Deaths of Despair or Drug Problems?

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Abstract

The United States is in the midst of a fatal drug epidemic. This study uses data from the *Multiple Cause of Death Files* to examine the extent to which increases in county-level drug mortality rates from 1999-2015 are due to "deaths of despair", measured here by deterioration in medium-run economic conditions. Multiple proxy methods are used to address the issue that no single variable adequately captures all aspects of the economy. Robustness tests are included, as well as examination of the sensitivity of the main results to controlling for selection on unobservables. The primary finding is that counties experiencing relative economic decline did experience higher growth in drug mortality than those with more robust growth, but the relationship is weak and mostly explained by confounding factors. In the preferred estimates, changes in economic conditions account for just one-ninth of the variation in growth of drug mortality rates, with a slightly greater portion of heroin-involved overdose death rates explained but virtually none of the increase opioid analgesic mortality. The contribution of economic factors is even less when accounting for selection on unobservables. These results suggest that the "deaths of despair" framing, while provocative, fails to explain the main sources of the fatal drug epidemic and that efforts to improve economic conditions in distressed locations, while desirable for other reasons, are not likely to yield significant reductions in drug mortality.

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1. Introduction

The United States is in the midst of a fatal drug epidemic. The number of Americans dying from drugs rose from 16,849 to 52,404 between 1999 and 2015 (Hedegaard et al. 2017), with provisional (and incomplete) data indicating a further increase to at least 64,070 for the 12-month period ending in January of 2017 (National Center for Health Statistics 2017). Drug overdoses are the leading cause of injury deaths in the United States, exceeding the number of motor vehicle fatalities since 2009 (Paulozzi 2012). The rapid growth in drug mortality originally involved prescription opioids like OxyContin, often in combination with other drugs (Jones, Mack, and Paulozzi 2013; Paulozzi, Mack, and Hockenberry 2014). However, the 20,145 and 15,446 fatalities during the latest 12-month period with available data reported to involve involving synthetic opioids (mostly fentanyl) and heroin substantially exceeded the 14,427 fatalities involving opioid analgesics (National Center for Health Statistics 2017).

Poisonings, over 90 percent of which are now due to drugs, are by far the most important factor explaining the declines in life expectancy observed since 1999 initially among 45-54 year old non-Hispanic whites by Anne Case and Angus Deaton (2015) and subsequently among a broader age range of mid-life whites (Kochanek, Arias, and Bastian 2016; Kolata and Cohen 2016; Squires and Blumenthal 2016). Case and Deaton attribute this rising mortality to "deaths of despair" (Case and Deaton 2017; Deaton 2017) which they view as a form of suicide that "respond(s) more to prolonged economic conditions than to short-term fluctuations, and especially social dysfunctions … that come with prolonged economic distress" (Deaton 2017, p.

3).[1] In their view, it is the social and economic environment rather than opioids (and presumably drugs more generally) that are the fundamental cause of the increased death rates.

At first glance, the particularly large increase in drug deaths in Appalachia and the rust-belt seems consistent with the deaths of despair hypothesis. However, other areas not associated with declining economies also have experienced high overdose fatality rates[2] and potential confounding factors in hard-hit area, such as race/ethnicity or education characteristics, might actually be the source of the geographic differences. Moreover, it is difficult to reconcile this mechanism with a number of important patterns of life expectancy and mortality. For instance, why has the increase in drug mortality been dramatically larger for whites than non-whites, even though the latter group has faced greater economic insecurity and worse economic conditions? And why aren't similar increases being observed among midlife adults in other developed countries that have also faced difficult economic times?[3]

These questions raise the possibility that changing economic conditions are *not* the primary mechanism for the rapid rise in overdose mortality. One alternative is that it is changes in the availability and use of risky drugs that are of particular importance – in short that the drug environment rather than economy – is the key driver in rising drug fatalities. Under such an explanation, whites might have been more affected than nonwhites because they have more widely been prescribed opioids (K. O. Anderson, Green, and Payne 2009; Burgess et al. 2014;

[1] Others have asserted potential roles for rising income inequality, international trade, stagnant wages, increased unemployment or general social and economic decline (Stiglitz 2015; Meara and Skinner 2015; Pierce and Schott 2016).
[2] For instance, New Hamphire had the highest state opioid fatality rate in 2014 s and Massachusetts had the fourth highest rate (Ruhm 2017b).
[3] For example, Case and Deaton (2017) present evidence showing that there has been little change in drug, alcohol and suicide mortality since the turn of the century for 50-54 year olds in France, Germany, Sweden, the United Kingdom, Canada and Australia.

Singhal, Tien, and Hsia 2016) and deaths in the United States might have increased more than in other countries because the large majority of opioid consumption has occurred in the U.S.[4]

This study examines the extent to which deteriorating economic conditions can explain the rapid rise in fatal overdoses. Although drug death rates have increased far more over time than other sources of mortality, Case and Deaton (2015) also emphasize the importance of deaths due to suicide and alcoholic liver disease (hereafter referred to as "alcohol"). Dowell et al. (2017) confirm that mortality rates from these sources have also risen over time, albiet by fairly small amounts. With this in mind, while focusing on drug-related mortality, I also analyze deaths from drugs, suicides and alcohol (DSA) as a group and, separately, those from nondrug suicides and alcohol (nondrug DSA).

To operationalize the examination of "deaths from despair", I focus on relatively long-run changes in a variety of economic factors including dimensions related to labor market outcomes, household wealth and international trade shocks. This is distinguished from prior literature that has examined how *transitory* economic fluctuations have affected various types of drug use or abuse (Arkes 2007; Ruhm 2015; Carpenter, McClellan, and Rees 2017; Martin Bassols and Vall Castelló 2016; Hollingsworth, Ruhm, and Simon 2018). The working assumption is that economic conditions *cause* changes in drug use and problems. However, there is some evidence of reverse causation – whereby rising opioid use has had negative effects on labor markets (Krueger 2017). To the extent this occurs, the analysis below may *overstate* the role of economic conditions as a contributor to the fatal drug epidemic.

Economists and other social scientists have previously examined how specific factors or policies are related to opioid use or drug fatalities including the roles of: medical marijuana

[4] In 2007 the United States contained 4.6 percent of the world's population but constituted 80 percent of global opioid and 99 percent of global hydrocodone consumption (Manchikanti et al. 2010).

(Powell, Pacula, and Jacobson 2015; Chu 2015; Bradford and Bradford 2016), abuse-deterrent drug formulations (Alpert, Powell, and Pacula 2017; Evans, Lieber, and Power 2017), Naloxone availability (Rees et al. 2017; Doleac and Mukherjee 2017), Medicare Part D (Powell, Pacula, and Taylor 2015), and state policies influencing the availability of prescription opoioids (Dowell et al. 2016; Meinhofer 2016; Buchmueller and Carey 2018). However, any observed effects would, explain, at most, only a small portion of the overall change in overdose deaths.[5] This study is attempting to examine the broader question of the sources of overall rise in drug deaths. The analysis implements methods of measuring the combined effects of multiple proxies for economic conditions, accounting for the incomplete reporting of drug involvement on death certificates, and testing the sensitivity of the findings to the presence of uncontrolled for confonding factors.

The analysis conducted to this point reveals three main findings. First, counties that suffered relative or absolute decline did also have larger increases in drug and total DSA mortality rates than counties with better economic performance. This pattern shows up using most or all of the economic proxies examined below, in part because they are generally reasonably highly correlated with each other. Second, the estimated impact of the economy dramatically attenuated – by more than half for drug fatalities, two-thirds for all DSA deaths, and by over three-quarters for those involving opioid analgesics – when adding controls for county-level characteristics, implying that the observed correlations are likely to be largely spurious. Third, changes in economic conditions are estimated to explain less than one-sixth of the observed increase in drug deaths occurring between 1999 and 2015. The portion of the rise in opioid analgesic deaths accounted for is an even smaller 3 to 6 percent (and virtually none of that

[5] For example, Dowell et al. (2016) find that implementing a combination of two state policies designed to reduce access to prescription opioids (pain clinic laws and mandated provider review of information in prescription drug monitoring programs) would reduce drug overdose deaths by around 12 percent.

for nondrug DSA mortality rates), whereas 8 to 14 percent of the rise in illicit opioid fatality rates may be explained. In sensitivity tests, a slightly larger share of the increase in drug deaths may be explained by economic factors for some groups and, even using the multiple proxy (MP) methods, it is possible that there is modest remaining attenuation bias. On the other hand, even small amounts of remaining selection on unobservables would be sufficient to eliminate most or all of the remaining contributions of economic factors. Overall, these results strongly refute the hypothesis that economic decline is a primary cause of rising overdose mortality.

2. **Methods**

2.1 Basic Framework

I examine the extent to which sustained deterioration in economic conditions is a driver of the increase in fatal overdoses by performing a county-level analysis where the outcomes are changes in various types of drug and DSA mortality rates and the key explanatory variables are five measures for economic conditions. In all cases, the dependent variables and economic proxies represent "long-changes", covering substantial periods of time. In the main model, changes in county level fatal overdose rates cover the period 1999 through 2015, with subperiods examined in additional analyses. Most of the economic measures measure changes over the same or similar periods but others, particularly exposure to import competition, cover an earlier timespan. This partially reflects data limitations but also may be desirable to the extent that the fatal drug epidemic is affected by lagged changes in economic conditions.

The basic econometric model is:

$$M_k = \boldsymbol{E}_k\beta + \boldsymbol{X}_k\gamma + \varepsilon_k, \quad (1)$$

where M_k is the change in the specified mortality rate (per 100,000) in county k between two years (usually 1999 and 2015), $\boldsymbol{E}_k$ measures changes in one or more proxies for economic conditions, $\boldsymbol{X}_k$ is a vector of supplementary covariates (included in most specifications) and ε_k is the regression error term.

The coefficients of interest, $\hat{\beta}$, show estimated economic effects on mortality growth. A requirement for unbiased estimates is $\text{cov}(E_k, \varepsilon_k) = 0$, implying that $\boldsymbol{X_k}$ must adequately control for influences on mortality trends and are spuriously correlated with $\boldsymbol{E}_k$. However, the estimates will be attenuated if the vector of supplementary covariates contains variables that are caused by changes in economic conditions. This issue is addressed by testing the sensitivity of the results to including a vector of supplementary covariates measured at or near the ending year of analysis (usually 2015) versus one using the same set of potential confounders but using first year (usually 1999) values.

There are advantages and disadvantages of each approach. Specifically, evaluating $\boldsymbol{X_k}$ at 2015 values is likely to better control for spurious correlation[6] but may also be more likely to suffer from bias related to reverse causation. Conversely, including predetermined (1999) covariates in the model largely eliminates this source of potential endogeneity but may less adequately control for confounding factors. The supplementary regressors, described below, include county population characteristics, rural-urban status, proxies for the medical infrastructure, and state policies related to drug use and abuse. Reverse causation does not seem like a major issue for most of these. For example, the county share of non-Hispanic whites might be affected by the growth in drug mortality rates, but probably only slightly. On the other hand,

[6] This need not be the case but is likely for this application because drug poisoning death rates have risen so rapidly over time. For instance, in this analysis, the growth and 2015 levels of drug mortality are very highly correlated (R=0.89 using sample weights) while there is a slight negative correlation between 1999 levels of drug mortality rates and changes from 1999-2015 (R=-0.19).

this could be a bigger issue for some covariates (e.g. the share of female-headed households or whether the state has implemented a strong prescription drug monitoring program by 2015).[7] Thus, while I believe that the models with 2015 supplementary covariates are likely to be preferable (more precision with minimal endogeneity bias), I also generally present findings with the starting year characteristics controlled for.[8]

In most models, observations are weighted by 2015 county populations, to avoid attributing undue influence to the treatment effects observed in small counties.[9] However, since weighting can reduce efficiency under some circumstances (Wooldridge 1999; Solon, Haider, and Wooldridge 2015), sensitivity of the results to use of unweighted estimates is explored.

Throughout the econometric analysis, the explanatory variables, $\boldsymbol{E}$ and $\boldsymbol{X}$, are standardized to have a mean of zero and a standard deviation of one (by subtracting the mean and dividing by the standard deviation). As a result, the regression coefficients show estimated "effect sizes" of a one standard deviation change in the regressor and the intercept term indicates the average change in the dependent variable.

The general empirical strategy is to use the econometric results from equation (1) to estimate how changes in economic conditions affect trends in fatal overdoses and then to compare these predicted impacts to the total change over the period. In a model with only a single proxy for economic conditions, this is measured as:

$$(2) \qquad \%\ of\ M\ Explained = \frac{\widehat{\beta}}{\sigma_M}\ x\ 100\%$$

[7] For example, Autor, Dorn and Hanson (2017) show that localities hit by international trade shocks experience a reduction in the supply of marrigeable men and an increase in the fraction of children born to unwed mothers.
[8] Conversely, reverse causation would be a much bigger issue for models that controlled for *changes* over time in $\boldsymbol{X_k}$, since the large levels effect would be differenced away.
[9] For example, in 2015, the smallest 50 percent of counties contained just 5.8 percent of the U.S. population.

where $\hat{\beta}$ is the regression coefficient on $\boldsymbol{E}$, from estimating equation (1), and σ_M is the standard deviation of the change in mortality rates. Since $\boldsymbol{E}$ has been standardized $\frac{\hat{\beta}}{\sigma_M}$ shows the standard deviation change in mortality rates expected to result from a one standard deviation increase in the economic proxy. For example, if a one standard deviation increase in $\boldsymbol{E}$ predicts a one-half standard deviation increase in M (i.e. if $\hat{\beta} = 0.5\sigma_M$), 50 percent of the mortality growth is accounted for by changing economic conditions.

