

RESEARCH ARTICLE

Geographic disparities and determinants of COVID-19 incidence risk in the greater St. Louis Area, Missouri (United States)

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Abstract

Background

Evidence seems to suggest that the risk of Coronavirus Disease 2019 (COVID-19) might vary across communities due to differences in population characteristics and movement patterns. However, little is known about these differences in the greater St Louis Area of Missouri and yet this information is useful for targeting control efforts. Therefore, the objectives of this study were to investigate (a) geographic disparities of COVID-19 risk and (b) associations between COVID-19 risk and socioeconomic, demographic, movement and chronic disease factors in the Greater St. Louis Area of Missouri, USA.

Methods

Data on COVID-19 incidence and chronic disease hospitalizations were obtained from the Department of Health and Missouri Hospital Association, respectively. Socioeconomic and demographic data were obtained from the 2018 American Community Survey while population mobility data were obtained from the SafeGraph website. Choropleth maps were used to identify geographic disparities of COVID-19 risk and several sociodemographic and chronic disease factors at the ZIP Code Tabulation Area (ZCTA) spatial scale. Global negative binomial and local geographically weighted negative binomial models were used to investigate associations between ZCTA-level COVID-19 risk and socioeconomic, demographic and chronic disease factors.

Results

There were geographic disparities found in COVID-19 risk. Risks tended to be higher in ZCTAs with high percentages of the population with a bachelor's degree ($p < 0.0001$) and obesity hospitalizations ($p < 0.0001$). Conversely, risks tended to be lower in ZCTAs with high percentages of the population working in agriculture ($p < 0.0001$). However, the

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association between agricultural occupation and COVID-19 risk was modified by per capita between ZCTA visits. Areas that had both high per capita between ZCTA visits and high percentages of the population employed in agriculture had high COVID-19 risks. The strength of association between agricultural occupation and COVID-19 risk varied by geographic location.

Conclusions

Geographic disparities of COVID-19 risk exist in the St. Louis area and are associated with sociodemographic factors, population movements, and obesity hospitalization risks. The latter is particularly concerning due to the growing prevalence of obesity and the known immunological impairments among obese individuals. Therefore, future studies need to focus on improving our understanding of the relationships between COVID-19 vaccination efficacy, obesity and waning of immunity among obese individuals so as to better guide vaccination regimens and reduce disparities.

Introduction

Since the first reported case in Wuhan (China) in December 2019, Coronavirus Disease 2019 (COVID-19) has spread worldwide with over 273 million confirmed cases and over 5.3 million deaths as of December 18, 2021 [1]. Within the United States, there have been over 50 million confirmed cases and over 805,000 reported deaths with Missouri reporting over 961,000 confirmed cases and 15,000 deaths [2, 3].

Evidence seems to suggest that the risk of COVID-19 might vary across communities due to differences in population characteristics and movement behavior that if identified may guide disease control. For instance, some studies have reported higher prevalence of COVID-19 in regions with high densities of Black and/or Hispanic populations [4, 5]. There have also been reports of associations between COVID-19 incidence risk and both healthcare and non-healthcare related occupations [6–8]. During the initial stages of the COVID-19 pandemic, stay-at-home and social distancing measures were implemented to minimize contacts between infected or potentially infected and susceptible individuals so as to curb disease transmission [9, 10]. These measures were based on the understanding that more interactions between infected and susceptible individuals in the population would lead to more cases, reflecting the potential association between COVID-19 incidence risk and the movement of individuals. Chang and co-workers used population mobility, derived from SafeGraph mobile phone data, and susceptible-exposed-infectious-removed (SEIR) model and predicted high infection rates among disadvantaged racial and socioeconomic groups [11]. The study noted that the identified differences were solely due to differences in mobility since disadvantaged groups were not able to reduce their mobility as much as their non-disadvantaged counterparts and that they tended to visit crowded places that were inherently associated with higher infection/disease risks [11].

Understanding the geographic disparities in the distribution of COVID-19 risk and the associations of these disparities with socioeconomic, demographic and chronic disease factors at the local level is critically important in identifying communities at highest risk. This information is important in guiding local health policies as well as resource allocation for targeting interventions such as distribution of testing kits and vaccines. Thus, the objective of this study

was to identify geographic disparities in COVID-19 incidence risk in the greater St. Louis area of Missouri and to simultaneously investigate sociodemographic, chronic condition and population movement determinants of the identified disparities.

Methods

Ethics approval

This study was approved by the North Carolina State University Institutional Review Board (IRB number: 22342) and all study methods were carried out in accordance with relevant guidelines and regulations. The study used anonymized secondary data provided to the investigators, by the Hospital Industry Data Institute, in such a manner that the identity of human subjects cannot be ascertained directly or through identifiers linked to the subjects. The investigators did not contact the subjects and did not re-identify subjects.

Study area

This retrospective ecological study was conducted in Missouri in an area that included a total of 108 ZIP Code Tabulation Areas (ZCTAs) located in 6 counties: Franklin, Jefferson, St. Charles, St. Louis City, St. Louis, and Warren counties. The area has a total population of approximately 2 million people comprised of about 20% Black, 3% Hispanic or Latino, 3% Asian and 74% White individuals. Forty-eight percent of the population was male, while 52% was female. The ZCTA-level population density ranged from 10 people per square mile in St. Charles County to 9,368 in St. Louis City County.

Data sources

Confirmed COVID-19 data. Data on confirmed cases of COVID-19 reported in the study area between March 23rd and October 8th, 2020 were obtained from the county Departments of Health. These data were aggregated to the ZCTA-level to obtain cumulative incidence risks of confirmed COVID-19 cases over the study period for each ZCTA.

Sociodemographic and base map data. Data on ZCTA-level sociodemographic factors, including age, sex, racial composition, population density, household size, education level, employment industry (occupation), and median income were obtained from the U.S. Census Bureau 2018 American Community Survey (ACS) 5-year estimates [12]. Cartographic boundary files used as base maps for all cartographic displays were obtained from the US Census Bureau Website [13].

