

**Deaths of Despair from the Cities to the Hollers: Explaining Spatial Differences in U.S.
Drug, Alcohol, and Suicide Mortality Rates**

Shannon M. Monnat, PhD

Assistant Professor of Rural Sociology, Demography, and Sociology
Population Research Institute
Pennsylvania State University
110B Armsby Bldg
University Park, PA 16802
Email: smm67@psu.edu
Phone: 814-867-2871

Paper prepared for the 2017 Population Association of America Annual Meeting. Chicago, IL.

ACKNOWLEDGEMENTS: The author acknowledges funding from the United States Department of Agriculture (USDA) Economic Research Service, support from the Population Research Institute at The Pennsylvania State University, which receives core funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (R24-HD041025), and support from the USDA Agricultural Experiment Station Multistate Research Project: W3001.

ABSTRACT

IMPORTANCE: Differences in mortality rates from drugs, alcohol, and suicide between U.S. counties are large. It is unknown whether mortality rate differences reflect county population composition, economic composition, and/or contextual factors.

OBJECTIVE: To determine associations between county compositional and contextual characteristics and drug, alcohol, and suicide (DAS) mortality rates.

DATA, SETTING, AND PARTICIPANTS: Spatial analyses were conducted on county-level factors and pooled age-adjusted DAS mortality rates from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research data system, 2006-2015.

EXPOSURES: County-level population and socioeconomic composition, labor market change, income inequality, and health-promoting infrastructure.

MAIN OUTCOME AND MEASURES: Pooled age-adjusted drug-related, alcohol-related, and suicide deaths per 100,000 population in 3,083 U.S. counties. Regression models included state fixed effects and 16 county-level characteristics.

RESULTS: In 2006-2015, the average county-level age-adjusted DAS mortality rate was 43.4 (95% CI, 42.8 to 43.9). In adjusted models, compared to counties in the lowest quartiles of each predictor, average DAS mortality rates were higher among counties with the largest shares of socioeconomically disadvantaged residents (23.3%, 95% CI, 19.5% to 27.1%; $P<.001$), military veterans (12.4%, 95% CI, 9.5% to 15.2%; $P<.001$), and age 65+ (13.8%, 95% CI, 10.4% to 17.2%; $P<.001$). Average rates were lower among counties in the highest quartile of percent black (-10.0%, 95% CI, -13.8% to -6.2%; $P<.001$) and presence of social-capital promoting establishments (-3.7%, 95% CI, -6.9% to -0.4%; $P=.03$). Counties with declines in median income since 1980 had an average DAS mortality rate that was 7.2% higher than counties with the largest income gains (95% CI, 4.4% to 10.1%; $P<.001$). In the unadjusted model, average DAS mortality rates were higher in rural (12.2%, 95% CI, 9.1% to 15.3%; $P<.001$), micropolitan (8.3%, 95% CI, 4.9% to 11.7%; $P<.001$), and small urban (7.6%, 95% CI, 4.4% to 10.8%; $P<.001$) versus large urban counties, but this was due to differences in demographic and socioeconomic composition.

CONCLUSIONS AND RELEVANCE: High DAS mortality rates are not randomly distributed across the U.S. In addition to rapid-response interventions in economically disadvantaged areas, the public health community and policymakers should consider efforts to address underlying macro-economic drivers of DAS mortality.

Nationwide, mortality from drug and alcohol poisoning and suicide has increased by 63% since 1999.¹ Most of this increase was driven by a surge in opioid overdoses, but overdoses from other drugs, suicides by other means, and alcohol-induced deaths also increased over this period (see Figure 1)¹. Drug, alcohol, and suicide deaths are not a random collection; they often derive from depression, hopelessness, and chronic pain.² Especially striking is that drug, alcohol, and suicide (DAS) mortality has increased during a period of declining mortality for other major causes of death.³⁻⁸

County-level differences in DAS mortality rates are large,⁷⁻⁹ but empirical explanations for this spatial heterogeneity are limited. Population composition differences (demographic, socioeconomic) likely contribute to this spatial variation. DAS mortality rates are much higher among non-Hispanic whites and American Indians than among blacks and Hispanics.^{1,8} Therefore, unlike other major causes of death, DAS mortality rates may be higher in counties with larger shares of whites relative to blacks and Hispanics. DAS mortality rates may also be higher in places with larger shares of elderly residents and military veterans, as these groups often suffer from chronic pain for which opioids are prescribed and have high rates of depression and substance misuse.^{10,11} Socioeconomic disadvantage (e.g., unemployment, poverty, lack of health insurance), lower educational attainment, and disabilities limiting daily functioning also increase risk of substance misuse and suicide.¹²⁻¹⁵ Accordingly, counties with comparatively larger shares of socioeconomically disadvantaged residents should have higher DAS mortality rates. Chronic outmigration from distressed rural areas and small cities over the past four decades has led to larger concentrations of vulnerable residents in these places. Beyond these compositional factors, counties also differ in their contextual features. Research shows that structural economic factors (e.g., income inequality, labor markets) and health-promoting

institutions (e.g., social capital-promoting establishments, health care infrastructure) are associated with all-cause mortality rates.¹⁶⁻¹⁹ It is unknown whether these same factors contribute to spatial differences in mortality from drugs, alcohol, and suicide – deaths that may derive more directly from depression, hopelessness, and chronic pain than other major causes of death.^{20,21} Some have described DAS mortality as “deaths of despair” and suggested that they are linked to economic dislocation and place-level downward mobility.^{4,22-24} This contention, though yet to be empirically tested, is well justified: the past two-decade increase in DAS mortality has corresponded with significant economic stressors, including de-industrialization, wage stagnation, and growing income inequality.²⁵⁻²⁹ Therefore, high DAS mortality rates may reflect place-level economic precarity, downward mobility, and social isolation.^{23,30-33}

Distinguishing the contributions of county-level compositional and contextual features to DAS mortality rates is essential for identifying place-level strategies to reduce rates of deaths from these preventable causes. Therefore, I examined associations between several county-level factors and DAS mortality rates (2006-2015). Because many of these factors may also be related to other cause-specific mortality rates, I compared associations from DAS mortality models to models examining heart disease, cancer, and chronic lower respiratory disease mortality rates.

Methods

Mortality

I extracted pooled county-level mortality rates (2006-2015) from the U.S. Centers for Disease Control and Prevention’s Wide-Ranging Online Data for Epidemiologic Research (WONDER) multiple cause-of-death (MCD) files, which identify assigned causes of death from all death certificates filed in the 50 states and D.C.¹ Categorization of presumed causes of death used

International Statistical Classification of Diseases, 10th revision (ICD-10) codes: *drug related* (accidental poisoning; poisoning of undetermined intent by exposure to drugs [X40-X44, Y10-Y14]; drug-induced diseases [D52.1, D59.0, D59.2, D61.1, D64.2, E06.4, E16.0, E23.1, E24.2, E27.3, E66.1, G21.1, G24.0, G25.1, G25.4, G25.6, G44.4, G62.0, G72.0, I95.2, J70.2-J70.4, K85.3, L10.5, L27.0, L27.1, M10.2, M32.0, M80.4, M81.4, M83.5, M87.1, R50.2]; drugs in the blood [R78.1-R78.5]; mental/behavioral disorders due to drugs [F11.0-F11.5, F11.7-F11.9, F12.0-F12.5, F12.7-F12.9, F13.0-F13.5, F13.7-F13.9, F14.0-F14.5, F14.7-F14.9, F15.0-F15.5, F15.7-F15.9, F16.0-F16.5, F16.7-F16.9, F18.0-F18.5, F18.7-F18.9, F19.0-F19.5, F19.7-F19.9]); *alcohol-related* (alcohol-induced diseases [E24.4, G31.2, G62.1, G72.1, I42.6, K29.2, K70.0-K70.4, K70.9, K85.2, K86.0, R78.0]; mental/behavioral disorders due to alcohol [F10.0-F10.9]; accidental poisoning and poisoning of undetermined intent by alcohol [X45, Y15]); and *suicides* (all intentional self-poisoning and self-harm [X60-X84, X87.0]). Because I did not separately examine drug, alcohol, and suicide mortality rates, deaths are counted only once in county-level rates.

There are practical and conceptual reasons for using MCD versus underlying cause-of-death (UCD) files for these analyses. First, data suppression for counties with fewer than 10 deaths results in missing mortality rates for over one-third of counties in the UCD data. Excluding those counties introduces significant bias because they are more likely to be rural. More deaths are captured in the MCD files, resulting in fewer counties with suppressed mortality rates. Second, using MCD data reduces risk of undercounting due to misclassification, which has been especially pronounced for suicide.³⁴⁻³⁶ Third, identifying a single factor as the underlying cause of death is an oversimplification of clinical and pathological processes that lead to death³⁷

and does not account for the possibility that the death may not have occurred without the presence of drugs or alcohol.

County Factors

County-level predictors came from the U.S. Census Bureau,^{38,39} the USDA Economic Research Service,⁴⁰ the Northeast Regional Center for Rural Development,⁴¹ and the Health Resources and Services Administration Area Health Resource Files.⁴² I used measures that capture conditions before 2006-2015 to reduce reverse causality bias. Based on research discussed earlier,^{8-21,23-33} I examined several demographic and socioeconomic composition factors and structural economic and health-promoting institution factors. Variable sources and descriptive information are provided in Table 1. *Population composition* was measured with percent non-Hispanic black, American Indian, foreign born, ages 65+, and veterans. *Socioeconomic composition* was measured with a factor-weighted index for economic precarity/disadvantage and an index for working-class presence. *Structural economic characteristics* included change in median household income 1980-2000, industry transformation 1980-2000, and income inequality. *Health-promoting institutional factors* included presence of Putnam-style social capital-promoting establishments,⁴⁹ presence of “rent-seeking”/special interest organizations,¹⁶ and designations as primary and mental health professional shortage areas. I included persistent population loss and metropolitan status as proxies for resource supply and (dis)investment.¹⁶ I recoded all continuous variables into quartiles to allow for nonlinear relationships with mortality rates and to address multicollinearity problems that arose from leaving them in their continuous forms.