2.2 Multiple Proxy Estimates

Implementing the strategy just described faces multiple challenges. There is not a clear conceptual framework determining what aspects of the economy are likely to be most important determinants of growth in drug mortality, nor exactly what is meant by changes in economic conditions. This is addressed by including proxies for multiple, potentially overlapping, aspects of the economy including: labor market conditions, the level and distribution of income, housing prices which are an important component of household wealth, and exposure to international trade.

Since no single economic indicator completely captures the effects of interest, estimates from a lone measure will suffer from attenuation bias. The primary strategy to address this is to implement the method developed by Lubotsky and Wittenberg (2006) for simultaneously including multiple proxies in the model and then including a weighted sum of the coefficients to minimize attenuation bias.

In this approach, E_k^* is a latent variable for economic conditions that affects changes in mortality rates according to:

$$M_k = \beta E_k^* + \boldsymbol{X}_k\gamma + \varepsilon_k. \quad (3)$$

We do not observe E_k^* but instead have multiple proxies, E_{kj}, where the additional subscript indicates the j^{th} proxy, which are related to the latent variable according to:

$$E_{kj} = \rho_j E_{kj}^* + \mu_{kj}. \tag{4}$$

The key assumptions are that E_k^* is uncorrelated with ε_k and that all of the μ_{kj} are uncorrelated with E_k^* and ε_k. The second assumption implies that the proxy variables operate only through their effect on E_k^* and do not independently affect M_k. A key advantage of this framework is that the covariances between the error terms of the economic proxies (μ_{kj}) are unrestricted and, specifically, are allowed to be non-zero.[10]

Equations (3) and (4) cannot be directly estimated, since E^* is unobserved, but Lubotsky and Wittenberg (LW) show that attenuation bias can be minimized by simultaneously including all of the economic proxies in the model in the regression model:

$$M = \sum_{j=1}^{k} \beta_j E_j + \boldsymbol{X}_k \gamma + \varepsilon, \tag{5}$$

(where $k = 5$ in this application), and then calculating the weighted sum of the proxy coefficients as:

$$\hat{\beta} = \sum_{j=1}^{k} \frac{cov(M,E_j)}{cov(M,E_1)} \hat{\beta}_j, \tag{6}$$

where E_1 is the proxy chosen as the base. I use as E_1 the proxy with the largest regression coefficient magnitude ($\hat{\beta}_j$) in a model that includes all economic condition measures but without supplementary covariates. LW show that $\hat{\beta}$, calculated in this manner, has the same scale as E_1.[11]

[10] By contrast, potential alternative approaches, including instrumental variables estimates and factor or principal component analyses require zero covariances. The estimated effects of models with a single economic proxy will suffer from attenuation bias. For example, suppressing the supplementary covariates and under the simplifying normalization that $\rho_1 = 1$, the OLS estimator of $M_k = \beta_1 E_{k1} + \varepsilon_k$ converges to $\hat{\beta}_1 = \beta \frac{var(E^*)}{var(E^*)+var(\mu_1)}$, which is biased towards zero for all positive $var(\mu_1)$.

[11] For these estimates, I "reverse code" the standardized changes in median household incomes and home prices (by switching the sign on the variables) so that positive coefficients on all of the economic proxies indicate that deteriorating economic conditions raise the growth rate of drug deaths.

Since the explanatory variables are all standardized, $\hat{\beta}$ can also be interpreted indicating effect sizes for changes in the latent variable E^*. However, to the extent that the vector of proxy variables does not fully account for all aspects of E^*, some attenuation bias may remain.

As an alternative, I address the issue of attenuation bias through a series of instrumental variables (IV) models, estimated by generalized methods of moments (GMM) to increase efficiency with heteroskedastic errors, where each of the economic proxies is instrumented by the other four. These are not the primary estimates for two reasons. First, the IV procedure assumes that the error terms, μ_{kj}, for the individual proxies in equation (4), are uncorrelated with each other. This is unlikely and implies that the IV estimates could be biased either upwards or downwards. Second, the estimates may vary sharply depending on which of the economic proxies is instrumented for.

Robust standard errors, clustered at the commuter zone level, are displayed on the tables.[12] All analyses was conducted using STATA Statistical Software: Release 15 (StataCorp 2017).

2.3 Incomplete Specification of Drug Categories Involved in Overdose Deaths

Identifying the drug involved in fatal overdoses is complicated because no specific drug category is identified on the death certificates on around one-fifth of drug fatalities, leading to a substantial understatement of mortality rates.[13] Corrected mortality rates were obtained using information from death certificate reports where at least one specific drug category was

[12] Clustering is at the commuter zone this is the level of the observations on the import exposure variable, as discussed below.
[13] This was the case for 21.9 percent of overdose fatalities in 1999 and 17.2 percent in 2015. For these fatalities, the death certificate lists only an unspecified category of drugs (ICD T-Code 50.9).

identified to impute drug involvement for cases where none was using a procedure, previously implemented by Ruhm (2017b).

Year-specific probit models were first estimated, by maximum likelihood, for the sample of fatal overdoses with at least one drug specified on the death certificate. The dependent variables in these models were equal to one if opioid analgesics or illicit opioids, respectively, were mentioned and zero if not. Dichotomous explanatory variables included: sex, race (white, black, other nonwhite), Hispanic origin, marital status (currently married at the time of death versus not), education categories (high school dropout, high school graduate, some college, college graduate), age categories (≤20, 21-30, 31-40, 41-50, 51-60, 61-70, >70), day-of-the-week of death indicators, location of death (hospital inpatient, hospital outpatient/ED, dead on arrival at hospital/ED, home, other) and census region. Predicted probabilities of opioid analgesic involvement were next imputed, using the probit estimates, for deaths without mention of specified drug category. Robustness of the results to the use of uncorrected mortality rates was also examined.

2.4 Selection on Unobservables

A condition for obtaining unbiased estimates of the economic measures of key interest, $\hat{\beta}$ in equation (1), is that cov(E_k, ε_k) = 0 or, equivalently, that the supplementary covariates $\boldsymbol{X}$ account for all relevant confounding factors. However, if there are omitted variables that affect mortality rates and are correlated with E, cov(E_k, ε_k) $\neq$ 0) and $\hat{\beta}$ will be biased. This is referred to below as selection on unobservables. I examine this issue using the methods developed by Oster (2016) that extend on those introduced by Altonji, Elder and Taber (2005).

Some additional notation is useful for describing the method. Define β^o and the R^o as the coefficient on E and R-squared from the "short" regression of equation (1), that excludes controls for $\boldsymbol{X}$; $\tilde{\beta}$ and $\tilde{R}$ are the corresponding coefficient and R-squared from the "long" equation that includes the supplementary covariates. Let R_{max} be the R-squared that would be obtained from a hypothetical regression that includes an additional vector of covariates, $\boldsymbol{W}$, that are orthogonal to $\boldsymbol{X}$ and capture all remaining determinants of mortality rates. At first glance, it might appear that $R_{max} = 1$; however, the value will be if there is measurement error in the dependent variable.[14] Finally, δ measures the relative importance of selection of observables and unobservables, where δ=1 implies the two are equally important and δ<1 indicates that selection on observables is more important.[15]

Oster (2016) shows that the true treatment effect is approximated by:

$$\beta^* \approx \tilde{\beta} - \delta(\beta^o - \tilde{\beta}) \left(\frac{R_{max} - \tilde{R}}{\tilde{R} - R^o}\right). \tag{7}$$

The magnitude of the difference between β^* and $\tilde{\beta}$ is therefore increasing in δ, $\beta^o - \tilde{\beta}$, $R_{max} - \tilde{R}$, and $R^o - \tilde{R}$. Verbally, the difference between β^* and $\tilde{\beta}$ increases as selection on unobservables becomes more important, the difference between the observed R-squared (from the long regression) and maximum hypothetical model R-squared increases, the change in estimated treatment effects between the long and short regression models grows, and the change in R-squared between the short and long models falls. $\beta^o, \tilde{\beta}, R^o$ and $\tilde{R}$ are obtained by estimating the "long" and "short" regressions; values for δ and R_{max} must be assumed.

[14] For instance, this could occur because of misclassification in the cause of death or the drugs involved in fatal overdoses.

[15] Specifically, defining σ_{XE} as the covariance between $\boldsymbol{X}$ and $\boldsymbol{E}$ and σ_{WE} as the covariance between $\boldsymbol{W}$ and $\boldsymbol{E}$, and with σ_X^2 and σ_W^2 being the variances in $\boldsymbol{X}$ and $\boldsymbol{W}$, then: $\delta = \frac{\sigma_{WE}/\sigma_W^2}{\sigma_{XE}/\sigma_X^2}$.

Manipulation of equation (7) also allows the relative importance of selection on unobservables that would eliminate the estimated treatment effect to be computed as:

$$\delta^* \approx \left(\frac{\tilde{\beta}}{(\beta^o - \tilde{\beta})}\right)\left(\frac{\tilde{R} - R^o}{R_{max} - \tilde{R}}\right) \quad (8)$$

and the R_{max} that would do so to be approximated by:

$$R^*_{max} \approx \tilde{R} + \left(\frac{\tilde{\beta}}{\delta(\beta^o - \tilde{\beta})}\right)(\tilde{R} - R^o) \quad (9)$$

3. **Data and Variables**

3.1 Dependent Variables

The outcomes examined are mortality rates due to drug poisonings, nondrug suicides and alcoholic liver disease (DSA deaths), as well as overdose deaths involving prescription and illicit opioids. Primary data come from death certificates for 1999 through 2015, as provided on the Centers for Disease Control and Prevention *Multiple Cause of Death (MCOD)* files, described in detail elsewhere (Centers for Disease Control and Prevention 2017b). Each certificate contains a single underlying cause of death, up to 20 additional causes, and demographic data. Information is utilized on cause of death, using four-digit *International Classification of Diseases, Tenth Revision* (ICD-10) codes, county of residence, age, race/ethnicity, gender, education, year, and weekday of death. The geographic information on county of residence is restricted and permission to use these data were also obtained. The Institutional Review Board for the Social and Behavioral Sciences at the University of Virginia reviewed this project and determined that it did not involve the use of human subjects.

The analysis covers the universe of DSA fatalities to US residents between 1999 and 2015 (foreign residents dying in the US were excluded). The study begins in 1999 because ICD-9 codes, used prior to 1999, are not fully comparable to ICD-10 categories.(R. N. Anderson et al. 2001). ICD-10 underlying cause of death (UCD) codes are used to classify the reason for death,

where the UCD is the "disease or injury which initiated the chain of events leading directly to death" (Centers for Disease Control and Prevention 2017a). Drug poisonings are defined conventionally as fatalities with ICD-10 codes: X40-X44, X60-X64, X85, Y10-Y14 or Y352. Nondrug suicides include ICD-10 codes X65-X84, Y87.0 and *U03; alcohol deaths refer to ICD-10 code K70.

For overdoses, the death certificate lists one or more drug categories involved as immediate or contributory causes of death. These were included separately in the *MCOD* files as ICD-10 "T-codes" and are referred to below as drug involvement. The drug categories examined are opioid analgesics (e.g. oxycodone), and illicit opioids, which include both heroin and synthetic opioids, defined by ICD-10 T-codes 40.2, 40.1 and 40.4 (www.icd10data.com/ICD10CM/Codes/S00-T88). Synthetic opioids include several drugs, the most important of which is fentanyl. Fentanyl has legal uses but recent increases in deaths from this source are largely driven by non-prescription consumption (Rudd et al. 2016). Although around half of fatal overdoses involve the use of more than one drug category (Ruhm 2016, 2017a), the analysis below does not examine drug combinations.

Death counts were converted into county mortality rates per 100,000 using population data obtained from the National Cancer Institute's *Surveillance Epidemiology and End Results (SEER)* program (https://seer.cancer.gov/popdata/). The SEER data are designed to supply more accurate population estimates for intercensal years than standard census projections, and to adjust for population shifts in 2005, resulting from Hurricanes Katrina and Rita.

In addition to total death rates, mortality rates were separately calculated for males and females, non-Hispanic whites (hereafter "whites") and nonwhites or Hispanics (hereafter "nonwhites"), education groups (high school graduate or less, some college but not graduated,

college graduate or more), and separately for 25-54 year olds and 25-54 and 45-54 year old whites, since these groups experienced particularly large increases in overdose deaths over the study period and because Case and Deaton (2015) emphasize mortality increases among the latter group.

Several challenges are encountered when calculating education-specific mortality rates. First, education is sometimes reported on death certificates in years rather than specific thresholds. In these cases, ≤12, 13–15 and ≥16 years are classified as high school graduate or less, some college and college graduate. Second, schooling status is missing on around 5 percent death certificates for overdoses.[16] Education-specific mortality rates are calculated by assuming that the county-specific distribution of educational attainment was the same for these missing cases as when schooling was reported. Third, the *SEER* data does not provide education-specific population estimates. These were obtained by multiplying total or group-specific population by the county education group share.[17]

3.2 Economic Indicators

Five county-level proxies for changes in economic conditions are included in the analysis: unemployment and poverty rates, median household incomes and home prices, and exposure to imports. These are designed to capture multiple aspects of the economy across the domains of labor market conditions, income, wealth and international trade.

