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Yadah Ampofo March 25, 2022

An Ecological Analysis of Overcrowded Housing, Vaccination coverage, and COVID-19 Case and Death Rates

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Abstract

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Social distancing and COVID-19 vaccinations are core public health mitigation measures to curb the spread of the SARS-CoV-2 virus in the United States. Overcrowded housing limits the ability to socially distance, and low community vaccination coverage leads to population susceptibility to the virus. We sought to investigate the association of overcrowded housing and vaccination coverage with new monthly COVID-19 case and death rates in 2021.

The unit of analysis was the county. The primary exposures include the proportion of households that were overcrowded (defined >1 person per room) and the cumulative population percentage that was vaccinated at the end of each month. Study outcomes were monthly new COVID-19 case and death rates per 100,000 population. We characterized monthly variations in the study exposures and outcomes and estimated their correlation by month in the 2021 year using Pearson coefficients. County vulnerability was categorized into four groups as: “High” (Top 25% overcrowded housing and Bottom 25% vaccination coverage); “High Overcrowded Housing” (Top 25% overcrowded housing and Top 75% vaccination coverage); “Low vaccination coverage” (Bottom 75% overcrowded housing and Bottom 25% vaccination coverage); and “Low” (Bottom 75% overcrowded housing and top 75% vaccination coverage). Associations of the composite vulnerability measure rates with COVID-19 case and death rates were estimated using linear regression. All statistical analyses accounted for calendar month through stratification or adjustment.

Data from 2,137 U.S. counties were analyzed. The correlation of overcrowded housing and vaccination rates with COVID-19 outcomes remained weak throughout the year (range of r= -0.259 to r=0.2030). The proportion of counties categorized as having high vulnerability reduced from 24.9% in January to 0.084% in December. In the adjusted model accounting for county-level socio-demographic factors and calendar month, there were no statistically significant associations between high vulnerability and COVID-19 case rates (β = 2.18; 95% CI -32.8, 37.1 p = 0.963) or death rates (β = 0.80, 95% CI -0.3,1.9, p = 0.162).

Despite weak monthly correlations among overcrowded housing, vaccination coverage, and COVID-19 outcomes at a county-level, we found no association of combined high overcrowded housing and low vaccination coverage with COVID-19 case or death rates during the 2021 year.

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Chapter 1: Introduction

1.0 Background

In the last two years, the COVID-19 Pandemic has resulted in the surge of catastrophic public health events in the United States. The frequent spikes in COVID-19 infections and hospitalizations, have caused health systems to become extremely overburdened and significantly affected patient health outcomes in hospitals across the country (Karan & Wadhera, 2021). According to the data published by the Centers for Disease Control and Prevention (CDC) COVID Data Tracker, as of 31st December 2021, there had been 54.74 million confirmed cases and 825.8 thousand deaths in the United States since the beginning of the pandemic (CDC, 2020). Public health officials have advised the use of social distancing, masking wearing, and vaccinations as key precautions against the disease and its complications. However, these precautions have been heavily politicized and publicly disputed (Bazant & Bush, 2021). Nevertheless, in the last few years, U.S. public health institutions have made great strides in boosting vaccine confidence and encouraging civilians to get vaccinated. According to the CDC COVID Data Tracker, as of January 11th 2022, 62.6% of the total population has been fully vaccinated, and 74.4% have received at least one dose (CDC, 2020).

Despite the remarkable vaccine uptake statistics, a significant proportion of the U.S. population is still not vaccinated. This can be attributed to vaccine hesitancy and physical vaccine accessibility barriers. The hesitancy stems from personal mistrust in vaccine safety and efficacy (Gonzales et al., 2021) which is largely influenced by the individual's cultural beliefs, political stance and public opinions (Beleche, 2021). However, for individuals who trust and want the vaccine, existing physical access barriers hinders their ability to do so. These barriers include the geographic proximity to the vaccine location sites, transportation expenses, complexities involved in vaccine scheduling as well as the immobility of elderly homebound individuals (Gonzales et al., 2021). Although there have been Federal interventions to combat vaccine hesitancy and breakdown these barriers, much more needs to be done. Until these issues are successfully addressed, unvaccinated individuals would continue to be extremely vulnerable to virus.

The dangers of this vulnerability is further reinforced by the association between high rates of COVID-19 cases and deaths and counties with low vaccination coverage (McLaughlin et al., 2022). Especially considering the various highly transmissible SARS-CoV-2 strains identified so far (van Oosterhout et al., 2021). The alarming mutation rate of the virus, only underscores the need for mass immunizations to successfully curb the possible increased transmission (Anderson & May, 1985) associated with emerging variants as well as decrease COVID-19 case and death rates.

Although there have been incidences of breakthrough COVID-19 cases, (Parums, 2021) the overall effectiveness of the COVID-19 vaccines is yet to be negated. Previous publications have shown that vaccinated individuals with breakthrough cases only experience mild symptoms (Duarte et al., 2021). Furthermore, they are also less likely to experience severe illness and hospitalizations compared to unvaccinated individuals (Klompas, 2021).

As a result, an unvaccinated status combined with the inability to social distance, puts unvaccinated overcrowded housing inhabitants at a much greater risk of contracting the virus (Fazio et al., 2021). Previous research publications have presented a linkage between overcrowding and negative physical health outcomes. Overcrowding has shown to increase the risk of infections, severe disease and the risk of having long term effects associated with the infectious disease (Gray et al., 2001). Furthermore, due to the fact that the virus is transmitted through physical contact, aerosols and respiratory droplets (Khan et al., 2020), overcrowded households could play a significant role in the transmission of the virus (Gray et al., 2001). The intrafamily transmission experienced within these crowded home settings, results in an increase in community transmissions which continues to propagate the spread of the virus (Khan et al., 2020). As a result, the inability to adequately practice social distancing within crowded homes, serves as a major public health threat.

Although some individuals make the personal decision to be unvaccinated and live in overcrowded settings, existing racial and ethnic disparities are also drivers in the creating the proportion of the population that is both unvaccinated and living in crowded housing. The factors that influence vaccination disparities include transportation difficulties (Bergal 2021), vaccine availability, barriers to access pharmacies, vaccination scheduling (Select Subcomitee on the cornavirus crisis, 2021) and the distrusts resulting from poor historical medical treatments and discriminatory experiences in healthcare (Committee on Equitable Allocation of Vaccine for the Novel Coronavirus et al., 2020).

In addition to racial and ethnic vaccination disparities, there are also racial disparities in the exposure to overcrowded housing. People of color and people of low income, are severely impacted compared to other races and ethnicities (Blake et al., 2007). Blacks and low-income individuals are 1.7 times and 2.2 times more likely to be residents of poor quality housing compared to the general population (Krieger & Higgins, 2002). Due to extreme economical vulnerability, some people may be forced to live in poor quality conditions with multiple roommates in order to reduce rent costs. However, crowded housing arrangements have been associated with the fast spread of infections. As a result, the economic benefit could sometimes be at the expense of their health (Dougherty, 2020).

Although adequate indoor ventilation and mask wearing must also be taken into account when assessing disease transmission within crowded indoor settings (Bazant & Bush, 2021), the need for low-income housing may cause tenants to accept certain structural inadequacies (The Joint Center for Housing Studies of Harvard University, 2017) such as the lack of ventilation. Furthermore, although mask-wearing is effective in reducing intra-family transmissions (Wang et al., 2020), the probability of people not wearing masks inside their homes still exists.

As a result, inadequate ventilation, and the probability that the overcrowded house may be a non-mask-wearing home, only leaves poor-quality housing residents with social distancing and vaccinations as their only arsenal against virus transmission. Recent research simulation results have shown that the combination of vaccinations and social distancing has an even greater effect in reduce COVID-19 mortality, compared to vaccinations alone (Gumel et al., 2021). However, in a crowded poor-quality housing setting, residents who are most likely blacks and low-income individuals (Krieger & Higgins, 2002) are deprived of basic structural requirements, the opportunity to practice social distancing, and are continually faced with vaccination barriers (Gonzales et al., 2021). These existing housing problems, combined with the low vaccination coverage experienced by the same black and low-income population, underscores how vulnerable a fraction of the population is to COVD-19 cases and deaths.

Chapter 2: Literature Review

2.0 COVID-19 Origins and Epidemiology

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a respiratory illness-causing virus that was first detected in the Chinese city of Wuhan in the Hubei Sheng Province. The associated illness is commonly known as COVID-19. Epidemiological investigations have revealed that most of the earliest cases recorded, were all connected to the Huanan Seafood Wholesale Market. Although, the precise primary reservoir of the SARS-CoV-2 virus is still unknown (Wu et al., 2020), studies soon lent credence to the virus' human-to-human transmission pathway soon after it was detected (Li et al., 2020). The increased prevalence of the coronavirus worldwide, resulted in the World Health Organization (WHO) classification of COVID-19 as a pandemic on March 11, 2020 (Cucinotta & Vanelli, 2020).

Since the virus' first detection in China, it has undergone several adaptive mutations that have resulted in multiple alarming variants. These include the Alpha (B.1.1.7); Beta (B.1.351); and Gamma (P.1); Delta (B.1.617.2), and Omicron (B.1.1.529) variants. The fact that each new emerging variant has the potential to be more transmissible and severe than the preceding variant (Aleem et al., 2022) only makes containing the virus even more challenging, thus worsening the public fear and uncertainty surrounding the virus and the entirety of the pandemic.

2.1 COVID-19 Transmission

COVID-19 is a transmissible illness that is spread through tiny aerosols released when an infected person coughs, sneezes or talks. Anyone in close contact with infected person, could result in the aerosols spreading into their mouth or nose and can easily be inbreathed into their lungs (Harvard Health Publishing, 2020). The common symptoms associated with coronavirus diseases include fever, cough, dyspnea, sputum production, myalgia, arthralgia, headache, diarrhea, rhinorrhea, and sore throat. However, incidents of anosmia (the loss of taste) and ageusia (the loss of smell) has also been reported (Lechien et al., 2020). Although most symptoms are treatable, long-term symptoms can persist even after patient tests negative for the SARS-CoV-2 virus. A recent meta-analysis study published shows that COVID-19 can have long term post-infection effects on numerous organs such as the lungs, heart, kidney, and the liver (Zarei et al., 2021).

