Objective: Both COVID-19 deaths and opioid overdose deaths continue to increase in the United States. Little is known about the characteristics of counties with high rates of mortality for both. Methods: We analyzed county-level data on COVID-19 mortality from January 1 to May 31, 2020, and on opioid overdose mortality during 2014-2018. The outcome variable, “high-risk county” was a binary indicator of high mortality rates (above 75% quartile) for both COVID-19 and opioid overdose. We conducted geospatial logistic regression models separately for urban and rural counties to identify social determinants of health associated with being a high-risk county.

Results: After adjusting for other covariates, the overall mortality rate of COVID-19 is higher in counties with larger population size and a higher proportion of racial/ethnic minorities, although counties with high rates of opioid overdose mortality have lower proportions of racial/ethnic minorities, a higher proportion of females, and are more economically disadvantaged. Significant predictors of rural counties with high mortality rates for both COVID-19 and opioid overdose include higher proportions of Blacks (Adjusted odds ratio [aOR], 1.04; 95%CI, 1.01–1.07), American Indians and Alaska Natives (aOR, 1.07; 95%CI, 1.02–1.13), and two or more races (aOR, 1.34; 95%CI, 1.13–1.60). Additional predictors for high-risk urban counties include population density (aOR, 1.12; 95%CI, 1.04–1.22) and higher unemployment rates during the COVID-19 pandemic (aOR, 1.23; 95%CI, 1.07–1.41).

Conclusions: Rural counties with high proportions of racial/ethnic minorities and urban counties with high unemployment rates are at high mortality risk for COVID-19 and opioid overdose.

Key Words: COVID-19, rural, opioid overdose, social determinants of health

Although the United States is still in the midst of the COVID-19 pandemic, the nation’s opioid crisis is on the rise again. After preliminary success to bring down opioid overdose deaths from 47,885 in 2017 to 47,096 in 2018, there were 50,312 in 2019, and actual numbers could be worse in 2020. More than 40 states have reported increases in opioid-related deaths during the COVID-19 pandemic. Both COVID-19 and opioid overdose are deadly. By the end of May 2020, more than 100,000 individuals in the U.S. died from COVID-19. Approximately 450,000 people died from an overdose involving any opioid between 1999 and 2018.

Thus far, there is no effective medication to treat COVID-19. Although there are approved medications for the treatment of opioid use disorder (MOUD), the availability of MOUD has been limited in many U.S. counties, particularly in rural areas. COVID-19 could worsen the opioid crisis as COVID-19 shelter-in-place orders have pushed individuals battling recovery into isolation and have reduced access to treatment. Although federal and state policies have made quick adjustments to allow easier access to MOUD during this public health emergency, socio-economic conditions and healthcare infrastructure within counties are slow to change. Social determinants of health (SDOH), which are conditions in the environments that affect people’s health risks and outcomes, provide a useful context to help characterize the factors that contribute to health disparities in communities.

Hence, the present study aims to identify SDOH for rural and urban U.S. counties with high mortality rates for COVID-19 and opioid overdose during the initial phase of the COVID-19 pandemic.

METHODS

Study Population

We analyzed characteristics associated with U.S. rural (n = 1,976) and urban (n = 1,166) counties with high mortality rates of COVID-19 and opioid overdose using geospatial cross-sectional analysis in 2020. We obtained county-level data including COVID-19 mortality from January 1 to May 31, 2020, and opioid overdose mortality during 2014–2018.
from the Center for Disease Control and Prevention (Appendix definitions of primary outcomes, available online, http://links.lww.com/JAM/A271). Other county-level data were from several sources (Appendix Table 1, available online, http://links.lww.com/JAM/A271). Institutional review board approval was not required for this study, which used only publicly available data.

Measures
Separately examining rural and urban counties, we defined counties with rates of both COVID-19 and opioid overdose mortality in the above 75% quartile as “high risk” counties, and counties with rates of both below 75% quartile are “low risk” counties. The county-level SDOH includes demographics, education, income, unemployment rate, population size, population density, urban-rural location, and availability and access to healthcare professionals (Appendix Table 2, available online, http://links.lww.com/JAM/A271).

Statistical Analysis
First, we fit 4 generalized additive models with a thin-plate spline term of spatial coordinates to identify county-level factors associated with COVID-19 and opioid overdose mortality rates of rural and urban U.S. counties. Adding county latitude and longitude into the model was to account for the spatial trend. Second, we modeled the probability of being a high-risk county as a function of all county-level covariates using generalized additive models with a logit link function and spatial coordinates among rural and urban counties, respectively. Significance was defined as $P < 0.05$. We carried out all analyses in R and SAS software.