Data from the Bureau of Labor Statistics *Local Area Unemployment Statistics Database* (www.bls.gov/lau/) are used to calculate three-year averages of unemployment rates, ending in

[16] Education is missing for 7.2 percent of fatal overdoses in 1999 and 4.7 percent in 2015.
[17] These data are from the 2000 Census and a five-year average of data from the 2011-2015 American Community Surveys, as provided in the USDA Economic Research Service (*ERS*) County Level Data Sets, www.ers.usda.gov/data-products/county-level-data-sets/county-level-data-sets-download-data/. The education shares refer to persons 25 and over and so the county shares are calculated for the percentage of the population over this age in the specified education group.

the year specified (e.g. 1997-1999 for the 1999 analysis year). Unemployment rates are averaged to smooth short-term fluctuations or measurement error, which will be particularly severe for smaller counties. Information on three-year averages in poverty rates and median household incomes (ending in the year specified) are obtained from the Bureau of the Census *Small Area Income and Poverty Estimates* (www.census.gov/did/www/saipe/). Data on median home prices in 2000, the earliest year used, are from the US Census; later data are 5-year averages from the American Community Survey (*ACS*) for the periods 2005-2009, 2007-2011 or 2011-2015. These data are obtained from various issues of the Area Resource File/Area Health Resource File (*ARF)*, http://www.arf.hrsa.gov, and from *American FactFinder* (https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml). Median household incomes and home prices are converted to $2015 using the All-Items Consumer Price Index (www.bls.gov/cpi/). The last economic proxy reflects changes in exposure to Chinese import competition between 1990 and 2007, using a measure constructed by Autor, Dorn and Hanson (2013).[18]

3.3 Additional Covariates

Most models control for additional covariates designed to capture the potential effects of confounding variables. Unless otherwise noted, each of these were available for each year during the analysis period. The *SEER* data were used to calculate county population shares of: females, Hispanics, black non-Hispanics, other nonwhite non-Hispanics, seven age categories (15-24, 25-34, 35-44, 45-54, 55-64, 65-74, ≥75 years old); county percentages of persons ≥25 years old with

[18] Differences in measured trade exposure occur because of variations in local industry employment structure in 1970. They use an instrumental variables procedure to account for the potential endogeneity of US trade exposure; the instruments are growth of Chinese imports to eight other developed countries. Their trade exposure measure is calculated at the commuter zone rather than the county level. For this analysis, all counties within a commuter zone are assumed to have the commuter zone level of import exposure, using a crosswalk of 1990 commuter zones to counties. The import exposure and crosswalk files were obtained from: www.ddorn.net/data.htm.

some college or who were college graduates was also included, using previously described information from the *ACS*.[19] The percentage of household headed by females in 2000 and 2010, and of foreign-born persons in the county in 2000, 2006-2010 and 2011-2015 were obtained from the *ARF*. Information on the number of hospital beds and active non-federal physicians per 1,000 population were provided from the same source and included to proxy the county's health infrastructure.[20]

The USDA ERS county level data sets, described above, also contain information on the 2013 "rural-urban" continuum code of the county, containing the following nine categories: metropolitan with population ≥1,000,000, 250,000 - 999,999 and <250,000 (three classifications); urban area with population ≥20,000 and 2,500 – 20,000 and adjacent to or not adjacent to a metropolitan area (four classifications); rural area with population <2,500 adjacent to or not adjacent to a metropolitan area (two classifications). In the regression models, dummy variables for eight of the classifications are included, with the largest metropolitan areas as the excluded reference group.

Finally, two measures of the state-level legal environment related to drug use are incorported. The first indicates whether the state has a prescription drug monitoring program (*PDMP*) that requires reporting to it by drug dispensers. The second controls for whether the state has legalized marijuana use for medical or recreational purposes. Data for both variables comes from the *Prescription Drug Abuse Policy System* (www.pdaps.org). They are included because there is evidence that each may influence drug use and abuse (Bachhuber et al. 2014; Bradford and Bradford 2016; Buchmueller and Carey 2018).

[19] Thus, in the regressions, the excluded (reference) categories are population shares of males, whites, <15 year olds and the non-college educated.
[20] The number of hospital beds was not available for 2011 and 2015. The former was calculated by averaging values for 2010 and 2012; the latter by using the 2014 number of beds.

Table A.1 provides summary statistics on the dependent variables, economic proxies, and additional covariates measured in (approximately) 1999 and 2015, with observations weighted by 2015 county populations. The analysis sample consists of 3,098 counties with boundries that are consistent over the time period and with data available for all of the economic proxies.[21] The table shows actual values; however, as mentioned, the independent variables are standardized in the regressions. Also, while the table shows actual changes in median household incomes and home prices, these are reverse-coded (opposite signed) in the econometric models, so that positive coefficients always indicate that worsening economic conditions are associated with higher growth in mortality.

4. **Descriptive Patterns**

Before turning to the econometric estimates, I show descriptive patterns of drug mortality over the 1999-2015 period. Figure 1 illustrates the changes in total drug death rates, suicide and alcohol mortality, as well as opioid analgesic and illicit opioid involved drug mortality rates. The overall drug fatality rate rose steadily over time, from 6.0 to 16.3 per 100,000 from 1999 to 2015, a 170 percent increase. Nondrug suicide death rates started out considerably higher (9.3 per 100,000 in 1999) but rose more slowly, reaching 12.1 per 100,000 in 2015. Alcohol deaths also increased relatively slowly (from 4.3 to 6.5 per 100,000) whereas opioid analgesic and illicit opioid death rates grew extremely rapidly: from 1.3 and 1.2 per 100,000 in 1999 to 4.8 and 7.4 per 100,000 in 2015. However, the patterns of increases quite different for the two categories of opioids. All of the increase in opioid analgesic mortality occurred from 1999-2011, whereas illicit opiod death rates rose modestly from 1999-2006, reaching 2.1 per 100,000 in the latter

[21] Three counties were dropped because information on education shares was missing; 24 and 2, respectively, were excluded because of missing information on import exposure and home prices.

year, and then considerably more rapidly thereafter, particularly from 2010 to 2015, where the increase was from 2.6 to 7.4 per 100,000.[22]

Figures 2 and 3 show corresponding patterns of drug and nondrug DSA mortality for subgroups stratified by sex, race/ethnicity, age and education. In both cases, death rates are higher in all years for males than females and for those without a college degree than for the college educated. Whites also have higher death rates and faster mortality growth from both sources towards the end of the sample period but, interestingly, the drug mortality rate were quite similar for whites and blacks (but higher than for Hispanics of other nonwhites) in 1999, whereas nondrug DSA mortality rates were already higher for whites than nonwhites in the initial analysis year. The age relationships are somewhat more complicated. Drug mortality rates rose fastest for 25-64 year olds and were generally highest for these groups, whereas nondrug DSA deaths were highest for those 45 and over and barely rose over time at younger ages.

Figure 4 provides additional information on opioid mortality rates and shows that: illicit opioid death rates exploded for males after 2010, while growing much more slowly for females; the particularly rapid rise in opioid analgesic death rates for whites, relative to nonwhites, occurred between 1999 and 2011, whereas that in illicit opioid mortality primarily after 2006; and that the rise in illicit opioid death rates was skewed towards relatively young addults – particularly 25-34 year olds, whereas increases in opioid analgesic fatalities mainly affected an older age group.

Appendix Figures A.1 through A.4 displays detailed results for drug and nondrug sources of mortality for sex, race/ethnicity, age and education subsamples. In addition to the findings already described, they show that sex differentials are larger for nondrug than drug deaths

[22] Heroin death rates grew 437 percent between 2006 and 2015, with the fastest rise (276 percent) from 2010-2015. Synthetic opioid death rates increased throughout the period but started from a low level, 0.4 per 100,000 in 1999, reaching 1.3 per 100,000 in 2013, and then exploding to 3.5 per 100,000 by 2015.

andthat mortality growth has been faster for whites than nonwhties for all types of DSA deaths. Perhaps most interesting are the age differences. As discussed, illicit opioid deaths skew younger than those due to analgesics, particularly in the later years. Rates of nondrug suicides are fairly similar for age groups older than 25, although with the fastest growth over time for 45-64 year olds, while alcohol mortality is heavily concentrated among persons 45 and older, with the fastest growth among 55-64 year olds. These patterns raise doubts about whether a single set of economic determinants could the source the differential increases in mortality rates or indicate that, if they are, they must operate through multiple mechanisms affecting the groups differently.

5. **Econometric Estimates**

I next present econometric results, first showing models controlling for the proxies for economic conditions, but without supplementary covariates, then including additional covariates, providing a series of robustness checks, results for population subgroups, and an investigation of the effects of remaining selection on unobservables.

5.1 Models without Supplementary Covariates

Table 1 shows regression coefficients for the economic proxies where the dependent variables are growth from 1999-2015 in the specified type of DSA mortality (all drugs, opioid analgesics, illicit opioids, all DSA and nondrug DSA), without controls for potential confounding factors. As mentioned, changes in median household incomes and home prices have been reverse-coded so that positive coefficients always imply that worse economic performance is associated with faster increases in mortality. Also, all regressors have been standardized so that the coefficients show estimated effects of a one-standard deviation change in the explanatory

variable. The top panel of the table shows results where the economic measures have been included separately, with every cell representing the results of a different regression. In the second panel, the five economic proxies have been included simultaneously, so that each column displays findings from a single regression. The third panel shows the multiple proxy (MP) estimate from the model with the five economic proxies but no additional covariates, as well as the percent of the total mortality change explained by economic conditions.

When entered separately, coefficients on the economic proxies are positive for all types of drug mortality and, except for import exposure, highly significant (top panel). For example a one-standard deviation decrease in county median household incomes ($2,817 in 2015 dollars) is associated with a 2.07 per 100,000 faster growth in overdose mortality and a 0.68 per 100,000 increase in the opioid-analgesic-involved drug death rate. Since the standard deviations for these two outcomes are 10.37 and 3.58 per 100,000, these estimates suggest that a one standard deviation reduction in income predicts around a 20 percent increase in mortality rates from these sources. The uniformly positive coefficients indicate that counties experiencing relative economic deterioration had higher than average growth in all types of drug mortality. Conversely, even when entered separately, the coefficients on the measures of economic conditions are smaller and, except for median home prices, statistically insignificant for nondrug DSA deaths, indicating that economic factors play little role for these types of mortality. Also, for this reason, the coefficient estimates are smaller in relative terms for all DSA deaths than for drug mortality.

The middle panel of Table 1 shows results when including the five economic proxies simultaneously. Doing so, substantially attenuates the coefficient estimates in virtually all cases. For instance, the coefficient on median household income is reduced almost 90 percent for

overall drug mortality, 99 percent for illicit opioif deaths and switches sign for opioid analgesic mortality. This is expected because the economic variables are reasonably highly correlated with each other, except for import exposure which is barely associated with the other four measures (see Appendix Table A.2). Controlling for the other economic proxies, changes in median home prices and poverty rates have the largest magnitudes for most outcomes. The R-squared is also uniformly low, ranging between 0.012 and 0.083, providing a further indication of the limited explanatory power of changes in economic conditions. With that said, the p-values from the test that the coefficients for the five economic proxies are jointly equal to zero are always low, indicating that there is some association between them and changes in death rates.

The third panel of Table 1 shows multiple proxy estimates, obtained using the Lubotsky/Wittenberg procedure, as well as the estimated percentage of the growth in mortality rates accounted for. The MP estimate exceeds the coefficient for any single economic measure in either the top or middle panel of the table by at least 14 percent (and generally much more), indicating the importance of correcting for attenuation bias. Dividing the multiple proxy estimate by the standard deviation of the dependent suggests that changes in economic conditions explain 33 percent of the rise in drug mortality rates, 26 percent of all DSA death rates and 26 to 28 of those involving opioid analgesics and illicit opioids but just 15% of the change in nondrug DSA fatality rates. However, these estimates are likely to suffer from serious omitted variable bias, an issue to which I turn next.

5.2 Models With Additional Covariates

The models just described control exclusively for (one or more of) the economic proxies and so do not account for the effects of potential confounding factors. Table 2 begins to remedy

this by summarizing models where the dependent variable is the change in drug mortality rates from 1999-2015 and various sets of controls are included. Column (a) repeats the results from Table 1, with the five economic variables included simultaneously but nothing else. Column (b) adds to this the set of 1999 county characteristics and column (c) includes characteristics measured at or near 2015. As mentioned, the 2015 supplementary variables will probably control for confounding factors better than the 1999 characteristics, and so I anticipate the MP estimates on the economic variables will be most attenuated in model (c).

Controlling for 1999 characteristics reduces the multiple proxy estimate by 55% (from 2.98 to 1.35) and accounting for 2015 supplementary controls does so by two-thirds (to 0.98), indicating that much of the observed relationship between changes in mortality rates and economic conditions is due to confounding factors. In model (b), "deaths of despair" are estimated to explain 15 percent of the rise in drug mortality, and 11 percent in column (c), compared to 33 percent in specification (a). The MP estimate remains statistically significant in specifications (b) and (c), suggesting that changes in economic factors may continue to play some role, but at least 85 percent of the rise in drug death rates results from other factors.

The first panel of Table 3 repeats the MP estimate and percentage change in drug deaths rates from 1999-2015 accounted for by economic factors. The next four panels show corresponding estimates for changes in opioid analgesic, illicit opioid, all DSA and nondrug DSA mortality rates. Comparing results for models (b) and (c) to (a) indicates that 67 to 88 percent of the original correlation between economic conditions and various types of drug mortality growth is due to confounding factors, with the greatest attenuation occurring for opioid analgesics, as is over three-quarters and greater than 90 percent, respectively, of that for all DSA deaths and nondrug DSA fatalities. The estimated change in mortality rates accounted for by

worsening economic conditions ranges from 3 percent to 6 percent for opioid analgesics, 8 to 14 percent for illicit opioids, and much less for all DSA or nondrug DSA deaths. These findings indicate that "deaths of despair" never account for more than one-sixth of the rise in mortality and considerably less in most cases. In addition, the change explained is always smaller when controlling for 2015 rather than 1999 county characteristics. Unless reverse causation is a major issue, which seems unlikely, the percentage of increased mortality explained is even smaller – accounting for just one-ninth of the rise in overall drug mortality and less for the other categories.