Statistical Analysis

Analyses included 3,083 of the 3,143 U.S. counties. All counties in Alaska (29) and Hawaii (5) were excluded due to unavailable data for several variables. I excluded four counties due to county boundary changes since 1980 (Broomfield County, CO; Bedford City, VA; La Paz County, AZ; Cibola County, NM). I excluded 22 counties with percent American Indian exceeding 40% because they are extreme outliers that dramatically skew the findings; the mean DAS mortality rate for these 22 counties was 153.8 compared to a mean rate of 43.4 for all other counties. CDC data suppression criteria resulted in suppression for 118 counties (3.8%). Because the majority of these counties are rural (82%), excluding them would bias results. Therefore, I conducted multiple imputation using the Markov Chain Monte Carlo method with several auxiliary variables either correlated with DAS mortality rates or likely to be associated with suppression.⁴³

Linear regression analysis proceeded in two stages. First, I separately regressed each county-level predictor on the logged DAS mortality rate, controlling for state fixed effects. State fixed effects account for the clustering of counties within states and unobserved state-level differences in policies and other factors. Second, I conducted multivariable regression with all county-level factors in the same model. To account for spatial autocorrelation (spillover effects), I calculated spatial weights for DAS mortality using first-order queen contiguity in GeoDa⁴⁴ and included those weights as a parameter in the regression model. For each county, the spatial weight represents the average DAS mortality rate among neighboring counties. To adjust for heteroscedasticity, I weighted by the log of county population, thereby giving less weight to counties with smaller populations whose mortality rates tend to vary more widely. Regression

analyses were conducted in Stata/MP 13.1 (StataCorp). Analysis of publicly available secondary data is exempt from Institutional Review Board review by Pennsylvania State University.

Sensitivity Tests

To determine whether the factors associated with DAS mortality rates are also associated with mortality rates for other major causes of death, I used seemingly unrelated regression (SUR) to run simultaneous regressions with the same predictors on DAS mortality, cancer mortality (ICD 10 codes: C00-C97), coronary heart disease mortality (I09, I11, I13, I20-I51), and chronic lower respiratory disease mortality (J40-J47). This procedure corrects for correlated errors across regression models. To enable comparisons of coefficients across models, I standardized the four mortality rates (mean=0, standard deviation=1). T-tests were used to compare differences in coefficient magnitudes for DAS mortality rates compared to the others ($P < .05$). To ensure that deaths were not included in more than one rate, I used the UCD files for coronary heart disease, cancer, and chronic lower respiratory disease.

I performed several additional sensitivity analyses. I substituted county-level factors measured in 2000 with those temporally proximate to or overlapping with the 2006-2015 mortality rates (See Table 1). I tested different thresholds for manufacturing and natural resource dependence and loss, ranging from 20% to 40%. I substituted various health care supply measures. Finally, I compared results to those from both weighted least squares and random-effects models. Findings were robust to these alternate specifications.

Results

The mean county-level age-adjusted DAS mortality rate was 43.4 (min=12.2; max=191.0). There was significant spatial clustering (Moran's $I=0.46$) with above average

mortality clusters in New England, central Appalachia, the Industrial Midwest, Oklahoma, northern California, the Pacific Northwest, and much of the Mountain West (Figure 2).

In unadjusted models (Table 2), percent American Indian, percent veterans, percent ages 65+, socioeconomic precarity, working-class presence, income inequality, manufacturing and natural resource job losses and declines in median household income since 1980, presence of social capital-promoting and rent-seeking establishments, health care shortage, persistent population loss, and higher mortality rates in neighboring counties (spatial spillover) were associated with higher DAS mortality rates. Small urban, micropolitan, and rural counties had significantly higher rates than large urban counties. Higher percent black and foreign-born were associated with lower DAS mortality rates.

In the adjusted model (Table 2), percent black remained associated with lower DAS mortality rates, whereas percent American Indian, percent veterans, percent ages 65+, and socioeconomic precarity remained associated with higher DAS mortality rates. Compared to counties with the smallest concentrations of socioeconomically disadvantaged residents, the average DAS mortality rate was 23.3% higher among counties with the largest concentrations (95% CI, 19.5% to 27.1%, $P < .001$). Industry transition lost significance in the adjusted model. This was explained by concomitant median income decline. Compared to counties with the largest increases in median household income, counties where income declined had an average DAS mortality rate that was 7.2% higher (95% CI, 4.4% to 10.1%, $P < .001$). High presence of social capital-promoting establishments was associated with lower DAS mortality rates, whereas high presence of rent-seeking establishments was associated with higher DAS mortality rates. Average DAS mortality rates were significantly *lower* in small urban, micropolitan, and rural counties compared to large urban counties. Additional analyses (not shown but available from

author upon request) demonstrated that both socioeconomic and demographic composition explained the nonmetropolitan and small urban disadvantage observed in the unadjusted models.

Comparison to other Mortality Rates

With few exceptions the spatial distribution of DAS mortality rates varies from heart disease, cancer, and lower respiratory disease mortality rates (eFigure 1). Standardized model comparisons (Table 3) show that some factors were associated with all four types of mortality, but there were also important differences. Unstandardized model comparisons are presented in eTable 1. In fully adjusted models, economic precarity and median income decline were positively associated with all four mortality rates, but the associations were strongest with DAS mortality. High presence of social capital-promoting establishments was inversely associated with only DAS mortality, whereas high presence of rent-seeking establishments was positively associated with only DAS mortality. Higher percent black was associated with higher heart disease and cancer mortality rates but lower DAS mortality rates. Percent ages 65+ was most strongly associated with drug, alcohol, and suicide mortality rates.

Discussion

This is the first national U.S. study to identify specific compositional and contextual factors contributing to county-level differences in drug, alcohol, and suicide (DAS) mortality rates – the so-called ‘deaths of despair’.²²⁻²⁴ Consistent with recent research on accidental overdose and suicide mortality rate trends,^{7,9,54} this study highlights significant spatial variation in DAS mortality rates and identifies the characteristics of counties that are bearing the heaviest DAS mortality burdens.

Compositionally, average DAS mortality rates were higher among counties with larger shares of socioeconomically disadvantaged residents, American Indians, military veterans, and elderly residents, and rates were lower among counties with larger shares of black residents. Contextually, job losses in manufacturing and natural resources in counties that were dependent on those industries and concomitant declines in median household income are associated with higher DAS mortality rates. Due to their comparative socioeconomic and demographic composition disadvantages, nonmetropolitan and small urban counties had higher average DAS mortality rates than large urban counties.

Although this study did not test specific mechanisms, findings suggest links between DAS mortality and both absolute economic distress and place-level downward mobility. These findings are consistent with research showing associations between county-level poverty and suicide rates,¹³ and sociological literature showing that socioeconomic status is a major social determinant of health and fundamental cause of preventable disease disparities.^{45,46} DAS mortality rates were higher in counties that experienced occupational losses in manufacturing and natural resource industries, explained by concurrent declines in median household income. Economic distress, out-migration, and community-level instability following major labor market shifts²⁶⁻²⁸ can manifest in collective psychosocial distress⁴⁷ and social disorders like substance misuse.²⁹⁻³³ Economic insecurity and instability also contribute to family and community breakdown,^{27,48} undermining important supports against depression and substance misuse.

Social capital may play a unique role in buffering against “deaths of despair”. Net of other county-level factors, average DAS mortality rates were lowest in counties with the largest presence of social capital promoting establishments. This association was not observed for heart, cancer, or respiratory mortality. Opportunities for civic engagement facilitate social interactions,

trust, goodwill, and social cohesion, and increase residents' sense of community belonging.⁴⁹ Average DAS mortality rates were higher in counties with high presence of rent-seeking establishments, like political and business associations. Rent-seeking organizations may undermine community well-being by diverting resources from education, health, and social services to corporate tax incentives and/or property development.¹⁶

Unlike other major causes of death, blacks have lower rates of DAS mortality than whites,⁵⁰ contributing to significantly lower DAS mortality rates in the highest percent black counties. This is a demographic and epidemiological conundrum, given that high percent black counties fare collectively worse on several key health measures and face considerable economic disadvantage. Lower drug-related mortality rates may be related to physicians being less likely to prescribe opioids to black patients,⁵¹ but blacks also have lower alcohol-related and suicide mortality rates⁵⁰ and lower rates of depression and anxiety than whites.⁵² Reference group theory may be at play⁵³; non-Hispanic whites, especially those without a college degree living in rural areas and small cities have experienced declining employment opportunities for several decades.²⁶⁻²⁹ This group may be comparing their conditions to prior generations of working-class whites that had better opportunities for upward mobility. Conversely, blacks and Hispanics may compare themselves to prior generations that had fewer opportunities.⁵³ Collectively, whites' reference group may leave them feeling worse off, whereas blacks' and Hispanics' reference groups may leave them feeling as though progress has been made. Future research should explore the potential roles of reference groups, collective mobility and resilience, and social support as buffers against DAS mortality in economically disadvantaged predominantly black and Hispanic communities.

