The economic underpinnings of the drug epidemic

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A B S T R A C T

U.S. labor markets have experienced transformative change over the past half century. Spurred on by global economic change, robotization, and the decline of labor unions, state labor markets have shifted away from an occupational regime dominated by the production of goods to one characterized by the provision of services. Prior studies have proposed that the deterioration of employment opportunities may be associated with the rise of substance use disorders and drug overdose deaths, yet no clear link between changes in labor market dynamics in the U.S. manufacturing sector and drug overdose deaths has been established. Using restricted-use vital registration records between 1999 and 2017 that comprise over 700,000 drug deaths, I test two questions: First, what is the association between manufacturing decline and drug and opioid overdose mortality rates? Second, how much of the increase in these drug-related outcomes can be predicted by manufacturing decline? The findings provide strong evidence that the restructuring of the U.S. labor market has played an important upstream role in the current drug crisis. Up to 92,000 overdose deaths for men and up to 44,000 overdose deaths for women are predicted by the decline of state-level manufacturing over this nearly two-decade period. These results persist in models that adjust for other social, economic, and policy trends changing at the same time. Critically, the findings signal the value of policy interventions that aim to reduce persistent economic precarity experienced by individuals and communities, especially the economic strain placed upon the middle class.

1. Introduction

The ongoing drug epidemic is one of the most consequential public health issues in the United States right now. Drug overdose deaths in the United States continued to rise through 2017, reducing overall life expectancy for the third year in a row – a trend in life expectancy that has not occurred in over a century (Hedegaard, Warner, and Miniño 2018; Murphy et al., 2018; Woolf and Schoomaker 2020). Nationally, drug overdose death rates increased from 6.1 deaths per 100,000 population in 1999 to 21.7 deaths per 100,000 population in 2017 (Murphy et al., 2018,). Despite a slight decline to 20.7 deaths per 100,000 in 2018 (Hedegaard et al., 2020), preliminary counts of overdose deaths from 2019 indicate a resurgence to 2017 levels (Ahmad et al., 2020).

Researchers have debated the extent to which social and economic determinants of health are meaningful explanations of the U.S. drug and opioid epidemic, with a particular emphasis on the opioid epidemic (Case and Deaton 2015, 2018; Dasgupta, Beletsky, and Ciccarone 2018; Ruhm, 2019). While some emphasize the importance of pharmaceutical companies in increasing the legal supply of prescription opioids to the public (e.g. Ruhm, 2019), others emphasize the role of structural economic change and economic despair as demand-side drivers of rising

rates of substance use (e.g. Case and Deaton 2015; 2017; Monnat, 2019). Yet, this framing of dueling supply-side and demand-side explanations overlooks the endogenous interrelationship between both supply and demand. Drug and opioid overdose deaths are not distributed randomly across the country, but are clustered in places with longstanding economic decline. Analyses of the geospatial patterning of the opioid epidemic indicate that areas with higher economic precarity – higher rates of poverty, higher rates of unemployment, and lower median home values, for instance – also had higher rates of filled opioid prescriptions, opioid-related hospital visits, and ultimately, opioid overdose deaths (Ghertner & Groves, 2018; Monnat, 2019; Schoenfeld et al., 2019). A full accounting of the origins of the opioid epidemic therefore necessitates a broader examination of how contextual economic conditions are associated with the rise of opioid deaths.

Prior studies have proposed that long-term changes in economic conditions, including the deterioration of employment opportunities in U.S. labor markets and the rise of economic insecurity for families, may be associated with the rise of substance use disorders and drug overdose mortality rates more generally (Betz and Jones 2018; Case & Deaton, 2017; Ghertner & Groves, 2018; Hederos et al., 2017; McLean, 2016; Monnat, 2018; Nosrati et al., 2017). Understanding this relationship is

necessary for multiple reasons. Establishing whether drug-related overdose deaths are attributable to upstream social and economic factors opens additional avenues of clinical, public health, and public policy intervention to stem the ongoing rise of drug overdose deaths. It may also shed light on regional variation in epidemic intensity and facilitate prediction of trends in these rates. Many of the hardest hit regions of the ongoing drug and opioid crisis have also endured decades of deteriorating economic conditions (Dasgupta et al., 2018; Ezzati et al., 2008; Zoorob & Salemi, 2020). Investigating this relationship informs social scientists about the scope conditions under which social and economic contexts are salient predictors of population-level health outcomes.

The present study considers how structural economic change – specifically, the decline of employment opportunities in the manufacturing sector – are associated with the rise of drug deaths since the late 1990s. Over the past half century, the United States labor market has experienced an industrial restructuring that has fundamentally reshaped the employment opportunities available to American workers, particularly for those with only a high school degree (Acemoglu & Autor, 2011; Autor & Dorn, 2013; Autor et al., 2006; Kalleberg, 2009). Spurred on by global economic change, robotization, and the decline of labor unions, U.S. labor markets have shifted away from an occupational regime dominated by the production of manufactured goods to one characterized by the provision of services. This new occupational structure has prompted the job polarization of U.S. labor markets, wherein the decline of largely middle-wage employment in manufacturing sectors has been accompanied by the rise of employment growth in low-wage and high-wage service sectors (Autor et al., 2006).

Although this structural transformation of U.S. labor markets began in the 1970s, the decline of employment opportunities in the manufacturing sector accelerated rapidly during the 2000s with the loss of nearly 5.4 million jobs (Atkinson et al., 2012). In comparison to the 1980s and the 1990s, when manufacturing employment decreased on average by about 0.5% per year, manufacturing employment decreased on average by 3.7% per year in the 2000s (Fig. 1). And although the manufacturing sector experienced a resurgence of employment growth following the Great Recession throughout the 2010s, only about 1.3 million manufacturing jobs were regained out of the initial 5.4 million that were lost since the early 2000s. Additionally, these new manufacturing jobs were less likely to pay as well as manufacturing jobs created in past decades (Jacobs et al., 2016). Overall, the decline of manufacturing jobs has resulted in the stagnation of wage growth and

the depletion of financial resources for the American middle class (Kalleberg, 2009; Kalleberg & von Wachter, 2017). Middle-income households held 62% of aggregate household income at the start of the 1970s. They now hold less than 43% of aggregate household income, largely the result of declining middle-wage jobs (Pew Research Center, 2015).

Recent research in the social and biomedical sciences has raised important questions about the implications of these and other structural economic changes on the mental health and emotional well-being of the middle class. Scholars theorize that the restructuring of labor markets, the rise of precarious work arrangements, and an overall stagnation of economic opportunity for many, has stimulated the rise of economic anxiety (Brand, 2015; Case & Deaton, 2015; Kalleberg, 2018; Kirsch & Ryff, 2016; Lim, 2017; McCall et al., 2017; Thiede & Monnat, 2016). Job loss, economic disinvestment, and out-migration from local labor markets and communities influence perceptions of economic opportunity, which in turn are associated with several indicators of worsened physical and mental health (Burgard et al., 2009; Catalano, 1991; Charles & DeCicca, 2008; McLean, 2016; Zivin et al., 2011). One of the clearest manifestations of this hypothesized process is the recent intensification of diagnoses of substance use disorders and drug overdose deaths (Gaydosh et al., 2019; Murphy et al., 2018). Both quantitative and qualitative research accounts suggest that local risk environments characterized by dampened economic opportunity can influence substance use (McLean, 2016; Monnat, 2019; Venkataramani et al., 2020). In this sense, drug deaths may represent a particularly extreme version of individual-level responses to societal pressures.

The present study contributes a sociological perspective to literature on the ongoing drug and opioid epidemic by emphasizing the role of institutions in shaping both social and economic contexts that impact health outcomes. Legislative and regulatory strategies for spurring industrial growth and addressing the oversupply of prescription opioids vary considerably across state borders, which motivates the importance of state-level comparisons that account for heterogenous social, economic, and political contexts.

Using this state-level framework, I combine economic and business activity data from multiple sources with annual drug and opioid overdose mortality data from the National Center for Health Statistics to answer two questions. First, what is the association between manufacturing decline and drug and opioid overdose mortality rates? Second, how much of the increase in these overdose mortality outcomes can be predicted by manufacturing decline? I use a research design that
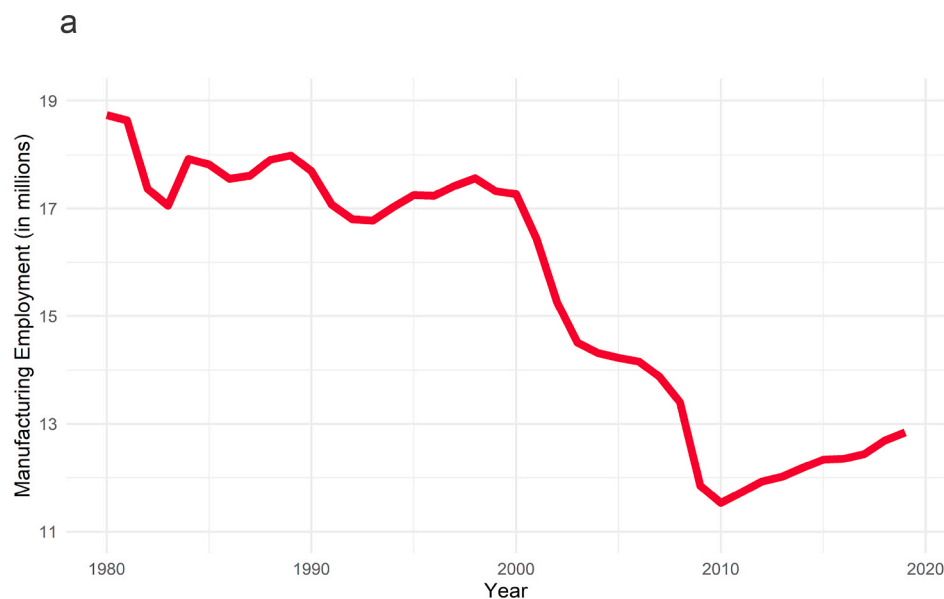
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Fig. 1a. Total number of workers employed in the manufacturing sector, 1980–2019.
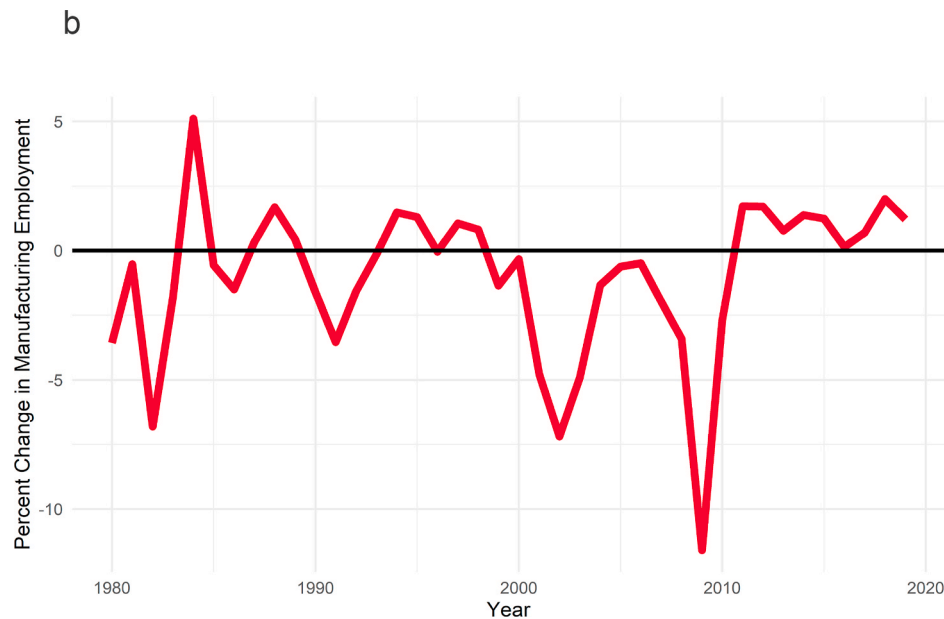
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Fig. 1b. Annual Percent Change in Manufacturing Employment, 1980-2019.
Data Source: U.S. Bureau of Labor Statistics, All Employees, Manufacturing [MANEMP], retrieved from FRED, Federal Reserve Bank of St. Louis; https://fred.stloui sfed.org/series/MANEMP, January 28, 2020.