2.2 COVID-19 Detection

The COVID-19 illness is commonly diagnosed using molecular, antigen, and antibody tests. The Polymerase Chain Reaction (PCR) test, which is a type of molecular testing, involves amplifying small quantities of ribonucleic acid (RNA) in SARS-CoV-2 and embedding RNA into deoxyribonucleic acid (DNA). The DNA is then replicated until the presence of the SARS-CoV-2 is identified (Cleaveland Clinic 2021).The antigen COVID-19 test involves an “immunoassay” of the SARS-CoV-2 virus to detect a “specific viral antigen” that would identify the presence of the virus in the body (CDC 2020). Furthermore, the antibody test involves looking for SARS-CoV-2 antibodies produced in the blood to confirm a previous infection. As a result, the antibody tests can only detect past COVID-19 infections and cannot be used to detect active COVID-19 infections (Texas Department of State Health Services, 2021).

2.3 COVID-19 Mitigation and Prevention Measures

(a) Non-pharmaceutical measures

Prior to the availability of vaccines, several non-pharmaceutical measures were established by the CDC to halt the transmission of the virus. These measures include hand washing, mask-wearing, and social distancing. A recent study published last year revealed that the SARS-CoV-2 virus can live on plastic and steel surfaces for up to 72 hours. As a result, frequent handwashing is considered a very effective way to protect oneself. The study also showed the virus also remained viable in aerosols for up to 3 hours (van Doremalen et al., 2020). Consequently, wearing a mask is an effective way to reduce the spread of the virus in a compromised environment. In addition to mask wearing, adherence to the social distancing measures of being 6ft apart, could also decrease the probability of being in close contact with an infected person, thus reducing the chances of virus transmissibility.

(b) **Pharmaceutical measures**

COVID-19 Vaccines

In response to the severity of the pandemic, scientists and governments across the globe conducted an unprecedented collaboration to create COVID-19 vaccines that would help curb the transmission of the virus and reduce mortality across the globe. The FDA approved vaccines include Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson). Research studies lent credence to their effectiveness against severe COVID-19 illness, disease and hospitalizations (National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases., 2021). However, despite the public health campaigns' emphasis on the vaccine benefits and the large-scale vaccination rollout in the United States, a fraction of the population remains unvaccinated for various reasons.

A recent survey study conducted by the Kaiser Family Foundation (KFF) still shows that there is still some hesitancy surrounding vaccine uptake in the United States. According to the survey, 12% of the population sampled in the study would never agree to take the COVID-19 Vaccines (Hamel et al., 2020). On the other hand, individuals who would want to get the vaccine, are impeded by vaccine access barriers especially in areas habited by marginalized persons. Examples of these barriers include transportation inaccessibility, language barriers as well as vaccine scheduling conflicts (Lee & Davis, 2021). The personal decision to not get a vaccine and the existing vaccination barriers, leaves a fraction of the population with a much lower level of immune protection against the virus compared to vaccinated persons.

(c) Vaccine Derived Herd Immunity

In addition to the individual level protection provided by vaccinations, the population level-protection through herd immunity has also been proposed since the beginning of the pandemic. Herd immunity occurs when an entire population has individual level immunity, that statistically reduces the probability of an infected person engaging with an uninfected person. As a result, the probability of close contact infections becomes too small to create an outbreak. Attaining herd immunity through natural infections is considered improbable. However, obtaining herd immunity through vaccinations is the considered most ethical and feasible pathway (Aschwanden, 2020).

However, the population proportion required to attain vaccine-derived herd immunity, has historically remained unclear due to multiple factors. These factors include the vaccine immunity duration, the contagiousness of the virus, the inevitable virus mutations, and the interference of environmental factors such as humidity and ultraviolet rays (Bach et al., 2021).

2.4 Demographic Differences in COVID-19 Health Outcomes

Although everyone is susceptible to the virus, some individuals are more vulnerable than others. Research has shown that COVID-19 disproportionately affects elderly individuals compared to younger individuals. This has been primarily attributed to a much weaker immune system and the increased risk of underlying comorbidities among the elderly population (Crimmins, 2020). Deaths and hospitalizations for patients with comorbidities were respectively 6 times and 12 times higher than those without comorbidities (Stokes et al., 2020). Furthermore, recent studies have also presented gender differences in the virulence and mortality of the virus. According to the study, men are more likely to experience virulent health outcomes and deaths compared to women, even when controlling for age (Jin et al., 2020). In addition to gender differences, racial and ethnic differences in the virulence of the virus have also been analyzed. Previous publications have shown that Black and Asian individuals are at a higher risk of experiencing severe coronavirus infections compared to white individuals (Sze et al., 2020).

In addition to the socio-demographic factors that increase an individual's COVID-19 vulnerability, the weather has also been presented as a factor that can influence disease transmission through behavioral and biological changes. Although there have been inconsistencies in previous study findings, a recent systematic analysis showed that temperature had a significant effect on COVID-19 incidence in majority of the research studies. Weather changes have been shown to increase the transmission dynamics, host susceptibility and virus survival. During the winter season, studies have presented an inverse relationship between temperature and COVID-19 transmissibility via host susceptibility and the virus viability (McClymont & Hu, 2021), thus increasing the risk of COVID-19 infections and mortality.

2.5 The Socioeconomic Impact of the Disease

In addition to the catastrophic public health losses stemming from the spread of the COVID-19 virus, the pandemic has also resulted in an unprecedented socioeconomic crisis which affected many jobs. Overall employment decreased by 22 million jobs between February and April 2020. Similar to the racial and ethnic disparities in COVID-19 health outcomes, people of color were also disproportionately affected. Studies have shown that Black and Hispanic workers were more likely to experience job losses compared to white workers, thus highlighting the socioeconomic vulnerability faced by minority groups in the United States.

For people who did not experience job layoffs, the pandemic disrupted their ability to work. The day care closures meant that working parents had to make the decision stay home to care for their own children. As a result, employees had to either reduce working hours or completely resign from their jobs (Meade 2021).

Ultimately, the immense job losses resulted in a drastic decrease in the U.S economic GDP output. The pandemic is estimated to cost the U.S. a total of $16 trillion in finical losses. Further underscoring the need to strengthen public health interventions and infrastructures that aid in curbing the virus (Cutler & Summers, 2020).

2.6 Overcrowded Housing

According to the Department of Housing and Urban Development (HUD), overcrowding is defined as having more than one person per room (PPR) (Blake et al., 2007). However, this measure of overcrowding has been heavily contested. This is primarily because the person per room measure fails to take into account the different sizes of the rooms (Gray et al., 2001), and it disregards the cultural differences in sleeping arrangements made based on age and sex relationships (Greenfield & Lewis, 1969). However, the existing debate simply underlines the problems associated with delineating the statistical definition of overcrowded housing from the sociocultural norms in our diverse society (Gray et al., 2001).

2.7 The History of Crowded Housing and Health in the United States

Historically, the United States has consistently battled with overcrowded housing and the Public Health risks associated with it. The issue can be traced as far back as the tenement-housing problem during the early 19th Century. As a result of the increased foreign migration (Murphy, 2021) into more urban settings during that time period, many immigrants had to live in overcrowded settings due to affordability. However, such economical housing was often at the expense of each occupants' health, due to the increased risk of infectious diseases.

Although the current HUD overcrowded housing measure is heavily debated, the standard was not always, >1 PPR. Historically, in the 1940s local governments declared overcrowded housing as > 2PPR but due to the public health undertaking to reduce crowding, it was reduced to > 1.50 PPR during the 1950s. In the 1960s, it was then finally reduced to the > 1.00 PPR measure, existing today (Myers et al 1996).

Irrespective of the fact that the implementation of public health measures was able to drastically reduce the spread of infectious diseases among 19th-century tenants, overcrowded housing still exists in the 21st century. Today, overcrowded housing residents cannot practice effective social distancing protocols. As a result, there is an increased risk of infections among overcrowded housing residents (Cope, 1901) and an imperative need to amplify vaccine coverage in the most vulnerable areas.

2.8 Overcrowded Housing: A potentially critical dimension of virus transmission

The socioeconomic crisis caused by the pandemic, has also increased the likelihood of household instability. These instabilities have exacerbated the pre-existing affordable housing crisis for low-income families and increased the overall household “cost burden”. This has also led to increased late rent payments, evictions, and a higher risk of homelessness for renters of color who are disproportionately affected (Winston 2021).

Many low-income families were forced to find affordable joint household living arrangements, including overcrowded housing, to save money on rent and utilities. However, recent publications have reported the overcrowding involved in some joint household arrangements increased the risk of COVID-19 transmission. Due to the lack of sufficient rooms in certain households, these joint household arrangements reduced an individual's ability to self-isolate after COVID-19 exposure (Vandenberg, 2021). Reports by HUD have also confirmed racial disparities among overcrowded housing inhabitants. Based on the report, the Non-Hispanic, White population are less likely to reside in overcrowded settings compared to other races and ethnicities (Blake et al., 2007) who can be classified as marginalized persons. In addition to being more likely to inhabit overcrowded spaces, marginalized community members are often space deficient and have insufficient financial resources to isolate sick persons within the household. According to a recent Wall Street Journal analysis, 28% of the COVID-19 cases reported as of June 7^{th} 2020, were derived from 10% of the U.S counties with the highest rates of overcrowding (Lovett et al., 2020). Knowledge from such studies, combined with the fact that marginalized persons have a higher risk of COVID-19 hospitalization due to a high prevalence of comorbidities (Lopez et al., 2021) shows that overcrowded housing poses an alarming public health threat to our society.

Knowledge gaps

Although there has been research published about relationship between overcrowded housing and COVID-19 outcomes as well as vaccination coverage and COVID-19 outcomes, the compounded association of both overcrowded housing and low vaccination coverage with COVID-19 outcomes across U.S. counties overtime, remains unclear.

Objectives

The study had four inter-related aims. First, we identified the monthly variations in the new average COVID-19 case, death and vaccination rates per 100,000 population. Second, we investigated the relationships between the primary exposures which comprised of the county-level proportion of households that were overcrowded (> 1 person per room) as well as the cumulative percentage of the population that was vaccinated at the end of each month and study outcomes which comprised of COVID-19 case and death rates per 100,000 population. Third, we developed a cross-sectional regional analysis of the U.S. county-level vulnerability categories during the 2021 calendar year. Lastly, we presented the estimated associations between a priori predictors and the key study variables using vulnerability categories.

Chapter 3: Methods

3.0 Study Design

The research was conducted using an ecological study design with the county as the unit of analysis. The research explored the relationship between overcrowded housing, vaccination coverage and COVID-19 outcomes. The exposures were the county-level proportion of households that were overcrowded and the cumulative county-level vaccination coverage. The primary study outcomes were the new monthly COVID-19 cases and deaths per 100,000 population.