Thus far, policy efforts have focused on opioid prescribing guidelines, expanding access to naloxone and treatment services, and reducing heroin supply entering at the U.S./Mexico border. But the problem is bigger than opiates. Although opiate overdoses increased the most over the past 15 years, deaths due to other drugs, alcohol, and suicides also increased.¹ Moreover, pooled mortality rates for alcohol-induced and suicide deaths exceed those for drug-induced deaths, and less than a quarter of recent DAS deaths involved opiates.⁵⁰ Most suicides are caused by guns, and most drug-induced suicides are caused by benzodiazepines,¹ for which opiate reversal agents have no effect. Focusing only on opiates, rather than considering the underlying connections between drugs, alcohol, and suicide, and failing to recognize the substantial spatial variation in DAS mortality rates may lead to costly and ineffective policy strategies. My findings suggest that, in addition to targeting treatment and prevention interventions toward communities with significant economic distress, places that have experienced major labor market shifts and income decline over the past four decades are important targets for intervention. Policymakers could consider spatially-targeted strategies to improve employment and training opportunities for those without a college degree, particularly in places most affected by blue-collar manufacturing and natural resource job losses.

Results should be considered in light of important limitations. First, analyses were ecologic and cannot account for characteristics of individuals who died within each county. Moreover, data suppression prevented disaggregating rates by race/ethnicity, sex, and age. There is significant demographic variation in DAS mortality.⁵⁰ Associations between county-level factors and mortality rates may vary across these demographic groups. Third, this study did not examine changes in mortality. The factors associated with increases in DAS mortality may differ from those associated with this pooled cross-section from 2006-2015. Fourth, death certificates

may misclassify causes of death. Pooling drug, alcohol, and suicide deaths and using MCD files somewhat reduces the likelihood of undercounting deaths due to misclassification.³⁵ Results may also be biased by unexamined heterogeneity in cause-of-death reporting, but state-level variation in reporting was controlled via state fixed effects. State fixed effects also accounted for unobserved heterogeneity in state programs and policies that may affect drug access, but national county-level data on such programs, narcotic supply, and other factors associated with mortality risk are unavailable.

Conclusions

Drug, alcohol, and suicide mortality rates are not randomly distributed across the U.S. Nonmetropolitan and small urban counties with comparatively larger concentrations of economically vulnerable residents, and counties that have experienced income declines due to manufacturing and natural resource job losses are shouldering a much heavier burden than others. The results of this study provide a comparative context for clinicians, public health professionals, and policymakers to give higher priority to the macro-economic drivers of DAS mortality. In concert with immediate and rapid-response treatment interventions, long-term economic policies that address the underlying causes of high rates of DAS mortality are likely to facilitate reducing these preventable deaths.

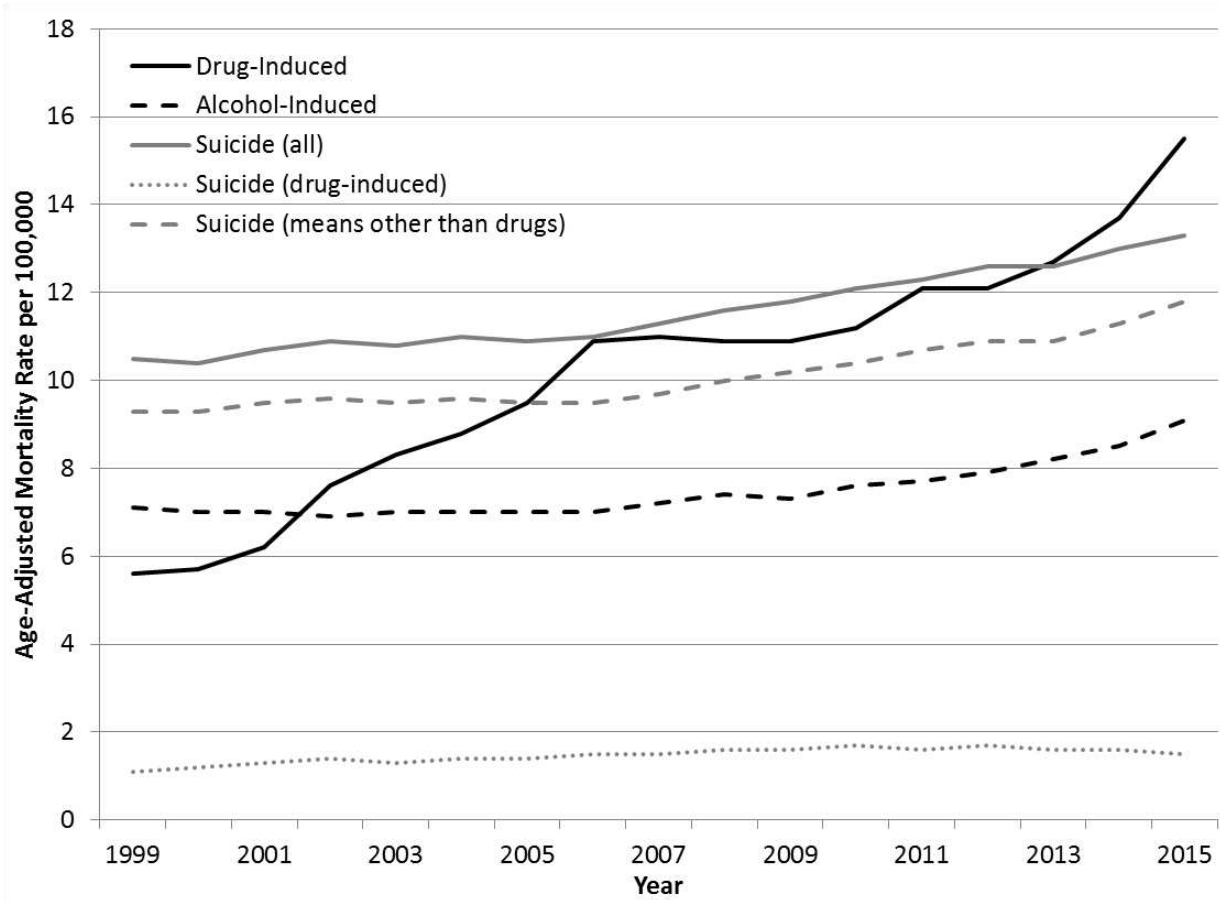
REFERENCES

1. U.S. Centers for Disease Control and Prevention. Wide-Ranging Online Data for Epidemiologic Research. <http://wonder.cdc.gov/>. Accessed January 25, 2016.
2. Zajacova A, Montez JK. Macro-level perspective to reverse recent mortality increases [published online January 25, 2017]. *The Lancet*. doi:10.1016/S0140-6736(17)30186-1.
3. Garcia MC, Faul M, Massetti G, et al. Reducing potentially excess deaths from the five leading causes of death in the rural United States. *MMWR*. 2017;66(2):1-7.
4. Case A, Deaton A. Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. *JAMA*. 2015;112(49):15078-15083.
5. Sidney S, Quesenberry CP, Jaffe MG, et al. Recent trends in cardiovascular mortality in the United States and public health goals. *JAMA Cardiol*. 2016;1(5):594-599.
6. Brandi P, Silver D, Mijanovich T, Macinko J. Temporal trends in motor vehicle fatalities in the United States, 1968 to 2010 - a jointpoint regression analysis. *Inj Epidemiol*. 2015;2(1):1-11.
7. Rossen LM, Bastian B, Warner M, Khan D, Chong Y. Drug Poisoning Mortality: United States, 1999–2014. National Center for Health Statistics. <https://blogs.cdc.gov/nchs-data-visualization/drug-poisoning-mortality/>. Accessed January 20, 2016.
8. Shiels MS, Chernyavskiy P, Anderson WF, et al. Trends in premature mortality in the USA by sex, race, and ethnicity from 1999 to 2014: an analysis of death certificate data [published online January 25, 2017]. *The Lancet*. doi: 10.1016/S0140-6736(17)30187-3.
9. Buchanich, JM, Balmert LC, Pringle JL, Williams KE, Burke DS, Marsh GM. Patterns and trends in accidental poisoning death rates in the US, 1979-2014. *Prev Med*. 2016;89:317-323.
10. West NA, Severtson SG, Green JL, Dart RC. Trends in abuse and misuse of prescription opioids among older adults. *Drug Alcohol Depend*. 2015;149:117-21.
11. Tanielian T, Jaycox LH, Schell T, et al. Invisible wounds: mental health and cognitive needs of America's returning veterans. RAND Corporation. http://www.rand.org/pubs/research_briefs/RB9336.html. Accessed February 8, 2017.
12. Frاسquilho D, Matos MG, Salonna F, et al. Mental health outcomes in times of economic recession: a systematic literature review. *BMC Public Health*. 2016;16:115.
13. Kerr WC, Kaplan MS, Huguette N, Caetana R, Giesbrecht N, McFarland BH. Economic recession, alcohol, and suicide rates: comparative effects of poverty, foreclosure, and job loss [published online November 14, 2016]. *Am J Prev Med*. doi:10.1016/j.amepre.2016.09.021.
14. Bush DM, Lipari RN. Substance use and substance use disorder by industry. The CBHSQ Report. 2015. https://www.samhsa.gov/data/sites/default/files/report_1959/ShortReport-1959.html. Accessed February 2, 2017.
15. McIntosh WL, Spies E, Stone D, Lokey C, Trudeau AT, Bartholow B. Suicide rates by occupational group – 17 states, 2012. *MMWR*. 2016;65(25):641-645.
16. McLaughlin DK, Stokes CS, Smith PJ, Nonoyama A. Differential mortality across the United States: the influence of place-based inequality. In: Lobao LM, Hooks G, Tickamyer A, eds. *The Sociology of Spatial Inequality*. Albany, NY: State University of New York Press. 2007.
17. Montez JK, Zajacova A, Hayward MD. Explaining inequalities in women's mortality between U.S. states. *SSM Popul Health*. 2016;2:561-571.