leverages variation both within states and within time periods to side-step endogeneity concerns that complicate identification. I use data from the Census Bureau's County Business Patterns program to examine how the decline in the relative share of state-level employment and earnings in manufacturing industries impacts drug and opioid mortality, net of factors that shape the supply of opioids and changes in other state-level contextual and compositional processes. This analysis is augmented by the estimation of a series of alternate specifications, including county-level models, to further evaluate the robustness of the results. The findings suggest strong evidence that the industrial restructuring of the U.S. labor market – the decline of manufacturing, in particular – has likely played an important upstream role in the current drug and opioid crisis. Up to 92,000 overdose deaths for men and up to 44,000 overdose deaths for women are predicted by the decline of state-level manufacturing over this nearly two-decade period.

2. Background

2.1. Economic deterioration and negative health outcomes

Social scientists have increasingly turned their attention towards the link between macroeconomic conditions, individual-level experiences of the labor market, and physical and mental health outcomes. Prior individual-level analyses on job displacement and plant closures in the U.S. and in European countries have demonstrated that involuntary job loss is associated with an array of negative health related outcomes, including decreased mental and physical health functioning (Riu-mallo-Herl et al., 2014; Schaller & Stevens, 2015), decreased self-reported health (Huijts et al., 2015; Strully, 2009), increased ciga-rette smoking and alcohol consumption (Black et al., 2015; Gallo et al., 2001), and increased short-term and long-term risks of all-cause mor-tality (Browning & Heinesen, 2012; Sullivan & von Wachter, 2009). Studies have documented how increased economic strain (Schaller & Stevens, 2015; Strully, 2009; Sullivan & von Wachter, 2009), decreased employment prospects and precarious employment situations (Janoski, Luke, & Oliver, 2014; Strully, 2009), and reduced access to health in-surance and reduced health care use (Jolly & Phelan, 2017; Schaller & Stevens, 2015; Sullivan & von Wachter, 2009) raise the likelihood of experiencing adverse health outcomes and behaviors, including alcohol

and cigarette usage.

Population substance use, including opioid use, may increase during periods of economic deterioration through multiple pathways. This may occur directly through the heightened stress of job displacement on in-dividuals and their families, or indirectly through population health impacts initiated by dampened economic opportunity and increased economic insecurity within labor markets. The individual-level experi-ence of job displacement, and the resultant economic strain and reduction of resources, fosters a risk-environment that increases the likelihood of substance abuse (Mclean, 2018; Merline et al., 2004; Rhodes, 2009; Rolfs et al., 2012).

Yet, the direct experience of job displacement for laid off workers does not fully account for the massive growth of substance use disorders and drug overdose deaths in communities that have experienced eco-nomic deterioration over the past several decades. Several pathways operate outside of individual-level effects. For example, the economic consequences of job loss and business disinvestment from labor markets extend beyond displaced workers to their families and to the broader community; these effects appear to have spillover health costs (Adda & Fawaz, 2019; Broman et al., 1990; Colantone et al., 2019; Lang et al., 2019). Long-term economic change like manufacturing decline alters the opportunity structures of labor markets and influences perceptions of economic uncertainty, which in turn increases physical and mental health issues (Colantone et al., 2019; Lang et al., 2019).

Indeed, several recent studies have suggested a link between eco-nomic deterioration in labor markets and increased opioid deaths. Monnat (2018), found a cross-sectional association between manufacturing dependence and average drug-related mortality rates across U.S. counties. In a separate analysis, Monnat (2019) found that drug mortality rates for non-Hispanic whites are larger in counties designated as service sector-dependent in comparison to counties designated as non-specialized. Likewise, Pierce and Schott (2016), examining the impact of U.S. trade policy on cause-specific mortality from three categories of deaths of despair, found that the implementa-tion of trade liberalization policies predicted increased mortality rates from accidental poisonings for white men and women, but not for other racial/ethnic groups. In contrast to these findings, Ruhm (2019), examining changes in county-level drug mortality rates between 1999 and 2015, reported a positive, albeit non-significant, association

between Chinese import penetration and increased drug mortality rates; but overall, he concludes that economic conditions (including other economic measures besides import penetration) explain less than 10% of the drug epidemic. Finally, Venkataramani et al. (2020) research on the relationship between automotive plant closures in local communities and opioid overdose mortality suggests that discrete economic shocks within commuting zone labor markets are associated with county-level increases in opioid overdose deaths.

The present study builds on and contributes to this literature by using an identification strategy that supports attribution of drug and opioid deaths to upstream economic change—and the shift from manufacturing to service employment in particular. I leverage annual variation in state-level manufacturing change to estimate drug and opioid overdose mortality. The panel design models a data generating process in which yearly fluctuations in employment conditions have immediate impacts on substance use and drug overdose deaths.

Though past findings have asserted that the rise of drug deaths throughout this time period are mostly concentrated among middle-age white men (e.g. Case & Deaton, 2015), recent studies have documented a counter-narrative: deaths of despair have substantially increased for a more expansive set of racial/ethnic groups, as well as for women (Alexander, Kiang, and Barbieri 2018; Gaydosh et al., 2019; Woolf et al., 2018). In light of these findings, I further investigate whether structural economic changes have differentially influenced drug mortality across racial/ethnic and gender subgroups by estimating a set of sensitivity models that predict age-, sex-, and race/ethnicity-specific drug deaths.

2.2. State-level heterogeneity in socio-political policy regimes

Rising differentiation in state-level health and economic policies have contributed to an increasingly common practice of conceptualizing the state as a laboratory to study population welfare (Montez et al., 2020; Montez, Hayward, and Zajacova 2019). Indeed, state-level contexts and policies are important determinants of population health outcomes, specifically (Bradley et al., 2016; Kim & Jennings Jr., 2009; Montez et al., 2019). State legislative and regulatory decisions influence population health outcomes directly through health policies such as tobacco control and Medicaid expansion, but also indirectly through social and economic policies in domains such as education and the criminal justice system (Massoglia & Remster, 2019; Miller et al., 2019; Montez et al., 2020), which stratify health outcomes within and across state populations. Policies concerning economic development and the rise of opioid prescriptions vary dramatically across states, and rather than being viewed as distinct, separate state policies, are better conceptualized as components of broader socio-political policy regimes that influence the daily lives of residents. As noted by Montez et al. (2019), state-level authority has increasingly taken precedence over both federal- and local-level authority over the past several decades.

Additionally, the pace and character of industrial change over the past three decades has differed markedly across states. These differences arise in part because of differences across state labor markets in the routinizability and offshoreability of occupational tasks in certain manufacturing sectors (Acemoglu & Autor, 2011; Autor & Dorn, 2013),[1] but also because of state-level policies that create incentives for manufacturers to stay put or to relocate plants. That is, states actively contend with one another as well as with international competitors to retain and attract manufacturing jobs. In order to promote economic development and industrial growth, policy approaches used by states have included financial incentives, corporate tax subsidies, labor deregulation, and the softening of environmental regulations, among others (Eisinger, 1988; Grant and Wallace 1994; Bartik, 1988; Gray and Lowery, 1990; Giroud

and Rauh, 2019). Variation in the legislation and implementation of these state-level industrial policies and labor contexts as well as the outcomes of these policies further motivate the importance of state-level comparisons and the usage of state fixed effects. Nationally, the share of jobs in manufacturing industries declined by an average of 5.8 percentage points between 1998 and 2016, from 15.2% in 1998 to 9.4% in 2016 (Fig. 2A, data and measurement described below). In this same time period, the share of total annual payroll in manufacturing industries declined by an average of 7.2 percentage points, from 18.6% in 1998 to 11.4% in 2016 (Fig. 2B). This average national decline masks substantial state-level variation. Arkansas, Rhode Island, Tennessee, North Carolina, and South Carolina experienced large declines in manufacturing employment of over 8 percentage points, while states such as Nevada, Wyoming, and Hawaii experienced declines of less than 2 percentage points.

An analysis examining the effects of state-level economic change on health and mortality must also be attentive to other contemporaneous social, economic, and compositional changes that might confound estimation. To address this concern, the models adjust for a set of theoretically relevant, time-varying compositional and contextual population-level characteristics, including educational attainment, race/ethnicity, marital status, population age structure, and self-reported health (Chetty et al., 2016; Schoenfeld et al., 2019). Based on prior literature that documents how companies move production operations to labor markets with cheaper labor costs and labor protections (Grant and Wallace 1994), I adjust for state-level trends in the percentage of workers represented by labor unions.[2] I adjust for state-level trends in labor force participation rates because shifts in labor force participation are associated with changes in population health outcomes and cause-specific mortality rates, including deaths from drugs and alcohol (Case & Deaton, 2017). The labor force participation rate is conceptually distinct from the relative share of manufacturing employment since it quantifies attachment to the labor force rather than the industrial characteristics or qualities of jobs in a labor market.