5.3 Robustness

I tested the robustness of the results to several changes in specifications, estimation methods and samples. Table 4 shows the results of models where observations are unweighted, rather than using 2015 population weights (middle panel) and using reported, rather than corrected, opioid analgesic and illicit opioid death rates (lower panel). Using unweighted data, the percentage of changes in mortality rates explained by economic conditions is smaller than with weighting: for example, 5 to 8 percent of the growth in total drug death rates is explained, compared to 11 to 15 percent with weighting. Some of this difference occurs because the standard deviations on the dependent variables are usually substantially larger in the unweighted data, so that a given estimated effect will explain less of the overall change; however, the MP estimates are also smaller in most cases.[23] Economic conditions are estimated to have somewhat greater explantory power when using reported rather than corrected opioid mortality rates: 5 to 8 percent of the change in opioid analgesic death rates, versus 6 to 7 percent with the corrected

[23] The unweighted sample means of the dependent variables are also generally larger than the weighted means, indicating higher mortality growth in smaller counties. However, the pattern is reversed for deaths involving illicit opioids.

data, and 12 to 18 percent of the rise in illicit opioid fatalities, compared to 8 to 13 percent. However, these do not change the overall findings.

Next, I addressed examined the results from a series of instrumental variables (IV) models where each economic proxy was instrumented by the other four. As discussed, IV estimates can eliminate attenuation bias but require the strong assumption that error terms between the five proxies and the latent variable are uncorrelated. Results of these models, with 2015 supplementary controls included, are summarized in Table 5. Estimation is by generalized method of moments (GMM), to provide efficient estimates with heteroskedastic errors, with the 2015 set of county characteristics controlled for.

Generally, the IV and multiple proxy estimates (repeated on the bottom panel of Table 5) are quite similar. For instance, for all drug mortality, the instrumented estimates for the poverty, household income, home price and unemployment proxies range between 0.7 and 1.3, implying that 9 to 15 percent of the change from 1999-2015 is explained, versus the multiple proxy estimate of 11 percent. The IV estimates for these four proxies imply that a smaller portion of the change in opioid analgesic and illicit opioid rates is explained by economic conditions than when using the multiple proxy approach, with statistically insignificant predicted effects in most cases. For all DSA deaths, the IV coefficients on the four economic measures just discuss suggest that economic conditions could explain between 7 and 14 percent of the rise in overall, mortality rates, exceeding the 6 percent accounted for using the multiple proxy estimate but not changing the fundamental conclusion of limited explanatory power.

The one exception is for import exposure, where the IV estimates are quite large, although not precisely measured, for drug, illicit opioid and all DSA mortality. However, as mentioned, this explanatory variable is barely correlated with the other economic proxies (see

Table A.2) and so is likely to suffer from a "weak instruments" problem (Bound, Jaeger, and Baker 1995; Staiger and Stock 1997).[24] The bottom-line is that both the MP and IV estimates indicate that changing economic conditions explain only a small portion of county-differences in increased drug fatalities rates.

Appendix Table A.3 provides estimates for sub-periods where growth in the specified category of opioid mortality was highest: 1999-2011 for opioid analgesic deaths and 2006-2015 for illicit opioid fatalities. The motivation is that including periods with little change in mortality rates may introduce noise into the estimates. However, using data for shorter periods comes at considerable cost, both because the changes in economic conditions cover a shorter period and since data restrictions imply that the dates over which they are measured may not be ideal. For example, home price information in the *American Community Survey* is averaged over a five-year period (e.g. 2011-2015) to obtain sufficient sample sizes. When examining changes in opioid analgesic mortality from 1999-2011, median home prices averaged from 2007-2011 are compared to those in 2000. When studying illicit opioid fatality rates from 2006-2015, median home prices averaged from 2005-2009 are compared to those averaged from 2011-2015. These poorly captures the dates over which mortality growth is measured.[25] The table indicates that economic conditions may explain a slightly larger portion – up to 8 percent – of the increase in opioid analgesic fatality rates from 1999-2011, but a smaller fraction – -2 to 6 percent – of the growth in illicit opioid mortality rates from 2006-2015.

5.4 Subgroups

[24] As evidence of this, the F-statistic on the first-stage instruments is 98.7, 142.8, 34.9 & 36.7 for poverty, incomes, home prices & unemployment but just 3.8 for import exposure.

[25] The table note provides additional detail on differences in the variables included for sub-periods. Other home price series do not provide sufficient information of this analysis. For example, Zillow Research (https://www.zillow.com/research/) provides county-level home value data but only for some (generally larger) counties.

Table 6 shows the multiple proxy estimates, associated standard errors and percent of the change in mortality explained for population sub-groups stratified by sex, race/ethnicity and education, with additional results for 25-54 year olds and non-Hispanic whites aged 25-54 and 45-54. Growth in drug mortality rates, of all types examined, increased relatively more for whites, 25-54 year olds, whites aged 25-54 (but not 45-54 year olds) and those without a college education than for their counterparts (see Appendix Table A.4). Declining economic conditions were generally also associated with the largest *absolute* increases in fatality rates for these groups and explained a greater percentage share of the mortality rate change for them. For example, overall drug mortality rates grew by 13.9 per 100,000 for whites versus 4.8 per 100,000 for nonwhites from 1999-2015. The multiple proxy estimates differed by a similar proportion (1.6 to 2.2 per 100,000 for whites versus 0.4 to 0.7 per 100,000 for nonwhites) and economic conditions explained an even larger share of the change for whites (15 to 21 percent versus 3 to 5 percent). However, this was not always the case. For instance, overdose mortality rates grew relatively rapidly for 25-54 year olds but county-level changes in economic conditions did not account for an unusually large percentage of the growth. Similarly, drug mortality grew faster for men than women, and the absolute size of the economic effect is larger for them, but the share of the mortality growth explained is fairly similar.[26]

6. **Selection on Unobservables**

The analysis to this point assumes that the vector of supplemental covariates (***X***) is sufficiently comprehensive to account for all relevant omitted variables, such that $\text{cov}(E_k, \varepsilon_k) =$

[26] Economic conditions explained a much larger percentage of the change in illicit opioid death rates for females than males (16 to 18 versus 4 to 11 percent), but mainly because of the dramatically slower mortality growth for women than men (3.6 versus 9.1 per 100,000).

0. This is a fairly strong assumption. The methods developed by Oster (2016) are implemented to examine how the results change if there is remaining selection on unobservables. As discussed, the key parameters are $\beta^o, \tilde{\beta}$, R^o and $\tilde{R}$, the multiple proxy coefficients and R-squared from the "short" and "long" regression of equation (1), as well as δ and R_{max}, for which values must be assumed. For many applications, Altonji et al., (2005) and Oster (2016) recommend setting δ=1, implying equal importance of selection on observables and unobservables. However, since it seems likely that this analysis most important aspects of the selection process will have been accounted for, I provide results assuming that δ = 0.5, implying that selection on observables is twice as important as that on unobservables. Choosing a higher δ value would further reduce the size of the estimated treatment effect. For the base model, I also set $R_{max} = 0.75$, which allows for considerable measurement error in the dependent variable. These values are somewhat arbitrary and so I also present estimates of δ^*, the relative importance of unobservables versus observables, at which the estimated treatment effect would be zero, $R_{max} = 0.75$, as well as for R^*_{max}, the hypothetical maximum R-squared to give a zero treatment effect, with δ = 0.5. The findings are summarized in Table 7. Column (a) shows the MP estimate without accounting for selection on unobservables. Columns (b) and (c) display the section-corrected estimated effect and percentage of the total change explained, with δ = 0.5 and $R_{max} = 0.75$. The last two columns show δ^* and R^*_{max}.

The striking result from Table 7 is that even small amounts of selection on unobservables would be sufficient to eliminate any estimated role for economic conditions as an explanation for rising mortality rates. For instance, with δ = 0.5 and $R_{max} = 0.75$, β^* is less than zero in eight of 10 specifications and, in most of these cases, δ > 0.3 or an $R_{max} > 0.5$ would be sufficient to eliminate the effect. The two specifications that are most supportive of *some* remaining effect are

for all drug or illicit opioid involved mortality when controlling for 1999 covariates. In these cases, the estimated β^* (with $\delta = 0.5$ and $R_{max} = 0.75$) remains positive and δ would need to be greater than 0.7 and R_{max} above 0.9 to eliminate the treatment effect. However, even in these cases, economic conditions are predicted to explain just 5 percent of the growth in total drug mortality rates and 7 percent of those involving illicit opioids.

7. **Discussion**

Counties experiencing economic decline had higher rates of growth in mortality due to drugs, suicide or alcohol than those with more robust economic growth. However, the relationship is fairly weak and is mostly of it is due to other county characteristics that are spuriously correlated with changes in economic conditions. Controlling for 2015 observable characteristics, just one-ninth of the increase in drug mortality rates from 1999-2015 is explained by changes in economic factors, with 8 percent of the growth in illicit opioid-involved overdose death rates between accounted but just 3 percent of the increase in opioid analgesic deaths and less than one percent of the change in nondrug suicide or alcohol fatalities. The portions accounted for are modestly higher when controlling for predetermined county characteristics, but the portions of the mortality change explained by economic conditions never reach 15 percent. In correcting for even modest amounts of remaining selection on unobservables would be sufficient eliminate most of the observed treatment effects. When doing so, the largest portion of the mortality change explained – occurring for illicit opioid involved deaths when using supplemental controls from 1999 – is below 7 percent of the overall amount.

These results suggest that the "deaths of despair" framing, while provocative, largely fails to explain the main sources of the fatal drug epidemic and imply that efforts to improve

economic conditions in distressed locations, while desirable for other reasons, are unlikely to yield significant reductions in drug mortality. Such a result probably should not be surprising since drug fatalities have increased substantially – including a rapid acceleration of illicit opioid deaths – after the end of the Great Recession (i.e. subsequent to 2009), when economic performance has considerably improved.

Evidence that declining economic conditions are not a major cause of the rapid increase in drug mortality does not identify the key causes. One hypothesis, to be examined in future work, is that individuals and groups are differentially at risk of drug abuse and fatal overdose. These risks depend on the public health environment and vary across locations and over time. For example, young adults and males probably have a relatively high rate of illegal drug use, whereas mature adults and women relatively more often consume legal drugs (although not always for their intended uses). The availability of opioid analgesics increased rapidly during the first decade of the 21st century, and flattened after 2010, whereas the heroin problem accelerated after 2006 and again subsequent to 2010, while fentanyl did so beginning in 2014. A possible empirical test of the health environment hypothesis, therefore, is to examine whether groups were differentially affected over time in ways consistent with these risk profiles.

The findings of this analysis suggest that efforts to lessen the fatal drug epidemic should probably focus on the primary prevention of drug problems and on the treatment of them once they emerge. To date, the greatest progress has been made in addressing the harms from opioid analgesics. These efforts have included establishing drug monitoring programs; restricting the ability of pain clinics and online pharmacies to dispense controlled substances; developing abuse-deterrent drug formulations; establishing opioid prescription guidelines emphasizing pre-treatment goals, increased screening prior to prescribing, prescribing the lowest effective dosage;

avoiding concurrent use of other opioids or benzodiazepines where possible; and proposals for mandatory provider education (Alexander, Frattaroli, and Gielen 2015; Meinhofer 2015; Jones et al. 2016; Meara et al. 2016; Dowell, Haegerich, and Chou 2016; FDA 2016; Madras 2017).

Expanded treatment options should almost certainly play a role in efforts to reduce opioid deaths, given the effectiveness of medication-based approaches utilizing methadone, buprenorphine and naltrexone (Schwartz et al. 2013; Woody et al. 2014; Mattick et al. 2008). Only a small proportion of addicts currently receive treatment and, among those who do, medication-based approaches are limited and often at insufficient dosages (Substance Abuse and Mental Health Services 2011; Volkow et al. 2014; D'Aunno et al. 2014). Naloxone administration saves lives and efforts are underway to raise its availability to first-responders and caregivers (Compton and Throckmorton 2013; Coffin and Sullivan 2013; Jones, Lurie, and Compton 2016; Rees et al. 2017), although this may be offset by increased use due to a reduction in risk from any single overdose (Doleac and Mukherjee 2017). Primary prevention of risky drug use is also critical but we know less about how to achieve this. Ongoing physician education efforts are also important, particularly in light of recent evidence that graduates of highly ranked medical schools or in specialties receiving specific training on the use of opioids after graduating from medical school provide fewer opioids than their counterparts (Schnell and Currie 2017). Community-based prevention strategies have shown promising results (Hawkins et al. 2008; Albert et al. 2011) and efforts to staunch the supply of illicit fentanyl and its analogs are certainly important.