18. Yang TC, Jensen L. Exploring the inequality-mortality relationship in the US with Bayesian spatial modeling. *Popul Res Policy Rev.* 2015;34:437-460.
19. Pierce JR, Schott PK. Trade liberalization and mortality: evidence from U.S. counties. Finance and Economics Discussion Series 2016-094. Washington, DC: Board of Governors of the Federal Reserve System. <http://www.federalreserve.gov/econresdata/feds/2016/files/2016094pap.pdf>. Accessed February 2, 2017.
20. Cheatle MD. Depression, chronic pain, and suicide by overdose: on the edge. *Pain Med.* 2011;12:S43-S48.
21. Russ TC, Kivimaki Morling JR, Starr JM, Stamatakis E, Batty GD. Association between psychological distress and liver disease mortality: a meta-analysis of individual study participants. *Gastroenterol.* 2015;148:958-966.
22. Stobe M. 'Deaths of despair' drag life expectancy lower for whites. Associated Press. June 3, 2016. <http://bigstory.ap.org/article/08c85b511f0245e5ada2db8e3d7c33a5/deaths-despair-overdoses-drinking-suicides-hit-whites>. Accessed February 2, 2017.
23. Chen VT. *Cut Loose: Jobless and Hopeless in an Unfair Economy.* Oakland, CA: University of California Press; 2015.
24. Monnat SM. Deaths of despair and support for Trump in the 2016 election. University Park, PA: Pennsylvania State University. <http://aese.psu.edu/directory/smm67/Election16.pdf>. Accessed November 4, 2016.
25. Saez E, Zucman G. Wealth inequality in the United States since 1913: evidence from capitalized income tax data. *Q J Econ.* 2016;131(2):519-578.
26. Bailey C, Jensen L, Ransom E. *Rural America in a Globalizing World: Problems and Prospects for the 2010s.* Morgantown, WV: West Virginia University Press; 2014.
27. Smith KE, Tickamyer AR. *Economic Restructuring and Family Well-Being in Rural America.* University Park, PA: Pennsylvania State University Press; 2011.
28. Brown DL, Swanson LE. *Challenges for Rural America in the Twenty-First Century.* University Park, PA: Pennsylvania State University Press; 2003.
29. Sherman J. *Those Who Work, Those Who Don't: Poverty, Morality, and Family in Rural America.* Minneapolis, MN: University of Minnesota Press; 2009.
30. Kaplan MS, Huguet N, Caetano R, Giesbrecht N, Kerr WC, McFarland BH. Economic contraction, alcohol intoxication and suicide: analysis of the National Violent Death Reporting System. *Inj Prev.* 2015;21:35-41.
31. McLean K. "There's nothing here": deindustrialization as risk environment for overdose. *Int J Drug Policy.* 2016;29:19-26.
32. Alexander B. *Glass House: The 1% Economy and the Shattering of the All-American Town.* New York, NY: Macmillan St. Martin's Press; 2017.
33. Quinones S. *Dreamland: The True Tale of America's Opiate Epidemic.* New York, NY: Bloomsbury Press; 2015.
34. Kapusta ND, Tran US, Rockett IR, et al. Declining autopsy rates and suicide misclassification. *Arch Gen Psychiatry.* 2011;68(1):1050-1057.
35. Rockett IR, Kapusta ND, Coben JH. Beyond suicide: action needed to improve self-injury mortality accounting. *JAMA Psychiatry.* 2014;71:231-232.
36. Rockett IR, Lilly CL, Jia H, et al. Self-injury mortality in the United States in the early 21st century: a comparison with proximally ranked diseases. *JAMA Psychiatry.* 2016;73(10):1072-1081.

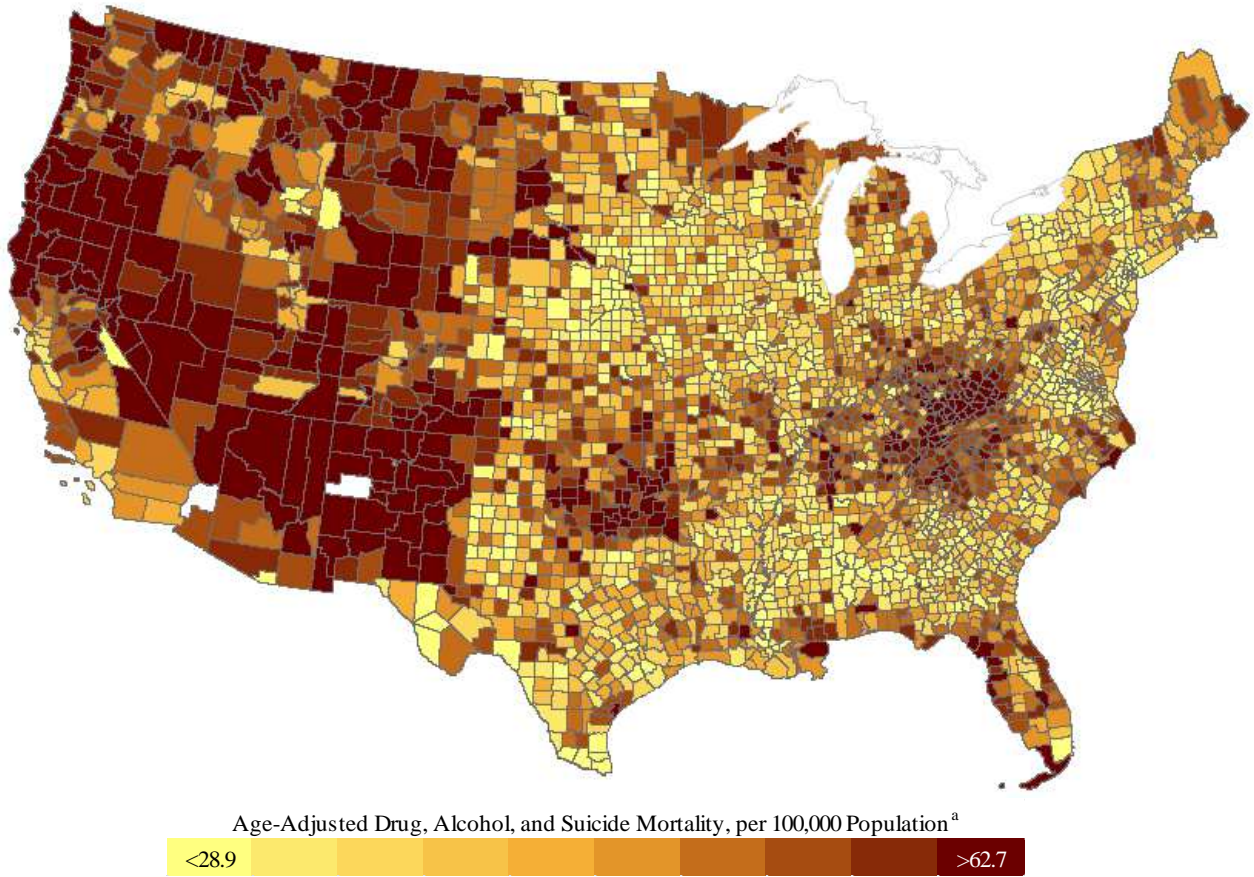
37. Fedeli U, Zoppini G, Goldoni CA, Avossa F, Mastrangelo G, Saugo M. Multiple cause of death analysis of chronic diseases: the example of diabetes. *Pop Health Met.* 2015;13:21.
38. U.S. Census Bureau. Decennial Censuses, 1980, 1990, 2000, 2010. <https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml>. Accessed January 15, 2016.
39. U.S. Census Bureau. American Community Survey, 2010-14. <https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml>. Accessed January 15, 2016.
40. U.S. Department of Agriculture, Economic Research Service. County Typology Codes, 2015 Edition. <https://www.ers.usda.gov/data-products/county-typology-codes/>. Accessed January 15, 2016.
41. Rupasingha A, Goetz SJ, Freshwater D. County-Level Measure of Social Capital. Northeast Regional Center for Rural Development. <http://aese.psu.edu/nercrd/community/social-capital-resources>. Accessed June 30, 2016.
42. U.S. Department of Health and Human Services, Health Resources and Services Administration. Area Health Resource Files Database. <http://ahrf.hrsa.gov/download.htm>. Accessed May 13, 2016.
43. Allison PD. *Missing Data*. Thousand Oaks, CA: Sage University Press; 2002.
44. Anselin L. *Exploring Spatial Data with GeoDa: A Workbook*. Santa Barbara, CA: Center for Spatially Integrated Social Science; 2005.
45. Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff.* 2002;21(2):60-76.
46. Link BG, Phelan JC. Social conditions as fundamental causes of disease. *J Health Soc Behav.* 1995;35:80-94.
47. Catalano R, Dooley D. Health effects of economic instability: a test of economic stress hypothesis. *J Health Soc Behav.* 1983;24(1):46-60.
48. Burgess EW. Economic, cultural, and social factors in family breakdown. *Am J Orthopsychiatry.* 1954;24(3):462-470.
49. Putnam RD. *Bowling Alone: The Collapse and Revival of American Community*. New York, NY: Touchstone Books; 2001.
50. Monnat SM. Drugs, alcohol, and suicide represent growing share of U.S. mortality. Carsey School of Public Policy. <https://carsey.unh.edu/publication/drugs-alcohol-suicide>. Accessed February 8, 2017.
51. Singhal A, Tien YY, Hsia RY. Racial-ethnic disparities in opioid prescriptions at emergency department visits for conditions commonly associated with prescription drug abuse. *PLoS One.* 2006;11(8).
52. Breslau J, Aguilar-Gaxiola S, Kendler KS, Su M, Williams D, Kessler RC. Specifying race-ethnic differences in risk for psychiatric disorder in a USA national sample. *Psychol Med.* 2006; 36(1):57-68.
53. Cherlin A. 2016. "Why are white deaths rising?" *The New York Times*. Feb. 22, 2016. https://www.nytimes.com/2016/02/22/opinion/why-are-white-death-rates-rising.html?_r=0. Accessed March 16, 2017.
54. Kegler SR, Stone DM, Holland KM. Trends in suicide by level of urbanization – United States, 1999-2015. *MMWR*;66(10):270-273.