Chronic disease data. Data on hospitalizations attributed to chronic conditions, by ZCTA of residence, were obtained from the Hospital Industry Data Institute, a not-for-profit organization founded by the Missouri Hospital Association that summarizes state-level hospital discharge data. The data included the number of unique patient hospitalizations with ICD-10 codes for obesity, tobacco use, cancer, chronic obstructive pulmonary disease (COPD), chronic kidney disease, heart failure, and diabetes. These variables were selected due to their hypothesized potential associations with COVID-19 risk. Therefore, risks of hospitalization with each of the above conditions were computed and used in subsequent analyses to investigate their associations with COVID-19 risk.

Movement data. Data on daily movement patterns of individuals into and within the study area from March 23rd to October 8th 2020 were obtained from the Social Distancing Metrics cellphone dataset of SafeGraph [14]. SafeGraph is a company that aggregates anonymized location data from smartphones. The data are useful for studying population mobility patterns. The metrics selected from the dataset were the origin census block group (CBG),

which represents the home location of the owner of a device, and the destination CBG. For privacy reasons, the data did not include CBGs which had less than 5 recorded devices. To allow ZCTA-level analysis, point-in-polygon joins were used to link CBGs to ZCTAs using CBG geographic centroids and ZCTA polygon data obtained from the U.S. Census Bureau [13]. A total of 5 CBGs did not match any ZCTA and could not be linked to the ZCTA polygon file. Thus, the final dataset had a total of 103 of the original 108 ZCTAs in the study area. Therefore, all subsequent analyses included 103 ZCTAs.

Population movement metrics were defined to describe the different types of movements observed in the study area. Travel from outside the study area into one of the 103 study area ZCTAs was called an “*outside visit*”. Travel from one study area ZCTA to another study area ZCTA was referred to as a “*between visit*” while travel within a study area ZCTA was called a “*within visit*”. Each of these movement metrics was expressed either as: (a) *raw values*: total number of visits in a ZCTA or (b) *per capita (population-adjusted) values*: total number of visits in a ZCTA divided by the population of the ZCTA. The per capita values were particularly important in situations where there were disproportionate numbers of movements in a ZCTA relative to the size of the ZCTA’s population (e.g. a large number of visits to sparsely populated ZCTAs).

Descriptive analysis and identification of geographic disparities in COVID-19 risk

Descriptive analyses were performed in R version 4.1.0 [15] and implemented in RStudio version 1.4.1103 [16]. The Shapiro-Wilk test was used to assess for normality of distribution of continuous variables. Medians as well as 1st and 3rd quartiles were reported for each variable since all were non-normally distributed. To investigate geographic disparities in COVID-19 incidence risk, choropleth maps were generated in QGIS [17] using Jenk’s optimization classification scheme [18] to determine the break-points. Jenk’s optimization, also known as natural breaks, uses a statistical approach which identifies groupings and patterns inherent in the data. The approach minimizes the sum of the within class variance while maximizing the difference between classes thereby attaining a high goodness of variance fit of 0.91. The approach also maximizes information about both the map area and the parameter being mapped resulting in a very efficient map.

Investigation of predictors of the geographic disparities of COVID-19 risk

Global models. Univariable global Poisson models were used to investigate associations between each of the investigated factors and COVID-19 incidence risk. The response variable of interest was the ZCTA-level number of confirmed COVID-19 cases offset by the natural log of the population in each ZCTA. The explanatory variables investigated were ZCTA-level sociodemographic factors, chronic condition risks, and movement patterns between and within ZCTAs. The models were fit using the Generalized Linear Model framework (glm function) in R [15], specifying Poisson distribution and log link. Variables with a p-value less than 0.15 were considered potentially associated with the outcome and investigated further. The linear relationships between the log of the incidence risk and the potential predictors were assessed graphically.

Bivariate Spearman rank correlation analyses were used to identify pairs of highly correlated ($r \geq 0.7$) potential predictors. To avoid multicollinearity during the subsequent multivariable modeling, only one of a pair of highly correlated variables were assessed in the multivariable model. Backwards elimination process was then used to build a multivariable Poisson model using an alpha of 0.05 to assess statistical significance. The final Poisson model

showed evidence of overdispersion based on the fact that the ratio of residual deviance to residual degrees of freedom was much greater than 1, implying the Poisson model was not appropriate for the data.

To account for overdispersion, a negative binomial (NB) model was fit to the data using the same approach described above for Poisson model. The NB model was fit using the `glm.nb` function of the MASS package in R [15] specifying negative binomial distribution and log link. Potential confounding variables were investigated by assessing if removal of a suspected confounding variable from the model resulted in a change of at least 20% of the coefficients of any of the variables still in the model. If this happened, then the suspected confounding variable would be retained in the model regardless of its statistical significance, otherwise, it would be removed from the model unless it had a significant p-value in which case it would be retained in the model as an important predictor. Two-way biologically meaningful interaction terms between predictors in the final main effects multivariable model were assessed and significant ones retained in the model. Goodness-of-fit of the final multivariable negative binomial model was assessed using Pearson and Deviance chi-square goodness-of-fit tests in STATA 16.1 [19].

Local models. A geographically weighted negative binomial (GWNB) model, proposed by Silva and Rodrigues [20], was fit to the data to assess if the association between each of the predictors and COVID incidence risks varied by geographic location. The same outcome, offset, distribution, link function, and predictors used in the final global multivariable NB model were used for this model. The GWNB theoretically estimates as many regression coefficients as the number of ZCTAs in the study area. This is unlike the global multivariable model which estimates one regression coefficient for each predictor and assumes that the strength of association with the outcome remains constant across all ZCTAs in the study area.

SAS/IML macro [21] of SAS version 9.4 [22] was used to fit the local GWNB model. The estimation of local regression coefficients was based on a biquadratic kernel weighting function [21], while the bandwidth was estimated using the adaptive method which allows the size of the bandwidth to vary based on the density of observations. Bias-corrected Akaike Information Criteria (AICc) was used to determine the optimum kernel bandwidth and compare the goodness-of-fit of the global NB and GWNB models. A lower AICc value indicated a better fitting model.

Stationarity of the GWNB coefficients were assessed using: (a) randomization non-stationarity test based on 999 replications [23]; (b) comparison of the interquartile range of the local GWNB model coefficients with the standard error estimates of the global NB model. Local coefficients with interquartile ranges larger than twice the standard error of the regression coefficient from the global NB model were considered non-stationary [24, 25].