RESULTS
Table 1 shows the results of four separate regression models investigating characteristics associated with mortality rates of COVID-19 and opioid overdose. Rural and urban counties with higher rates of COVID-19 mortality had larger population size, higher proportions of racial/ethnic minorities, and higher median household income. Rural and urban counties with higher rates of opioid overdose mortality had lower proportions of Blacks, lower proportions of males, and lower median household income.

In Table 2, factors associated with being at greater risk for both high mortality rates of COVID-19 and opioid among rural counties were: a larger population (Adjusted odds ratio [aOR], 1.17; 95% CI, 1.03–1.33 per 10,000 increment); higher proportions of Blacks (aOR, 1.04; 95%CI, 1.01–1.07), American Indians and Alaska Natives (aOR, 1.07; 95%CI, 1.02–1.13), or two or more races (aOR, 1.34; 95%CI, 1.13–1.60); and a higher proportion of the population

![Table 1](http://links.lww.com/JAM/A271)
TABLE 2. County-level Factors Associated with County with High Mortality Rates of both COVID-19 and Opioid Overdose among U.S. Rural and Urban Counties

| Population characteristics | Rural (n = 1,182) | Urban (n = 789) |
|----------------------------|------------------|-----------------|
| Population (10,000)       | 1.17 (1.03, 1.33)* | 1.01 (1.00, 1.02) |
| Population density per square mile (100) | 1.06 (0.83, 1.36) | 1.12 (1.04, 1.22)** |
| Race/Ethnicity, %          |                  |                 |
| Hispanic or Latinx         | 1.02 (0.96, 1.09) | 0.98 (0.87, 1.10) |
| Black                      | 1.04 (1.01, 1.07)* | 1.03 (0.97, 1.09) |
| American Indian and Alaskan Native | 1.07 (1.02, 1.13)** | 0.86 (0.40, 1.88) |
| Asian                      | 0.54 (0.25, 1.14) | 0.95 (0.73, 1.24) |
| Native Hawaiian and Other Pacific islanders | 0.68 (0.07, 7.07) | 0.00 (0.00, 0.10)* |
| Other races                | 1.12 (0.36, 3.50) | 0.15 (0.03, 0.90)* |
| Two or more races          | 1.34 (1.13, 1.60)** | 1.23 (0.71, 2.13) |
| Male, %                    | 0.93 (0.81, 1.07) | 0.78 (0.52, 1.19) |
| Age, %                     |                 |                 |
| 25 to 64                   | 1.12 (0.98, 1.29) | 1.03 (0.84, 1.28) |
| ≥ 65                      | 1.12 (1.02, 1.23)* | 1.09 (0.93, 1.27) |
| Education, %               |                 |                 |
| High school                | 1.04 (0.94, 1.14) | 0.85 (0.67, 1.06) |
| Some college or higher     | 1.02 (0.94, 1.12) | 0.86 (0.74, 1.05) |
| Socioeconomic characteristics |                 |                 |
| Median household income ($1,000s) | 0.99 (0.94, 1.04) | 1.03 (0.98, 1.08) |
| Unemployed, %              | 0.95 (0.88, 1.02) | 1.23 (1.07, 1.41)** |
| Health care characteristics |                 |                 |
| Physicians per 10,000 population | 1.00 (0.97, 1.03) | 0.99 (0.97, 1.02) |
| Healthcare professional shortage area score | 1.03 (0.97, 1.10) | 0.99 (0.92, 1.06) |

CI = 95% confidence interval. Boldface indicates statistical significance.

High mortality of COVID-19 and opioid counties are defined as those with mortality rates of COVID-19 and opioid overdose both above 75% quartile (Rural = 97 vs Urban = 103).

The reference group of generalized additive models was counties with rates of COVID-19 and opioid overdose both below 75% quartile (Rural = 1,085 vs Urban = 958).

*P < 0.05.
**P < 0.01.
***P < 0.001.

≥ 65 years of age (aOR, 1.12; 95%CI, 1.02–1.12). Urban counties with higher population density were associated with greater odds of being high risk (aOR, 1.12; 95%CI, 1.04–1.22). Higher proportions of Native Hawaiians and Other Pacific islanders (aOR, 0.00; 95%CI, 0.00–0.10) or other races (aOR, 0.15; 95%CI, 0.03–0.90) were inversely associated with increased odds of being high-risk urban counties. A higher unemployment rate during the COVID-19 pandemic increased the odds of being a high-risk urban county (aOR, 1.23; 95%CI, 1.07–1.41).

DISCUSSION

Our study findings revealed distinctive community-level factors associated with COVID-19 and opioid overdose mortality rates for rural and urban U.S. counties. Higher proportions of racial/ethnic minorities increased the odds of being “high risk” rural counties, whereas higher unemployment rates during the COVID-19 pandemic increased odds of being “high risk” urban counties.