Figure 1. Age-Adjusted Mortality Rates for Drug-Induced, Alcohol-Induced, and Suicide Deaths from 1999 to 2015



Note: Drug- and alcohol-induced rates exclude intentional self-poisonings which are captured in the suicide category.

Figure 2. County-Level Drug, Alcohol, and Suicide Mortality Rates, 2006-2015



^a Legend categories represent mortality rate deciles.

Table 1. Variable Information and Data Sources^a

Variable	County-Level Mean (SD) or %	Source/Years for Main Analysis	Source/Years for Sensitivity Analysis
POPULATION COMPOSITION			
percent non-Hispanic black	8.8 (14.5)	U.S. Decennial Census, 2000	American Community Survey 5-year estimates, 2010-14
percent American Indian	1.1 (3.0)		
percent foreign born	3.5 (4.8)		
percentage age 65 and older	14.8 (4.1)		
percentage of the population age 18-64 who are veterans	10.7 (2.7)		
SOCIOECONOMIC COMPOSITION			
<u>Economic Precarity Index</u> (standardized $\alpha=0.77$)	46.8 (12.1)	U.S. Decennial Census, 2000	American Community Survey 5-year estimates, 2010-14
poverty rate for ages 18-64	12.6 (5.7)		
percentage of adults age 16+ in labor market who are unemployed	3.4 (1.3)	Small Area Health Insurance Estimates (SAHIE), 2005 ^b	
percentage of adults age 16+ with a work disability	19.7 (5.1)		
percentage of families with children that are headed by a single-parent	26.0 (7.2)		
percentage of households receiving public assistance	3.3 (1.7)		
percentage ages 18-64 without health insurance	18.0 (6.1)		
<u>Working-Class Index</u> (standardized $\alpha=0.89$)	127.4 (14.6)	U.S. Decennial Census, 2000	
percentage of residents age 25 and older without a 4-year college degree	83.5 (7.8)		
percentage of employed residents in food/personal service and manual labor occupations (food service, serving, personal care and service, farming, forestry, fishing, construction, extraction, maintenance, production, transportation, and material moving)	44.0 (7.5)		
STRUCTURAL ECONOMIC CHARACTERISTICS			
<u>Industry Transformation</u> - Counties grouped into four categories: 1. not dependent on manufacturing or natural resource employment (counties where less than 25% of all employed workers were in manufacturing or natural resource [extraction, forestry/fishing, farming] occupations in 1980)	47.5%	U.S. Decennial Censuses, 1980 & 2000	Change between 1980 (U.S. Decennial Census) and 2010-14 (American Community Survey 5-year estimates)

2. manufacturing job loss (counties where at least 25% of employed workers were in manufacturing occupations in 1980, but the number of workers employed in manufacturing occupations declined by at least 20% 1980-2000)	13.4%		
3. natural resource job loss counties where at least 25% of employed workers were in extraction, forestry/fishing, or farming occupations in 1980, but the number of workers employed in those occupations declined by at least 20% 1980-2000)	12.5%		
4. manufacturing or natural resource industry stability or growth (counties where at least 25% of employed workers were in manufacturing or natural resource occupations in 1980 and either gained jobs in those industries or lost fewer than 20% of the jobs in those industries 1980-2000)	26.7%		
Percent change in median household income, 1980-2000 (constant \$)	16.5 (14.7)	U.S. Decennial Censuses, 1980 and 2000	Change between 1980 (U.S. Decennial Census) and 2010-14 (American Community Survey 5-year estimates)
Income inequality (gini coefficient)	0.43 (0.04)	U.S. Decennial Census, 2000	American Community Survey 5-year estimates, 2010-14
HEALTH-PROMOTING ORGANIZATIONAL/INSTITUTIONAL FACTORS			
<u>Social capital-promoting establishments</u> : number of religious, civic, bowling, fitness, golf, sports organizations and associations per 10,000 population	12.9 (6.5)	Rupasingha et al. - County Level Measures of Social Capital, 2005	Rupasingha et al. - County Level Measures of Social Capital, 2009
<u>Rent-seeking special interest establishments</u> : number of labor, professional, and political organizations and business associations per 10,000 population	1.7 (1.6)		
<u>Health care infrastructure</u> : Designation as primary care health professional shortage area (0=no; 1=yes) Designation as mental health care professional shortage area (0=no; 1=yes)	63.1% 54.8%	Area Health Resource Files	NA

Persistent population loss (number of residents declined between 1980 and 1990 censuses and between 1990 and 2000 censuses)	19.4%	U.S. Decennial Censuses, 1980, 1990, 2000	U.S. Decennial Censuses, 1990, 2000, and 2010
<u>metropolitan status:</u>			
<i>large urban</i> (county in a metro area with ≥ 1 million residents)	14.0%	USDA, Economic Research Service Urban Influence Codes, 2013	NA
<i>small urban</i> (county in a metro area with < 1 million residents)	23.6%		
<i>micropolitan</i> (nonmetropolitan county in labor market area centered on an urban cluster with population $>10,000$ and $< 50,000$)	20.5%		
<i>rural</i> (counties located outside of metro/micropolitan areas)	41.9%		

SD = standard deviation

a Final variable selection came after assessing multiple measures and testing for multicollinearity. Other health care measures tested in preliminary models included: Medicare Part D opioid claims per enrollee; presence of at least one community mental health center, psychiatric hospital, hospital with alcohol/drug inpatient or outpatient care, and hospital with pain management services; per capita supply of active MDs, psychiatrists, psychologists, social workers, occupational, physical, and recreational therapists, occupational medicine MDs, and physical rehabilitation MDs; and the ratio of population to mental health providers and primary care providers. Multicollinearity prevented the inclusion of median household income (correlated with economic precarity) and percent Hispanic (correlated with percent foreign-born).

b Although percent non-Hispanic white would arguably be a better racial/ethnic composition variable for a study on drug, alcohol, and suicide mortality, it was too strongly correlated with many of the economic indicators (even when using quartiles) to include it in regression models.

c County-level health insurance rates are not available in the Decennial Census. 2005 is the first year for which SAHIE estimates are available

Table 2. Associations Between County-Level Factors and Drug, Alcohol, and Suicide Mortality Rates in the United States, 2006-2015

Independent Variables	Unadjusted Percentage Difference in AAMR ^a		Adjusted Percentage Difference in AAMR ^{ab}	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
<u>Population Composition</u>				
<i>Percent non-Hispanic black</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	-1.7 (-4.6 to 1.2)	.259	0.5 (-2.0 to 3.0)	.668
Quartile 3	-2.8 (-6.1 to 0.4)	.090	-0.1 (-3.0 to 2.8)	.952
Quartile 4	-14.5 (-18.5 to -10.6)	<.001	-10.0 (-13.8 to -6.2)	<.001
<i>Percent American Indian</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	1.3 (-1.5 to 4.2)	.361	1.4 (-1.0 to 3.8)	.238
Quartile 3	2.9 (-0.2 to 6.0)	.069	2.1 (-0.6 to 4.8)	.125
Quartile 4	14.5 (10.9 to 18.1)	<.001	3.3 (0.2 to 6.5)	.039
<i>Percent foreign born</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	0.5 (-2.3 to 3.4)	.710	1.0 (-1.5 to 3.4)	.442
Quartile 3	-0.8 (-3.8 to 2.3)	.614	3.0 (0.2 to 5.8)	.035
Quartile 4	-13.3 (-16.7 to -9.9)	<.001	-1.0 (-4.3 to 2.3)	.547
<i>Percentage aged 18-64 who are veterans</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	7.5 (4.7 to 10.3)	<.001	5.9 (3.4 to 8.3)	<.001
Quartile 3	12.4 (9.6 to 15.2)	<.001	8.4 (5.9 to 11.0)	<.001
Quartile 4	18.5 (15.6 to 21.5)	<.001	12.4 (9.5 to 15.2)	<.001
<i>Percent aged 65+</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	11.1 (8.5 to 13.8)	<.001	6.7 (4.3 to 9.1)	<.001
Quartile 3	14.1 (11.3 to 16.9)	<.001	7.3 (4.5 to 10.2)	<.001
Quartile 4	21.9 (19.0 to 24.8)	<.001	13.8 (10.4 to 17.2)	<.001
<u>Socioeconomic Composition</u>				