Results

Descriptive statistics

The median percentages of male, Black, and Hispanic populations across ZCTAs were 48.6%, 3.7% and 2.2% of the study population, respectively, while the median percentage of individuals aged ≥ 65 years was 15% (Table 1). The median average household size was 2.5 and the median household income was \$59,769 with 9.5% of the population living below the poverty line. Regarding education, individuals with a high school or lower education comprised the highest percentage (38.2%) of the population followed by those with some college education (23%). As for occupation, most of the population worked in education or healthcare (23.6%), followed by manufacturing (11%) and the least were employed in agriculture (0.5%) (Table 1).

Of the chronic conditions assessed for potential association with COVID-19, chronic kidney disease (CKD) had the highest median hospitalization risk (7.6%) while heart failure had

Table 1. Summary statistics of ZCTA-level potential predictors of COVID-19 risk in the Greater St. Louis Area, Missouri (USA).

Type of Variable	Variable	Median	1 st Quartile	3 rd Quartile
Demographic Factors				
	% male population	48.6	47.4	50.3
	% black population	3.7	0.9	34.2
	% Hispanic/Latino population	2.2	1.0	3.2
	% over 65	15.0	12.3	17.8
	Average household size	2.5	2.3	2.7
Economic Variables				
	% below poverty level	9.5	5.8	16.8
	median household income	59,769	46,005	77,504
Educational Variables				
	% with ≤ high school education	38.2	23.9	47.6
	% with some college education	23.0	19.8	25.6
	% with associate's degree	8.6	6.6	10.6
	% with bachelor's degree	18.0	9.4	25.9
Occupation Variables				
	% in agriculture ¹	0.5	0.2	1.0
	% in construction	5.2	3.38	9.5
	% in retail	10.8	8.3	12.0
	% in transportation	4.45	3.1	6.05
	% in manufacturing	11.0	8.7	13.0
	% in education or healthcare	23.6	20.6	27.7
Health Behavior (ZCTA-level number of hospitalized patients that use tobacco per 100 persons)				
	% tobacco ²	10.4	6.8	14.5
Co-morbidities (ZCTA-level number of hospitalized patients with specific condition per 100 persons)				
	% obesity	7.0	5.6	8.0
	% cancer	3.8	3.3	4.3
	% COPD ³	4.0	3.1	4.9
	% CKD ⁴	7.6	6.4	8.9
	% heart failure	3.2	2.6	3.8
	% diabetes	7.5	6.5	9.2
Movement variables				
	Outside visits	44,501	16,974	71,724
	Within visits	181,031	78,776	401,433
	Between visits	163,655	71,337	298,681
	Per capita outside visits	2.4	1.5	4.3
	Per capita within visits	13.2	9.0	18.8
	Per capita between visits	9.7	6.8	1.4

¹Percent of population employed in agriculture, forestry, fishery and mining.

²ZCTA-level % hospitalized patients that were tobacco users.

³Chronic Obstructive Pulmonary Disease.

⁴Chronic Kidney Disease.

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the lowest (3.2%). Regarding movement of the population, the largest median number of movements across all study ZCTAs were within ZCTA visits (median: 181,031) while the fewest number of visits were outside visits (median: 44,501). The values of the per capita (population adjusted) visits followed the same ordering as the above raw (unadjusted) visits with the

highest median number of per capita visits being within ZCTA visits (median: 13.2) and the lowest being visits from outside the ZCTA (median: 2.4).

Predictors of COVID-19 incidence risk

Global model. Using a relaxed alpha of 0.15, several variables had potential univariable associations with COVID-19 incidence risk (Table 2). These included: (a) socioeconomic and demographic variables: percentage of male and Black populations, average household size and median household income; (b) all education and occupation variables, with the exception of the percentage of the population with an associate's degree and those employed in retail and transportation; (c) all chronic disease and movement variables (except risks of hospitalizations attributable to tobacco use and COPD, within ZCTA visits and between ZCTA visits) (Table 2).

Based on the final global multivariable negative binomial model, the incidence risk of COVID-19 tended to be higher in ZCTAs that had high percentages of the population with bachelor's degrees ($p < 0.0001$) and those hospitalized due to obesity ($p < 0.0001$) (Table 3). In contrast, COVID-19 risks tended to be lower in ZCTAs which had high percentages of the population employed in agriculture if the ZCTAs had no (zero) per capita between ZCTA visits (Table 3). The significant ($p < 0.0001$) interaction between percentage of the population in agriculture and the per capita between ZCTA visits implies that the latter was a significant effect modifier of the relationship between COVID-19 risk and percentage of the population employed in agriculture.

Thus, although COVID-19 risk tended to be lower in ZCTAs that had a high percentage of the population employed in agriculture but no between ZCTA per capita visits, the risk of COVID-19 was higher in ZCTAs that had both high percentage of the population employed in agriculture and high per capita between ZCTA visits.

The geographic distribution of COVID-19 risks and each of the predictors in the final model are shown in Fig 1. Note that the white patches in the maps indicate ZCTAs with missing data. The risks of COVID-19 were higher in the Eastern region of the study area, with pockets of high risks in ZCTAs located in St. Louis, St. Louis City and St. Charles counties while the lowest risks were observed in ZCTAs in Warren, Jefferson and Franklin counties. The distribution of the percentage of the population with bachelor's degrees followed similar spatial patterns. The ZCTAs that had high percentages of the population employed in agriculture tended to have low COVID-19 risks (Fig 1).

Local model. The randomization non-stationarity test results indicate that the coefficients of the association between percentage of the population employed in agriculture and COVID-19 risk was non-stationary ($p = 0.049$) and, therefore, varied by geographic location (Table 4). This is further supported by the fact that the interquartile range of the GWNB model coefficient for percentage of the population employed in agriculture (0.1232) is greater than twice the standard error of the global coefficient (0.0652) for percentage of the population employed in agriculture (Table 4).

The strength of the negative association between percentage of the population in agriculture and COVID risk varied considerably by geographic location and showed a gradient increasing from East to West, with the strongest association occurring in the West (Fig 2) which also has the highest percentage of the population employed in agriculture (Fig 1). When there is no (zero) per capita between ZCTA visits, the direction of this association stayed consistently negative across all ZCTAs in the study area (Fig 2). However, this association was modified and reversed by the number of per capita between ZCTA visits with COVID-19 risk increasing as both the percentage of population in agriculture and the number of per capita between ZCTA

Table 2. Univariable associations between ZCTA-level COVID-19 risk and potential predictors in the Greater St. Louis Area, Missouri (USA).