For the study of opioids specifically, there is also relevant state-level variation in policies that have facilitated the local *supply* of opioids. State governments have enacted an array of policy strategies to address the opioid epidemic. For instance, the creation of Prescription Drug Monitoring Program's (PDMPs), state-run electronic databases that allow prescribers, dispensers, and other health authorities to track the prescription patterns of controlled substances for individual patients, has become a widely adopted policy intervention used by states to reduce the amount of opioid painkillers prescribed to patients (Bao et al., 2017; Cerdá et al., 2020; Fink et al., 2018). States have also enacted other policy interventions such as laws that aim to regulate pain management clinics, increase access to naloxone, and improve legal protections for bystanders who report drug overdoses as they are occurring. The outcomes of these policies, whether effective in reducing substance use and opioid deaths or not, has varied (e.g. Doleac and Mukherjee 2018). I adjust for the implementation of PDMPs, naloxone access laws, and Good Samaritan laws, to account for these major drug policy interventions. Given data availability limitations for the full 19-year time period, I adjust for state-level trends in the supply of legally dispensed opioid prescriptions in sensitivity analyses that span the years 2007-2017, thereby netting out the supply of legal opioids. As an alternative strategy, I additionally test for differences across states that had implemented "triplicate" programs – early versions of PDMPs – in the 1990s. States with triplicate policies have experienced slower growth in opioid overdose deaths over the past two decades, largely the result of receiving a smaller supply of prescription opioids than non-triplicate states (Alpert et al., 2019).

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[1] For instance, manufacturing employment in the automobile industry decreased for midwestern states while increasing for southern states (Cutcher-Gershenfeld et al., 2015).

[2] I also tested for the percentage of workers in a state labor force who were *members* of labor unions rather than those covered/represented by labor unions. The results are approximately the same.
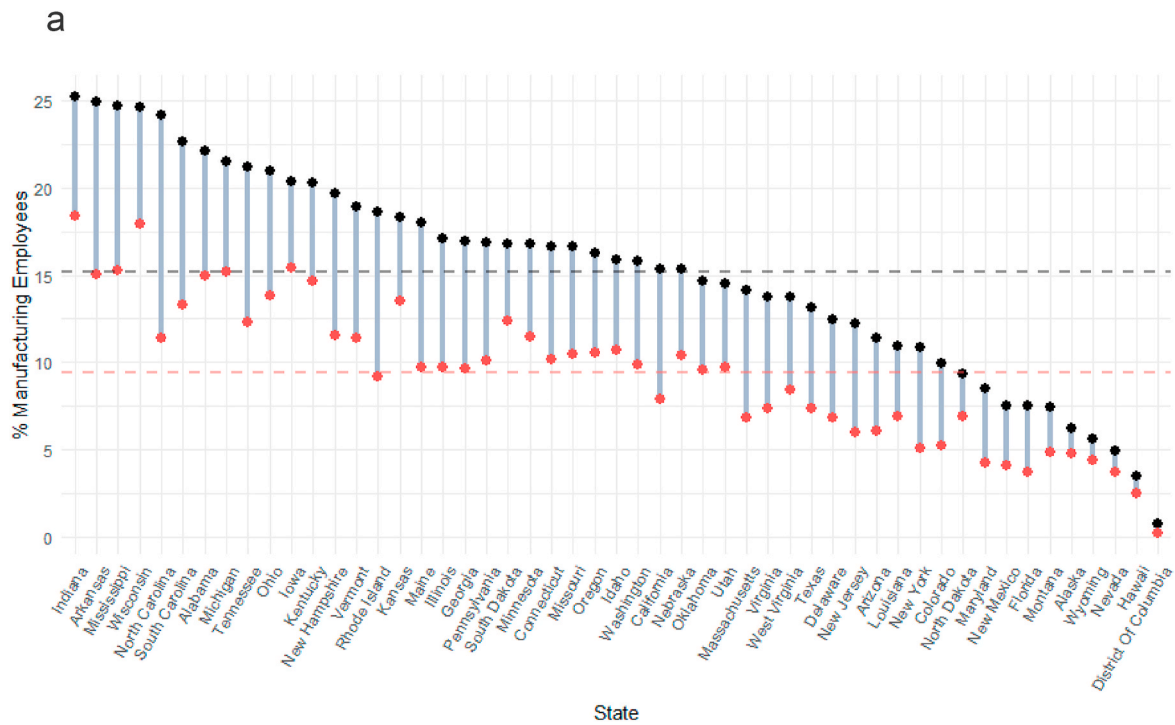
Fig. 2a. Change in the Share of Employees in Manufacturing Sector by State, 1998-2016.
Notes: Black dots represent percentage of workers employed in manufacturing in 1998; Red dots represent percentage of workers employed in manufacturing in 2016; Vertical lines represent overall percentage point decline between 1998 and
2016. Horizontal grey dotted line represents state average in 1998; Horizontal pink dotted line represents state average in 2016. Data: U.S. Census Bureau, County Business Patterns Program.. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Situating the present analysis at the state-level therefore facilitates modeling how regional variation in ecological risk environments contributes to variation in the concentration of a pressing public health concern, specifically, drug and opioid overdose mortality. It also facilitates an opportunity to address the implementation of several important state-level policy changes that are widely considered relevant to the unfolding of the U.S. opioid epidemic. Capturing annual variation in these processes both increases the precision of identification and advances a theoretical model of how labor market dynamics shape contexts of substance use and drug overdose.

3. Data and methods

3.1. Drug overdose mortality rates

Rates of annual state-level drug and opioid overdose mortality between 1999 and 2017 were calculated using the restricted-use multiple cause of death file from the National Center for Health Statistics (NCHS) in combination with bridged-race population estimates from the NCHS. Mortality data used in this study are based on approximately 47.7 million death certificate records of U.S. residents reported to the National Vital Statistics System (NVSS) between 1999 and 2017. For drug overdose mortality rates, this data represents approximately 260,000 deaths to women and 440,000 deaths to men, among which 326,000 of those male deaths are for non-Hispanic white men ages 15–64. For opioid mortality rates, this data represents approximately 134,000 deaths to women and 262,000 deaths to men.

Drug overdose mortality rates were constructed and defined using

the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) underlying cause of death codes X40-44, X60-64, X85, and Y10-14 (Hedegaard et al., 2018). These classifications include drug deaths recorded as unintentional, suicide, homicide, or of undetermined intent, although nearly 90% are recorded as unintentional. Opioid overdose mortality rates were constructed using the previous ICD10 underlying cause of death codes in conjunction with any of the following ICD10 multiple cause of death codes T40.0 (Opium), T40.1 (Heroin), T40.2 (Other Opioids), T40.3 (Methadone), T40.4 (Other Synthetic Narcotics), or T40.6 (Other Unspecified Narcotics). Appendix Table S1 presents the full description of all ICD10 codes used to define drug and opioid mortality rates.

Between 1999 and 2017, 21% of drug overdose deaths in the NCHS multiple cause of death file were coded as involving a single unspecified drug, medicament, or biological substance (ICD10 code T50.9). The high proportion of unclassified drug overdoses on death certificates has likely resulted in an undercount of opioid involved overdoses (Boslett et al., 2020; Buchanich et al., 2018; Ruhm, 2017; Warner et al., 2013). Using correction techniques, researchers estimate that nearly 3/4 of these unclassified drug overdose deaths were likely to involve opioids, with substantial variation across states and time (Boslett et al., 2020; Ruhm, 2017). To address the undercount, I implemented a correction procedure that predicted opioid involvement in unclassified drug overdose deaths using logistic regression models and a parsimonious set of decedent characteristics as predictors (Boslett et al., 2020). The full methodology for this correction procedure is described in Appendix Note S1. For analyses in the present study that test for the association between manufacturing decline and opioid deaths, I present estimates
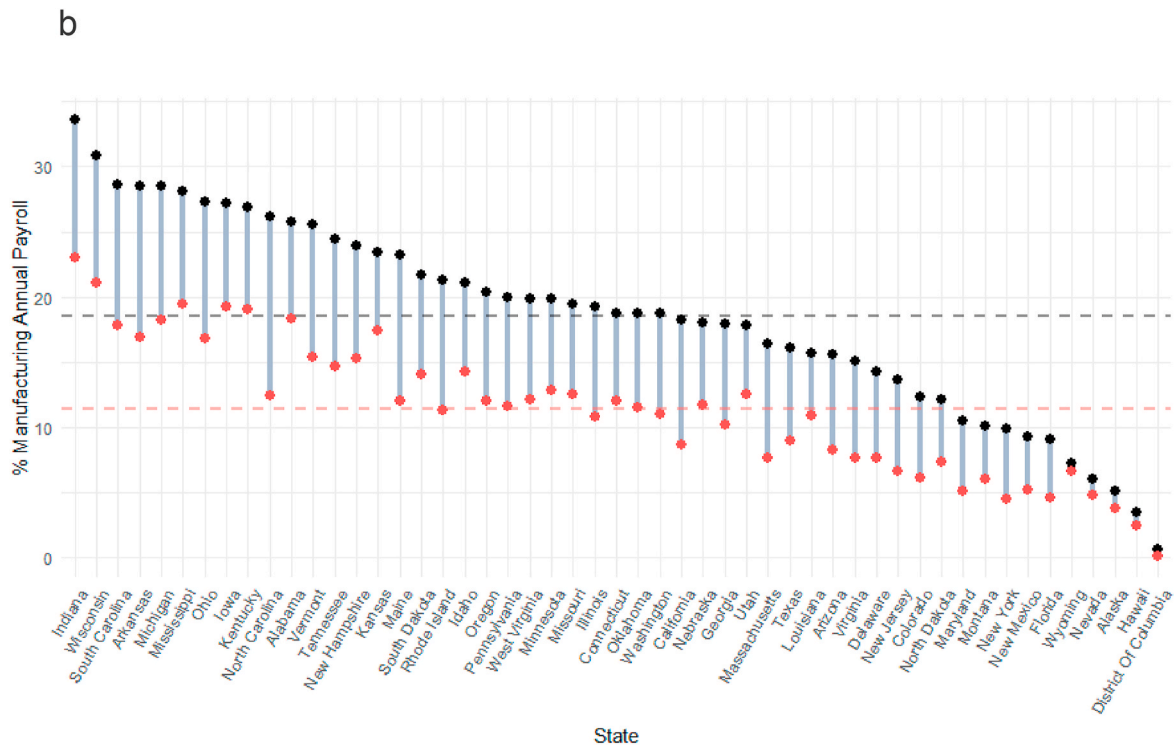
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Fig. 2b. Change in the Share of Annual Payroll in Manufacturing Sector by State, 1998-2016.
Notes: Black dots represent percentage of annual payroll in manufacturing in 1998; Red dots represent percentage of annual payroll in manufacturing in 2016; Vertical lines represent overall percentage point decline between 1998 and
2016. Horizontal grey dotted line represents state average in 1998; Horizontal pink dotted line represents state average in 2016. Data: U.S. Census Bureau, County Business Patterns Program. . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

for both the non-corrected opioid mortality rates and the corrected opioid mortality rates.