<i>Economic precarity</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	18.9 (16.2 to 21.7)	<.001	12.4 (9.8 to 15.0)	<.001
Quartile 3	28.2 (25.2 to 31.3)	<.001	19.9 (16.7 to 23.1)	<.001
Quartile 4	27.1 (23.9 to 30.4)	<.001	23.3 (19.5 to 27.1)	<.001
<i>Working class presence</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	9.0 (6.2 to 11.8)	<.001	1.2 (-1.4 to 3.8)	.349
Quartile 3	10.6 (7.8 to 13.5)	<.001	2.6 (-0.2 to 5.5)	.072
Quartile 4	10.9 (7.8 to 13.9)	<.001	1.7 (-0.5 to 6.2)	.096
<u>Structural Economic Characteristics</u>				
<i>Employment industry transition, 1980 to 2000</i>				
Not manufacturing or natural resource dependent in 1980				
(REF)	0.0		0.0	
Manufacturing loss	5.0 (1.7 to 8.2)	.003	-0.4 (-3.3 to 2.4)	.759
Natural resource loss	4.5 (0.9 to 8.1)	.014	1.7 (-0.8 to 5.9)	.132
Manufacturing or natural resource stability or growth	-1.2 (-3.9 to 1.5)	.395	1.0 (-1.4 to 3.4)	.404
<i>Change in median household income, 1980 to 2000 (constant \$)</i>				
Quartile 1 (decline/stagnation)	15.7 (12.6 to 18.8)	<.001	7.2 (4.4 to 10.1)	<.001
Quartile 2	7.5 (4.6 to 10.4)	<.001	4.2 (1.7 to 6.6)	.001
Quartile 3	5.1 (2.3 to 7.9)	<.001	2.2 (-0.2 to 4.5)	.070
Quartile 4 (largest increase) (REF)	0.0		0.0	
<i>Income inequality</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	9.7 (6.9 to 12.5)	<.001	2.1 (-2.9 to 4.6)	.084
Quartile 3	12.1 (9.2 to 15.0)	<.001	1.8 (-0.9 to 4.6)	.186
Quartile 4	7.9 (4.8 to 11.1)	<.001	-0.3 (-3.5 to 2.9)	.852
<u>Health-Promoting Organizational/Institutional Characteristics</u>				
<i>Putnam-type social capital-promoting establishments</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	6.5 (3.6 to 9.3)	<.001	2.5 (0.03 to 5.0)	.047

Quartile 3	8.1 (5.1 to 11.1)	<.001	-0.04 (-2.8 to 2.7)	.975
Quartile 4	4.4 (1.1 to 7.7)	.009	-3.7 (-6.9 to -0.4)	.027
<i>Rent-seeking establishments</i>				
Quartile 1 (REF)	0.0		0.0	
Quartile 2	0.8 (-2.0 to 3.6)	.569	1.3 (-1.0 to 3.6)	.262
Quartile 3	2.8 (0.01 to 5.6)	.049	1.5 (-0.8 to 4.0)	.204
Quartile 4	6.5 (3.6 to 9.5)	<.001	5.2 (2.6 to 7.7)	<.001
<i>Primary health care professional shortage area</i>				
No (REF)	0.0		0.0	
Yes	3.1 (1.0 to 5.3)	.005	-0.7 (-2.5 to 1.1)	.467
<i>Mental health care professional shortage area</i>				
No (REF)	0.0		0.0	
Yes	5.9 (3.6 to 8.3)	<.001	0.8 (-1.3 to 2.8)	.464
<i>Persistent population loss, 1980-2000</i>				
No (REF)	0.0		0.0	
Yes	6.8 (3.9 to 9.6)	<.001	1.0 (-1.7 to 3.6)	.478
<i>Metropolitan Status</i>				
Large urban (REF)	0.0		0.0	
Small urban	7.6 (4.4 to 10.8)	<.001	-5.9 (-8.7 to -3.1)	<.001
Micropolitan	8.3 (4.9 to 11.7)	<.001	-8.0 (-11.3 to -4.7)	<.001
Rural	12.2 (9.1 to 15.3)	<.001	-9.2 (-12.6 to -5.8)	<.001
Spatial Weight – Rho ^d	18.4 (17.1 to 19.7)	<.001	13.8 (12.5 to 15.0)	<.001

N=3,083 counties

^aAAMR = age-adjusted mortality rate; all models include state fixed effects

^bAdjusted R-square=.574

^cQuartiles are ordered so that Quartile 1 represents the lowest 25th percentile and Quartile 4 represents the highest 25th percentile.

^dMoran's I=.460; the spatial weight is standardized to have a mean of 0 and standard deviation of 1

Table 3. Comparison of Associations between County-Level Factors and Standardized Cause-Specific Mortality Rates in the United States, 2006-2015

	Model-Adjusted Standardized Percentage Difference in AAMR ^a							
	<u>Drugs, Alcohol, Suicide</u>		<u>Heart Disease</u>		<u>Cancer</u>		<u>Respiratory Disease</u>	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
<u>Population Composition</u>								
<i>Percent non-Hispanic black</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.009 (-.064 to .082)	.801	.086 (.022 to .150)	.009	.088 (.013 to .163)	.021	.090 (.013 to .167)	.022
Quartile 3	-.023 (-.109 to .064)	.607	.154 (.078 to .230)	<.001 *	.117 (.028 to .205)	.010 *	.150 (.059 to .240)	.001 *
Quartile 4	-.334 (-.447 to -.222)	<.001	.242 (.145 to .339)	<.001 *	.246 (.133 to .359)	<.001 *	.001 (-.115 to .117)	.985 *
<i>Percent American Indian</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.043 (-.028 to .114)	.238	-.022 (-.085 to .041)	.493	-.012 (-.085 to .061)	.749	-.018 (-.093 to .057)	.631
Quartile 3	.063 (-.016 to .141)	.118	.007 (-.063 to .076)	.853	.047 (-.033 to .127)	.252	.057 (-.026 to .139)	.180
Quartile 4	.086 (-.006 to .179)	.068	.017 (-.065 to .098)	.685	.135 (.040 to .230)	.005	.076 (-.022 to .173)	.128
<i>Percent foreign born</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.028 (-.044 to .100)	.446	-.021 (-.085 to .043)	.521	-.031 (-.105 to .043)	.406	-.024 (-.100 to .052)	.528
Quartile 3	.086 (.004 to .167)	.040	-.051 (-.123 to .022)	.171 *	-.016 (-.100 to .068)	.712 *	.063 (-.023 to .149)	.153
Quartile 4	-.043 (-.140 to .054)	.381	-.134 (-.221 to -.048)	.002	-.146 (-.246 to -.045)	.004	-.065 (-.167 to .038)	.216
<i>Percentage aged 18-64 who are veterans</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.163 (.091 to .235)	<.001	.052 (-.012 to .115)	.111 *	.151 (.077 to .224)	<.001	.263 (.187 to .339)	<.001 *
Quartile 3	.236 (.160 to .313)	<.001	.040 (-.028 to .107)	.247 *	.149 (.071 to .228)	<.001	.271 (.191 to .352)	<.001
Quartile 4	.360 (.276 to .444)	<.001	.073 (-.001 to .147)	.054 *	.244 (.158 to .330)	<.001 *	.346 (.257 to .434)	<.001
<i>Percent aged 65+</i>								

Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.197 (.122 to .271)	<.001	.031 (-.034 to .097)	.345 *	.120 (.044 to .196)	.002	.003 (-.075 to .081)	.934 *
Quartile 3	.215 (.130 to .300)	<.001	.085 (.010 to .160)	.026 *	.111 (.024 to .198)	.013 *	.017 (-.073 to .107)	.708 *
Quartile 4	.397 (.296 to .498)	<.001	.082 (-.007 to .171)	.071 *	.135 (.032 to .238)	.010 *	-.005 (-.112 to .101)	.923 *
Socioeconomic Composition								
<i>Economic precarity</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.361 (.284 to .437)	<.001	.207 (.139 to .274)	<.001 *	.222 (.144 to .301)	<.001 *	.262 (.182 to .343)	<.001 *
Quartile 3	.585 (.490 to .679)	<.001	.356 (.273 to .438)	<.001 *	.434 (.338 to .530)	<.001 *	.386 (.287 to .484)	<.001 *
Quartile 4	.689 (.577 to .801)	<.001	.586 (.487 to .684)	<.001	.598 (.483 to .712)	<.001	.421 (.303 to .538)	<.001 *
<i>Working class presence</i>								
Quartile 1 (REF)	0.0		0.0		0.0		0.0	
Quartile 2	.050 (-.027 to .128)	.202	.322 (.254 to .390)	<.001 *	.290 (.211 to .369)	<.001 *	.275 (.194 to .357)	<.001 *
Quartile 3	.086 (.001 to .171)	.048	.506 (.431 to .581)	<.001 *	.414 (.327 to .501)	<.001 *	.322 (.233 to .412)	<.001 *
Quartile 4	.085 (-.015 to .185)	.094	.591 (.503 to .679)	<.001 *	.481 (.379 to .583)	<.001 *	.416 (.311 to .521)	<.001 *
Structural Economic Characteristics								
<i>Employment industry transition, 1980 to 2000</i>								
Not manufacturing or natural resources dependent in 1980 (REF)	0.0		0.0		0.0		0.0	
Manufacturing loss	-.016 (-.101 to .069)	.713	.029 (-.047 to .104)	.455	-.015 (-.102 to .073)	.745	.077 (-.013 to .167)	.095
Natural resource loss	.070 (-.023 to .163)	.142	.023 (-.059 to .105)	.584	-.018 (-.113 to .077)	.713	.217 (.119 to .316)	<.001 *
Manufacturing or natural resource stability or growth since 1980	.029 (-.043 to .100)	.430	.021 (-.042 to .083)	.521	.001 (-.072 to .074)	.979	.112 (.037 to .187)	.004
<i>Change in Median Household Income, 1980 to 2000 (constant \$)</i>								
Quartile 1	.218 (.135 to .301)	<.001	.109 (.036 to .182)	.004 *	.183 (.098 to .268)	<.001	.157 (.069 to .245)	<.001
Quartile 2	.127 (.053 to .200)	.001	.154 (.089 to .219)	<.001	.133 (.058 to .209)	.001	.170 (.092 to .248)	<.001
Quartile 3	.068	.057	.089	.005	.088	.016	.061	.105