Type of Variable	Variable	Coefficient	95% Confidence Interval	p-values
Demographic Factors				
	% male population	0.014	-0.002, 0.030	0.110
	% black population	0.003	0.001, 0.005	0.007
	% Hispanic/Latino population	0.020	-0.009, 0.050	0.168
	% over 65	-0.007	-0.019, 0.005	0.245
	Average household size	-0.150	-0.330, 0.030	0.114
Educational Variables				
	% with ≤ high school education	-0.003	-0.007, 0.001	0.147
	% with some college education	-0.010	-0.022, 0.001	0.079
	% with associate's degree	-0.007	-0.028, 0.013	0.482
	% with bachelor's degree	0.007	0.001, 0.013	0.024
Economic Variables				
	% below poverty level	0.002	-0.004, 0.008	0.595
	median household income (\$10,000s)	0.017	-0.002, 0.037	0.091
Occupation Variables				
	% in agriculture ¹	-0.055	-0.10, -0.005	0.030
	% in construction	-0.035	-0.048, -0.021	<0.0001
	% in retail	0.001	-0.010, 0.030	0.308
	% in transportation	0.009	-0.015, 0.033	0.478
	% in manufacturing	-0.019	-0.032, -0.006	0.003
	% in education or healthcare	0.011	0.001, 0.022	0.032
Health Behavior (ZCTA-level number of hospitalized patients that use tobacco per 100 persons)				
	% tobacco ²	0.007	-0.004, 0.018	0.245
Co-morbidities (ZCTA-level number of hospitalized patients with specific condition per 100 persons)				
	% obesity	0.047	0.017, 0.078	0.004
	% cancer	0.059	0.024, 0.094	0.002
	% COPD ³	0.009	-0.036, 0.053	0.692
	% CKD ⁴	0.046	0.021, 0.072	0.001
	% heart failure	0.080	0.022, 0.140	0.007
	% diabetes	0.035	0.010, 0.060	0.006
Movement variables				
	Outside visits (1,000,000s)	0.980	-0.099, 2.100	0.074
	Within visits (1,000,000s)	0.082	-0.120, 0.290	0.427
	Between visits (1,000,000s)	0.230	-0.110, 0.570	0.171
	Per capita outside visits	0.016	0.005, 0.028	0.004
	Per capita within visits	0.008	0.003, 0.014	0.008
	Per capita between visits	0.016	0.010, 0.022	<0.0001

¹Percent of population employed in agriculture, forestry, fishery and mining.

²ZCTA-level % hospitalized patients that were tobacco users.

³Chronic Obstructive Pulmonary Disease.

⁴Chronic Kidney Disease.

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visits increased as evidenced by the significant interaction term (Table 3). It is worth noting that the coefficient of the interaction term was stationary (Table 4) implying that the strength of the modified association was the same across all ZCTAs in the study area.

Table 3. Final global negative binomial model showing significant predictors of COVID-19 risk in the Greater St. Louis Area, Missouri (USA).

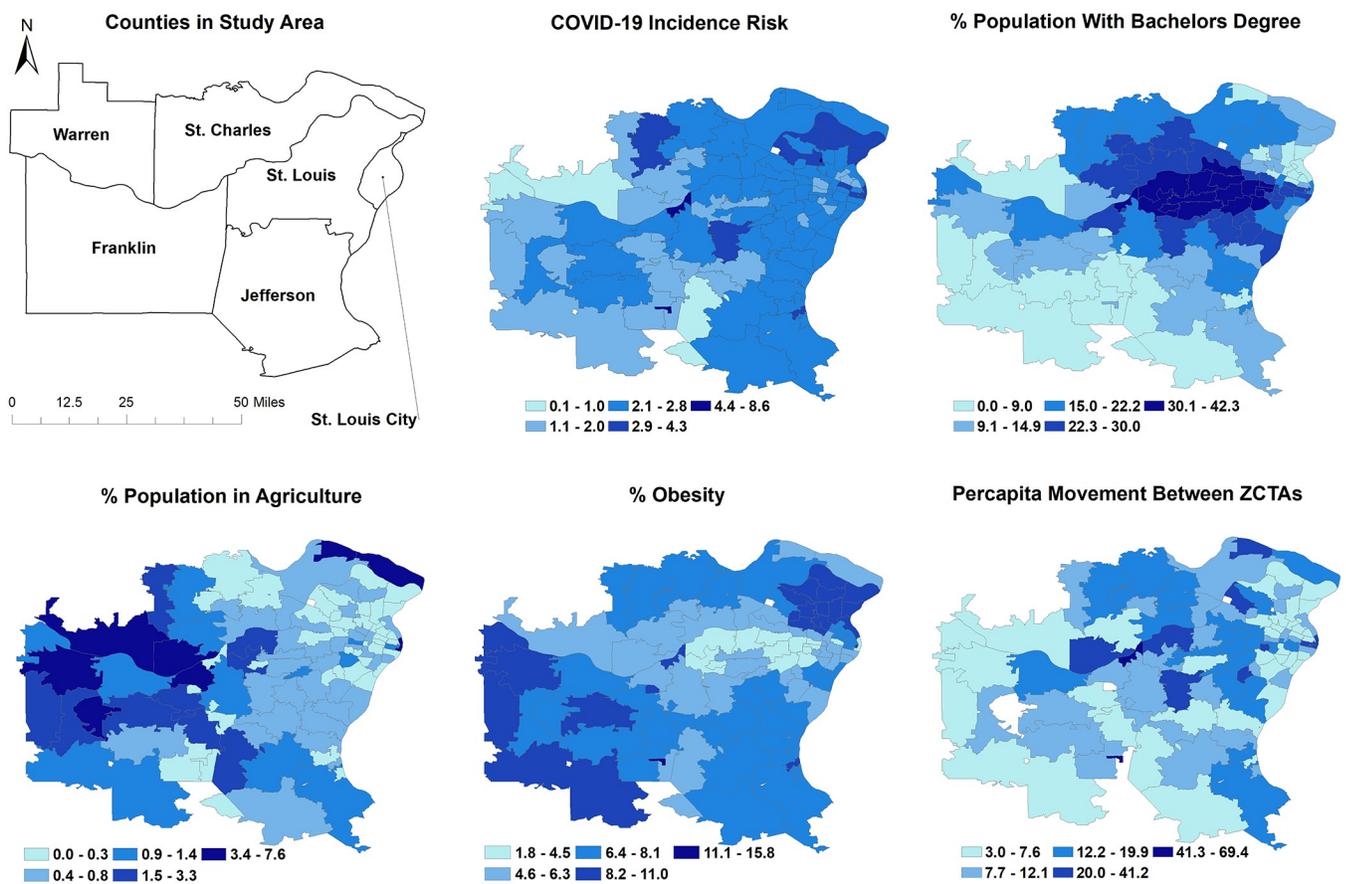
Name	Coefficient	95% Confidence Interval	p-value
% with bachelor's degree	0.018	0.011, 0.025	<0.0001
% obesity ¹	0.121	0.087, 0.155	<0.0001
% in agriculture	-0.181	-0.245, -0.117	<0.0001
Per capita between visits	0.002	-0.005, 0.009	0.600
% in agriculture* per capita between visits	0.008	0.005, 0.011	<0.0001