3.1 Data Sources

The county-level overcrowded housing 5-year average data estimates were derived from the 2014 - 2018 Comprehensive Housing Affordability Strategy (CHAS) database. The CHAS database is a subset of the U.S Census Bureau's American Community Survey (ACS). However, the CHAS database specifically provides information about housing issues and housing needs for low-income households.

In the county-level CHAS dataset, the 'persons per room' variable was the only variable of interest. The variable represented the different categories for number the persons which occupied a room in each occupied housing unit. Based on the U.S. Department of Housing and Urban Development (HUD) definition of overcrowded housing as "more than one person per room" (Blake et al., 2007), only subgroups with more than one person per room were included in generating the final overcrowded housing proportion variable.

The daily COVID-19 county-level vaccination data from 1st January 2021 – 31st December 2021 was obtained from the Centers for Disease Control and Prevention (CDC)

COVID Data Tracker website. In the dataset obtained, the 'at least one dose' variable was the only vaccination variable of interest. The variable represented the number of persons who had received at least one dose according to their respective state of residence, including boosters (CDC, 2020).The ‘at least one dose’ variable was selected to ensure that persons in process of completing their vaccination sequence were not excluded from the study.

The daily U.S county-level COVID-19 case and death data were obtained from the New York Times GitHub database from 1st January 2021 – 31st December 2021. Each observation was sourced from data published by states and local health personnel (Times, 2020). Although CDC, Johns Hopkins and other COVID-19 data repositories exist, the New York Times GitHub, was the first institution to track and provide a detailed historical record of the COVID-19 cases within the United States (Times, 2022).

The socio-demographic covariates such as the county-level percent minority and socioeconomic status, were derived from the American Community 2018 Survey 5-year estimates data. Multiyear estimates are “period” estimates that represent data collected over a period of time. Multiyear estimates, like the ACS 5-year estimates, provide overall data for small populations in the United States (U.S. Census Bureau, n.d.).

3.2 Calculation of the Overcrowded Housing Proportion and Percent Variable

Overcrowded housing was defined as county-level proportion of all housing units with more than 1 person per room between 2014 – 2018. The overcrowded housing proportion variable was created using the Department of Housing and Urban Development (HUD) definition of overcrowded housing (>1 person per room). The variable was created by adding all the county-level housing units with more than 1.0 person per room and dividing the total by the total number of housing units in the county. The percent overcrowded housing variable was also created by multiplying the final county-level overcrowded housing proportion by 100.

3.3 Vaccination Variables

Using the CDC vaccination dataset, a total of 21,241 county-level observations with missing FIPS code data were removed and 37,218 county-level observations with missing data for the 'at least one dose" variable were removed from the dataset. In addition to the missing observations, county-level observations from U.S territories (ie. Puerto Rico, Hawaii, Guam, Virgin Islands, Northern Mariana Islands and American Samoa) were also excluded.

The cumulative percent vaccinated variable was created by dividing the total number of administered first doses by the estimated total county population and multiplying the proportion by 100.

The new monthly COVID-19 vaccinations per 100,000 population variable was first created by adding all the daily 'at least one dose' vaccinations administered at the end of each month within a county and then dividing the total value by estimated county population. Second, the total vaccinations administered in the previous month was then subtracted from the current month to generate the new monthly vaccinations administered variable. The proportion was then multiplied by100,000 to generate the new vaccination rates per 100,000 population.

3.4 New Monthly COVID-19 Case and Death Rate Variables

The new monthly COVID-19 cases and death rates per 100,000 population were created by first aggregating the number of daily deaths and cases recorded at the end of each month, dividing the total by the estimated county population, and then multiplying that number by 100,000. Second, the total cases and deaths recorded in the previous month was then subtracted from the current month to generate the new monthly COVID-19 case and death rates per 100,000 population.

3.5 Composite Housing and Vaccination Vulnerability

To develop a measure of county vulnerability to COVID-19 that considered simultaneously crowded housing and under-vaccinated communities, we created a four-level composite variable that ranked counties as (1) high risk on both high risk overcrowded housing and low vaccinations, (2) high risk in overcrowded housing only, (3) high risk in low vaccination coverage only, and (4) low risk on both low risk overcrowded housing and high vaccination coverage. The counties in category (1) were counties in the top 25% of the county overcrowded housing ranking and the bottom 25% of the county at least one dose vaccination coverage rankings. The counties in the overcrowded housing category (2), were in the top 25% of overcrowded housing county rankings and in the top 75% of the vaccination coverage. Furthermore, the counties in the low vaccination coverage category (3) were in the bottom 25% of the at least one dose county vaccination coverage rankings and the bottom 75% of overcrowded housing county rankings. Lastly, the counties in the low-risk vulnerability category (4), were in the bottom 75% of overcrowded housing county rankings and in the top 75% of at least one dose county vaccination coverage rankings. The creation of these categories allowed for a visual depiction of the monthly vulnerability frequency changes over the 2021 calendar year.

3.6 County-Level Covariates

(a) **Socio-demographic**

The socio-demographic variables were sourced from the 2018 ACS 5-year estimates dataset coalited by the U.S Census Bureau. The variables selected were the percentage of those > 65 years, county-level percent male and county-level percent minority.

(b) **Socio-economic**

The socio-economic data was also obtained from the 2018 ACS 5-year estimates dataset. The variables included in the analysis included average household income (adjusted based on the 2018 inflation), % in poverty (percentage population with income below the poverty level in the last 12 months), % with college (percentage of population >25years with a bachelor's degree).

(c) **Rurality**

Furthermore, Urban-rural categories based on metropolitan statistical areas (MSAs) were also included in the study. These comprised of Large Central Metro (counties with >1 million population in an inner city MSA), Medium Metro (counties with MSAs of 250,000- 999,999 population) Noncore/Nonmetro (nonmetropolitan counties in a micropolitan statistical areas), Large Fringe Metro (counties with >1 million population in a suburban area MSA), Small Metro (counties with MSAs between 50,000 - 249,999 population), Micropolitan/Nonmetro (counties outside micropolitan statistical areas) (Ingram & Franco, 2012).

3.7 Statistical Methods/Analysis

(a) Sample Size

The final analytic sample comprised of 25,644 county-month observations with 2,137 counties in each month. In order to create the sample, all observations were required to have data for the month, date, year, new COVID-19 cases, new COVID-19 deaths, CHAS overcrowded housing proportion, at least one dose administered and the estimated county population variables. 5,070 missing one or more of these study variables were identified and excluded from the final analytic sample.

Furthermore, all observations above the 99th percentile of the monthly cumulative county rates variables and the final overcrowded housing proportion variable were classified as outliers and 1,417 more observations were dropped from the dataset.

In order to eliminate sampling bias in the analysis, a balanced panel containing observations for all 12 months was created. This ensured that the same number of counties were present in each month. Only data for counties with all 12 monthly data observations were kept in the final analytic dataset. As a result, 8,964 observations with less than 12 monthly data observations were identified and removed from the dataset.

(b) Data Analysis

All statistical analysis were conducted using Stata/MP statistical software (version 16.1). All datasets were downloaded in a CSV format and imported into Stata and cleaned. To identify the monthly variations in the average new COVID-19 case, death, and vaccination rates per 100,000 population a time-series bar chart was constructed to visualize the monthly trends during the year. In order to investigate the relationships between the primary variables of interest, multiple bivariate Pearson correlations were conducted. The Pearson correlation allowed for a preliminary assessment about the correlations between the primary exposure and outcome variables in the study.

(c) Linear and Multiple Regression Analysis

Linear and multiple regression analysis were also conducted to present the estimate associations between the vulnerability measure and the primary outcomes. The analyses adjusted for county-level socio-demographic characteristics (age, gender, county-level percent minority), socio-economic factors, rurality, U.S. regions and the calendar month. The regression allowed for the simultaneous consideration of multiple key covariates alongside the vulnerability measure in relation to the COVID-19 case and death rates per 100,000 population.

(d) Sensitivity Analyses

Subsequently, a sensitivity analyses was also conducted by estimating the associations between an alternative four-category-vulnerability measure and the new COVID-19 case and death rates per 100,000 population. The alternative vulnerability measure applied different vaccination coverage thresholds to define the risk categories: <25% (high risk), <50% and <75% (low risk).

3.8 Human Error & Bias

All datasets used in the study were derived from public records which could also be prone to human errors and sampling bias. Human errors included the missing observations in the county-level datasets used in the study analysis.

These human errors were addressed by ensuring that there was consistency in the number of counties in each month for the 2021 calendar year using a panel design for all 12 months. This ensured that all the county-level observations included in the final analytical frame representative of each month within the 2021 calendar year.

Chapter 4: Results

4.0 Descriptive Characteristics

A total of 2,137 counties with monthly data for the 2021 calendar year yielded 25,644 county-month observations in the analytic sample. **Table 1** presents the descriptive characteristics of the counties in the study that is also depicted by **Figures 1-3**.

The table and figures summarize the means and standard deviations of the average new monthly COVID-19 cases, deaths and vaccinations from January 2021 to December 2021. The average new monthly COVID-19 case and death rates followed a decreasing trend from January to July, after which both case and death rates started positively trending and began increasing. Average new monthly cases rates per 100,000 population were the highest in September and lowest in June. On the other hand, new monthly death rates per 100,000 population were highest in January and lowest in July. Notably, the highest between-month difference for the new monthly average case rates per 100,000 was observed between July and August with a 256.5% increase. However, the highest between-month difference for the new monthly average death rates 100,000 was observed between August and September with a 357.1% increase.

During the July and August case surge, the average new monthly vaccination rates per 100,000 population also showed the highest between-month difference, with 54.2% increase. Based on the results presented in the table, most vaccinations were administered during the first quarter of the year, in March. However, June had the lowest record of vaccinations administered. Generally, there were monthly variations in the mean and standard deviations for the primary time-specific variables.

Table 2 presents the correlations among key study variables at the county-level. In all months, there was a positive correlation between the new COVID-19 case and death rates, ranging from a low of r= 0.02 in March to a high of r= 0.48 in August. The direction of the two-way correlations among all other variables fluctuated from month to month. We observed negative correlations between the vaccination rates (i.e., new vaccinations per 100,000 population) and the new COVID-19 case rates and death rates in 3 and 8 months of the year respectively. All the positive correlations between the case, death and vaccination rates observed in the rest of the months, were all in the weak to moderate range.