I calculated age-adjusted mortality rates to account for shifts in the age distribution of state populations over time as well as differences in the age distribution of populations across states. I then log-transformed the age-adjusted mortality rates because the non-transformed mortality rates are right-skewed and nonnormal (Figure S1). Since there were only a couple of state-year observations with drug or opioid death rates of zero, I allowed the log transformation to render these values as undefined and excluded them from my analysis. I used the "direct" method of age standardization to derive age-adjusted death rates based on the weighted age distribution of the total U.S. population in the year 2000 as the standard (Anderson & Rosenberg, 1998). I accessed bridged-race population estimates from the NCHS for population denominators. I then evaluated the accuracy of the calculated age-adjusted mortality rates by comparing equivalent non-suppressed, publicly available age-adjusted mortality rates for state-year observations that had more than 9 deaths through the CDC WONDER database. The correlation between the rates I calculated and those accessed through CDC WONDER ranged from $r = 0.9998$ to $r = 0.9999$, indicating that the calculations were performed correctly. The advantage of using the restricted-use multiple cause of death file is that the present analysis includes non-zero, state-year observations that would otherwise be suppressed in the public-use file.

3.2. Measures

3.2.1. Manufacturing decline

The decline of the U.S. manufacturing sector in state labor markets was assessed using relative measures of the total number of employees and total annual payroll concentrated in the manufacturing sector. Both measures were lagged one-year to achieve appropriate temporal ordering. I obtained state-level data on annual employment and payroll between 1998 and 2016 from the U.S. Census Bureau's County Business Patterns program (CBP) which compiles subnational business establishment data according to 6-digit North American Industry Classification System (NAICS) codes (U.S. Census Bureau, 2018). CBP relies primarily on business establishment data from the Census Bureau's Business Register (BR) which contains a complete list of all business establishments in the United States with paid employees. The relative share of annual employment and payroll was calculated by dividing the number of employees and payroll in the manufacturing sector (NAICS 2-digit codes 31–33) by the number of employees and payroll in all business sectors.

3.2.2. Covariates

I included a set of theoretically relevant, time-varying covariates in the models which might plausibly confound the direct association between manufacturing decline and mortality rates. Based on extant literature on the economic and geographic determinants of mortality and life expectancy (e.g. Chetty et al., 2016; Elo et al., 2019; Woolf and Schoomaker 2020), the models adjust for state-level compositional and

contextual characteristics including the labor force participation rate, the percentage of workers represented by labor unions, the percentage of the population with a college degree, the percentage of the population ever married, the percentage of the population who are Hispanic, the percentage of the population who are Black, the age structure of the population, the percentage of the population living in metropolitan area counties, and scores of self-reported health.

The findings of several recent studies (Currie et al., 2019; Krueger, 2017) have suggested a reverse causal direction between economic conditions and the opioid epidemic: that is, substance use might causally impact rates of unemployment and labor force participation. I use an estimation strategy that lags all predictors by one year to achieve well-defined temporal ordering, but I additionally test specifications that adjust for a set of state-specific drug regulatory policies that might plausibly be associated with both growth or contraction in manufacturing industries (or labor markets more broadly) and drug use. These policies include annual binary indicators for the initial and ongoing implementation of Prescription Drug Monitoring Programs (PDMPs), naloxone access laws, and Good Samaritan laws. The outcomes of these policies, whether effective in reducing substance use and opioid deaths, has varied (for Naloxone access laws, see Doleac and Mukherjee 2018; for PDMPs, see Fink et al., 2018, Finley et al., 2017, or Grecu et al., 2019); yet, they represent the implementation of extensive state-level interventions that might explain trends in drug and opioid deaths.

Data on state-level labor force participation rates were accessed from the U.S. Census Bureau's Local Area Unemployment Statistics program (LAUS) (Bureau of Labor Statistics, 2018). Data on annual state-level union coverage come from the Union Membership and Coverage Database (Hirsch & Macpherson, 2003) which estimates statistics on union membership using the Current Population Survey (CPS). Data used to calculate the percentage of the state population living in metropolitan counties were accessed from the USDA Economic Research Service's 2013 rural-urban continuum codes dataset (United States Department of Agriculture 2019). Data used to calculate compositional racial/ethnic and age structure covariates were accessed from the NCHS bridged-race population estimates. Data on other state-level social, economic, health, and compositional characteristics between 1999 and 2017 were calculated using micro-data from the U.S. Census Bureau's CPS Annual Social and Economic Supplement accessed through the Integrated Public Use Microdata System (IPUMS) at the University of Minnesota (Flood et al., 2020). I applied person-level weights when generating these state-level characteristics. Finally, data on the implementation of state-level drug policies were acquired from the Prescription Drug Abuse Policy System (PDAPS) (Bao et al., 2017). Table 1 displays the means and standard deviations of variables for the entire sample during the full period of the study, 1999–2017.

3.3. Analytic approach and model specification

This study leverages annual variation within state labor markets over nearly two decades to evaluate how declining shares of manufacturing jobs and earnings contribute to changes in drug and opioid overdose mortality. I estimated a set of two-way, state-level fixed effects regression equations predicting log-transformed, age-adjusted rates of drug and opioid overdose deaths, for women and men separately. The first specification adjusted for state and year fixed effects as well as contextual and economic characteristics. I then introduced measures of several state-level time-varying policies that might plausibly confound the association between manufacturing decline and overdose mortality. To test the robustness of the results to measurement choices, I operationalized the decline of manufacturing in two separate ways: first, as the percentage of workers employed in the manufacturing sector, and second, as the percentage of total annual payroll concentrated in the manufacturing sector. Parameter estimates and clustered standard errors at the state-level are reported for all estimated regression models. In

Table 1
Descriptive statistics.

Variables	1999–2017		
	Mean	S.D.	State-Year Observations
Drug Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	9.5	5	969
Male	15.9	9.4	969
Opioid Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	5.3	4.1	969
Male	9.9	8.3	969
Corrected Opioid Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	7	4.7	969
Male	12.3	8.7	969
Logged Drug Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	2.1	0.6	969
Male	2.6	0.6	969
Logged Opioid Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	1.4	0.8	967
Male	2	0.8	968
Corrected Logged Opioid Overdose Age-Adjusted Death Rate (per 100,000 population)			
Female	1.7	0.8	967
Male	2.3	0.7	968
Logged Emergency Department Visits (per 100,000 population)			
Female	4.8	0.6	381
Male	4.9	0.7	381
Logged Inpatient Hospital Stays (per 100,000 population)			
Female	5.3	0.5	553
Male	5.2	0.6	553
Manufacturing Measures			
Manufacturing Employment (%)	11.5	5.0	969
Manufacturing Annual Payroll (%)	13.9	6.3	969
State-Level Covariates			
Labor Force Participation Rate	65	4.3	969
College Graduates (%)	19.6	5	969
Ever-Married (%)	56.5	3.5	969
Hispanic (%)	9.3	9.7	969
Black (%)	11.3	11.5	969
% Population Ages 15-64	66.7	1.6	969
% Population Ages 65 or Above	13.3	2	969
Population Living in Metropolitan Area Counties (%)	75.6	18.5	969
Self-Reported Health Score (1-Excellent to 5-Poor)	2.2	0.12	969
State-Level Labor and Drug Policy Covariates			
Union Coverage (%)	12.8	5.5	969
Prescription Drug Monitoring Program			
# of states in 1999	16	–	950
# of states in 2017	50	–	950
Naloxone Access Laws			
# of states in 1999	0	–	969
# of states in 2017	48	–	969
Good Samaritan Laws			
# of states in 1999	0	–	969
# of states in 2017	37	–	969
Opioid Prescriptions Filled (per 100 population)	81	23	561

Note: All covariates are lagged one year.

the main analyses, I omit state-level population weights because states are conceptualized here as distinct administrative entities with different sets of social, economic, and health policies. Nevertheless, I present supplementary analyses that weight for population size to test whether the results hold up under a different set of assumptions. The models are specified as follows:

$$\log(M_{st}) = \boldsymbol{\beta} \boldsymbol{x}_{st} + \boldsymbol{\alpha}_s + \boldsymbol{\mu}_{st} \qquad \text{Eq. 1}$$

where log (M_{st}) refers to the log-transformed age-adjusted mortality rate for state s during year t; $\boldsymbol{\beta}$ refers to a vector of estimated coefficients; $\boldsymbol{x}_{st}$ refers to a vector that measures the relative share of state-level manufacturing, either the percentage of employment or annual payroll concentrated in manufacturing industries, and vectors of state-level compositional and contextual characteristics as well as additional

state-level policies, in addition to binary-coded year vectors; α_s refers to a vector of state-specific intercepts; and μ_{st} refers to state- and year-specific error terms.

3.4. Subgroup and sensitivity analyses

I conducted several additional analyses to (1) further investigate subgroup heterogeneity, (2) evaluate whether the results persist when predicting *county*-level drug and opioid overdose mortality rates, (3) test for differences across states with and without "triplicate" programs in the 1990s, and, alternatively, explicitly adjust for the state-level supply of prescription opioids, (4) assess whether the results persist when using negative binomial regression equations as an alternative modeling strategy, (5) include population weights in the model estimation, (6) adjust for additional potential sources of omitted variable bias and gauge the extent to which unobserved omitted variables might influence the results, and (7) test whether the results persist when using non-fatal outcomes of substance use: opioid-related inpatient hospitalizations and emergency department visits.

First, I constructed models that predicted age-specific counts of drug deaths, binned across 10-year age intervals between the ages 25–64, for non-Hispanic whites and Blacks separately by sex.[3] To account for an excess of state-year observations with zero deaths for these racial/ethnic and age subgroups as well as overdispersion, I estimated negative binomial models predicting counts of drug and opioid overdose deaths instead of logged rates as in Eq. (1).

Second, to evaluate whether the results persist when accounting for *within*-state variation, I estimated models predicting logged county-level drug and opioid overdose mortality rates with measures of manufacturing employment and annual payroll at three different levels of aggregation: the county-level, commuting zone-level, and state-level. For all specifications, I include county-level fixed effects and year fixed effects to maintain the two-way fixed effects modeling strategy. I incorporate county-level population weights, measured at the beginning of the time period (1999), to downweight counties with small populations that are likely to yield less stable annual mortality rates, and upweight counties with large populations that are likely to yield more stable annual mortality rates. I address the issue of substantial nonrandom data suppression of employment values in the county-level Census Bureau CBP dataset by estimating specifications that include manufacturing employment measures calculated from (a) the original CBP dataset, and (b) an imputed CBP dataset (Eckert et al., 2020) that relies on data suppression flags and the hierarchical structure of the Census CBP database to impute missing values using a linear programing algorithm.[4]

The commuting zone- and state-levels of aggregation for the manufacturing employment and annual payroll measures are preferable to counties because they account for relevant geographic spillovers of labor market conditions – that is, employment opportunities extend beyond one's county of residence (Venkataramani et al., 2020). Commuting zones identify clusters of contiguous counties, not bounded by state borders, where people both live and work based on commuter flows (Tolbert and Sizer 1996). Aggregating measures of manufacturing employment and earnings at these higher geographic levels capture pertinent information that would not necessarily be detectable at a lower level of geographic scale, such as the county-level (Lindo, 2015). For all county-level models, I adjust for county-level compositional covariates (% non-Hispanic Black, % Hispanic, and detailed population age structure in 5-year age bins), county-level level labor force participation rates (for residents of the county), state-level characteristics (% college educated, % ever-married, % of state living in metropolitan area counties, % foreign born) and policy variables (naloxone access law implementation, PDMP implementation, Good Samaritan law implementation, and % workers covered by labor unions).

