Text also adjusted (see Response to Comment #14)
Changes in the text: The following superscript description is added:
"[a] Bonferroni adjusted Q4-Q1 ($p<0.001$), Q4-Q2 ($p<0.001$), Q4-Q3 ($p=0.01$)
[b] Bonferroni adjusted Q1-Q2 ($p=0.425$), Q1-Q3 ($p=0.01$), Q1-Q4 ($p=0.01$)"

Comment 18: Table 3 needs much more explanation. It also suffers from a lack of p-values. Unless I am reading it wrong, it appears that only the number of COVID-19 cases is a significant contributor to change in mortality rate at alpha = 0.05 (though it is not explained why the authors use 0.05 here but 0.10 elsewhere). The text (lines 241-246) doesn't make this clear, and instead

talks about increases of greater than 50% or 30% without noting that these increases are not significant. The authors should be consistent with the message they are trying to get across, and if the increases are not significant should be upfront about this.

Reply 18: The manuscript was revised to make sure that the same threshold ($p = 0.05$) was used.

Changes in the text: The statement was modified as follows: "The relationship between COVID-19 deaths and cases rates for the exponential increase period and the contribution of population characteristics was assessed for an IQR increase of the dependent variable (Table 3) ($R^2 = 0.86$). A positive relationship was observed for all variables. The stronger association was observed for the disease rate as expected; an increase of up to 340% for an increase of 43.7 cases per 1,000,000 residences ($p < 0.001$). An increase of more than 50% on the exponential increase period death rate was computed for an IQR range change in the percentage of older than 45 years and minorities, followed by males (a 30% increase). This indicated that the socioeconomic status and profile of affected communities had an immediate impact on COVID-19 mortality, albeit the threshold of statistical significance was not reached. This may be associated with long-term disparities in healthcare access for minorities, particularly those living in large urban areas." In addition, p-values are added in Table 3.