			(-.002 to .138)					(.027 to .151)						(.016 to .160)				(-.013 to .135)	
Quartile 4 (REF)			0.0					0.0						0.0				0.0	
<i>Income inequality</i>																			
Quartile 1 (REF)			0.0					0.0						0.0				0.0	
Quartile 2			.064	.083				.018	.580					-.031	.421 *			.042	.281
			(-.008 to .137)					(-.046 to .082)						(-.105 to .044)				(-.035 to .119)	
Quartile 3			.054	.197				-.014	.697					-.102	.016 *			.001	.976
			(-.028 to .135)					(-.086 to .058)						(-.185 to -.019)				(-.085 to .087)	
Quartile 4			-.017	.736				-.105	.015					-.135	.007 *			-.113	.028
			(-.113 to .079)					(-.190 to -.020)						(-.233 to -.036)				(-.214 to -.012)	
Health-Promoting Organizational/Institutional Characteristics																			
<i>Social capital-promoting establishments (Putnam type)</i>																			
Quartile 1 (REF)			0.0					0.0						0.0				0.0	
Quartile 2			.070	.065				.032	.343					.027	.479			.036	.371
			(-.004 to .144)					(-.034 to .097)						(-.048 to .103)				(-.042 to .114)	
Quartile 3			-.004	.926				.014	.708					-.008	.849			.029	.504
			(-.086 to .078)					(-.058 to .086)						(-.092 to .076)				(-.057 to .116)	
Quartile 4			-.117	.016				.017	.686 *					-.049	.323			-.003	.960 *
			(-.212 to -.022)					(-.066 to .101)						(-.146 to .048)				(-.102 to .097)	
<i>Rent-seeking establishments (Olson type)</i>																			
Quartile 1 (REF)			0.0					0.0						0.0				0.0	
Quartile 2			.035	.318				-.002	.945					.012	.735			-.114	.002 *
			(-.033 to .103)					(-.062 to .058)						(-.058 to .082)				(-.186 to -.043)	
Quartile 3			.043	.235				-.011	.720					.026	.478			-.154	<.001 *
			(-.028 to .113)					(-.074 to .051)						(-.046 to .098)				(-.228 to -.080)	
Quartile 4			.151	<.001				-.076	.024 *					.027	.490 *			-.159	<.001 *
			(.076 to .226)					(-.142 to -.010)						(-.050 to .104)				(-.238 to -.080)	
<i>Primary health care professional shortage area, 2000</i>																			
No (REF)			0.0					0.0						0.0				0.0	
Yes			-.020	.480				-.022	.358					-.023	.413			-.019	.509
			(-.074 to .035)					(-.070 to .025)						(-.079 to .032)				(-.077 to .038)	
<i>Mental health care professional shortage area, 2000</i>																			
No (REF)			0.0					0.0						0.0				0.0	
Yes			.018	.567				.032	.240					-.046	.150			.046	.159
			(-.043 to .079)					(-.022 to .086)						(-.108 to .017)				(-.018 to .111)	
<i>Persistent population loss, 1980-2000</i>																			
No (REF)			0.0					0.0						0.0				0.0	
Yes			.031	.430				.171	<.001 *					.098	.015			.067	.104
			(-.046 to .108)					(.103 to .239)						(.019 to .176)				(-.014 to .148)	

<i>Metropolitan Status</i>								
Large urban (REF)	0.0		0.0		0.0		0.0	
Small urban	-.181 (-.268 to -.093)	<.001	-.115 (-.193 to -.038)	.004	-.202 (-.291 to -.112)	<.001	-.079 (-.171 to .014)	.096
Metropolitan	-.241 (-.341 to -.142)	<.001	-.112 (-.200 to -.024)	.013 *	-.189 (-.291 to -.087)	<.001	-.055 (-.161 to .050)	.302 *
Rural	-.270 (-.372 to -.167)	<.001	-.111 (-.201 to -.020)	.017 *	-.245 (-.350 to -.141)	<.001	-.098 (-.206 to .010)	.074 *
<i>Spatial Weight - Rho</i>	.396 (.360 to .432)	<.001	.379 (.339 to .419)	<.001	.358 (.320 to .396)	<.001	.484 (.452 to .517)	<.001 *
R-Square	.581		.674		.560		.534	
Moran's I	.460		.593		.490		.481	

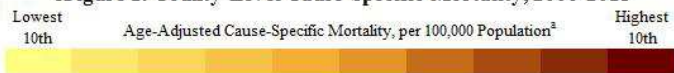
N=3,083 counties

^aAAMR = age-adjusted mortality rate (per 100,000 persons); logged mortality rates were standardized to have a mean of 0 and standard deviation of 1 to enable comparisons of coefficient magnitude across models; all models include state fixed effects

^bThe spatial weight is standardized to have a mean of 0 and standard deviation of 1

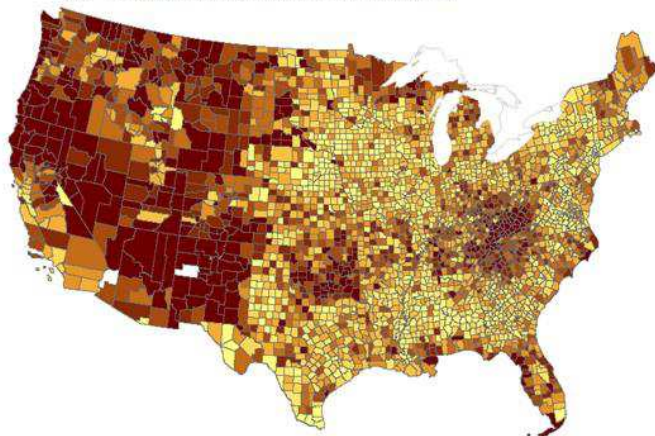
*Indicates that the coefficient is significantly different (P<.05) from the coefficient in the drug, alcohol, and suicide mortality model

eFigure 1. County-Level Cause-Specific Mortality, 2006-2015

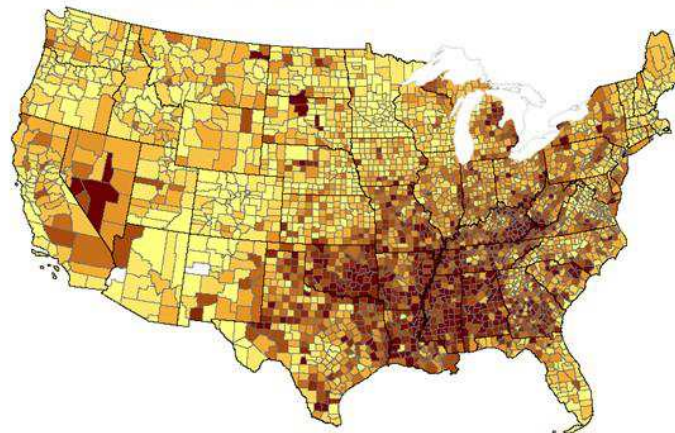


^aLegend categories represent cause-specific mortality rate deciles.

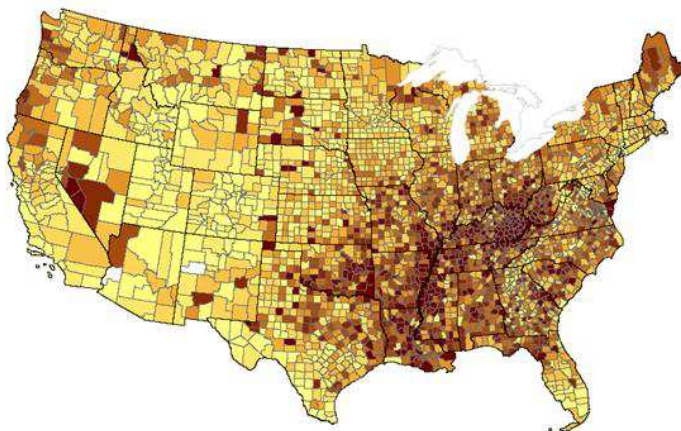
A. Drug, Alcohol, and Suicide Mortality



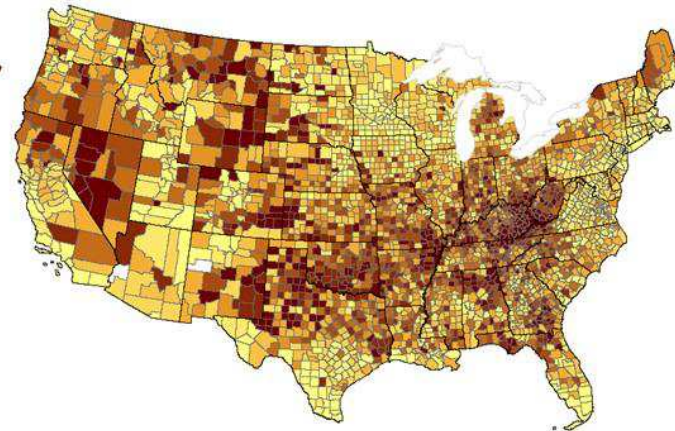
B. Coronary Heart Disease Mortality



C. Cancer Mortality



D. Chronic Lower Respiratory Disease Mortality



eTable 1. Associations between County-Level Factors and Heart Disease, Cancer, and Chronic Lower Respiratory Disease Mortality Rates in the United States, 2006-2015