Our analyses indicate the existence of population-level disparities and confirmed that racial/ethnic minorities are more impacted by COVID-19. Furthermore, having higher proportions of racial/ethnic minorities was associated with being a “high risk” rural county. Future studies should investigate underlying factors and ecological influences that may contribute to this disparity (eg, lack of health care access, or other indirect health determinants). We observed a positive association between median household income and COVID-19 mortality rate. When we divided median household income into four groups, counties below 25% and above 75% of median household income had higher average rates of COVID-19 mortality compared with the remaining counties. The potential reason could be that those with low income are more affected by unprotected workplace and dense housing, whereas those with high income could be more affected by international and vacation travel in the early stage of the pandemic.

Previous studies have shown positive associations between unemployment and overdose. Unemployment causes adverse changes in health behaviors (eg, substance use), which in turn leads to deterioration of health. Alternatively, pre-existing health conditions may be a common cause of both unemployment and mortality, which could be even more devastating among the poor. During the COVID-19 pandemic, U.S. unemployment reached 13.3% of the workforce in May 2020 and is expected to remain elevated. Efforts to mitigate COVID-19 related socioeconomic consequences and to reduce mortality should involve welfare and healthcare systems (eg, expansion of Medicaid coverage) that helps prevent risk-taking behaviors, including substance use leading to overdose mortality.

Limitations

This study has several limitations. First, we used measures at the county level, which cannot identify within-county
differences. Ecological study potentially suffers from the ecological fallacy, which limits the extension of findings to individuals within counties. Second, the cross-sectional study design limited the ability to make causal inferences. Given the continuing pandemic, factors influencing subsequent trends may change. Finally, residual confounding bias may exist because of unmeasured confounders.

CONCLUSIONS
The present study identified racial/ethnic minority and unemployment as upstream factors of health in rural and urban counties, indicating that those vulnerable populations were more severely affected by the COVID-19 pandemic and the opioid overdose crisis. Society needs to consider that the unintended consequences of strategies to reduce COVID-19 impacts may further exacerbate the opioid overdose crisis through increased social and economic marginalization. The study findings could encourage policymakers and program leaders to take geographic needs into consideration when developing practical responses to combat these public health crises.

REFERENCES
1. Ahmad F, Rossen L, Sutton P. Provisional Drug Overdose Death Counts.; 2020. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.html#references. Accessed November 11, 2020.
2. Alter A, Yeager C, Analyst O. COVID-19 Impact on US National Overdose Crisis. http://odmap.org/Content/docs/news/2020/ODMAP-Report-May-2020.pdf. Accessed November 11, 2020.
3. American Medical Association. Issue Brief: Reports of Increases in Opioid-Related Overdose and Other Concerns during COVID Pandemic. https://www.ama-assn.org/system/files/2020-11/issue-brief-increases-in-opioid-related-overdose.pdf. Accessed November 10, 2020.
4. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19): cases in the US. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html. Accessed August 7, 2020.
5. Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics. https://wonder.cdc.gov/. Published 2020.
6. Silva MJ, Kelly Z. The escalation of the opioid epidemic due to COVID-19 and resulting lessons about treatment alternatives. Am J Manag Care. 2020;26(7):e202–e204.
7. Agency for Health Research and Quality. Social Determinants of Health (SDOH). https://www.ahrq.gov/sdoh/index.html. Accessed February 25, 2020.
8. Wood SN. Thin plate regression splines. J R Stat Soc Ser B Stat Methodol. 2003;65(1):95–114.
9. Wang QQ, Kaelber DC, Xu R, Volkow ND. COVID-19 risk and outcomes in patients with substance use disorders: analyses from electronic health records in the United States. Mol Psychiatry. 2020;26(1):30–39.
10. Hollingsworth A, Ruhm CJ, Simon K. Macroeconomic conditions and opioid abuse. J Health Econ. 2017;56:222–233.
11. Hammarström A. Health consequences of youth unemployment. Public Health. 1994;108(6):403–412.
12. Huber M, Lechner M, Wunsch C. Does leaving welfare improve health? Evidence for Germany. Health Econ. 2011;20(4):484–504.
13. Bureau of Labor Statistics. The Employment Situation—May 2020. www.bls.gov/cps. Accessed August 7, 2020.
14. Kravitz-Wirtz N, Davis CS, Ponicki WR, et al. Association of Medicaid expansion with opioid overdose mortality in the United States. JAMA Network Open. 2020;3(1):e1919066.
15. Melamed OC, Hauck TS, Buckley L, Selby P, Mulsant BH. COVID-19 and persons with substance use disorders: Inequities and mitigation strategies. Subst Abus. 2020;41(3):286–291.