Third, recent findings by Alpert et al. (2019) document how states with "triplicate" programs – early versions of prescription drug monitoring programs – in place when OxyContin was initially introduced in 1996 experienced fewer opioid deaths over the following two decades. Alpert et al. (2019) argue that these state-level drug policies reduced the intensity of predatory marketing of prescription opioids by pharmaceutical companies, leading to lower long-term opioid prescribing rates. To evaluate whether the findings of the present study are robust to this important supply-side predictor of the opioid crisis, I estimated models that tested for differences in the association between manufacturing decline and opioid/drug overdose mortality according to whether states had implemented triplicate programs prior to OxyContin's introduction. I accomplished this by fully interacting the predictors in Eq. (1) with a binary indicator of whether a state had implemented a triplicate program in the years prior to the introduction of OxyContin.[5] The interaction coefficient for manufacturing employment/payroll and triplicate status tests for differences across triplicate states and non-triplicate states. I estimate these models at the county-level to rigorously test whether these group differences persist while accounting for within-state heterogeneity.

More broadly, the relationship between economic conditions and drug-related mortality and hospitalizations might be confounded by issues of drug supply (Monnat, 2019; Ruhm, 2019). Several recent studies have argued that the supply of prescription opioids is negatively associated with labor force outcomes, including unemployment rates and labor force participation (Currie et al., 2019; Hollingsworth, Ruhm & Simon, 2017; Krueger, 2017). State-level opioid supply might therefore confound the identification in Eq. (1) that models the relationship between lagged manufacturing decline and drug overdose mortality rates and opioid-related hospitalizations. Therefore, I conducted sensitivity tests that adjusted for the state-level rate of retail opioid prescriptions dispensed per 100 population, which accounts for the full supply of legally dispensed prescription pills.[6] These sensitivity models only cover the years 2007-2017 because of data availability. Data on the prescription opioid rate were accessed from the CDC which acquired prescription data from IQVIA, a health information technology and clinical research company (Centers for Disease Control and Prevention, 2019; Guy et al., 2020). Unfortunately, there is no comparable dataset which measures the supply of illegal drugs.

I next evaluated whether the results from the main specifications were sensitive to several important methodological decisions: modeling strategy, weighting procedure, potential over-adjustment, and potential omitted variable bias. I first estimated negative binomial regression models to predict counts of drug and opioid overdose deaths. I then re-estimated the main specifications with state-level population weights to address the concern that states with smaller populations might be biasing the results. I next removed the labor force participation rate from the set of covariates to address the potential issue that the process of deindustrialization might also alter the relative size of the labor force and therefore including this covariate might suppress the full effect. Finally, I tested for three potential sources of confounding: compositional shifts in the detailed age structure of state populations, the percentage of the state population born outside of the U.S., and state-by-year linear time trends. Following these tests, I additionally implemented a formal bounds analysis (Oster, 2019) to assess the sensitivity of the parameter estimates to unobservable variables.

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[3] In the age-, sex-, and race/ethnicity-specific set of sensitivity models, I include whites and Blacks, but not other racial/ethnic groups because most state-year values for other racial/ethnic groups are below 10 deaths and unreliable.

[4] Unfortunately, there are no equivalent imputed datasets for annual payroll.

[5] Triplicate states include California, Idaho, Illinois, New York, and Texas.

[6] This is a measure of pill quantity and not prescription strength (i.e. morphine milligram equivalents).

Mortality is the most dismal consequence of drug and opioid misuse; however, the drug epidemic has also devastated individuals and communities through an array of negative physical and mental health outcomes that require medical interventions. In a final sensitivity analysis, I consider whether structural changes in manufacturing employment and annual payroll are associated with two types of medical utilization: opioid-related emergency department visits and inpatient hospitalization stays. I accessed data on these outcomes through the Healthcare Cost and Utilization Project (HCUP) database from the Agency for Healthcare Research and Quality (AHRQ) at the U.S. Department of Health and Human Services. AHRQ draws on an annual sample of treat-and-release visits to emergency departments from the State Emergency Department Databases (SEDD) and a sample of short-term inpatient stays at community hospitals from the State Inpatient Databases (SID). Opioid-related emergency department visits and inpatient stays are coded according to ICD-9-CM codes (Weiss et al., 2017). These samples cover 98% of all inpatient discharges and 98.5% of all emergency department visits in the states that partner with AHRQ. For both measures, data are only available from 2005 to 2017, and the maximum number of states participating in the databases are 36 for the emergency department visits and 47 for the inpatient stays.

4. Results

4.1. Manufacturing decline and logged mortality from drug overdoses

Fig. 3 presents a series of maps of the U.S. that display the variation in age-adjusted drug overdose mortality rates across states in 1999, 2008, and 2017. For both men and women, rates of overdose mortality increased throughout the time period and were highest in West Virginia, Virginia, Ohio, and Washington, D.C. at the end of the period in 2017.

Table 2, Panel A presents the regression results predicting state-level logged mortality rates from drug overdoses for women and men using both measures of manufacturing decline in sepearate models (Full model output is presented in Appendix Table S2A). For the full age-adjusted log-transformed drug mortality rate models, Model 2, a one percentage point increase in the share of workers employed in manufacturing is associated with a −3.4% decrease in drug mortality rates for women and a −4.9% decrease in drug mortality rates for men.[7] This is equivalent to a decrease of −0.32 deaths per 100,000 population in the drug mortality rate for women and a decrease of −0.77 deaths per 100,000 population in the drug mortality rate for men. Using the annual payroll measure, a one percentage point increase in the share of overall annual payroll in manufacturing is associated with a −3.1% decrease in drug mortality rates for women and a −3.8% decrease in drug mortality rates for men. This is equivalent to a reduction of −0.29 in the drug mortality rate for women and a decrease of −0.61 in the drug mortality rate for men. For both measures, the results are statistically significant below the p < .001 threshold for men and below the p < .01 level for women. Manufacturing jobs, as a share of all jobs in state labor markets, declined by an average of 5.8 percentage points throughout the entire 1999–2017 period. Accordingly, changes in manufacturing employment accounted on average for an additional 1.8 drug deaths per 100,000 for women and 4.5 drug deaths per 100,000 for men based on the point estimates between the start and end of this period. Similarly, the average decline of manufacturing annual payroll by 7.2 percentage points accounts for an additional 2.3 drug deaths per 100,000 for women and 5.5 drug deaths per 100,000 for men between the start and end of this period.

The point estimates indicate that manufacturing decline between 1999 and 2017 predicts an additional 90,309 (annual payroll) to 92,511 (employment) drug overdose deaths for men and an additional 39,402 (annual payroll) to 44,710 (employment) drug overdose deaths for

women over this 19-year period, had the share of manufacturing employment and annual payroll remained at 1999 levels during each year of the present analysis. This means that manufacturing decline can explain approximately 21% of all overdose deaths for men and 15.2%–17.2% of all overdose deaths for women between the start and end of this period.

Fig. 4 displays the percentage of deaths between 1999 and 2017 attributable to changes in state-specific decreases in manufacturing employment and annual payroll for both women and men between 1999 and 2017. For states such as South Dakota, North Carolina, Mississippi, Nebraska, and Iowa, manufacturing decline predicts 40% or more of all overdose deaths for men and approximately 20% of all overdose deaths for women. Meanwhile, manufacturing decline predicts less than 5% of all overdose deaths for men and less than 2.5% of all overdose deaths for women in the District of Columbia and states such as Wyoming, Nevada, Hawaii, Alaska, and New Mexico. This map demonstrates the substantial and meaningful variation in the state-level association between manufacturing decline and drug overdose death rates – a range of over 50 percentage points for men and roughly 30 percentage points for women. Appendix Table S3 presents the predicted number of deaths in each state attributable to manufacturing decline based on the employment and annual payroll point estimates.

4.2. Manufacturing decline and mortality from opioid overdoses

Out of the 700,000 drug overdose deaths over the 1999–2017 period, approximately 400,000 deaths involved the specified use of opioids, including prescription opioids, heroin, and synthetic opioids such as fentanyl and fentanyl analogs. To investigate the role of manufacturing decline on the opioid crisis specifically, Table 2, Panel B presents regression results predicting state-level logged opioid mortality for women and men using both measures of manufacturing decline (Full model output is presented in Appendix Table S2B). For the full age-adjusted opioid mortality rate models, Model 2, a one percentage point increase in the share of workers employed in the manufacturing sector is associated with a −5.4% decrease in opioid mortality for women and a −6.9% decrease in opioid mortality for men. Using the annual payroll measure yields similar results: a one percentage point increase in the share of overall annual payroll in manufacturing is associated with a −4.8% reduction in opioid mortality for women and an −5.2% reduction in opioid mortality for men. The results are similar, although slightly larger in magnitude, when estimating models that use logged opioid mortality rates that have been corrected for death certificate records that undercount opioid involvement (Table 2, Panel C; Full model output is presented in Appendix Table S2C).

Throughout the entire 1999–2017 period, changes in manufacturing employment on average predict an additional 1.6 opioid deaths per 100,000 for women and 3.9 opioid deaths per 100,000 for men based on the point estimates. Changes in manufacturing annual payroll on average predict an additional 2.0 opioid deaths per 100,000 for women and 4.9 opioid deaths per 100,000 for men.

4.3. Subgroup analysis: manufacturing decline and overdose mortality across racial/ethnic-specific 10-year age groups

Researchers have documented how the rise of drug deaths – particularly opioid drug deaths – is concentrated among middle-age, non-Hispanic white males (Case & Deaton, 2015). The third column of Fig. 3 presents a set of maps which display the rapid and widespread increase in overdose deaths among non-Hispanic white males ages 45–54 in 1999, 2008, and 2017.