The correlation of the new COVID-19 case, death, and new vaccination rates per 100,000 with overcrowded housing proportions were negative in 7, 5, and 5 months of the year respectively. The 7 negative correlations between COVID-19 case rates and the overcrowded housing proportion were observed in from March to May and again from September until the end of the year. On the other hand, the positive correlations between both variables were primarily observed at the beginning of the year in January and February as well as consistently during the summer months from June to August.

The 5 negative correlations between the new COVID-19 death rates per 100,000 and the overcrowded housing proportions were noted during the early to mid-period of the year in January, February, May and towards the end of the year in December and November. In contrast, the positive correlations between both variables were noted from March to April and from June to October.

In terms of the correlations between the new vaccination rates per 100,000 and the overcrowded housing proportion, the 5 negative correlations were specifically observed during the entire first quarter of the year and in September and November. However, positive correlations were only observed from April to August and in October and December.

4.1 Temporal Analysis of U.S. County-Level Vulnerability

Figure 4 shows the percent monthly distribution of the counties meeting the criteria of high risk, high risk overcrowded housing only, low vaccination coverage only and low risk included in the analysis. As the year progressed, the majority of counties shifted from the high vulnerability category to lower vulnerability categories due to increasing vaccination uptake nationally. Specifically, the percentage of counties in the high-risk vulnerability category decreased from 24.9% January to 0.084% in December, while the percentage of counties in the low-risk vulnerability category increased from 0.09% January to 73.4% in December. In contrast, the overcrowded housing vulnerability only category gradually increased from 0.09% in January to 21.2% in May, and then subsequently remained relatively constant for the rest of the year between April to December.

Figure 5 depicts the county-level percent overcrowded housing based on the 2014 – 2018 Comprehensive Housing Affordability Strategy (CHAS) 5-year estimates dataset. The county-level percent overcrowded housing ranged from 0.00% to 9.98% and was based on the criteria that they were in the top 25% of the overcrowded housing observed in the country. According to the figure, counties with a higher percentage of overcrowded housing were predominantly located in the Western and Southern United States. The South had highest number of counties (248 counties) with high overcrowded housing. However, the Northeast Region had only 12 of counties with high overcrowded housing, which was the lowest (See **Table 3)**.

Furthermore, **Figure 6-7** heat maps visualize the county-level vulnerability risk category. The heat maps provide cross sectional geographic information on each county's vulnerability in January and December 2021. Notably, the Western and the Southern region of the United States, had the most significant change in the overall county-level vulnerability between January and December 2021.The South and the West had a 100% and 84.6% decrease in high-risk counties respectively by December 2021. Our results show that there were no high-risk counties Northeastern United States in January and December. The Midwest, Northeast and South had 0% high risk counties by December 2021. However, the 1.87% of the Western U.S. counties were still observed as high-risk counties in December 2021 (See **Table 3**).

4.2 Linear and Multiple Regressions

Table 4 and 5 present the findings from multiple linear regression models constructed to estimate associations between the study exposures and new monthly COVID-19 case and death rates, respectively. According to the **Table 4** results, the unadjusted model shows high-risk counties ($\beta = 43.4$, 95% CI 5.8,81.1, $p = 0.024$) and the low vaccination coverage counties ($\beta = 52.4$, 95% CI 27.2, 77.6, $p<0.001$) had slightly more cases per 100,000 compared to the low-risk county reference group. However, the counties within the overcrowded housing category ($\beta = -53.4$, 95% CI -78.6, -28.1, $p<0.001$) had fewer cases per 100,000 than counties in the reference group.

On the other hand, the fully adjusted model in **Table 4** was adjusted for socio-demographic characteristics (age, gender, county-level percent minority), socio-economic factors, rurality, U.S. regions and the calendar month. The results show that counties in the high-risk vulnerability category had slightly more cases per 100,000 as counties in the low-risk category ($\beta = 2.18$; 95% CI -32.8, 37.1 $p = 0.903$).

However, counties in the low vaccination coverage only category had fewer cases per 100,000 than counties in the reference group ($\beta = -57.0$, 95% CI -84.6, -30.8, $p < 0.001$). Similarly, we found that counties with high overcrowded housing only had fewer cases per 100,000 than counties in the reference group ($\beta = -30.1$, 95% CI -51.8, -8.5, $p=0.006$).

According to the **Table 5** results, the unadjusted model shows that counties in the high-risk category ($\beta = 8.0$, 95% CI 7.2,8.9, $p<0.001$) had slightly more deaths per 100,000 compared to the low-risk county reference group. Similarly, the low vaccination coverage counties ($\beta = 9.6$, 95% CI 9.1,10.2, $p <0.001$) and the counties in the overcrowded housing category ($\beta = 1.1$, 95% CI 0.50,1.6, $p<0.001$) were also observed to have more deaths per 100,000 than the reference group.

The fully adjusted model in **Table 5** (adjusted for socio-demographic characteristics (age, gender, county-level percent minority), socio-economic factors, rurality, U.S. regions and the calendar month) noted counties in the high-risk category ($\beta = 0.80$, 95% CI -0.3,1.9, $p = 0.162$) and the overcrowded housing category ($\beta = 0.38$, 95% CI -0.3,1.0, $p = 0.257$) which observed deaths per 100,000 that were more than the low-risk reference group, however they were both not statistically significant results. Furthermore, in this model, only the counties within the low vaccination coverage category had statistically significant results. The counties in the low vaccination category ($\beta = 1.7$, 95% CI 0.90,2.5 $p<0.001$) observed slightly more deaths per 100,000 compared to the counties in the low-risk reference group.

4.3 Sensitivity Analyses of the Vaccination Coverage Threshold Changes

The sensitivity analyses revealed that the estimated association between vulnerability and the new COVID-19 case and death rates per 100,000 population were sensitive to the changes in the county-level vaccination coverage used to define each vulnerability category. The modifications to the vaccination coverage thresholds at <25%, <50% and <75% in the overcrowded housing vulnerability category were estimated to be associated with fewer new COVID-19 cases per 100,000 compared to the low-risk reference group at all thresholds. The only statistically significant results for the low vaccination vulnerability category for the cases per 100,000 population, were the counties in the <25% and <50% of county-level vaccination rankings. Counties within these categories were estimated to be associated with fewer COVID-19 cases per 100,000 compared to the counties in the low-risk reference group. Furthermore, the only statistically significant results for the counties within the high-risk vulnerability category, involved counties in the <50% of the county-level vaccination coverage. Counties within the high-risk category were estimated to be associated with fewer cases per 100,000 compared to the low-risk reference group counties (See **Table 6** in Appendix)**.**

In contrast, in (**Table 7** in Appendix)**,** there were no statistically significant results for the counties in the overcrowded housing category at all thresholds. The only statistically significant results for counties within the low vaccination category were the counties in the <25% and in the <75% county-level vaccination coverage. Counties within these categories were estimated to be associated with slightly higher COVID-19 cases per 100,000 compared to the reference group. Furthermore, the only statistically significant results for the counties within the high-risk vulnerability category, involved counties in the <75% of the county-level vaccination coverage. Counties within the high-risk category were estimated to be associated with slightly more deaths per 100,000 compared to the low-risk reference group counties.