¹Percentage of hospitalized patients with obesity.

<https://doi.org/10.1371/journal.pone.0274899.t003>

Discussion

This study identified ZCTA-level geographic disparities of COVID-19 risk in the greater St. Louis area of Missouri. It also investigated predictors of the identified disparities. The identified significant association between COVID-19 incidence risk and percentage of the population with bachelor's degree is in contrast to findings from individual level studies that reported higher COVID-19 morbidity and mortality among individuals with lower educational attainment [26, 27]. It also contrasts with reports of a study in a county in Michigan that reported



Source: U. S. Census Bureau, 2018 American Community Survey; COVID Case Data from Missouri Department of Health

Fig 1. Geographic distribution of ZCTA-level COVID-19 risk and its significant predictors in the Greater St. Louis area, Missouri (USA).

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Table 4. Results of assessment of stationarity of the coefficients of the predictors of the COVID-19 risks in the Greater St. Louis Area, Missouri.

	NB SE ¹	2x(NB SE ¹)	GWNB IQR ²	GWNB IQR ² - 2x(NB SE ¹)	GWNB p-value ³	Is Coefficient Non-Stationary?
% with bachelor's degree	0.0035	0.007	0.0067	-0.003	0.102	No
% in agriculture	0.0326	0.0652	0.1232	0.058	0.049	Yes ⁵
% obesity ⁴	0.0174	0.0348	0.0255	-0.0093	0.322	No
Per capita between visits	0.0035	0.0007	0.0034	-0.0036	0.544	No
% in agriculture*per capita between visits	0.005	0.01	0.0043	-0.0057	0.085	No

¹Standard Error (SE) from the Negative binomial (NB) model.

²Interquartile range (IQR) of the geographically weighted negative binomial (GWNB) standard error.

³p-value of the predictor from the GWNB model.

⁴Percentage of hospitalized patients with obesity.

⁵Coefficients are non-stationary based on both the p-value of the stationarity test and GWNB IQR - 2x(NB SE) assessment.

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no association between COVID-19 incidence risk and level of education [4]. This may suggest that the importance of specific factors might vary by geographic location and might be driven by contextual factors. Additionally, the observed association between higher education