Table 3A estimates negative binomial regression models predicting state-level counts of drug overdose deaths for non-Hispanic white females and males between the age of 25–64, binned at 10-year intervals. Regardless of the measure of manufacturing decline, the results for all age groups are substantively large and statistically significant for white

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[7] For women, (exp(-0.034) − 1)*100 = −3.343; for men, (exp(-0.050) − 1)* 100 = −4.877.
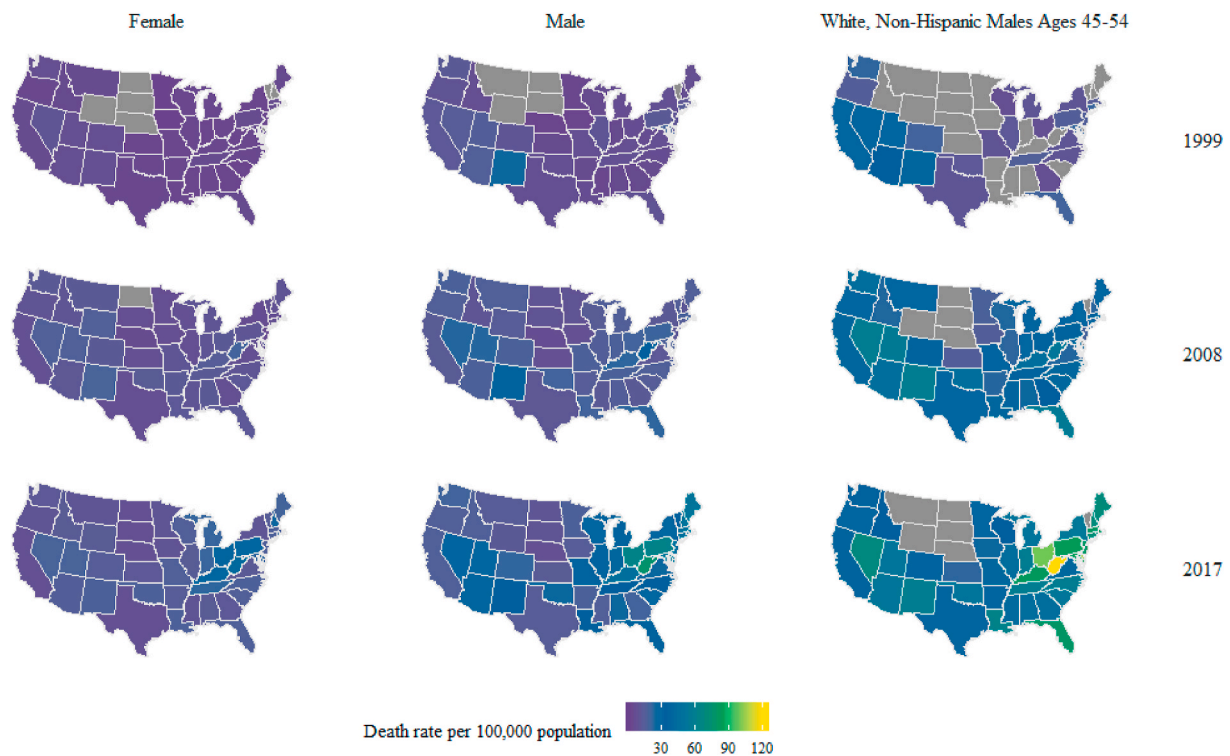
Fig. 3. State-Level Overdose Rates for Females, Males, and White, Non-Hispanic Males Ages 45-54.
Notes: Death rates are age-adjusted for females and males. Grey shading represents states with less than 10 deaths per year; rates are not displayed in accordance with requirements of the data use agreement with the NCHS.

males, with the effect size largest for white men ages 45–54. For the female age-specific models, the results are substantively large and statistically significant for both manufacturing measures in all age groups with the exception of the oldest 55–64 age group. In contrast to whites, manufacturing decline is generally not significantly associated with the rise of drug deaths for non-Hispanic Black females and males (Table 3B), but the association is largest and most precisely estimated for Black females ages 45–54 and Black males in the 35–44 and 55-54 age groups.[8]

4.4. County-level analyses

Table 4 presents a set of models predicting county-level logged drug and opioid mortality rates, which separately test measures of manufacturing employment and annual payroll at the county-, commuting zone-, and state-level. For the most part, the coefficients are sizable, precisely estimated, and increase in magnitude at higher levels of aggregation of the manufacturing measure, for both the drug and opioid mortality rate models. The pattern of these results is consistent with prior research on geographic scale and effect sensitivity (i.e. Lindo, 2015) that finds that coefficient estimates of economic conditions on mortality are downwardly biased at lower levels of aggregation. In the models that use commuting zone-level manufacturing measures – which consider across-county spillover effects of local labor markets – a one percentage point increase in manufacturing employment is associated with a −1.6% reduction in drug overdose mortality rates for women and a −2.0% reduction in drug overdose mortality rates for men.[9] County

population-weighted, commuting zone-level manufacturing employment decreased on average by 5.9 percentage points between 1999 and 2017. This indicates that reductions in commuting zone-level manufacturing employment between 1999 and 2017 can explain on average roughly 7.4% of the rise in county-level drug deaths for women and 8.3% of the rise in county-level drug deaths for men over this period. For the models that expand the definition of spillovers to include the entirety of state-level labor markets, a one percentage point increase in manufacturing employment is associated with a −3.2% reduction in drug overdose rates for women and a −4.7% reduction in drug overdose mortality rates for men. These effects explain on average roughly 16.6% of the total rise in drug mortality rates for women and 21.1% of the total rise in drug mortality rates for men. Overall, these county-level results largely correspond to the main state-level findings, which demonstrates that the association between manufacturing decline and the rise of drug and opioid overdose deaths persists when accounting for within-state variation.

4.5. Triplicate programs and prescription drug supply

Alpert et al. (2019) find extensive state-level variation in the growth of opioid overdose deaths according to whether state triplicate policies had been adopted prior to the introduction of OxyContin by Purdue Pharma in 1996. To evaluate whether the association between manufacturing decline and the rise of opioid overdose deaths persists regardless of state-level policies that limited the widescale prescribing of opioid medication, I estimated county-level models that tested for differences across triplicate and non-triplicate states (Table 5). The results show that there is no statistically significant difference below the p < .05 level in the effect size of manufacturing decline on overdose deaths between triplicate and non-triplicate states. This suggests that the ecological, demand-side influence of structural economic change remains a salient predictor of rising drug and opioid overdose deaths even in states that had adopted strict drug control policies in the 1990s which

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[8] The number of drug and opioid deaths for other racial/ethnic groups at the state level are too small to generate enough reliable annual mortality estimates for analysis.

[9] These calculations are based on the results from the CBP Imputed models. For women, (exp(-0.0158) - 1)*100 = −1.57; for men, (exp(-0.0204) - 1)*100 = −2.02.

Table 2

Regression analyses predicting logged drug, opioid, and corrected overdose mortality rates.

A. Logged Drug Overdose Mortality		
Manufacturing Measure	Model 1	Model 2
Female		
% Employees in Manufacturing	−0.033**	−0.034**
	(0.011)	(0.011)
% Annual Payroll in Manufacturing	−0.030**	−0.031**
	(0.010)	(0.009)
Male		
% Employees in Manufacturing	−0.049***	−0.050***
	(0.013)	(0.013)
% Annual Payroll in Manufacturing	−0.039***	−0.039***
	(0.011)	(0.011)
B. Logged Opioid Overdose Mortality		
Manufacturing Measure		
Female		
% Employees in Manufacturing	−0.051*	−0.055*
	(0.025)	(0.023)
% Annual Payroll in Manufacturing	−0.046*	−0.049**
	(0.020)	(0.018)
Male		
% Employees in Manufacturing	−0.067*	−0.071*
	(0.030)	(0.028)
% Annual Payroll in Manufacturing	−0.051*	−0.053*
	(0.023)	(0.021)
C. Logged Corrected Opioid Overdose Mortality		
Manufacturing Measure		
Female		
% Employees in Manufacturing	−0.057*	−0.061**
	(0.021)	(0.021)
% Annual Payroll in Manufacturing	−0.047**	−0.049**
	(0.017)	(0.016)
Male		
% Employees in Manufacturing	−0.074***	−0.077***
	(0.019)	(0.019)
% Annual Payroll in Manufacturing	−0.056***	−0.057***
	(0.016)	(0.015)
State and Year Fixed Effects	Yes	Yes
Compositional and Economic Covariates	Yes	Yes
Labor and Drug Policy Covariates	No	Yes

*p < .05, **p < .01, ***p < .001 (two tailed tests).

Notes: (a) All covariates are lagged one year. (b) State-clustered standard errors are in parentheses. (c) Drug overdose models have 969 observations, representing 50 states and the District of Columbia over 19 years. Uncorrected and corrected opioid overdose models have 967 observations for women and 968 observations for men. (d) Compositional and economic covariates include state-level measures of the labor force participation rate, the percentage with a college degree, the percentage who have ever been married, the percentage who are Hispanic, the percentage who are Black, the percentage who are ages 18–64, the percentage who are ages 65 or above, the percentage living in metropolitan counties, and the average self-reported health score. (e) Labor and drug policy covariates include state-level measures of the percent of workers covered or represented by labor unions, and binary indicators of whether states have implemented three types of drug policies: PDMPs, naloxone access laws, and Good Samaritan laws for reporting drug overdoses.

would ultimately reduce the supply of legal prescription opioids over the next two decades.

To further assess the importance of drug supply on the main results, I estimated a set of models (Appendix Table S4, first column) that adjusted specifically for the legal supply of opioid prescriptions per 100 population using data accessed from the CDC. For models estimating log-transformed age-adjusted rates of drug deaths, the results do not substantively change for men – the magnitude of both manufacturing measures remains, but is less precisely estimated for the annual payroll

measure – but the coefficient for percentage of annual payroll concentrated in manufacturing slightly attenuates and both measures lose precision for women. Similarly, the inclusion of this additional covariate into the models predicting log-transformed, age-adjusted rates of corrected opioid deaths increases the standard errors for females, but does not alter the results much for males. While caution should be used to interpret these models (they only cover the years 2007-2017, have a reduced number of state-year observations, and are not directly comparable to the main specifications), they indicate that the role of manufacturing decline on the broader drug epidemic cannot be simply explained away by state-level trends in the legal supply of opioid pain prescriptions.
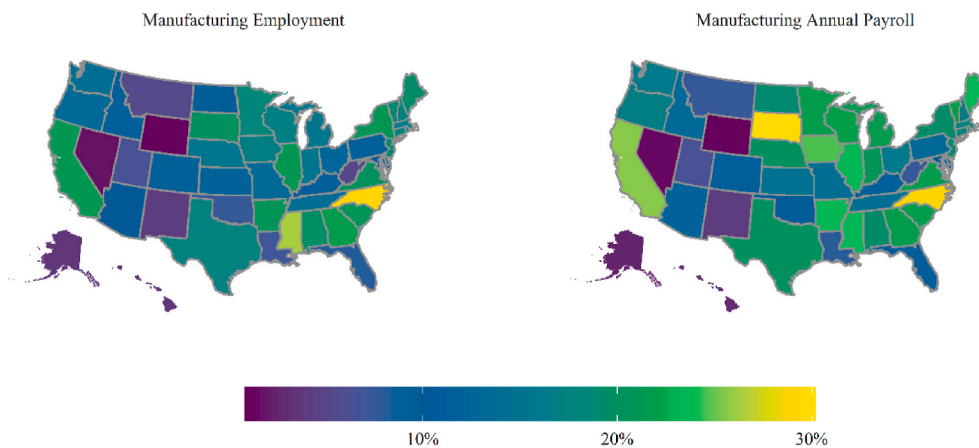
4.6. Additional sensitivity analyses

In a first set of additional sensitivity analyses, I evaluated whether the results were sensitive to the modeling strategy used. I re-estimated the main specifications using negative binomial regression models and a dependent measure of drug and opioid overdose death counts. The results, presented in the second column of Appendix Table S4, are similar in size and magnitude as those estimated from Eq. (1). I then re-estimated the main specifications with state-level population weights (third column, Appendix Table S4). These weighted models alter the theoretical interpretation of the main models because they give precedence to population size rather than treating each state as a comparable administrative unit. Nevertheless, the inclusion of population weights does not substantively alter the effect size or significance level of the results. Next, in the fourth column of Appendix Table S4, I considered whether the inclusion of the labor force participation rate covariate was obscuring the full relationship between manufacturing decline and drug and opioid overdose deaths. In comparison to the main specifications, little changes with removal of this covariate.