Results: Tables & Figures

Figure 1: Average New COVID-19 Cases per 100,000 Population

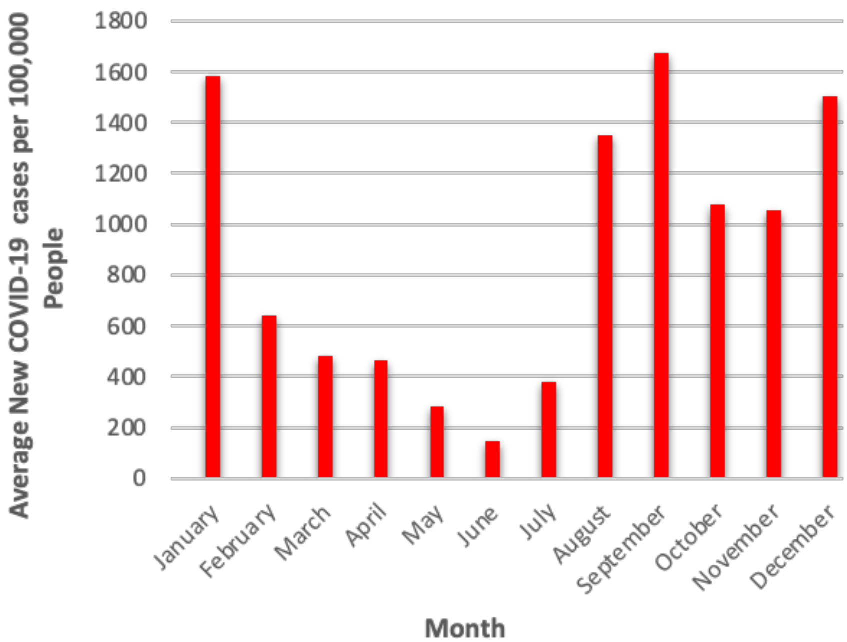


Figure 2: Average New COVID-19 Deaths per 100,000 Population

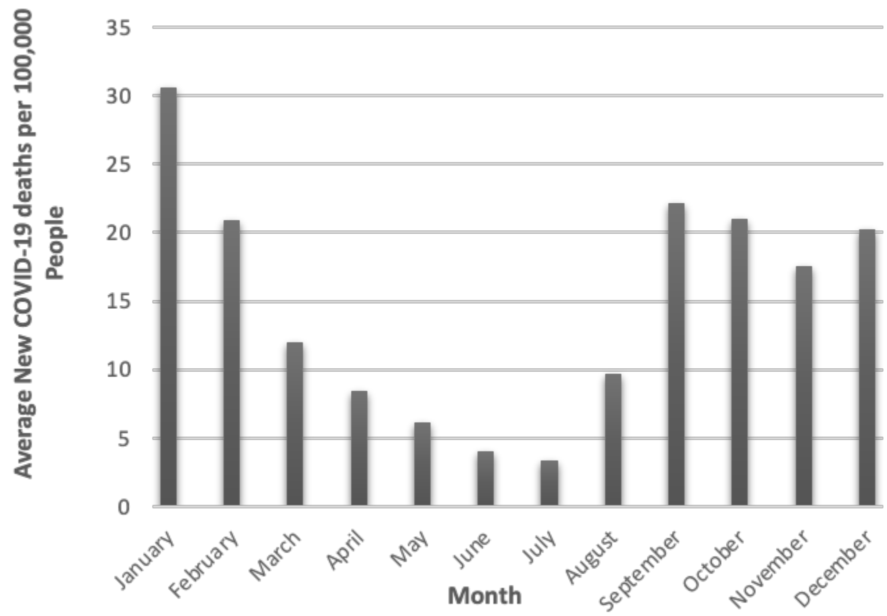


Figure 3: Average New COVID-19 Vaccinations per 100,000 Population

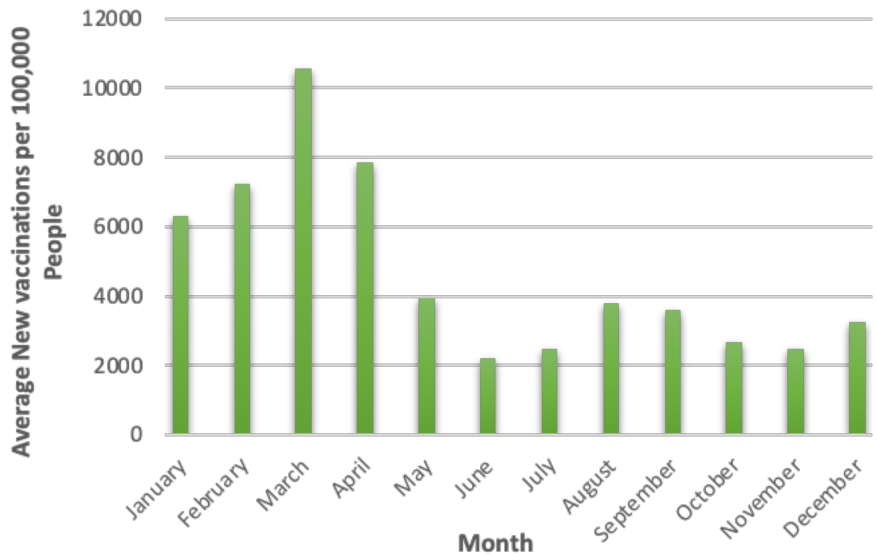


Figure 4: Percentage of U.S. Counties within each Vulnerability Risk Category from January - December 2021

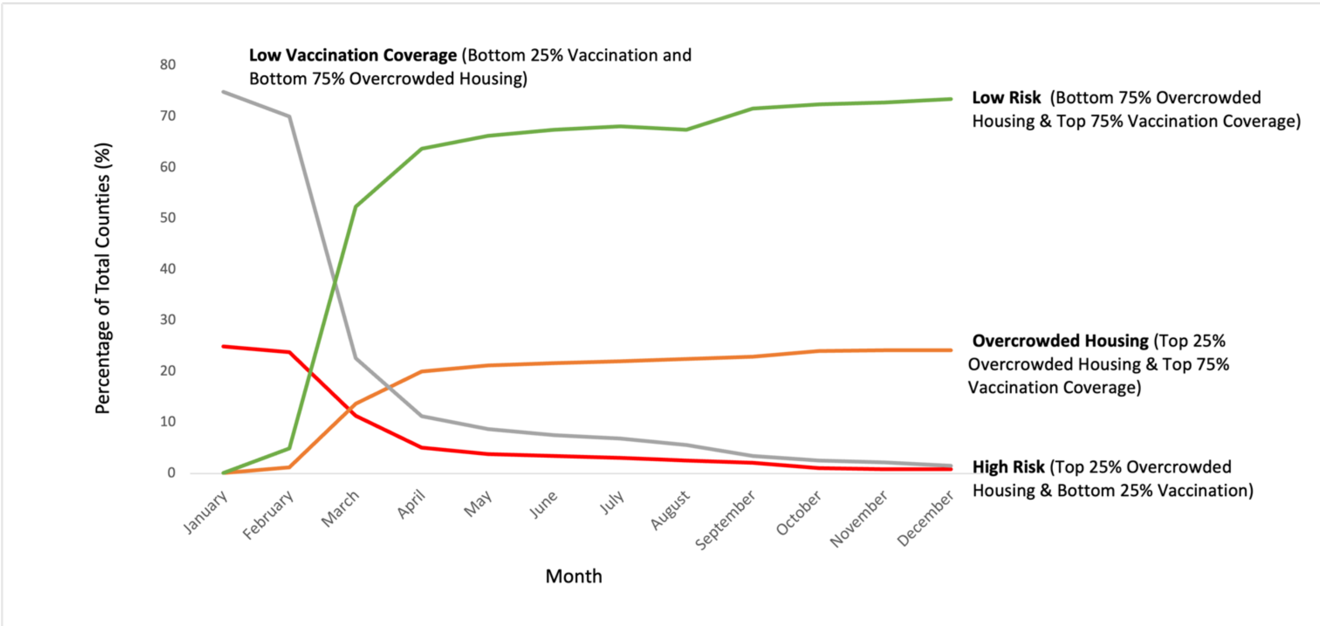
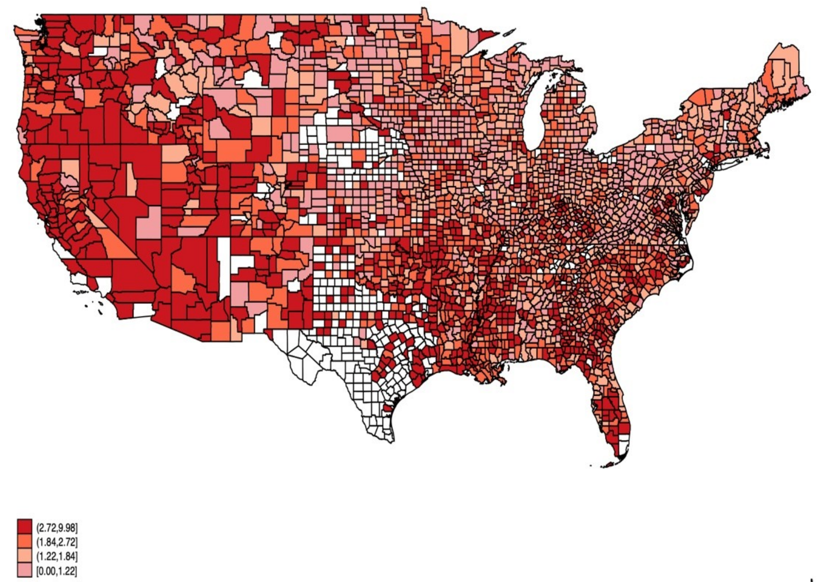
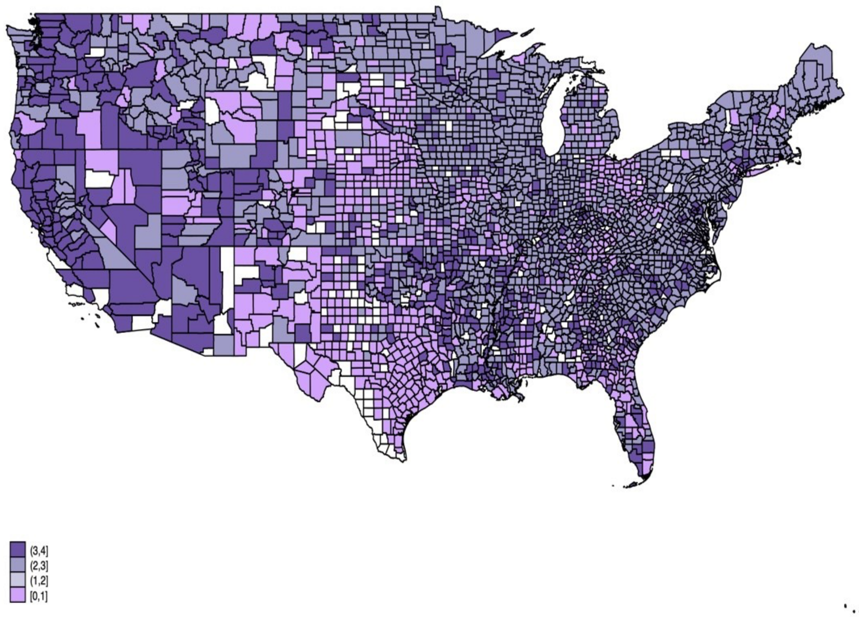


Figure 5: U.S. County-Level Heat Map of Percent Overcrowded Housing



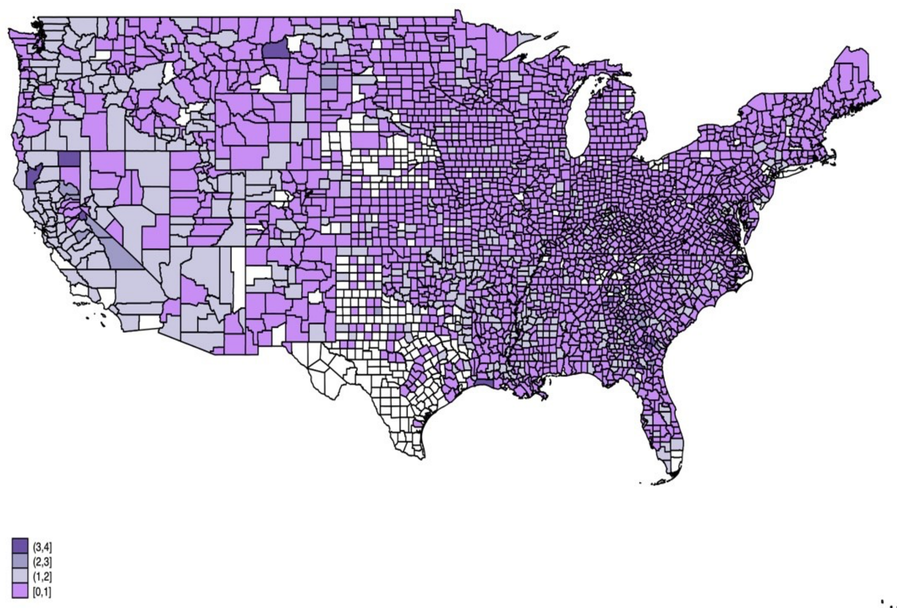
Note: Data sourced from the 2014 – 2018 Comprehensive Housing Affordability Strategy (CHAS) 5 – year estimates dataset. (n = 2,137)

Figure 6: January 2021 U.S. County-Level Heat Map of the County-level Vulnerability Risk Category



Note: Map created using a four-level composite variable that ranked each county (n = 2,137)
(1) High Risk: Top 25% Overcrowded Housing & Bottom 25% Vaccination
(2) Overcrowded housing(High Risk Overcrowded Housing): Top 25% Overcrowded Housing & Top 75% Vaccination Coverage
(3) Low vaccination coverage: Bottom 25% Vaccination and Bottom 75% Overcrowded Housing
(4) Low Risk: Bottom 75% Overcrowded Housing & Top 75% Vaccination Cove