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Table 1: Estimated Effect of Economic Conditions on Changes in Drug, Suicide and Alcohol (DSA) Death Rates, 1999-2015

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	All DSA	Nondrug DSA
Measures Included Separately					
Δ in Poverty Rate	2.205*** (0.560)	0.798*** (0.242)	1.334*** (0.446)	2.320*** (0.752)	0.115 (0.306)
Δ in Median Household Income	2.068*** (0.546)	0.679*** (0.254)	1.136** (0.496)	2.515*** (0.773)	0.447 (0.351)
Δ in Median Home Price	2.289*** (0.649)	0.908** (0.354)	1.158* (0.627)	2.840*** (0.680)	0.551** (0.255)
Δ in Unemployment Rate	1.370*** (0.464)	0.295** (0.131)	1.069*** (0.253)	1.144 (0.765)	-0.226 (0.356)
Δ in Import Exposure	0.500 (0.518)	0.171 (0.201)	0.577 (0.472)	0.247 (0.607)	-0.253 (0.216)
Measures Included Together					
Δ in Poverty Rate	1.106** (0.509)	0.554** (0.252)	0.727* (0.401)	0.818 (0.592)	-0.288 (0.225)
Δ in Median Household Income	0.219 (0.667)	-0.114 (0.334)	0.012 (0.526)	0.742 (0.953)	0.523 (0.391)
Δ in Median Home Price	1.473* (0.804)	0.725* (0.403)	0.616 (0.681)	1.970** (0.875)	0.497* (0.257)
Δ in Unemployment Rate	0.282 (0.443)	-0.144 (0.209)	0.487 (0.350)	-0.151 (0.663)	-0.432 (0.304)
Δ in Import Exposure	0.339 (0.476)	0.125 (0.180)	0.450 (0.456)	0.134 (0.549)	-0.205 (0.199)
R^2	0.083	0.056	0.056	0.060	0.012
P-Value	<0.001	0.002	<0.001	<0.001	0.013
Multiple Proxy Estimate	2.979*** (0.638)	1.104*** (0.347)	1.856*** (0.512)	3.246*** (0.750)	1.132*** (0.309)
% of Total Δ Explained	32.9%	26.2%	27.8%	26.2%	15.4%
Dep. Var. Mean [SD]	10.37 [9.06]	3.58 [4.22]	6.27 [6.67]	15.39 [12.38]	5.02 [7.35]

Note: In the top panel, each cell shows results of a different regression where the dependent variable is the specified drug death rate per 100,000 and only a single measure of economic conditions is included in the model (n=3,098). In the second panel, all five measures of economic conditions are controlled for simultaneously. Changes in median household incomes and home prices are "reverse coded" (i.e. the signs are switched from positive to negative and vice versa) so that, for all measures, positive coefficients indicate that worsening economic conditions are correlated with higher mortality rates. Observations are weighted by 2015 county populations. Regressors are standardized to have a mean of zero and a standard deviation of one, so that coefficient shows "effect sizes" of a one standard deviation change in the independent variable. Change in unemployment and poverty rates refer to three-year averages of

annual rates for the periods ending in 2015 versus 1999. Changes in median household incomes ($2015) are from 1999 to 2015. Drug poisoning deaths refer to cases where the ICD underlying cause of death code is X40-X44, X60-X64, X85, Y10-Y14 or Y352. Opioid Analgesic and illicit opioids refer to deaths involving ICD-10 codes T40.2 and T40.1 or T40.4 respectively. DSA indicates deaths from drug poisoning, nondrug suicides or alcoholic liver disease (alcohol) and nondrug DSA to deaths from nondrug suicides or alcoholic liver disease. Nondrug suicides refer to ICD-10 codes X65-X84, Y87.0 and *U03, and alcohol to ICD-10 code K70. Deaths involving opioid analgesics or illicit opioids are adjusted for non-reporting of the drugs involved in overdose deaths using the methods described in the text. Multiple proxy estimates refer to the model with all economic proxies simultaneously included and are estimated using the methods discussed in the text. Robust standard errors clustered at the commuter zone level are in parentheses. The percentage of total change explained is calculated by dividing the multiple proxy estimate by the standard deviation of the dependent variable. P-Value refers to the null hypothesis that the five economic measures are jointly equal to zero. *** p<0.01, ** p<0.05, * p<0.1

Table 2: Estimated Effect of Economic Conditions on 1999-2015 Change in Total Drug Death Rate, with Various Sets of Controls

Economic Conditions Proxy	(a)	(b)	(c)
Δ in Poverty Rate	1.106**	0.677*	0.979**
	(0.509)	(0.355)	(0.402)
Δ in Median Household Income	0.219	0.070	-0.679
	(0.667)	(0.395)	(0.421)
Δ in Median Home Price	1.473*	0.454	0.637
	(0.804)	(0.524)	(0.516)
Δ in Unemployment Rate	0.282	0.237	0.089
	(0.443)	(0.325)	(0.293)
Δ in Import Exposure	0.339	0.164	-0.166
	(0.476)	(0.276)	(0.274)
R^2	0.083	0.395	0.389
P-Value	<0.001	0.022	0.037
Multiple Proxy Estimate	2.979***	1.346***	0.984***
	(0.638)	(0.373)	(0.290)
% of Total Δ Explained	32.9%	14.9%	10.9%
Additional Controls	None	1999	2015

Note: See note on Table 1. Each column in table shows results of a different model where the dependent variable is the change in the total drug death rate per 100,000 from 1999-2015. The sample mean change in the weighted drug poisoning rate is 10.34 per 100,000 and the standard deviation is 9.06 per 100,000. Additional controls in include county population shares of: females, Hispanics, black non-Hispanics, other nonwhite non-Hispanics, age categories (15-24, 25-34, 35-44, 45-54, 55-64, 65-74, ≥75 years old), and person with some college or college graduates (among those ≥25 years old), % female headed households and foreign-born. Also included are controls for 8 urban-rural categories (metropolitan with population 250,000-999,999; metropolitan with population <250,000; urban with population ≥20,000 adjacent to a metropolitan area or not adjacent to a metropolitan area, urban with population 2,500-19,999 adjacent or not adjacent to metropolitan areas, and rural with population <2,500 and adjacent or not adjacent to metropolitan areas), active non-federal physicians and total hospital beds per 1,000 and whether the state legal medical/recreational marijuana and prescription drug monitoring program (two variables). These were measured in the year specified (1999 or 2015), except urban-rural location is from 2013, % female-headed households are from 2000 and 2010 and % foreign-born are from 2000 and the average from 2011-2015. *** p<0.01, ** p<0.05, * p<0.1

Table 3: Estimated Effect of Economic Conditions on 1999-2015 Changes in Various Types of Drug Death Rates

	(a)	(b)	(c)
<u>All Drugs</u>			
Multiple Proxy Estimate	2.979***	1.346***	0.984***
	(0.638)	(0.373)	(0.290)
% of Total Δ Explained	32.9%	14.9%	10.9%
<u>Opioid Analgesics</u>			
Multiple Proxy Estimate	1.104***	0.250**	0.138*
	(0.347)	(0.105)	(0.077)
% of Total Δ Explained	26.2%	5.9%	3.3%
<u>Illicit Opioids</u>			
Multiple Proxy Estimate	1.856***	0.917***	0.555**
	(0.512)	(0.269)	(0.270)
% of Total Δ Explained	27.8%	13.7%	8.3%
<u>All DSA</u>			
Multiple Proxy Estimate	3.246***	0.930***	0.782***
	(0.750)	(0.321)	(0.301)
% of Total Δ Explained	26.2%	7.5%	6.3%
<u>Nondrug DSA</u>			
Multiple Proxy Estimate	1.132***	0.131***	0.093***
	(0.309)	(0.037)	(0.029)
% of Total Δ Explained	15.4%	1.8%	1.3%
Additional Controls	None	1999	2015

Note: See notes on Tables 1 and 2. *** p<0.01, ** p<0.05, * p<0.1

Table 4: Estimated Effect of Economic Conditions on 1999-2015 Changes in Various Types of Drug Death Rates, Robustness Checks

	All Drugs		Opioid Analgesics		Illicit Opioids		All DSA		Nondrug DSA	
	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)
Main Model										
Multiple Proxy Estimate	1.346*** (0.373)	0.984*** (0.290)	0.250** (0.105)	0.138* (0.077)	0.917*** (0.269)	0.555** (0.270)	0.930*** (0.321)	0.782*** (0.301)	0.131*** (0.037)	0.093*** (0.029)
Dependent Var. Mean [SD]	10.37 [9.06]		3.58 [4.22]		6.27 [6.67]		15.39 [12.38]		5.02 [7.35]	
% of Total Δ Explained	14.9%	10.9%	5.9%	3.3%	13.7%	8.3%	7.5%	6.3%	1.8%	1.3%
Unweighted										
Multiple Proxy Estimate	1.082*** (0.308)	0.663** (0.257)	0.258*** (0.091)	0.097** (0.040)	0.846*** (0.176)	0.450*** (0.138)	1.059*** (0.346)	0.688*** (0.227)	-2.457*** (0.769)	-2.303*** (0.704)
Dependent Var. Mean [SD]	10.87 [13.08]		4.42 [7.05]		4.85 [7.42]		18.20 [23.93]		7.33 [19.88]	
% of Total Δ Explained	8.3%	5.1%	3.7%	1.4%	11.4%	6.1%	4.4%	2.9%	-12.4%	-11.6%
Unadjusted Mortality Rates										
Multiple Proxy Estimate			0.268** (0.112)	0.225** (0.096)	1.150** (0.450)	0.775* (0.406)				
Dependent Var. Mean [SD]			2.99 [4.09]		5.29 [6.41]					
% of Total Δ Explained			6.5%	5.5%	18.0%	12.1%				
Additional Controls	1999	2015	1999	2015	1999	2015	1999	2015	1999	2015

Note: See notes on Tables 1 through 3. Table shows multiple proxy estimates for models with additional controls for the 1999 or 2015 set of supplementary covariates. Top panel repeats the results shown in Table 2. The second panel shows estimates from corresponding models without weighting the data. Lower panel show results for changes in reported (rather than adjusted) opioid analgesic, heroin and synthetic opioid mortality rates. *** p<0.01, ** p<0.05, * p<0.1

Table 5: GMM (IV) Estimates of Effects of Economic Conditions on Changes in Drug Death Rates, 1999-2015

Economic Proxy	All Drugs	Opioid Analgesics	Illicit Opioids	All DSA	Nondrug DSA
GMM Estimates					
Δ in Poverty Rate	0.695*	-0.103	0.371	0.861*	0.150
	(0.394)	(0.181)	(0.318)	(0.497)	(0.239)
Δ in Median Household Income	1.333***	0.084	0.597*	1.223**	-0.169
	(0.458)	(0.194)	(0.345)	(0.506)	(0.265)
Δ in Median Home Price	0.813	0.032	0.462	1.262*	0.327
	(0.519)	(0.208)	(0.437)	(0.666)	(0.295)
Δ in Unemployment Rate	1.298*	-0.021	0.643	1.722**	0.274
	(0.682)	(0.245)	(0.495)	(0.803)	(0.387)
Δ in Import Exposure	3.991	-0.279	1.456	3.787	-0.670
	(2.460)	(0.800)	(1.475)	(2.572)	(1.195)
Multiple Proxy Estimate	0.984***	0.138*	0.555**	0.782***	0.093***
	(0.290)	(0.077)	(0.270)	(0.301)	(0.029)

Note: See notes on Tables 1 through 3. Each cell in the top panel of the table shows results of a different generalized method of moments estimate where the specific proxy of changes in economic conditions is instrumented by the other four proxies. The bottom panel repeats the corresponding multiple proxy estimates from Table 2. All specifications also control for the 2015 set of supplementary characteristics. Robust standard errors with clustering at the commuter zone level are shown in parentheses. *** p<0.01, ** p<0.05, * p<0.1

Table 6: Estimated Effect of Economic Conditions on 1999-2015 Changes in Drug Death Rates for Population Subgroups

Group	All Drugs		Opioid Analgesics		Illicit Opioids		All DSA		Nondrug DSA	
	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)	(a)	(b)
All	1.346***	0.984***	0.250**	0.138*	0.917***	0.555**	0.930***	0.782***	0.131***	0.093***
	(0.373)	(0.290)	(0.105)	(0.077)	(0.269)	(0.270)	(0.321)	(0.301)	(0.037)	(0.029)
	14.9%	**10.9%**	**5.9%**	**3.3%**	**13.7%**	**8.3%**	**7.5%**	**6.3%**	**1.8%**	**1.3%**
Males	1.820***	1.113***	0.275**	0.102**	1.170***	0.429**	1.279**	0.811**	0.240***	0.182***
	(0.532)	(0.369)	(0.107)	(0.046)	(0.312)	(0.208)	(0.525)	(0.343)	(0.081)	(0.061)
	14.3%	**8.8%**	**5.0%**	**1.8%**	**11.5%**	**4.2%**	**6.9%**	**4.4%**	**1.9%**	**1.4%**
Females	0.922***	0.824***	0.216**	0.156*	0.758***	0.681***	0.766***	0.833***	-0.113***	-0.166**
	(0.229)	(0.224)	(0.094)	(0.086)	(0.159)	(0.170)	(0.211)	(0.244)	(0.040)	(0.075)
	11.7%	**10.4%**	**5.1%**	**3.6%**	**17.8%**	**16.0%**	**7.7%**	**8.1%**	**-1.9%**	**-2.9%**
Whites	2.205***	1.632***	0.732***	0.409**	1.185***	0.741***	2.779***	2.347***	0.570***	0.462***
	(0.426)	(0.360)	(0.150)	(0.170)	(0.294)	(0.285)	(0.494)	(0.457)	(0.197)	(0.166)
	21.2%	**15.7%**	**15.0%**	**8.4%**	**15.4%**	**9.6%**	**19.7%**	**16.6%**	**6.5%**	**5.2%**
Nonwhite/Hispanics	0.672***	0.337**	0.103**	0.041**	0.223	0.032*	1.730***	1.557***	-1.186***	-1.225***
	(0.258)	(0.170)	(0.048)	(0.016)	(0.151)	(0.017)	(0.422)	(0.399)	(0.290)	(0.310)
	5.4%	**2.7%**	**1.5%**	**0.6%**	**3.0%**	**0.4%**	**7.8%**	**7.0%**	**-6.6%**	**-6.8%**
25-54 Years Old	2.569***	1.853***	0.371**	0.172**	2.258***	1.355***	1.600**	1.230**	0.551***	0.474***
	(0.705)	(0.641)	(0.180)	(0.084)	(0.507)	(0.510)	(0.701)	(0.619)	(0.164)	(0.164)
	13.0%	**9.4%**	**4.2%**	**2.0%**	**15.9%**	**9.5%**	**6.4%**	**5.0%**	**4.3%**	**3.7%**
Whites: Aged 25-54	4.812***	3.454***	1.268***	0.701**	2.842***	1.597***	4.286***	3.361***	0.700*	0.629*
	(0.937)	(0.748)	(0.286)	(0.273)	(0.659)	(0.563)	(1.001)	(0.806)	(0.360)	(0.382)
	21.3%	**15.3%**	**12.6%**	**6.9%**	**17.0%**	**9.6%**	**15.2%**	**11.9%**	**4.5%**	**4.1%**
Whites: Aged 45-54	1.705***	1.208***	0.728***	0.556**	0.597***	0.329**	1.780***	1.289***	0.536***	0.435**
	(0.406)	(0.360)	(0.164)	(0.220)	(0.176)	(0.154)	(0.419)	(0.441)	(0.197)	(0.211)
	16.8%	**11.9%**	**14.2%**	**10.9%**	**11.4%**	**6.3%**	**12.2%**	**8.8%**	**5.4%**	**4.3%**
≤ High School	2.253***	2.237***	0.354***	0.326***	1.558***	1.059**	1.551**	1.835**	-0.365***	-0.201**
	(0.838)	(0.677)	(0.128)	(0.115)	(0.529)	(0.493)	(0.773)	(0.758)	(0.124)	(0.089)
	9.9%	**9.8%**	**3.6%**	**3.3%**	**8.9%**	**6.0%**	**5.1%**	**6.0%**	**-2.0%**	**-1.1%**
Some College	0.818*	0.653***	0.145**	0.225**	0.737***	0.322**	0.296	0.474	0.568	0.448
	(0.418)	(0.246)	(0.073)	(0.114)	(0.197)	(0.136)	(0.413)	(0.395)	(0.386)	(0.433)
	6.6%	**5.2%**	**2.3%**	**3.6%**	**10.0%**	**4.4%**	**1.5%**	**2.3%**	**3.6%**	**2.9%**
College Graduate	0.889**	0.772**	0.182**	0.158***	0.351***	0.160**	0.605*	0.655	0.197	0.469
	(0.407)	(0.329)	(0.091)	(0.060)	(0.125)	(0.071)	(0.366)	(0.433)	(0.187)	(0.341)
	7.9%	**6.8%**	**3.3%**	**2.9%**	**7.1%**	**3.2%**	**2.8%**	**3.0%**	**1.1%**	**2.5%**
Additional Controls	1999	2015	1999	2015	1999	2015	1999	2015	1999	2015