Appendix Table S5 presents models that adjust for three additional potential sources of confounding: detailed population age structure (in 5-year age bins), the percentage of the population who were born outside of the U.S., and state-by-year linear time trends. For the specifications that adjust for the first two covariates, the substantive results do not change. For the specification that adjusts for state-by-year linear time trends, the estimates lose statistical significance below the p < .05 level and become positive. It is likely that the state-specific time trends are sweeping out part of the estimate of interest. Prior studies on the appropriateness of location-specific time trends (e.g. Wolfers, 2006) have documented how their inclusion can confound estimation, particularly in the context of analyzing dynamic, evolving processes over time. Since changes in manufacturing employment and payroll commence immediately at the beginning of the 1999–2017 period, these state-specific time trends are not adjusting for pre-existing differences in overdose mortality rates across states prior to the treatment, but rather are likely adjusting for trends in overdose mortality rates that are responding in part to changes in manufacturing employment and annual payroll after treatment. As a result, this specification risks over-controlling and confounding estimation.

I further investigated the role of omitted variable bias by conducting a formal bounds analysis (Oster, 2019). The results of this analysis, presented in Appendix Note S2, suggest that selection on unobserved omitted variables would have to be extreme to reduce the coefficient estimates from the main results down to zero.

Finally, I estimated models that predicted non-fatal outcomes of substance use: opioid-related emergency department visits and inpatient hospitalizations. Data on these outcomes are only available between 2005 and 2017 and most states do not have observations spanning those entire 13 years. The estimates, presented in Appendix Table S6, are consistent in direction and substantive magnitude as the primary findings presented above, particularly for emergency department visits, though the estimate precision varies by the years of the study. Overall, this series of additional sensitivity analyses indicates that the findings

A. Women

Manufacturing Employment   Manufacturing Annual Payroll

B. Men

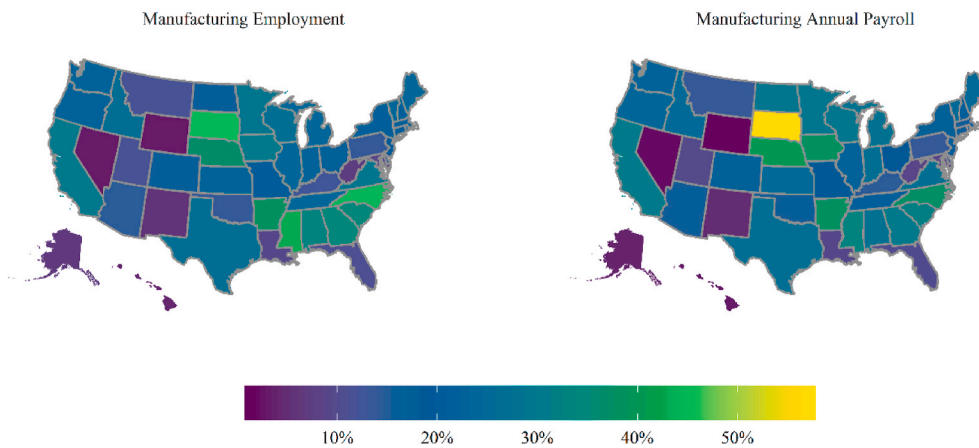Manufacturing Employment   Manufacturing Annual Payroll

Fig. 4. Percentage of drug deaths between 1999 and 2017 predicted by manufacturing decline.

from the main analysis generally hold up under different methodological decisions, different theoretical assumptions, different levels of geographic aggregation, and different outcomes of opioid use.

5. Discussion

The drug epidemic continues to disrupt the lives of individuals, families, and communities throughout the country. Since 1999, over 700,000 people in the U.S. have died from drug overdoses (including over 400,000 from opioid overdoses), and according to the most recent estimates, 2.1 million people suffered from an opioid use disorder in 2017 (Center for Behavioral Health Statistics and Quality, 2018). This study documents a large and substantively important state-level

relationship between annual declines in the U.S. manufacturing sector and increases in drug and opioid overdose mortality rates between 1999 and 2017. The findings demonstrate how the ongoing transformation of U.S. labor markets has altered ecological-level risk environments that shape population health outcomes.

Manufacturing decline, measured either as the share of manufacturing jobs in a state labor market or the share of total annual payroll concentrated in the manufacturing sector, can predict approximately 21% of all overdose deaths for men and 15.2%–17.2% of all overdose deaths for women between the start and end of the time period studied, 1999–2017. This represents an upward bound of an excess 92,000 male and 44,000 female drug overdose deaths that would otherwise have been avoided if the share of manufacturing employment

Table 3A

Negative binomial regression analyses predicting age-specific drug overdose deaths for white, non-Hispanic females and males for 10-year age groups.

Age-Specific Drug Deaths	White Females, non-Hispanic		White Males, non-Hispanic	
	Model 1	Model 2	Model 1	Model 2
Ages 25–34				
% Employees in Manuf.	−0.051***	−0.042***	−0.053***	−0.048***
	(0.013)	(0.013)	(0.011)	(0.011)
% Annual Payroll in Manuf.	−0.047***	−0.038***	−0.043***	−0.039***
	(0.010)	(0.010)	(0.008)	(0.008)
N	969	969	969	969
Ages 35–44				
% Employees in Manuf.	−0.050***	−0.046***	−0.068***	−0.062***
	(0.011)	(0.011)	(0.011)	(0.010)
% Annual Payroll in Manuf.	−0.045***	−0.041***	−0.056***	−0.051***
	(0.008)	(0.008)	(0.008)	(0.008)
N	969	969	969	969
Ages 45–54				
% Employees in Manuf.	−0.064***	−0.062***	−0.093***	−0.092***
	(0.011)	(0.011)	(0.011)	(0.011)
% Annual Payroll in Manuf.	−0.051***	−0.048***	−0.070***	−0.068***
	(0.008)	(0.008)	(0.008)	(0.008)
N	969	969	969	969
Ages 55–64				
% Employees in Manuf.	−0.026	−0.024	−0.058***	−0.058***
	(0.013)	(0.013)	(0.015)	(0.014)
% Annual Payroll in Manuf.	−0.017	−0.012	−0.041***	−0.038***
	(0.010)	(0.010)	(0.011)	(0.011)
N	969	969	969	969

*p < .05, **p < .01, ***p < .001 (two tailed tests).
Notes: (a) All covariates are lagged one year. (b) Exposure variable set to annual state-level sex-specific population size. (c) All models include state and year fixed effects. (d) Compositional and economic covariates (Model 1 and Model 2) include state-level measures of the labor force participation rate, the percentage with a college degree, the percentage who have ever been married, the percentage who are Hispanic, the percentage who are Black, the percentage who are ages 18–64, the percentage who are ages 65 or above, the percentage living in metropolitan counties, and the average self-reported health score. (e) Labor and drug policy covariates (Model 2) include state-level measures of the percentage of workers covered or represented by labor unions, and binary indicators of whether states have implemented three types of drug policies: PDMPs, naloxone access laws, and Good Samaritan laws for reporting drug overdoses.

Table 3B

Negative binomial regression analyses predicting age-specific drug overdose deaths for Black, non-Hispanic females and males for 10-year age groups.

Age-Specific Drug Deaths	Black Females, non-Hispanic		Black Males, non-Hispanic	
	Model 1	Model 2	Model 1	Model 2
Ages 25–34				
% Employees in Manuf.	−0.023	−0.022	−0.006	−0.005
	(0.030)	(0.030)	(0.021)	(0.021)
% Annual Payroll in Manuf.	−0.038	−0.031	−0.031	−0.028
	(0.023)	(0.023)	(0.017)	(0.017)
N	893	893	931	931
Ages 35–44				
% Employees in Manuf.	0.004	0.003	−0.016	−0.016
	(0.022)	(0.022)	(0.020)	(0.019)
% Annual Payroll in Manuf.	−0.010	−0.008	−0.052***	−0.049***
	(0.017)	(0.017)	(0.014)	(0.015)
N	893	893	969	969
Ages 45–54				
% Employees in Manuf.	−0.053*	−0.054*	−0.014	−0.015
	(0.022)	(0.022)	(0.017)	(0.017)
% Annual Payroll in Manuf.	−0.036*	−0.035*	−0.023	−0.021
	(0.017)	(0.017)	(0.014)	(0.014)
N	950	950	950	950
Ages 55–64				
% Employees in Manuf.	−0.015	−0.038	−0.037	−0.040
	(0.038)	(0.039)	(0.025)	(0.024)
% Annual Payroll in Manuf.	−0.002	−0.006	−0.058**	−0.052**
	(0.030)	(0.030)	(0.019)	(0.019)
N	874	874	912	912

*p < .05, **p < .01, ***p < .001 (two tailed tests).
Notes: (a) All covariates are lagged one year. (b) Exposure variable set to annual state-level sex-specific population size. (c) Missing state-year observations are the result of states with no combined race-, sex-, and age-specific drug deaths over the entire 19-year period between 1999 and 2017. (d) All models include state and year fixed effects. (e) Compositional and economic covariates (Model 1 and Model 2) include state-level measures of the labor force participation rate, the percentage with a college degree, the percentage who have ever been married, the percentage who are Hispanic, the percentage who are Black, the percentage who are ages 18–64, the percentage who are ages 65 or above, the percentage living in metropolitan counties, and the average self-reported health score. (f) Labor and drug policy covariates (Model 2) include state-level measures of the percentage of workers covered or represented by labor unions, and binary indicators of whether states have implemented three types of drug policies: PDMPs, naloxone access laws, and Good Samaritan laws for reporting drug overdoses.