Figure 7: December 2021 U.S. County-Level Heat of the County-level Vulnerability Risk Category



Note: Map created using a four-level composite variable that ranked each county (n = 2,137)
(1) High Risk: Top 25% Overcrowded Housing & Bottom 25% Vaccination
(2) Overcrowded housing (High Risk Overcrowded Housing): Top 25% Overcrowded Housing & Top 75% Vaccination Coverage
(3) Low vaccination coverage: Bottom 25% Vaccination and Bottom 75% Overcrowded Housing
(4) Low Risk: Bottom 75% Overcrowded Housing & Top 75% Vaccination Coverage

Table 1: Summary of County Case, Death and Vaccination Rates Per 100,000 Population by Month

	New Case Rates per 100,000 population	New Death Rates per 100,000 population	New Vaccination Rates[b] Per 100,000 population
Month[a]	(n = 25644)	(n =25644)	(n= 25644)
January	1583.5 ± 687.1	30.6 ± 22.3	6312.7 ± 3718.6
February	641.1 ± 345.6	20.9 ± 18.8	7237.8 ± 4004.3
March	479.4 ± 352.2	12.0 ± 12.4	10573.4 ± 4562.8
April	466.8 ± 384.5	8.5 ± 12.6	7846.5 ± 4547.3
May	283.2 ± 209.0	6.2 ± 8.0	3935.4 ± 2985.8
June	144.9 ± 152.5	4.1 ± 6.3	2199.1 ± 1138.9
July	378.1 ± 387.4	3.5 ± 6.3	2457.1 ± 1610.2
August	1347.9 ± 824.7	9.7 ± 12.3	3789.6 ± 3209.2
September	1676.1 ± 718.7	22.2 ± 20.1	3609.8 ± 4910.3
October	1077.1 ± 591.3	21.0 ± 17.4	2665.6 ± 4786.2
November	1056.6 ± 707.4	17.6 ± 17.9	2452.6 ± 1752.9
December	1505.6 ± 734.8	20.2 ± 18.8	3251.3 ± 6116.8

Data in table are presented as mean ± SD
[a]*The Month variable represents all the months for the 2021 Calendar year.*
[b]*The rate at which county civilians received at least one Dose by State of Residence per 100,000 population.*

Table 2: Monthly Pearson Correlations between New COVID-19 Case, Death and Vaccination rates per 100,000 and Overcrowded Housing proportion

		New Case Rates Vs. New Death Rates	New Case Rates Vs. New Vaccination Rates	New Death Rates Vs. New Vaccination Rates	New Case Rates Vs. Overcrowded Housing proportion	New Death Rates Vs. Overcrowded Housing proportion	New Vaccination Rates Vs. Overcrowded Housing proportion
Month[a]	January	0.305	0.0013	0.0021	0.0840	-0.0248	-0.0977
	February	0.2622	-0.2052	-0.1414	0.0357	-0.0174	-0.0898
	March	0.0201	0.0683	-0.1814	-0.0654	0.0085	-0.0758
	April	0.0271	0.3204	-0.1077	-0.1421	0.0128	0.0007
	May	0.200	0.1221	-0.0521	-0.0759	-0.01	0.0252
	June	0.1550	-0.0425	-0.0362	0.1156	0.001	0.1531
	July	0.2995	0.4299	0.110	0.177	0.0512	0.2030
	August	0.487	0. 1906	0.1748	0.1513	0.1033	0.1478
	September	0.410	0.0569	0.0084	-0.0260	0.0789	-0.0687
	October	0.1528	-0.0329	-0.1055	-0.11	0.0360	0.1084
	November	0.238	0.116	-0.145	-0.2134	-0.0124	-0.0311
	December	0.151	0.0304	-0.0084	-0.259	-0.1172	0.0176
	2021 Year	**0.413**	**-0.0254**	**0.0174**	**-0.0259**	0.0033	0.0039

Note [a]*The Month variable represents all the months for the 2021 Calendar year.*

Table 3: The Total Number Counties in the Top 25% of the County-Level Overcrowded Housing

Region	Frequency
Midwest	98
Northest	12
South	248
West	178

Note: Data sourced from the 2014 – 2018 Comprehensive Housing Affordability Strategy (CHAS) 5 – year estimates dataset

Table 4: County-Level Associations of Vulnerability Measures and Demographic Characteristics with COVID-19 Cases per 100,000 Population

	Unadjusted β (95% CI)	P Value	Adjusted β (95% CI)	P Value
Vulnerability				
Low Risk	Reference		Reference	
Overcrowded Housing	**-53.4**(-78.6,-28.1)	<.001	**-30.1** (-51.8,-8.5)	0.006
Low Vaccination Coverage	**52.4** (27.2, 77.6)	<.001	**-57.0** (-84.6,-30.8)	<.001
High Risk	**43.4** (5.8, 81.1**)**	0.024	2.18 (-32.8, 37.1)	0.903
% Age, 65+ years	**-2.9** (-5.1, -0.70)	0.010	**-9.9** (-12.1, -7.7)	<.001
% Male	**-4.9** (-9.5, -0.39)	0.033	**-6.5** (-10.8, -2.2)	.003
Metropolitan Classification				
Large Central Metro	Reference		Reference	
Large Fringe Metro	**116.6** (-1103.1, 704.3)	0.001	-17.4 (-66.1,31.3)	0.483
Medium Metro	**111.9** (-887.5, 902.4)	0.002	-37.7 (-85.5,10.2)	0.123
Small Metro	**107.4** (-953.7, 866.5)	0.003	**-55.5** (-105.8,-5.2)	0.030
NonCore (Nonmetro)	**86.1** (-655.2, 1194.8)	0.014	**-83.6** (-134.7, -32.6)	0.001
Micropolitan (Nonmetro)	**125.7** (-651.1, 1166.7)	<.001	**-52.5**(-102.1,-2.8)	0.038
% Minority	**-2.28** (-2.80,-1.76)	<.001	**-3.7**(-4.3, -3.1)	<.001
Median Income, $	**-0.0023** (-0.03, -0.002)	<.001	-.001(-0.002, 7.53e-06)	0.052
% Poverty	**2.3** (0.74, 3.8)	0.004	-0.22 (-2.5, 2.1)	0.855
% College	**-9.53** (-11.2, -7.8)	<.001	**-10.36** (-12.0,-7.9)	<.001
Region				
West	Reference		Reference	
Northeast	**131.4** (91.7,171.1)	<.001	**71.6** (38.3, 104.8)	<.001
Midwest	**106.4** (77.5,135.2)	<.001	20.9 (-5.5,47.4)	0.120
South	**135.3** (107.2,163.4)	<.001	**77.6** (50.9,104.2)	<.001
Month				
January	Reference		Reference	
February	**-942.4** (-975.6, -909.3)	<.001	**-944.9** (-968.7,-921.1)	<.001
March	**-1104**.1(-1137.3, -1071)	<.001	**-1129.9** (-1167.2,-1092.6)	<.001
April	**-1116.7** (-1149.9, -1083.6)	<.001	**-1147.0** (-1187.5,-1106.5)	<.001
May	**-1300.3** (-1333.45, -1267.2)	<.001	**-1331.7** (-1370.2,-1293.1)	<.001
June	**-1438.6** (-1471.8, -1405.5)	<.001	**-1470 (**-1507.9,-1433.2)	<.001
July	**-1205.4** (-1238.5, -1172.2)	<.001	**-1237.6** (-1275.4,-1199.7)	<.001
August	**-235.6** (-268.7, -202.4)	<.001	**-268.4** (-308.9, -227.8)	<.001
September	**92.6** (59.4,125.7)	<.001	**58.7** (16.0,101.4)	0.007
October	**-506.4** (-539.5, -473.2)	<.001	**-540.4** (-590.4, -490.4)	<.001
November	**-526.8** (-560, -493.7)	<.001	**-561.0** (-616.0, -506.0)	<.001
December	**-77.9** (-111.1, -44.8)	<.001	**-112.5** (-162.1, -62.8)	<.001

Note: Demographic and Socioeconomic Data sourced from 2018 American Community Survey.
Vulnerability Variable included a four-level composite variable that ranked each county (n = 2,137)
(1) High Risk: Top 25% Overcrowded Housing & Bottom 25% Vaccination
(2) Overcrowded housing (High Risk Overcrowded Housing): Top 25% Overcrowded Housing & Top 75% Vaccination Coverage
(3) Low vaccination coverage: Bottom 25% Vaccination and Bottom 75% Overcrowded Housing
(4) Low Risk: Bottom 75% Overcrowded Housing & Top 75% Vaccination Coverage

Table 5: County-Level Associations of Vulnerability Measures and Demographic Characteristics with COVID-19 Deaths per 100,000 Population