Note: See notes on Tables 1 through 3. Top entry for each group shows the multiple proxy estimate of the effect of economic conditions on changes in the specified death rate, per 100,000 from 1999-2015. Robust standard errors clustered by commuter zone are in parentheses. The percentage of the total change in specified drug mortality rate growth explained by economic conditions is in bold. *** p<0.01, ** p<0.05, * p<0.1

Table 7: Estimated of Effects of Economic Conditions on Changes in Drug Death Rates, 1999-2015, Accounting for Selection on Unobservables

Type of Drug/Additional Covariates	Unadjusted Estimate	Adjusted Estimates			
		δ=0.5, R_{max}=0.75		δ^*	R^*_{max}
		β^*	% of Δ Explained		
	(a)	(b)	(c)	(d)	(e)
All Drugs					
1999 Covariates	1.346	0.415	4.6%	0.723	0.908
2015 Covariates	0.984	-0.194	-2.1%	0.418	0.691
Opioid Analgesics					
1999 Covariates	0.250	-0.451	-10.7%	0.178	0.473
2015 Covariates	0.138	-0.081	-19.2%	0.073	0.357
Illicit Opioids					
1999 Covariates	0.917	0.461	6.9%	1.005	>1.00
2015 Covariates	0.555	-.0202	-0.3%	0.482	0.739
All DSA					
1999 Covariates	0.930	-0.537	-4.3%	0.317	0.609
2015 Covariates	0.782	-0.711	-5.7%	0.262	0.568
Nondrug DSA					
1999 Covariates	0.131	-1.627	-22.1%	0.037	0.218
2015 Covariates	0.093	-1.627	-22.1%	0.027	0.214

Note: See notes on Tables 1 through 3. Column (a) shows multiple proxy estimates without correction for selection on unobservables (from Table 3). Columns (b) and (c) show the selection-adjusted treatment effect and% of the change in mortality rates explained, assuming that δ=0.5 and R_{max}=0.75. Column (d) shows the value of δ that would give an estimated zero treatment effect, with R_{max}=0.75, and column (e) shows the R_{max} value that would do so, with δ=0.5.