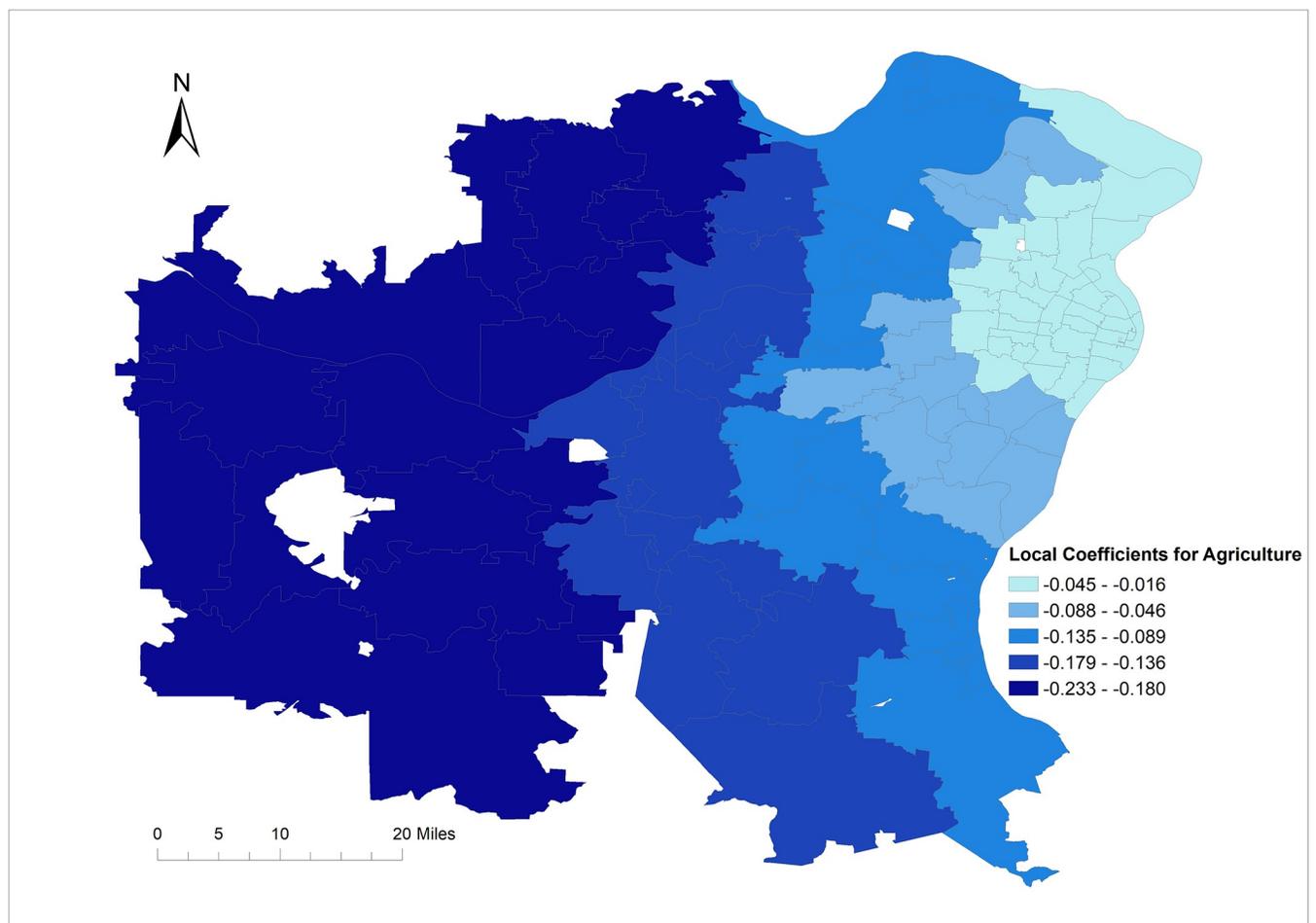


Fig 2. Geographically varying coefficients of local geographically weighted negative binomial model of COVID-19 risks in the Greater St. Louis Area, Missouri (USA).

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attainment and COVID-19 risk observed in this study might be more a reflection of access to COVID-19 testing and not necessarily differences in disease incidence. It is likely that individuals with higher education attainment had better access to COVID-19 testing, than those with lower education attainment, especially during the time covered by the study when testing was not yet widely available.

The significant association between risk of COVID-19 and obesity hospitalization risks observed in this study is consistent with reports from several studies [28–31]. A number of reports have also linked obesity to more severe COVID-19 illness, hospitalizations and deaths [32–37]. A UK study reported that, compared to individuals of normal weight, overweight and obese individuals had 44% and 97% higher risk of COVID-19, respectively [38]. A pooled analysis conducted as part of a meta-analysis by Popkin *et al.* reported that the odds of individuals with obesity testing positive for COVID-19 were 46% higher than among those who were not obese [37]. Some authors have suggested that excess ectopic fat deposition that occurs in obese individuals reduces protective cardiorespiratory reserve and potentiates the immune dysregulation that might mediate the progression to critical illness and organ failure in some COVID-19 patients [32]. Thus, obesity has harmful effects on lung function, reducing both forced expiratory volume and vital capacity [32]. Furthermore, obesity has modulatory effects on key immune cell populations critical in the response to SARS-CoV-2 virus. Increased anti-inflammatory cells inhibit the ability to reduce the infection, because inflammatory responses are needed to control viral spread [37]. This likely impairs the immune response to SARS-CoV-2. Obesity has also been reported to impair the development of immunological memory. For example, influenza vaccination in adults with and without obesity results in equivalent influenza-specific antibody titers at 30 days post vaccination, but antibody titers wane more among obese compared to non-obese adults 1 year after vaccination [37, 39].

The inflammatory factors involved in obesity play a role in the development of severe lung diseases. There is evidence that susceptibility to acute respiratory distress syndrome, associated with COVID-19, is significantly greater among obese than non-obese individuals [40]. Moreover, obesity has been shown to increase the risk of influenza morbidity and mortality [41] due to impaired innate and adaptive immune responses [42]. It is suspected that COVID-19 vaccines might be less effective among individuals with obesity due to this weakened immune response [37]. These immunological impairments among obese individuals might suggest faster waning of immunity following vaccination among obese than non-obese segments of the population. This is particularly concerning considering the growing prevalence of obesity. Future individual level studies will need to focus on improving our understanding of the relationship between obesity and COVID-19 vaccination efficacy and waning of immunity to better guide vaccination regimens.

The COVID-19 pandemic has occurred at a time when the prevalence of obesity is increasing throughout the world [37] with almost all countries today having prevalence of overweight/obesity greater than 20% [43–45]. Unfortunately, the movement and social distancing restrictions due to the COVID-19 pandemic have resulted in changes in food consumption and physical activity patterns that might exacerbate current trends in the prevalence of obesity. It is concerning that these changes might have implications lasting way past the pandemic period [37] not only in the study area, but other geographic regions as well.

Although, in the absence of per capita between ZCTA visits, the percentage of the population engaged in agriculture had a negative association with COVID-19 risk, this association was modified and even reversed by per capita between ZCTA visits since the interaction term between the percentage of the population in agriculture and per capita between ZCTA visits was positive and statistically significant. Other studies have reported higher prevalence of COVID-19 in regions with high percentages of individuals engaged in agricultural activities

[6, 8]. Based on the findings of the current study, while the number of per capita between ZCTA visits did not have a significant association with COVID-19 risk on its own, it was an effect modifier of the effect of agricultural occupation on COVID-19 risk. This suggests that, in the Greater St Louis Area, per capita movements between ZCTAs may have a more profound impact on COVID-19 risk in the more rural communities (which have more individuals engaged in agriculture) than in urban locales.

It is worth noting that although both total visits (not adjusted for population) and per capita visits (adjusted for population) were assessed for potential association with COVID-19 risk, only the per capita visits had significant association with COVID risk. This may be an indication of the fact that it is not just mobility that is important, but that where the individuals go and the kind of interactions they have may be equally, if not more important. The lack of association between race and COVID risk is contrary to findings from other studies that have reported significant associations between Black population and COVID-19 risk [4, 5, 46].

The fact that the coefficients for the percentage of the population in agriculture were non-stationary and hence varied by geographic location implies that the importance and potential impact of this variable is not constant across the study area but varies based on geographic location. Thus, the strength of association between percent of population in agriculture and COVID-19 risk changes by location implying that a global coefficient was not sufficient in describing this relationship. Therefore, the focus of control efforts might need to vary based on location since some factors may be more important in some locales than others.

Strengths and limitations

There is currently lack of standardized data collection approaches across ZCTAs potentially resulting in differences in case ascertainment across ZCTAs. Moreover, hospitalization data can be influenced by differences in access to healthcare and may not always be representative of the population at large. A limitation of the safe SafeGraph data is that it may not be representative of all the segments of the population. For instance, it uses data collected by applications on only smartphones and thus does not include data on individuals who do not use smartphones. Some smartphone users may also opt-out from the service that collects mobility data and hence their data may not be collected. Additionally, for privacy reasons, SafeGraph data from ZCTAs with less than 5 devices were not included in the analysis. Therefore, SafeGraph data may not be representative of the true population mobility and hence the findings should be interpreted with this limitation in mind. The primary strength of this study is that it used both global and local models to identify predictors of COVID-19 risk. This approach allows identification of geographically varying regression coefficients and better descriptions of the associations between predictors and outcomes so as to better guide geographically targeted local control and prevention efforts. Another strength of the study is the use of SafeGraph population mobility data. The relevance of population movements to the COVID-19 infection risk is evident from the stay-at-home and social distancing directives that were put in place during the pandemic. The statistical analysis conducted in this study provided an insight into the possible associations between COVID-19 risk and various types of movements into and within ZCTAs.