	Unadjusted *β* (95% CI)	P Value	Adjusted *β* (95% CI)	P Value
Vulnerability				
Low Risk	Reference		Reference	
Overcrowded Housing	**1.1** (0.50, 1.6)	<.001	0.38 (-0.3, 1.0)	0.257
Low Vaccination Coverage	**9.6** (9.1, 10.2)	<.001	**1.7** (0.9, 2.5)	<.001
High Risk	**8.0** (7.2, 8.9)	<.001	0.80 (-0.3, 1.9)	0.162
% Age, 65+ years	**0.3** (0.2,0.3)	<.001	**0.1**(0.02,0.18)	0.010
% Male	**-0.1** (-0.23, -0.03)	0.013	**-0.22** (-0.35, -0.1)	<.001
Metropolitan Classification				
Large Central Metro	Reference		Reference	
Large Fringe Metro	**3.2** (1.5, 4.8)	<.001	-0.37 (-1.3, 0.8)	0.483
Medium Metro	**4.2** (2.6, 5.8)	<.001	**-1.6** (-2.7 -0.6)	0.002
Small Metro	**4.5** (2.9, 6.1)	<.001	**-1.6** (-2.7, -0.5)	0.004
NonCore (Nonmetro)	**6.6** (5.0, 8.1)	<.001	**-1.8** (-3.0, -0.6)	0.002
Micropolitan (Nonmetro)	**5.8** (4.3,7.4)	<.001	**-1.4** (-2.5, -0.3)	0.011
% Minority	-0.010 (-0.0018,0.022)	0.098	-0.04 (-0.6, -0.02)	0.237
Median Income, $	**-0.0002** (-0.00021 -0.00019)	<.001	**-0.000050**(-0.000080, -0.000020)	0.007
% Poverty	**0.4** (0.4, 0.5)	<.001	**-0.13 (**0.1, 0.2)	0.015
% College	**-0.7** (-0.7, -0.6)	<.001	**-0.4** (-0.5, -0.3)	<.001
Region				
West	Reference		Reference	
Northeast	**-1.2** (-2.1, -0.3)	0.007	**-1.44**(-2.5, -0.397)	0.007
Midwest	0.6 (-0.1,1.2)	0.081	**-1.04**(-1.9, -0.2)	0.015
South	**5.3** (4.7,6.0)	<.001	**2.42**(1.6, 3.3)	<.001
Month				
January	Reference		Reference	
February	**-9.7**(10.6,-8.7)	<.001	**-9.6** (-10.6,-8.6)	<.001
March	**-18.7**(-19.6,-17.7)	<.001	**-17.7** (-18.8,-16.6)	<.001
April	**-22.2**(-23.1,-21.3)	<.001	**-21.0** (-22.1,-19.8)	<.001
May	**-24.5**(-2.4,-23.5)	<.001	**-23.3** (-24.3,-22.1)	<.001
June	**-26.6**(27.5,-25.6)	<.001	**-25.3** (-26.4,-24.1)	<.001
July	**-27.2**(-28.1,-26.3)	<.001	**-25.9**(-27.0,-24.8)	<.001
August	**-21**(-21.9,-20.1)	<.001	-**19.7** (-20.8,-18.5)	<.001
September	**-8.4**(-9.4,-7.5)	<.001	**-7.1** (-8.4,-5.8)	<.001
October	**-9.6**(-10.5,-8.7)	<.001	**-8.3**(-9.5,-6.9)	<.001
November	**-13.1**(-14,-12)	<.001	**-11.7**(-13.1,10.3)	<.001
December	**-10.5** (-11.4,-9.5)	<.001	**-9.1** (10.4,-7.8)	<.001

Note: Demographic and Socioeconomic Data sourced from 2018 American Community Survey.
Vulnerability Variable included a four-level composite variable that ranked each county (n = 2,137).
(1) High Risk: Top 25% Overcrowded Housing & Bottom 25% Vaccination
(2) Overcrowded housing (High Risk Overcrowded Housing): Top 25% Overcrowded Housing & Top 75% Vaccination Coverage
(3) Low vaccination coverage: Bottom 25% Vaccination and Bottom 75% Overcrowded Housing
(4) Low Risk: Bottom 75% Overcrowded Housing & Top 75% Vaccination Coverage

Chapter 5: Discussion

In this ecological study, we found no association between county vulnerability—defined by combined high overcrowded housing and low vaccination coverage—and county COVID-19 outcomes during the 2021 calendar year. Based on the results presented, there was no evidence that overcrowded housing, a community level indicator of the ability to socially distance within the home, was a relevant predictor of transmission rates or mortality across US counties in 2021. Although the high-risk counties were observed to have a slightly higher COVID-19 case and death rate per 100,000 population compared to the counties in the low-risk reference group in adjusted models, the high-risk category was not statistically significantly associated with case or death rates after adjusting for socio-demographic characteristics (age, gender, county-level percent minority, income, education), socio-economic factors, rurality, U.S. regions and month. This null associations highlights the inadequacy of combined overcrowded housing and low vaccination coverage as an ecological predictor of high risk of poor COVID-19 outcomes. Instead, based on covariates in the fully adjusted models, we found that socioeconomic and regional factors were more strongly associated with COVID-19 case and death rates. Furthermore, the analyses indicated substantial variations by month that were not accounted for by other covariates.

We observed an inverse association between low vaccination coverage counties and case rates, and a positive association between low vaccination coverage counties and death rates. This may be because of better case detection infrastructure in counties that have higher vaccination (which could lead to the detection of mild and asymptomatic cases), as well as the fact that the vaccine is most effective against severe infection and death. The upstream causes of unequal vaccination coverage may be political and societal factors—such as historical mistrust in the U.S.

healthcare system, anti-vaccination beliefs, and low educational attainment. While not directly examined in this study, these factors may have influenced vaccine hesitancy and vaccine uptake (Hildreth & Alcendor, 2021), leading to the unequal distribution of vaccination.

Interestingly, counties in the overcrowded housing category had statistically significantly lower case rates and equivalent death rates when compared with counties with no vulnerability. A possible explanation is the residual confounding by public health infrastructure. Overcrowded housing may be higher in urban areas where policies were more stringent or public health infrastructure was stronger. Similarly, in the adjusted model, county-level percent minority showed an inverse association with COVID-19 case rates and no association with death rates. This pattern may be because the counties with highest overcrowded housing and minority populations experienced highest case rates early in the pandemic and had milder epidemics by 2021 (e.g., the population was naturally inoculated from infection due to prior disease by 2021).

In adjusted models, non-metropolitan counties had higher case rates and death rates. After adjusting for socio-demographic characteristics, however, non-metropolitan counties were observed to have slightly fewer monthly COVID-19 case and death rates per 100,000 compared to the counties in the Large Central Metro reference group category. While it was not possible to do a mediation analysis with these data, they suggest that much of the risk in rural areas was driven by socio-economic and socio-demographic characteristics.

The regional results suggest that the West and the Southern United States regions contained the most high-risk counties in January 2021. These findings are consistent with the CDC map depiction of the total doses administered on the COVID-19 Data tracker website (CDC, 2020). However, the results show a decrease in the number of high-risk counties from January 2021 to December 2021. This could be attributed to the public health campaign successes through creative initiatives to address vaccine barrier issues. For example, companies such as Uber and Lyft offering free rides to and from vaccination sites to address the transportation barriers faced by many Americans (Siddiqui & Armour, 2021). In addition to solving transportation barriers, the CDC implementation of eviction moratoriums, also may have contributed to the decreased incidence of overcrowded housing living arrangements and prevented existing living arrangements from worsening (Jowers et al., 2021). Overall, the regional-cross sectional analysis depicts the great strides made by public health professionals to combat the spread of the virus at the community-level from the beginning to the end of the year and could have contributed to the lack of association observed in the study.

The month variables in the adjusted regression models reported fewer COVID-19 case rates per 100,000 population compared to reference month of January in all months except September, which was reported to have slightly higher cases per 100,000 population. The estimated association presented in September, could have been attributed to the lag in infection rates from the previous month of August which can be associated with an increase in summer activities and crowded gatherings. As a result, social distancing guidelines were likely to be followed (Rumain et al., 2021). In the adjusted model for the deaths, COVID-19 deaths per 100,000 population were associated with fewer deaths per 100,000 in each month compared to the January reference month. The overall downward monthly trends in the cases and deaths reported per 100,000 population could have also been driven by changes in vaccination. There was a higher percentage of high-risk U.S. counties compared to the low-risk U.S. counties until mid-February when the distribution rate had been increased and resulted in the percentage of low-risk counties surpassing that of the high-risk counties. This could also be attributed to the new administration’s ability to address most of the distribution issues and could have resulted in the decrease in the percentage of counties in the low vaccination coverage category as the year progressed. Although vaccination distribution delays were solved, the monthly variation in vaccination uptake trends could have indirectly influenced the monthly COVID-19 case rates and death rates observed per 100,000 population.

However, the limitations of the study methods could have also contributed to the fact that there was no association between the combined high overcrowded housing and low vaccination coverage with COVID-19 case and death rates during the 2021 calendar year.

First, exposure and outcome variables may have been defined using alternative approaches and they may have been measured imperfectly. For example, there is no universally accepted definition of overcrowded housing and there are various household living arrangements that can be categorized as overcrowded housing but fail to pose a public health threat. The person-per-room measure does not encompass the socio-cultural context in which people inhabit a room. In fact, previous research which highlights definition's failure to address the differences in sleeping arrangements based on age and sex relationships (Greenfield & Lewis, 1969). Furthermore, the use of overcrowded housing as a county-level indicator of social distancing, also excludes all other probable other settings such as workplaces and religious spaces, which are also possible locations for crowding and could have also contributed to the lack of association observed in the results at the ecological-level.

Similarly, the definition of vaccination coverage may have affected the findings. In some analyses, we considered new vaccinations per 100,000 population. The new monthly vaccination variable fails to capture the cumulative total of the population vaccinated, and this may be one reason for inconsistent correlations and the null and observed at the ecological level. Moreover, our primary measure of coverage was defined as the population with least one dose of vaccine.

We may have observed different associations had we used complete dosing or boosters to define the proportion of the population that was truly protected through vaccination. The possible increase in virulence due to the frequent mutation of the SARS-COV-2 virus may warrant more stringent definitions of vaccination coverage in future studies.

The fact that an ecological approach was used in the study, means that the results cannot be inferred to report associations between individual level exposures and outcomes. As a result, our null findings related to overcrowded housing and low vaccination coverage do not address whether at an individual level residing in overcrowded housing and/or being unvaccinated/ relate to probability of being infected with the COVID-19 disease or dying from it.

In addition to the ecological nature of the study, the dataset used in the study statistical analysis only represents a 70% of the total U.S. counties. There is also the added possibility of the underreporting of county-level overcrowded housing units, cases, deaths, vaccinations, county population estimates, and other socioeconomic factors included in the study. This could most likely be attributed to human errors as well as the fact that asymptomatic cases are less likely to be accurately encapsulated into public health records because they are less likely to seek testing. The underreporting of COVID-19 related deaths could also be due to fraction of people who died in their homes and were not recorded in the county database.

Furthermore, the study was conducted during the 2021 calendar year. By the year 2021, most overcrowded housing residents could have spent the whole of 2020 year implementing and perfecting COVID-19 safety measures that would reduce virus transmission within the homes, and these counties may have already experienced the most severe waves of the virus. As a result, by 2021 the long-term application of these safety measures implemented within the home, may have resulted in the lack of association between combined high overcrowded housing and low vaccination coverage with COVID-19 case rates and death rates observed by 2021.

Although the Metropolitan categories at the county-level were analyzed in the statistical analysis, the fact that the study only focused on the county-level geography and did not compare the results across finer levels of geography, such as Census tracts, is also a study method limitation that could have also contributed to the null results observed.

The fact that there is no universally acclaimed population proportion for herd immunity could have also played a role in the fact that the study presents no association between the combined high overcrowded housing and low vaccination coverage with COVID-19 case and death rates during the 2021 calendar year.