Figure 1: Drug, Nondrug Suicide and Alcohol (DSA) Mortality Rates

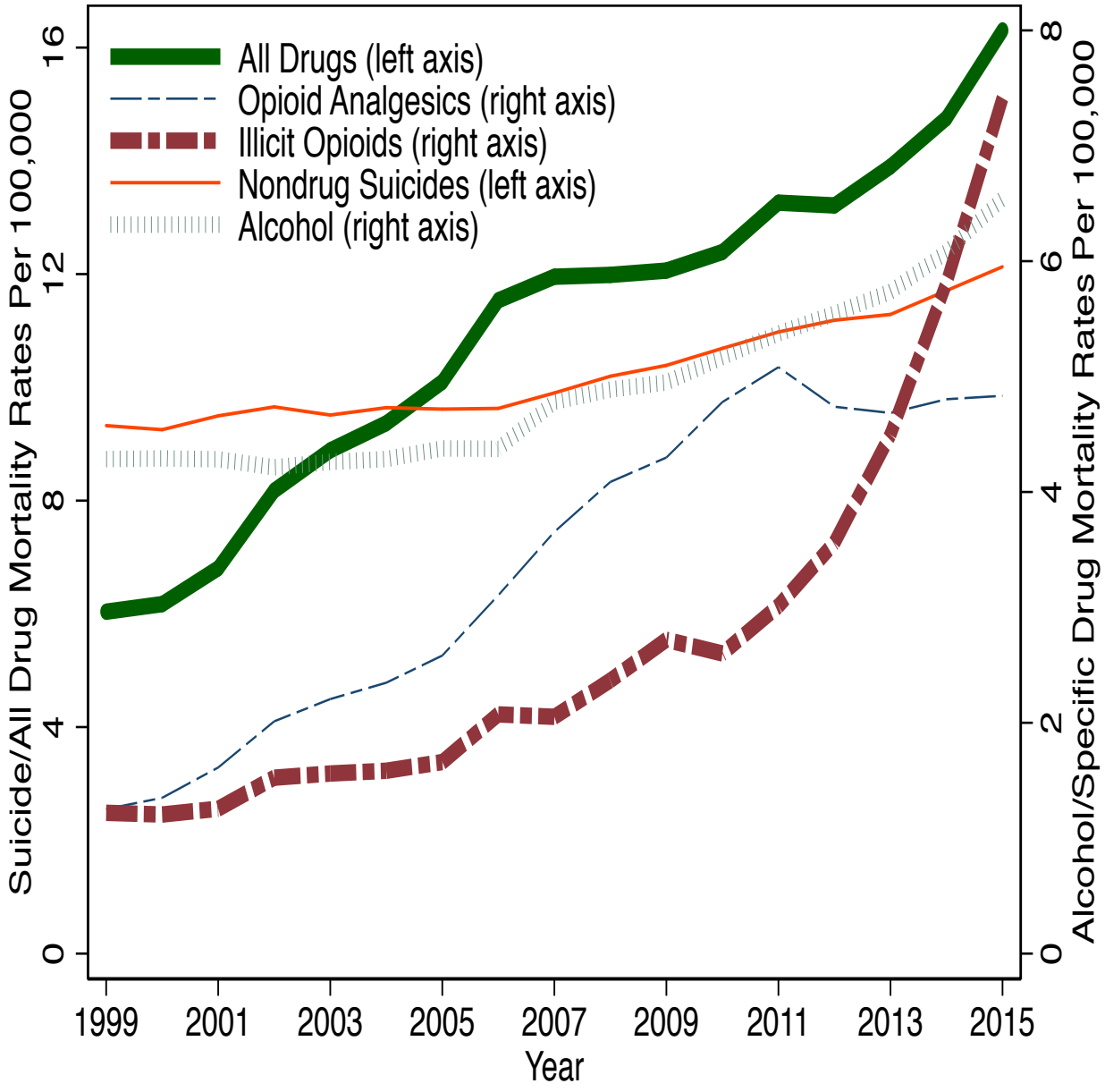

Figure 2: Drug Mortality Rates For Population Subgroups

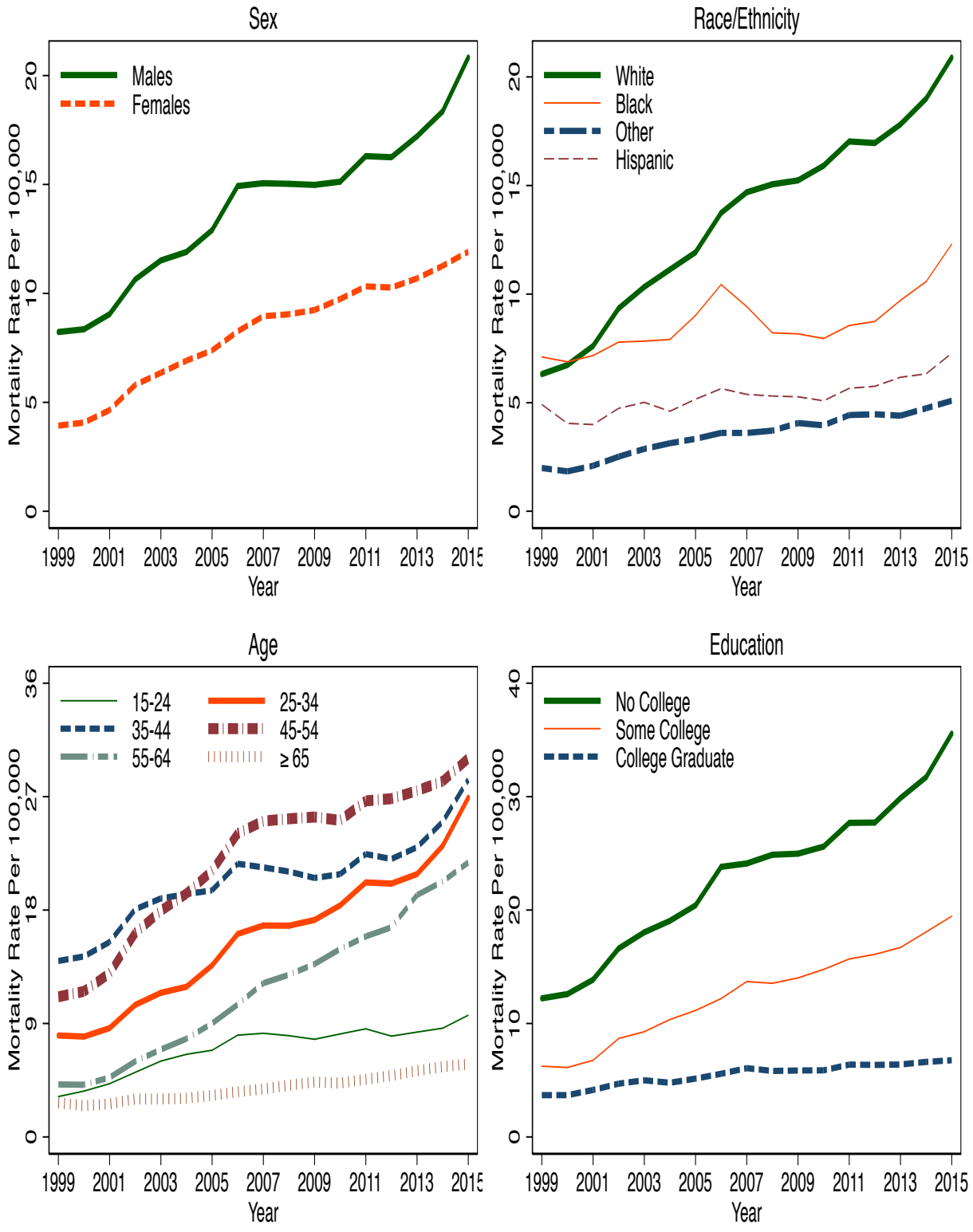

Figure 3: Nondrug Mortality Rates for Population Subgroups

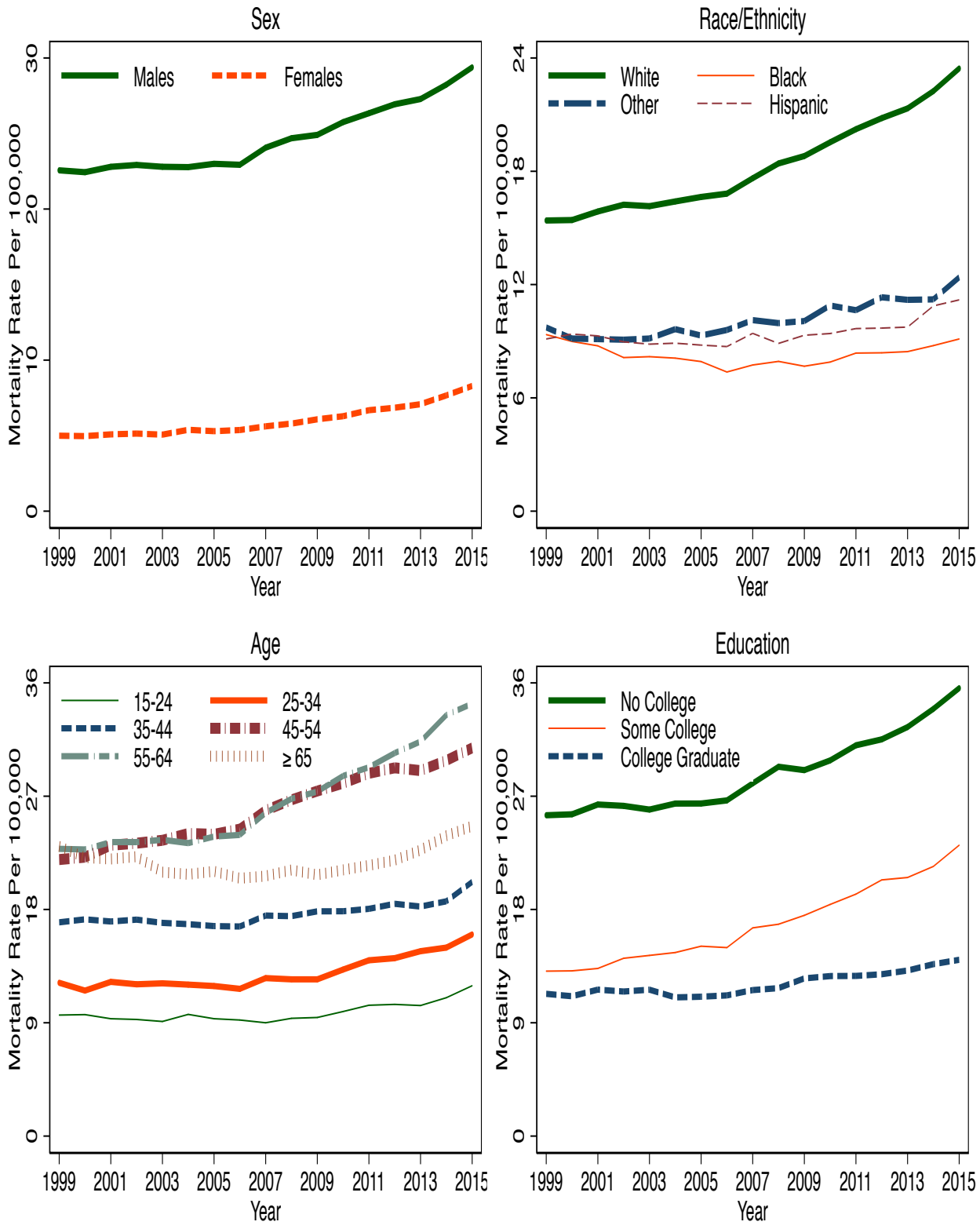

Figure 4: Opioid Analgesic and Illicit Opioid Mortality Rates for Selected Population Subgroups

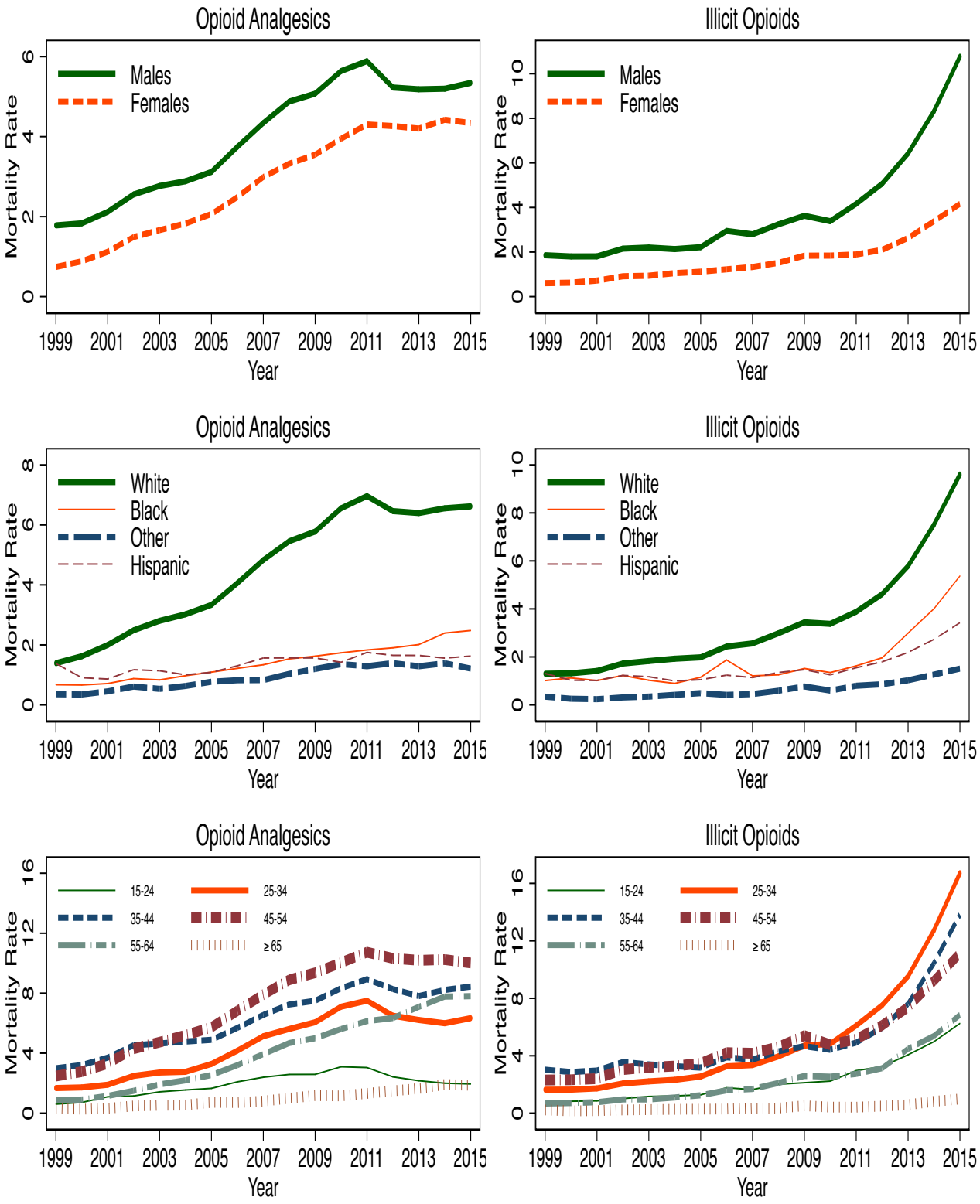

Table A.1: Summary Statistics for Variables Used in Main Analysis

Variable	Mean	Std. Dev
Outcomes: Δ in Drug Death Rates per 100,000 (2015 vs. 1999)		
All Drugs	10.37	9.06
Opioid Analgesics	3.58	4.22
Illicit Opioids	6.27	6.67
Drug, Suicide, Alcohol (DSA)	15.39	12.38
Nondrug DSA	5.02	7.35
Nondrug Suicide	2.76	5.67
Alcohol	2.26	4.21
Economic Proxies (Δ 2015 vs. 1999)		
Poverty Rate (3-year average)	2.93	2.47
Median Household Income (3-year average, 2015$	-2,817	5,586
Median Home Price, 2015$: %Δ (2011-2015 average vs. 2000)	17.85	22.31
Unemployment Rate (3-year average)	1.77	1.56
Instrumented Import Share of Employment (2007 vs. 1990)	3.29	2.03

Additional Covariates (1999 & 2015)	*1999*		*2016*	
Population Shares	Mean	SD.	Mean	SD.
Females	0.509	0.012	0.508	0.012
Hispanics	0.123	0.148	0.172	0.164
Non-Hispanic Blacks	0.121	0.128	0.131	0.127
Other Race (Non-Hispanics)	0.045	0.054	0.066	0.067
15-24 Year Olds	0.139	0.029	0.137	0.027
24-34 Year Olds	0.145	0.023	0.137	0.025
34-44 Year Olds	0.162	0.014	0.126	0.014
44-54 Year Olds	0.131	0.012	0.134	0.013
54-64 Year Olds	0.085	0.013	0.127	0.017
64-74 Year Olds	0.065	0.019	0.086	0.021
≥ 75 Year Olds	0.058	0.019	0.063	0.019
Some College (≥25 years old)	0.275	0.048	0.294	0.049
College Graduate (≥25 years old)	0.242	0.095	0.306	0.109
Female-headed Household (2000, 2010)	0.179	0.059	0.198	0.060
Foreign born (2000, 2011-2015)	0.109	0.102	12.924	0.105
Medical/Policy Variables (2015)				
Active Nonfederal MD's per 1000	2.514	1.903	2.761	2.054
Hospital beds per 1000: 2015	3.603	2.713	2.896	2.058
Marijuana Legal in State for Medical/Recreational Uses	0.160	0.367	0.465	0.499
State Prescription Drug Monitoring Program	0.195	0.396	0.919	0.273
Urban-Rural Status Share (2013)				
Metropolitan Area: Population 250,000 - 999,999	0.210	0.408	0.210	0.408
Metropolitan Area: Population <250,000	0.092	0.289	0.092	0.289
Urban Area: Population ≥20,000, adjacent to metro	0.043	0.203	0.043	0.203
Urban Area: Population ≥20,000, not adjacent to metro	0.015	0.122	0.015	0.122
Urban Area: Population 2,500-19,999, adjacent to metro	0.047	0.211	0.047	0.211
Urban Area: Population 2,500-19,999, not adjacent to metro	0.026	0.158	0.026	0.158
Rural Area: Population <2,500, adjacent to metro	0.007	0.082	0.007	0.082
Rural Area: Population <2,500, not adjacent to metro	0.008	0.089	0.008	0.089

Note: Variables are measured at the county level and weighted by 2015 county populations. Independent variables are standardized to have a mean of 0 and a standard deviation of 1 in the econometric analysis. Death rates involving opioid analgesics, heroin and synthetic opioids are adjusted for incomplete reporting on death certificates using the methods discussed in the text. Entries in parentheses indicate if

variable dates are different from 1999 or 2015. Prescription drug monitoring programs (PDMP) are those with requirement that dispensers must report data to PDMP. For poverty, unemployment rates and household incomes, the variables are three-year averages ending in the year specified.

Table A.2: Correlations Between Economic Proxies

	Poverty	Income	Home Prices	Unemployment	Imports
Poverty	1.000				
Income	-0.702	1.000			
Home Prices	-0.530	0.641	1.000		
Unemployment	0.487	-0.436	-0.284	1.000	
Imports	0.080	-0.016	-0.027	0.107	1.000

Note: Table shows correlations between economic proxies with observations weighted by 2015 county populations. Proxy names are abbreviated (e.g. “Unemployment” refers to the change in the unemployment rate.

Table A.3: Multiple Proxy Estimates of Effect of Economic Conditions on Changes in Various Types of Drug Death Rates For Selected Time Periods

	Opioid Analgesics		Illicit Opioids	
1999-2015				
Multiple Proxy Estimate	0.250**	0.138*	0.917***	0.555**
	(0.105)	(0.077)	(0.269)	(0.270)
Dependent Var. Mean [SD]	3.58 [4.22]		6.27 [6.67]	
% of Δ Explained	5.9%	3.3%	13.7%	8.3%
1999-2011				
Multiple Proxy Estimate	0.362***	0.396***		
	(0.105)	(0.124)		
Dep. Var. Mean	3.81 [4.76]			
% of Δ Explained	7.6%	8.3%		
2006-2015				
Multiple Proxy Estimate			0.249***	-0.085***
			(0.061)	(0.022)
Dep. Var. Mean			5.42 [6.15]	
% of Δ Explained			5.8%	-2.0%
Additional Controls	Start Year	End Year	Start Year	End Year

Note: See notes on Tables 1 through 4. Table shows multiple proxy estimates for models with additional controls for the start year (1999 or 2006) or end year (2011 or 2015) of analysis. When 2011 is the ending year, the ending period for measuring changes in home prices is 2007-2011 and 2011 covariates include the average share foreign born in 2006-2010. When 2006 is the first analysis year, initial year home prices are averaged from 2005=2009.
. *** p<0.01, ** p<0.05, * p<0.1

Table A.4: Dependent Variable Descriptive Statistics for Population Subgroups

Group	All Drugs		Opioid Analgesics		Illicit Opioids		All DSA		Nondrug DSA	
	Mean	Std. Dev	Mean	Std. Dev	Mean	Std. Dev	Mean	Std. Dev	Mean	Std. Dev
All	10.37	9.06	3.58	4.22	6.27	6.67	15.39	12.38	5.02	7.35
Males	12.79	12.70	3.57	5.51	9.08	10.17	19.56	18.61	6.77	12.61
Females	8.04	7.91	3.61	4.28	3.58	4.27	11.29	10.26	3.24	5.82
Whites	13.85	10.38	4.90	4.87	7.90	7.70	21.48	14.12	7.63	8.84
Nonwhite/Hispanics	4.81	12.49	1.45	7.03	3.53	7.42	6.55	22.30	1.74	18.05
25-54 Years Old	18.00	19.71	6.05	8.77	11.92	14.19	23.68	24.87	5.68	12.95
Whites: Aged 25-54	24.80	22.60	8.35	10.09	15.44	16.69	33.88	28.22	9.08	15.51
Whites: Aged 45-54	9.71	10.12	3.07	5.11	3.26	5.25	15.68	14.60	5.97	10.00
≤ High School	24.01	22.72	7.90	9.80	14.59	17.60	34.17	30.37	10.16	18.01
Some College	12.03	12.48	4.24	6.34	6.54	7.38	20.65	20.31	8.61	15.55
College Graduate	3.49	11.31	1.82	5.53	1.82	4.92	6.80	21.54	3.31	18.53

Note: Table shows average growth between 1999 and 2015 for specified type of drug mortality and population subgroup. Observations are weighted by 2015 county populations.