Conclusions

Geographic disparities of COVID-19 risks exist in the greater St Louis area. These disparities are, in part, explained by socioeconomic factors, chronic disease risks and population movement patterns that may be important in guiding efforts to control the disease and reduce disparities. Use of GIS, global, and local models help improve our understanding of geographic

disparities in disease risks and the determinants thereof. The identified association between COVID-19 risk and obesity as well as the known immunological impairments among obese individuals is concerning considering the growing prevalence of obesity. Future studies will need to focus on improving our understanding of the relationship between obesity and COVID-19 vaccination efficacy and waning of immunity to better guide vaccination regimens.

Supporting information

S1 Data.
(CSV)

S2 Data.
(XLSX)

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References

1. Johns Hopkins Coronavirus Resource Center. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). In: COVID-19 Dashboard, [Internet]. 2021 [cited 30 Nov 2021]. Available: <https://coronavirus.jhu.edu/map.html>
2. Centers for Disease Control and Prevention (CDC). COVID Data Tracker. In: Data Tracker, [Internet]. 2021 [cited 27 Nov 2021]. Available: <https://covid.cdc.gov/covid-data-tracker/#datatracker-home>
3. Centers for Disease Control and Prevention (CDC). COVID Data Tracker Weekly Review. In: Science and Research, [Internet]. 2021 [cited 27 Nov 2021]. Available: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html>

4. Akanbi MO, Rivera AS, Akanbi FO, Shoyinka A. An Ecologic Study of Disparities in COVID-19 Incidence and Case Fatality in Oakland County, MI, USA, During a State-Mandated Shutdown. *J Racial Ethn Heal Disparities*. 2020. <https://doi.org/10.1007/s40615-020-00909-1> PMID: 33124003
5. Mude W, Oguoma VM, Nyanhanda T, Mwanri L, Njue C. Racial disparities in COVID-19 pandemic cases, hospitalisations, and deaths: A systematic review and meta-analysis. *J Glob Health*. 2021; 11: 1–15. <https://doi.org/10.7189/JOGH.11.05015> PMID: 34221360
6. Zhang M. Estimation of differential occupational risk of COVID-19 by comparing risk factors with case data by occupational group. *Am J Ind Med*. 2021; 64: 39–47. <https://doi.org/10.1002/ajim.23199> PMID: 33210336
7. Le D, Hawkins D. Variation in Employment in Healthcare Occupations and County-Level Differences in COVID-19 Cases in the United States of America. *J Occup Environ Med*. 2021; 63: 629. <https://doi.org/10.1097/JOM.0000000000002230> PMID: 34184657
8. Lusk JL, Chandra R. Farmer and farm worker illnesses and deaths from COVID-19 and impacts on agricultural output. *PLoS One*. 2021; 16: e0250621. <https://doi.org/10.1371/journal.pone.0250621> PMID: 33909685
9. Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nat* 2020 5847820. 2020; 584: 257–261. <https://doi.org/10.1038/s41586-020-2405-7> PMID: 32512579
10. City of St Louis. COVID-19 Emergency Orders. In: City of St Louis, [Internet]. 2021 [cited 27 Nov 2021]. Available: <https://www.stlouis-mo.gov/government/departments/health/communicable-disease/covid-19/orders/index.cfm>
11. Chang S, Pierson E, Koh W, Gerardin J, Redbird B, Grusky D, et al. Mobility network models of COVID-19 explain inequities and inform reopening. *Nature*. 2021; 589. <https://doi.org/10.1038/s41586-020-2923-3> PMID: 33171481
12. Census Bureau U.S. American Community Survey 5-year estimates. In: U.S. Census Bureau [Internet]. 2018 [cited 17 Nov 2021]. Available: <https://www.census.gov/programs-surveys/acs>
13. US Census Bureau. Geography Mapping Files. In: US Census Bureau [Internet]. 2021 [cited 26 Nov 2021]. Available: <https://www.census.gov/programs-surveys/geography/geographies/mapping-files.html>
14. SafeGraph. SafeGraph. In: 2021 [Internet]. 2021 [cited 1 Mar 2021]. Available: www.safegraph.com
15. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>. 2021. Available: <https://www.r-project.org/>
16. Team RStudio. RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL <http://www.rstudio.com/>. Boston, MA: RStudio Team; 2021.
17. QGIS.org. QGIS Geographic Information System. QGIS Association; 2021. Available: <http://www.qgis.org>
18. Jenks GF. The Data Model Concept in Statistical Mapping. *Int Yearb Cartogr*. 1967; 7: 186–190.
19. StataCorp. STATA. College Station, TX: StataCorp; 2019.
20. Ricardo S, Carvalho R. Geographically Weighted Negative Binomial Regression—incorporating overdispersion. *Stat Comput*. 2014; 24: 769–783. <https://doi.org/10.1007/S11222-013-9401-9>
21. Ricardo Da Silva A. A SAS® Macro for Geographically Weighted Negative Binomial Regression. 2016. Available: <https://support.sas.com/resources/papers/proceedings16/8000-2016.pdf>
22. Institute SAS. Statistical Analysis System (SAS) Version 9.4. Cary, NC, USA. SAS Institute Inc. Cary, NC, USA: SAS Institute Inc; 2016.
23. Hope ACA. A Simplified Monte Carlo Significance Test Procedure on JSTOR. *J R Stat Soc Ser B Stat Methodol*. 1968; 30: 582–598. Available: <https://www.jstor.org/stable/2984263?seq=1>
24. Fotheringham AS, Brunson C, Charlton M. Geographically Weighted Regression: The Analysis of Spatially Varying Relationships. *Geographical Analysis*. West Sussex, England: John Wiley & Sons Ltd; 2002.
25. Brunson C, Fotheringham AS, Charlton ME. Geographically weighted regression: a method for exploring spatial nonstationarity. *Geogr Anal*. 1996; 28: 281–298. <https://doi.org/10.1111/j.1538-4632.1996.tb00936.x>
26. Concepción-Zavaleta MJ, Coronado-Arroyo JC, Zavaleta-Gutiérrez FE, Concepción-Urteaga LA. Does level of education influence mortality of SARS-CoV-2 in a developing country? *Int J Epidemiol*. 2020; 49: 2091–2093. <https://doi.org/10.1093/IJE/DYAA193> PMID: 33221908