	Model-Adjusted Percentage Difference in AAMR ^a					
	<u>Heart Disease</u>		<u>Cancer</u>		<u>Chronic Lower Respiratory Disease</u>	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
<u>Population Composition</u>						
<i>Percent non-Hispanic black</i>						
Quartile 1 (REF)	0.0		0.0		0.0	
Quartile 2	2.2 (0.6 to 3.7)	0.007	1.3 (0.2 to 2.4)	0.019	3.0 (0.6 to 5.4)	0.013
Quartile 3	3.7 (1.8 to 5.5)	<.001	1.8 (0.5 to 3.1)	0.006	4.9 (2.2 to 7.7)	0.001
Quartile 4	5.8 (3.5 to 8.1)	<.001	3.7 (2.0 to 5.3)	<.001	0.7 (-2.9 to 4.2)	0.715
<i>Percent American Indian</i>						
Quartile 1 (REF)	0.0		0.0		0.0	
Quartile 2	-0.5 (-2.0 to 1.0)	0.495	-0.1 (-1.1 to 1.0)	0.917	-0.5 (-2.7 to 1.8)	0.689
Quartile 3	-0.1 (-1.8 to 1.5)	0.868	0.6 (-0.6 to 1.7)	0.358	1.7 (-0.8 to 4.2)	0.188
Quartile 4 (high percent American Indian)	0.5 (-1.4 to 2.5)	0.598	2.0 (0.6 to 3.4)	0.006	2.7 (-0.3 to 5.7)	0.075
<i>Percent foreign born</i>						
Quartile 1 (REF)	0.0		0.0		0.0	
Quartile 2	-0.4 (-1.9 to 1.1)	0.619	-0.4 (-1.5 to 0.7)	0.504	-0.6 (-3.0 to 1.7)	0.589
Quartile 3	-1.0 (-2.8 to 0.7)	0.245	-0.2 (-1.4 to 1.0)	0.748	2.0 (-0.6 to 4.7)	0.128
Quartile 4	-3.0 (-5.1 to -0.9)	0.004	-2.0 (-3.5 to -0.6)	0.007	-2.0 (-5.1 to 1.1)	0.215
<i>Percentage aged 18-64 who are veterans</i>						
Quartile 1 (REF)	0.0		0.0		0.0	
Quartile 2	1.5 (0.0 to 3.0)	0.047	2.4 (1.3 to 3.5)	<.001	8.5 (6.2 to 10.8)	<.001
Quartile 3	1.2 (-0.4 to 2.7)	0.155	2.5 (1.3 to 3.6)	<.001	9.0 (6.6 to 11.4)	<.001
Quartile 4	2.0 (0.3 to 3.8)	0.024	3.9 (2.6 to 5.1)	<.001	11.3 (8.7 to 14.0)	<.001
<i>Percent aged 65+</i>						
Quartile 1 (REF)	0.0		0.0		0.0	
Quartile 2	0.7 (-0.8 to 2.2)	0.359	1.7 (0.7 to 2.8)	0.002	0.1 (-2.2 to 2.4)	0.927
Quartile 3	1.8 (0.1 to 3.6)	0.042	1.4 (0.2 to 2.7)	0.026	0.3 (-2.4 to 3.0)	0.843
Quartile 4	1.6 (-0.5 to 3.7)	0.132	1.8 (0.3 to 3.3)	0.019	-0.6 (-3.8 to 2.6)	0.708
<i>Persistent population loss, 1980-2000</i>						
No (REF)	0.0		0.0		0.0	

Yes	4.3 (2.7 to 6.0)	<.001	1.6 (0.4 to 2.7)	0.008	1.7 (-0.8 to 4.2)	0.178
<i>Metropolitan Status</i>						
Large urban (REF)	0.0		0.0		0.0	
Small urban	-2.8 (-4.6 to -1.1)	0.002	-3.0 (-4.3 to -1.8)	<.001	-2.5 (-5.2 to 0.1)	0.064
Micropolitan	-2.7 (-4.7 to -0.6)	0.010	-2.8 (-4.2 to -1.3)	<.001	-1.8 (-4.9 to 1.4)	0.270
Rural	-2.7 (-4.8 to -0.6)	0.013	-3.7 (-5.2 to -2.2)	<.001	-3.2 (-6.4 to 0.0)	0.051
<u>Socioeconomic Composition</u>						
<i>Economic precarity</i>						
Quartile 1 (low precarity) (REF)	0.0		0.0		0.0	
Quartile 2	5.1 (3.6 to 6.7)	<.001	3.6 (2.5 to 4.7)	<.001	8.1 (5.7 to 10.5)	<.001
Quartile 3	8.9 (6.9 to 10.8)	<.001	6.8 (5.4 to 8.2)	<.001	11.9 (8.9 to 14.8)	<.001
Quartile 4 (high precarity)	14.5 (12.2 to 16.9)	<.001	9.3 (7.6 to 11.0)	<.001	13.2 (9.7 to 16.8)	<.001
<i>Working class presence</i>						
Quartile 1 (small working class) (REF)	0.0		0.0		0.0	
Quartile 2	7.7 (6.1 to 9.3)	<.001	4.2 (3.0 to 5.3)	<.001	8.2 (5.8 to 10.7)	<.001
Quartile 3	12.1 (10.3 to 13.8)	<.001	6.1 (4.8 to 7.3)	<.001	10.0 (7.3 to 12.7)	<.001
Quartile 4 (high working class)	14.2 (12.1 to 16.3)	<.001	7.1 (5.6 to 8.6)	<.001	13.0 (9.9 to 16.2)	<.001
<u>Structural Economic Characteristics</u>						
<i>Employment industry transition, 1980 to 2000</i>						
Not manufacturing or natural resources dependent in 1980 (REF)	0.0		0.0		0.0	
Manufacturing loss	0.7 (-1.1 to 2.4)	0.465	-0.1 (-1.4 to 1.1)	0.840	2.2 (-0.4 to 4.9)	0.103
Natural resource loss	0.6 (-1.5 to 2.6)	0.587	-0.4 (-1.8 to 1.1)	0.595	6.2 (3.1 to 9.3)	<.001
Manufacturing or natural resource stability or growth since 1980	0.6 (-0.9 to 2.1)	0.443	0.2 (-0.8 to 1.3)	0.698	3.0 (0.8 to 5.3)	0.009
<i>Change in Median Household Income, 1980 to 2000 (constant \$)</i>						
Quartile 1 (decline or stagnation)	2.7 (0.9 to 4.4)	0.003	2.5 (1.3 to 3.8)	<.001	4.7 (2.0 to 7.3)	0.001
Quartile 2	3.5 (2.0 to 5.1)	<.001	1.8 (0.7 to 2.9)	0.001	5.0 (2.6 to 7.3)	<.001
Quartile 3	2.0 (0.6 to 3.5)	0.007	1.2 (0.2 to 2.2)	0.024	1.8 (-0.4 to 4.1)	0.107
Quartile 4 (large increase) (REF)	0.0		0.0		0.0	
<i>Income inequality</i>						
Quartile 1 (low inequality) (REF)	0.0		0.0		0.0	
Quartile 2	0.5 (-1.1 to 2.0)	0.548	-0.4 (-1.5 to 0.7)	0.476	1.0 (-1.3 to 3.4)	0.374
Quartile 3	-0.4 (-2.1 to 1.3)	0.622	-1.5 (-2.7 to -0.2)	0.018	-0.3 (-2.9 to 2.3)	0.805
Quartile 4 (high inequality)	-2.5 (-4.5 to -0.5)	0.014	-2.0 (-3.4 to -0.5)	0.007	-4.2 (-7.3 to -1.2)	0.007
<u>Organizational/Institutional Characteristics</u>						
<i>Social capital-promoting establishments (Putnam type)</i>						

Quartile 1 (low social capital) (REF)	0.0		0.0		0.0	
Quartile 2	0.8 (-0.7 to 2.3)	0.309	0.5 (-0.6 to 1.6)	0.379	1.2 (-1.1 to 3.6)	0.293
Quartile 3	0.4 (-1.3 to 2.1)	0.668	-0.1 (-1.3 to 1.2)	0.920	0.9 (-1.7 to 3.5)	0.481
Quartile 4 (high social capital)	0.7 (-1.3 to 2.7)	0.485	-0.5 (-1.9 to 0.9)	0.490	0.2 (-2.8 to 3.3)	0.883
<i>Rent-seeking establishments (Olson type)</i>						
Quartile 1 (low rent-seeking) (REF)	0.0		0.0		0.0	
Quartile 2	0.0 (-1.4 to 1.4)	0.979	0.2 (-0.8 to 1.3)	0.629	-2.8 (-4.9 to -0.6)	0.011
Quartile 3	-0.3 (-1.8 to 1.2)	0.695	0.4 (-0.6 to 1.5)	0.406	-4.1 (-6.3 to -1.8)	0.000
Quartile 4 (high rent-seeking)	-1.8 (-3.4 to -0.2)	0.030	0.5 (-0.7 to 1.6)	0.425	-4.1 (-6.5 to -1.6)	0.001
<i>Primary health care professional shortage area</i>						
No (REF)	0.0		0.0		0.0	
Yes	-0.4 (-1.6 to 0.7)	0.452	-0.3 (-1.1 to 0.5)	0.484	-0.9 (-2.6 to 0.8)	0.319
<i>Mental health care professional shortage area</i>						
No (REF)	0.0		0.0		0.0	
Yes	0.8 (-0.5 to 2.1)	0.209	-0.6 (-1.5 to 0.3)	0.186	1.4 (-0.5 to 3.3)	0.159
Spatial Weight – Rho ^b	9.2 (8.2 to 10.2)	<.001	5.6 (5.0 to 6.2)	<.001	15.9 (14.8 to 16.9)	<.001
R-Square	.684		.560		.534	
Moran's I	.592		.490		.481	

N=3,083 counties

^aAAMR = age-adjusted mortality rate (per 100,000 persons); all models include state fixed effects

^bThe spatial weight is standardized to have a mean of 0 and standard deviation of 1