Table A.5: Estimated Effect of Economic Conditions on Changes in Nondrug Suicide and Alcohol Death Rates, 1999-2015

Economic Proxy	Nondrug Suicide	Alcohol
No Covariates: Measures Included Separately		
Δ in Poverty Rate	0.012	0.103
	(0.195)	(0.182)
Δ in Median Household Income	0.228	0.220
	(0.191)	(0.200)
Δ in Median Home Price	0.387**	0.165
	(0.182)	(0.191)
Δ in Unemployment Rate	-0.289	0.063
	(0.184)	(0.194)
Δ in Import Exposure	-0.057	-0.196
	(0.138)	(0.136)
No Covariates: Measures Included Together		
Δ in Poverty Rate	-0.205	-0.083
	(0.181)	(0.158)
Δ in Median Household Income	0.279	0.243
	(0.238)	(0.206)
Δ in Median Home Price	0.440**	0.057
	(0.205)	(0.195)
Δ in Unemployment Rate	-0.434**	0.002
	(0.184)	(0.177)
Δ in Import Exposure	-0.010	-0.195
	(0.128)	(0.137)
R2	0.011	0.005
P-Value	0.001	0.532
Multiple Proxy Estimate	0.924***	0.422*
	(0.228)	(0.248)
% of Total Δ Explained	16.3%	10.0%
Dependent Var. Mean [SD]	2.76	2.25
Models with 1999 Covariates		
Multiple Proxy Estimate	0.190***	0.318***
	(0.049)	(0.094)
% of Total Δ Explained	3.4%	7.5%
Models with 2015 Covariates		
Multiple Proxy Estimate	0.181***	0.335***
	(0.051)	(0.072)
% of Total Δ Explained	3.2%	7.9%
GMM (IV) Estimates, Models with 2015 Covariates		
Δ in Poverty Rate	-0.384**	0.455***
	(0.170)	(0.155)
Δ in Median Household Income	-0.445***	0.376**
	(0.170)	(0.175)
Δ in Median Home Price	-0.408*	0.621***

	(0.222)	(0.236)
Δ in Unemployment Rate	-0.641**	0.860***
	(0.263)	(0.252)
Δ in Import Exposure	-2.473**	2.224***
	(1.045)	(0.843)

Note: See note on Tables 1-3 and 5. Models estimated are the same as in those tables, but with different sources of death.

Figure A.1: DSA Mortality Rates by Sex

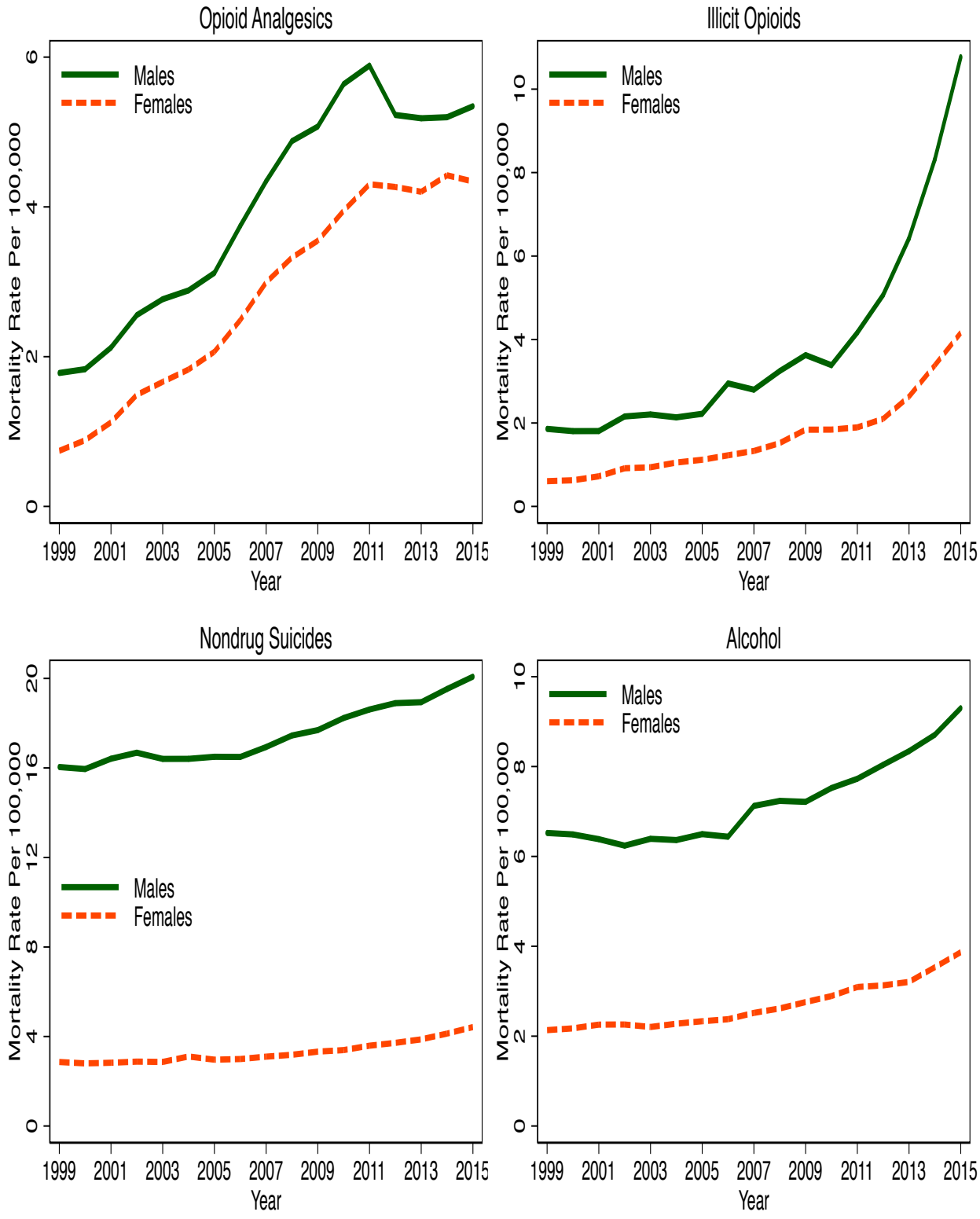

Figure A.2: DSA Mortality Rates by Race/Ethnicity

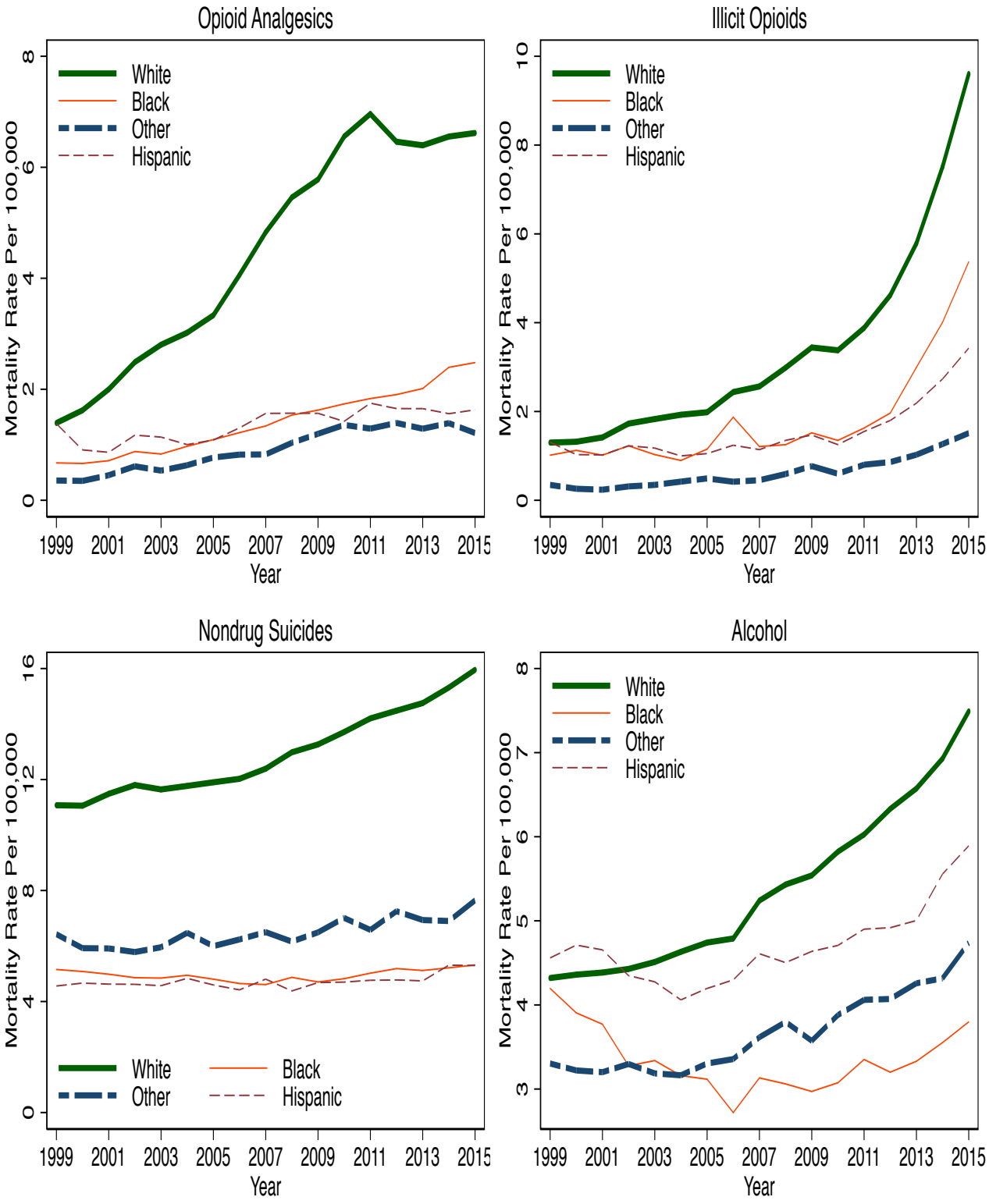

Figure A.3: DSA Mortality Rates by Age

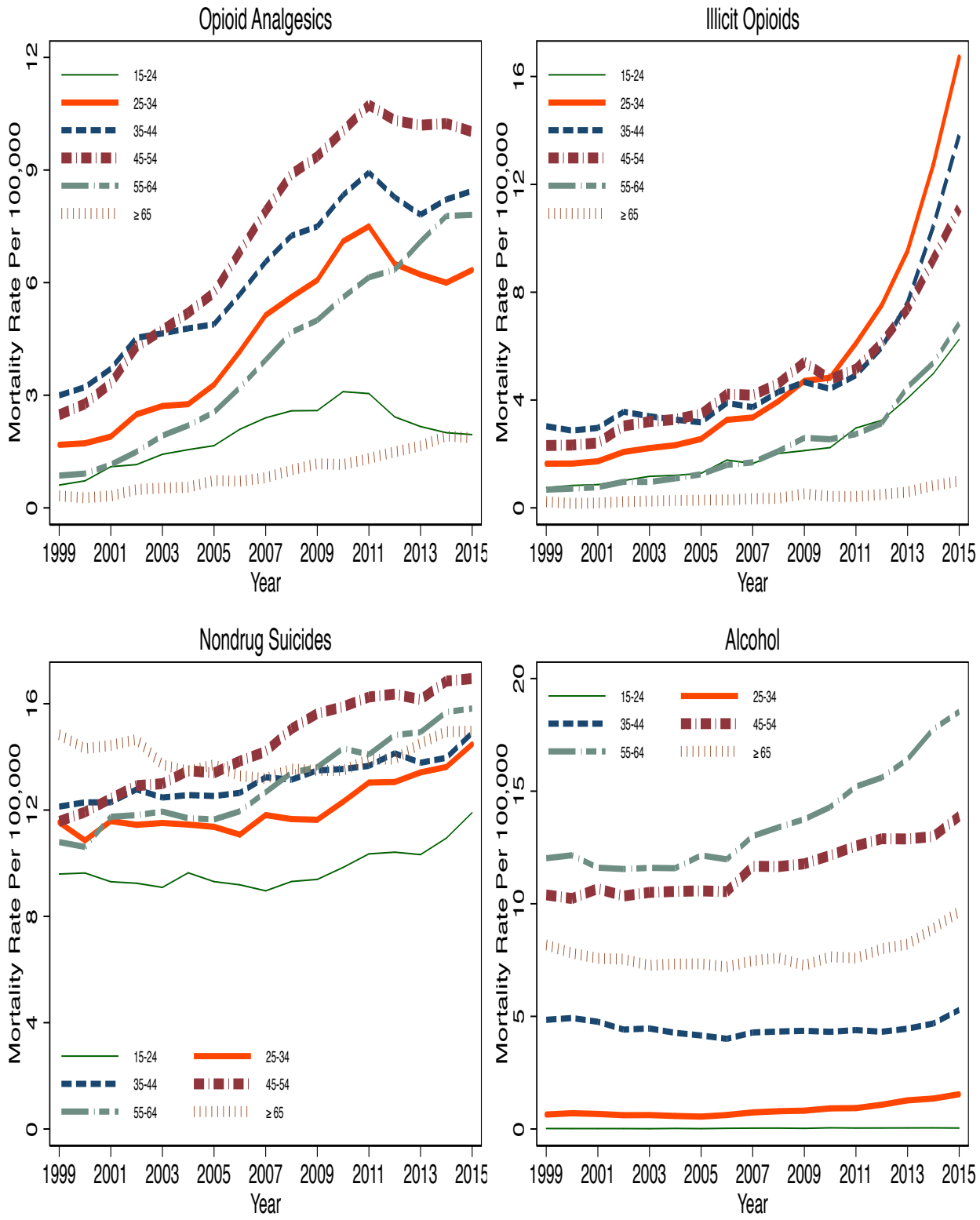

Figure A.4: DSA Mortality Rates by Education