27. Niedzwiedz CL O'Donnell CA, Jani BD, Demou E, Ho FK, Celis-Morales C, et al. Ethnic and socioeconomic differences in SARS-CoV-2 infection: Prospective cohort study using UK Biobank. *BMC Med.* 2020; 18: 1–14. <https://doi.org/10.1186/S12916-020-01640-8/FIGURES/4>
28. Rozenfeld Y, Beam J, Maier H, Haggerson W, Boudreau K, Carlson J, et al. A model of disparities: risk factors associated with COVID-19 infection. *Int J Equity Heal* 2020 191. 2020; 19: 1–10. <https://doi.org/10.1186/S12939-020-01242-Z> PMID: 32727486
29. Gao Y, Ding M, Dong X, Zhang J, Azkur AK, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: A review. *Allergy.* 2021; 76: 428–455. <https://doi.org/10.1111/all.14657> PMID: 33185910
30. de Lusignan S, Dorward J, Correa A, Jones N, Akinyemi O, Amirthalingam G, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *Lancet Infect Dis.* 2020; 20: 1034–1042. [https://doi.org/10.1016/S1473-3099\(20\)30371-6](https://doi.org/10.1016/S1473-3099(20)30371-6) PMID: 32422204
31. Hernández-Garduño E. Obesity is the comorbidity more strongly associated for Covid-19 in Mexico. A case-control study. *Obes Res Clin Pract.* 2020; 14: 375–379. <https://doi.org/10.1016/j.orcp.2020.06.001> PMID: 32536475
32. Sattar N, McInnes IB, McMurray JJV. Obesity Is a Risk Factor for Severe COVID-19 Infection: Multiple Potential Mechanisms. *Circulation.* 2020; 4–6. <https://doi.org/10.1161/CIRCULATIONAHA.120.047659> PMID: 32320270
33. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ.* 2020;369. <https://doi.org/10.1136/bmj.m1966> PMID: 32444366
34. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A, et al. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation. *Obesity (Silver Spring).* 2020; 28: 1195–1199. <https://doi.org/10.1002/oby.22831> PMID: 32271993
35. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F, et al. Obesity in Patients Younger Than 60 Years Is a Risk Factor for COVID-19 Hospital Admission. *Clin Infect Dis.* 2020; 71: 896–897. <https://doi.org/10.1093/cid/ciaa415> PMID: 32271368
36. Kompaniyets L, Goodman AB, Belay B, Freedman DS, Sucosky MS, Lange SJ, et al. Body Mass Index and Risk for COVID-19–Related Hospitalization, Intensive Care Unit Admission, Invasive Mechanical Ventilation, and Death—United States, March–December 2020. *MMWR Morb Mortal Wkly Rep.* 2021; 70: 355–361. <https://doi.org/10.15585/mmwr.mm7010e4> PMID: 33705371
37. Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, et al. Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obes Rev.* 2020; 21. <https://doi.org/10.1111/obr.13128> PMID: 32845580
38. Ho FK, Celis-Morales CA, Gray SR, Katikireddi SV, Niedzwiedz CL, Hastie C, et al. Modifiable and non-modifiable risk factors for COVID-19, and comparison to risk factors for influenza and pneumonia: results from a UK Biobank prospective cohort study. *BMJ Open.* 2020; 10: e040402. <https://doi.org/10.1136/bmjopen-2020-040402> PMID: 33444201
39. Sheridan PA, Paich HA, Handy J, Karlsson EA, Hudgens MG, Sammon AB, et al. Obesity is associated with impaired immune response to influenza vaccination in humans. *Int J Obes (Lond).* 2012; 36: 1072–1077. <https://doi.org/10.1038/ijo.2011.208> PMID: 22024641
40. Gong MN, Bajwa EK, Thompson BT, Christiani DC. Body mass index is associated with the development of acute respiratory distress syndrome. *Thorax.* 2010; 65: 44–50. <https://doi.org/10.1136/thx.2009.117572> PMID: 19770169
41. Louie JK, Acosta M, Samuel MC, Schechter R, Vugia DJ, Harriman K, et al. A novel risk factor for a novel virus: obesity and 2009 pandemic influenza A (H1N1). *Clin Infect Dis.* 2011; 52: 301–312. <https://doi.org/10.1093/cid/ciq152> PMID: 21208911
42. Karlsson EA, Milner JJ, Green WD, Rebeles J, Schultz-Cherry S BM. Chapter 10—Influence of obesity on the response to influenza infection and vaccination. In: Johnston RA SB, editor. *Mechanisms and Manifestations of Obesity in Lung Disease.* Cambridge, Massachusetts: Academic Press; 2019. pp. 227–259.
43. Bixby H, Bentham J, Zhou B, Di Cesare M, Paciorek CJ, Bennett JE, et al. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature.* 2019; 569: 260–264. <https://doi.org/10.1038/s41586-019-1171-x> PMID: 31068725
44. Di Cesare M, Bentham J, Stevens GA, Zhou B, Danaei G, Lu Y, et al. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet (London, England).* 2016; 387: 1377–1396. [https://doi.org/10.1016/S0140-6736\(16\)30054-X](https://doi.org/10.1016/S0140-6736(16)30054-X)

45. Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the Double Burden of Malnutrition and the Changing Nutrition Reality. *Lancet* (London, England). 2020; 395: 65. [https://doi.org/10.1016/S0140-6736\(19\)32497-3](https://doi.org/10.1016/S0140-6736(19)32497-3) PMID: 31852602
46. Samuel LJ, Gaskin DJ, Trujillo AJ, Szanton SL, Samuel A, Slade E. Race, ethnicity, poverty and the social determinants of the coronavirus divide: U.S. county-level disparities and risk factors. *BMC Public Heal* 2021 211. 2021; 21: 1–11. <https://doi.org/10.1186/S12889-021-11205-W> PMID: 34187414