In the sensitivity analyses, adjusting for socio-demographic characteristics (age, gender, county-level percent minority), socio-economic factors, rurality, U.S. regions and month, revealed that counties in the high-risk category in the case model were only statistically significantly estimated to be associated with fewer COVID-19 cases per 100,000 compared to the counties in the low-risk reference group only at the <50% threshold. The adjusted model for the deaths per 100,000 population revealed that counties in the high-risk vulnerability category had slightly more deaths per 100,000 population compared to the counties in the low-risk reference group but were only statistically significant at the at the <75% threshold. The variations in statical significance at various high-risk thresholds suggests that the threshold may have an ecological-level influence on the estimated associations presented in the regression models and could have been a study limitation that may contributed to the null results presented.

However, in addition to limitations, the study also contained strengths. Firstly, the research findings provided a county-level analysis of the association of overcrowded housing and low vaccination coverage with COVID-19 case and death ratees. Secondly, the study was also conducted over a 12-month period and accounted for the dynamic nature of the pandemic. Third, we included several county factors that may be confounders of the association of interest.

Chapter 6: Conclusion

At an ecological level, this study suggested that there was no county-level association of combined high overcrowded housing and low vaccination coverage with COVID-19 case and death rates per 100,000 population. The population-level statistical results obtained from the study cannot be inferred to make individual-level conclusions. Although these results show that there is no county-level association for this ecological study conducted in the 2021 calendar year, prior research highlighting the role of vaccinations and social distancing in COVID-19 incidence and mortality cannot be ignored. At an individual level, the inability to practice social distancing in crowded living arrangements may still place residents at an increased risk of COVID-19 and consequent death. Furthermore, vaccination is known to be protective of against serious illness and long-term damage, or death once diagnosed with COVID-19 infection in individuals. Our findings do not contradict the individual-level literature because they address how these phenomena operate at a county-level.

Furthermore, our analysis of monthly new average COVID-19 case, death and vaccination rates per 100,000 population could be a model for creating time-specific COVID-19 public health interventions. The detailed monthly breakdown of the new case, death and vaccination rates would allow public health officials to be more effective at improving the overall community health. For example, the monthly breakdown of when case and death rates are at their highest, would allow public health officials to know when to invest more in COVID-19 campaigns which educate and highlight the importance of practicing COVID-19 safety measures. The monthly breakdown of when vaccinations rates are at their highest, could be influential in the helping U.S. public health procurement department know how many vaccination vials should be ordered per month, in order to reduce wastage.

Future studies could focus on comparing how using different definitions of key study variables impact findings, and also how crowded housing and vaccination shape risk using individual-level data. Although a few social determinants of health such as education and economic status were included in the case and death rate regression models, future studies could also extensively explore the role of access to quality healthcare and the neighborhood/built environment and how each these variable influences the study results presented.

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Appendix A: Tables

Table 6: New Case rates per 100,000 regression results from fully adjusted multivariable models comparing counties with <25% versus <50% versus <75% high risk thresholds for Vaccine Coverage.

	<25% **Adjusted β (95% CI)**	<50% **Adjusted β (95% CI)**	<75% **Adjusted β (95% CI)**
Vulnerability			
Low Risk	*Reference*	*Reference*	*Reference*
Overcrowded Housing	**-38.7** (-60.5,-16.9)	**-65.2** (-94.9, -35.6)	**-104.6** (-147.6, -61.6)
Low Vaccination Coverage	**-55.0** (-81.4,-28.5)	**-67.2** (-89.4, -45.0)	10.7 (-16.5, 38.0)
High Risk	0.84 (-43.7, 92.4)	**-38.4** (-66.4, -10.4)	18.7(-13, 50.4)

Table 7: New Death rates per 100,000 regression results from fully adjusted multivariable models comparing counties with <25% versus <50% versus <75% high risk thresholds for Vaccine Coverage.

	<25% **Adjusted β (95% CI)**	<50% **Adjusted β (95% CI)**	<75% **Adjusted β (95% CI)**
Vulnerability			
Low Risk	*Reference*	*Reference*	*Reference*
Overcrowded Housing	0.13 (-0.53,0.79)	0.058 (-0.88,0.76)	-0.77 (-1.8,0.3)
Low Vaccination Coverage	**1.7** (0.89,2.5)	0.00022 (-0.63,0.63)	**2.47** (1.8, 3.1)
High Risk	0.58 (-0.55,1.70)	-0.36 (-1.2,0.54)	**2.29** (1.4,3.2)

Appendix B: Figures

Figure 8: 2021 Monthly Variations in the Percentage of U.S. Counties within each Vulnerability Category at the 25% Vaccination Coverage Threshold

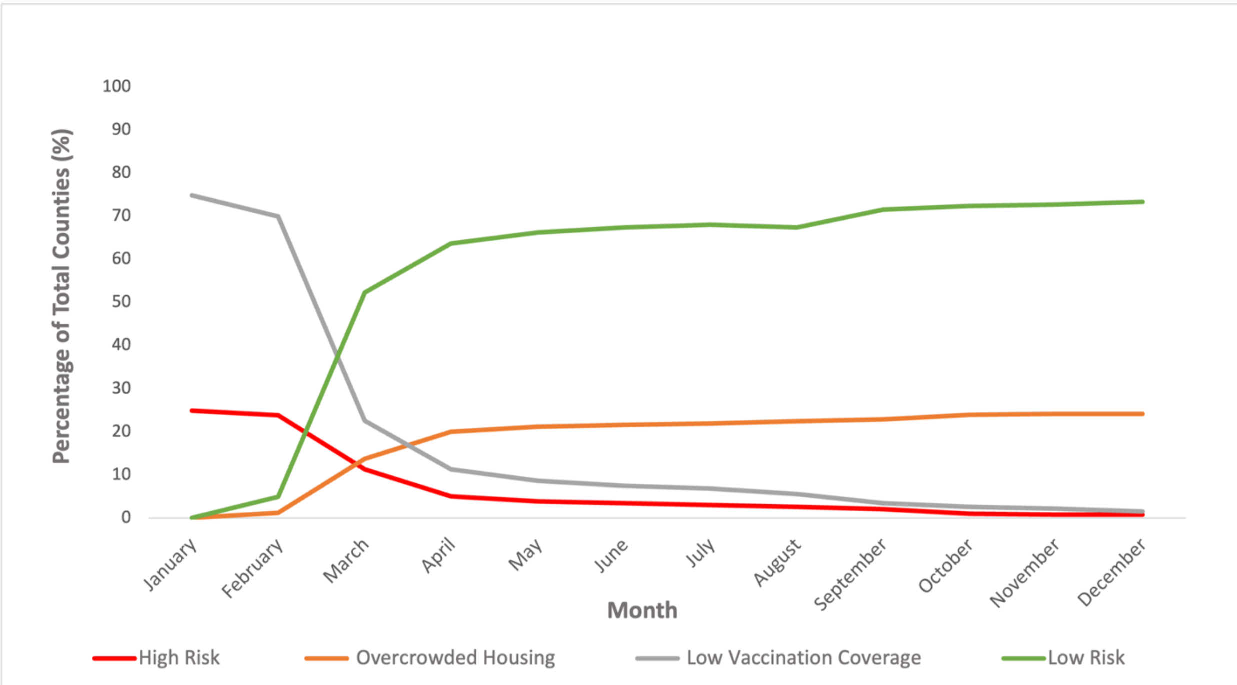

Figure 9: 2021 Monthly Variations in the Percentage of U.S. Counties within each Vulnerability Category at the 50% Vaccination Threshold

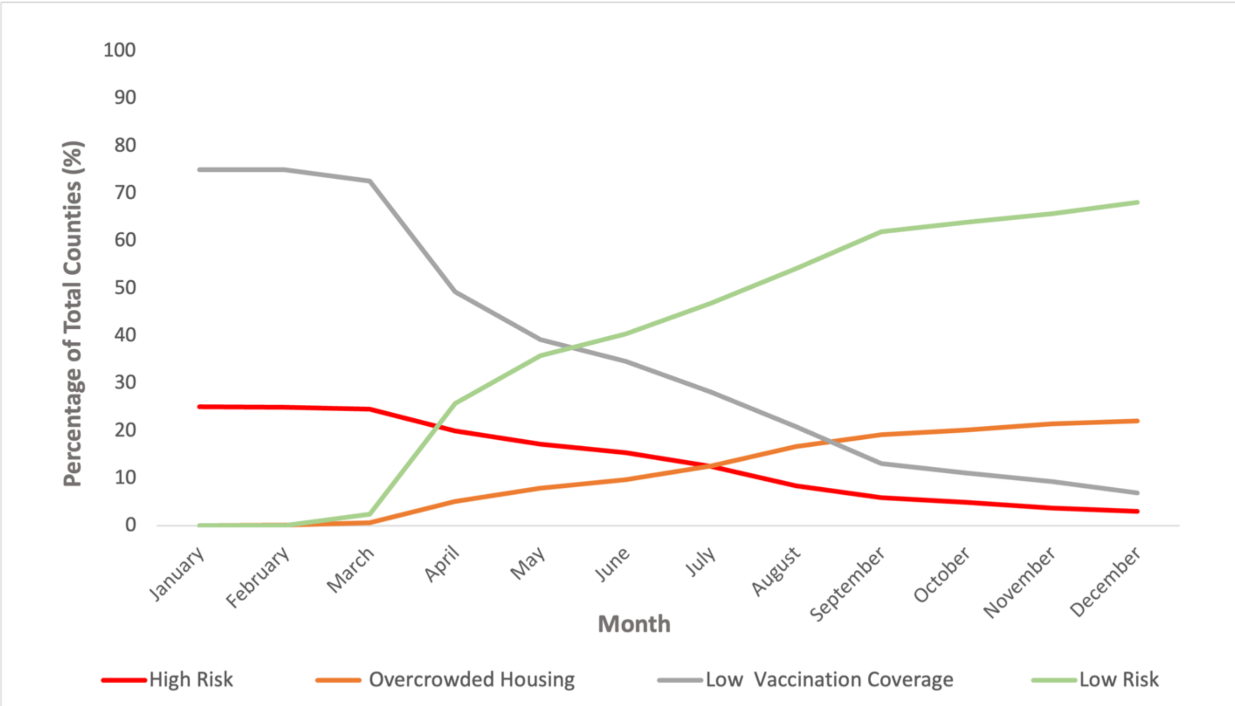

Figure 10: 2021 Monthly Variations in the Percentage of U.S. Counties within each Vulnerability Category at the 75% Vaccination Threshold