Table 4
Regression analyses predicting county-level drug and opioid mortality rates.

A. Logged Drug Overdose Mortality	Level of Manufacturing Measure Aggregation				
Manufacturing Measure	County		Commuting Zone		State
	CBP	CBP Imputed	CBP	CBP Imputed	CBP
Female					
% Employees in Manufacturing	−0.0045**	−0.0092***	−0.0116*	−0.0158*	−0.0324*
	(0.0014)	(0.0021)	(0.0049)	(0.0067)	(0.0122)
% Annual Payroll in Manufacturing	−0.0043**		−0.0110*		−0.0283**
	(0.0013)		(0.0044)		(0.0105)
Male					
% Employees in Manufacturing	−0.0053***	−0.0101***	−0.0138**	−0.0204**	−0.0479***
	(0.0015)	(0.0028)	(0.0051)	(0.0073)	(0.0119)
% Annual Payroll in Manufacturing	−0.0051**		−0.0125*		−0.0365**
	(0.0015)		(0.0048)		(0.0117)
Counties	2932	3120	3132	3132	3132
County-Year Observations	55,517	57,620	59,375	59,304	59,458
B. Logged Corrected Opioid Overdose Mortality					
Manufacturing Measure					
Female					
% Employees in Manufacturing	-0.0051**	-0.0105***	-0.0145*	-0.0194*	-0.0506*
	(0.0016)	(0.0026)	(0.0058)	(0.0082)	(0.0193
% Annual Payroll in Manufacturing	-0.0050**		-0.0132*		-0.0381*
	(0.0015)		(0.0051)		(0.0161)
Male					
% Employees in Manufacturing	-0.0063***	-0.0124***	-0.0144*	-0.0219**	-0.0699***
	(0.0017)	(0.0031)	(0.0058)	(0.0081)	(0.0180)
% Annual Payroll in Manufacturing	-0.0058***		-0.0122*		-0.0477**
	(0.0016)		(0.0052)		(0.0175)
Counties	2932	3120	3132	3132	3132
County-Year Observations	55,517	57,620	59,375	59,304	59,458
County and Year Fixed Effects	Yes	Yes	Yes	Yes	Yes
County, CZ, and State Covariates	Yes	Yes	Yes	Yes	Yes
State Labor and Drug Policy Covariates	Yes	Yes	Yes	Yes	Yes

Notes: (a) County and commuting zone manufacturing measures were constructed using the county-level County Business Patterns dataset while the state manufacturing measures were constructed using the state-level County Business Patterns dataset. The CBP Imputed data were accessed from Eckert et al. (2020). (b) The county-level CBP model (Column 1) excludes counties that have no information on manufacturing employment over the entire 1999–2017 period. (c) The CBP Imputed dataset does not have imputed annual payroll numbers. (d) All models are weighted by county population in 1999. (e) Standard errors are clustered at the state-level.

and annual payroll had remained at 1999 levels. These results persist in models that adjust for a set of state-level contextual, compositional, and labor and drug policy characteristics as well as sensitivity models that estimate this relationship at the county-level and test for differences across states that had triplicate drug monitoring programs prior to the introduction of OxyContin in 1996. The effect size of the coefficient was also substantively larger when looking at racial/ethnic and age subgroups, especially for non-Hispanic white males between the ages of 45-54, a demographic group that has been particularly hard-hit by the rise in drug deaths (Case and Deaton 2015, 2017; Okie, 2010).

Many explanations of the rise of the drug epidemic emphasize the important, mechanistic role of pharmaceutical companies and pill mills in deluging communities with inexpensive opioid pain relievers (Kolodny et al., 2015). The results presented here do not conflict with this supply-side explanation since it is likely that workers in manufacturing industries, already more likely to experience workplace-related pain ailments such as repetitive strain injuries (van Tulder, Malmivaara, and Koes 2007), were at higher risk of becoming addicted to prescription painkillers upon job loss and financial hardship (Dasgupta et al., 2018; Nagelhout et al., 2017). Areas with higher unemployment were also more likely to be targeted by pharmaceutical companies pushing opioid medications (Hadland et al., 2019). In fact, the results suggest that state-level differences in manufacturing decline represent a substantial amount of variation in drug and opioid overdose deaths. Future research would benefit from moving beyond the current scholarly debate about the opioid and broader drug epidemic that sets in opposition social/economic explanations and drug supply explanations.

The modeling strategy used in the present study – two-way fixed

effects – is well suited for evaluating the relationship between manufacturing decline and overdose mortality since it adjusts for all observed and unobserved time-invariant, state-specific confounders as well as for aggregate time trends (Allison, 2009). In addition, the models adjust for time-varying characteristics – state-level contextual, compositional, and drug and labor policy attributes – that might potentially confound the relationship between manufacturing decline and drug/opioid mortality. Equivalent county-level models that include county-level fixed effects further indicate that the results are robust when examining this process in local communities specifically. This evidence indicates strong support for the labor market explanation that has been widely theorized, but until now, not well supported empirically (Case & Deaton, 2015; Monnat, 2018; Ruhm, 2019). Nevertheless, the results presented here should be interpreted as associational and not causal.

The findings emphasize the importance of understanding the role of upstream social and economic factors when addressing the ongoing drug epidemic in the U.S. State-level differences in drug policies, labor environments, and broader socio-political policy regimes are salient facets of drug-risk environments that shape the health of populations. Critically, the results signal the value of policy interventions that would reduce the persistent economic precarity experienced by individuals and communities, especially the economic strain placed upon American workers. The value of implementing these upstream social and economic policies does not conflict with efforts made by government entities to hold pharmaceutical companies and pill mills accountable for overprescribing opioid medications to the public, nor does it conflict with the value of health policies aimed at reversing the opioid epidemic.

Table 5
County-Level Regression models testing for differences across triplicate and non-triplicate states.

A. Logged Drug Overdose Mortality		
Manufacturing Measure	Main Effect	Interaction Effect
Female		
% Employees in Manufacturing	-0.0096**	-0.0046
	(0.0028)	(0.0121)
% Annual Payroll in Manufacturing	-0.0080***	-0.0077
	(0.0022)	(0.0084)
Male		
% Employees in Manufacturing	-0.0125***	0.0003
	(0.0029)	(0.0128)
% Annual Payroll in Manufacturing	-0.0102***	-0.0036
	(0.0025)	(0.0083)
B. Logged Opioid Overdose Mortality		
Manufacturing Measure		
Female		
% Employees in Manufacturing	-0.0110**	0.0096
	(0.0039)	(0.0140)
% Annual Payroll in Manufacturing	-0.0083**	-0.0011
	(0.0027)	(0.0100)
Male		
% Employees in Manufacturing	-0.0120*	0.0088
	(0.0047)	(0.0155)
% Annual Payroll in Manufacturing	-0.0093*	0.0008
	(0.0037)	(0.0098)
C. Logged Corrected Opioid Overdose Mortality		
Manufacturing Measure		
Female		
% Employees in Manufacturing	-0.0146***	0.0017
	(0.0034)	(0.0127)
% Annual Payroll in Manufacturing	-0.0119***	-0.0028
	(0.0026)	(0.0096)
Male		
% Employees in Manufacturing	-0.0148***	0.0071
	(0.0037)	(0.0124)
% Annual Payroll in Manufacturing	-0.0112***	0.0006
	(0.0031)	(0.0082)

$*p < .05, **p < .01, ***p < .001$ (two tailed tests).
Notes: (a) All covariates are lagged one year. (b) State-clustered standard errors are in parentheses. (c) Employment models have 59,375 county-year observations; Annual payroll models have 59,379 county-year observations. (d) Main effect represents the coefficient for non-triplicate states; Interaction effect represents the difference in coefficient size and statistical significance between non-triplicate and triplicate states (i.e. the coefficient for triplicate states is equivalent to the Main Effect + the Interaction Effect). (e) Triplicate states include California, Idaho, Illinois, New York, and Texas. (f) All models include county fixed effects, year fixed effects, and all compositional, economic, and state labor and drug policy covariates included in the previous county-level models. (g) Employment and Annual Payroll measures are aggregated at the commuting zone-level. (h) All models are weighted by county population in 1999.

Future research should further investigate the complex relationship between structural unemployment, pain management, prescription drug use, and drug mortality.

This analysis should be interpreted with an understanding of the limitations of the data and analytic method. The data are ecological and do not model how individual-level labor market histories or perceptions of local economic opportunity are associated with mortality. As such, future research should identify datasets which allow for the modeling of individual-level labor market experiences and perceptions in conjunction with macro-level structural economic changes in labor markets. This sort of multi-level approach would further clarify the interrelationship between individual-level risk factors and ecological-level risk environments. Second, although fixed effects analyses adjust for time-invariant confounders which enter the model specifications linearly and additively, this method does not account for the full set of known and unknown confounders which vary across time. To address this issue,

this study adjusted for several important known sources of time-varying unobserved heterogeneity which have been identified by past research to impact mortality rates. Yet, it is still possible that there are omitted variables that might bias the results. Third, the covariates that adjust for state-specific supply-side factors of prescription painkillers (i.e. PDMPs, prescription opioid rates) are imprecise measures of the misuse of prescription opioids and have a number of limitations (Bao et al., 2017; Horwitz et al., 2018); yet, they represent the best available measures for evaluating policy changes that have altered the flow of prescription drugs. Fourth, drug and opioid overdose mortality rates used in this analysis were calculated according to deaths coded as having (or in the case of corrected opioid deaths, predicted to have) an underlying or contributing cause related directly to drug or opioid poisonings. Classifying individual-level death records that involve drug and opioid use as an *indirect* cause is not possible with NCHS vital statistics mortality records, but recent findings from Glei and Preston (2020) suggest that the scale of deaths from the drug epidemic was about two times larger in 2016 than drug-coded deaths when taking into account drug-associated mortality from indirect causes such as circulatory diseases, respiratory diseases, neoplasms, and external causes, to name a few. Finally, the single-year lag structure used in the specifications assesses the immediate relationship between manufacturing decline on overdose deaths. However, it is likely that the full direct and indirect impacts of structural economic change on substance use and ultimately overdose mortality might take a longer time to emerge than a single year (Venkataramani et al., 2020).

6. Conclusions

Manufacturing decline over the past two decades represents a continuation of long-term structural economic changes which have fundamentally altered the types of jobs available to U.S. workers, particularly those with only a high school degree. Since the 1980s, job growth has been concentrated in low-skill service industries that provide lower pay, fewer benefits, and decreased job security (Autor et al., 2006; Kalleberg, 2018). The findings of this study suggest that these economic changes can predict a substantial proportion of recent increases in U.S. mortality rates over the past two decades, especially for drug overdose deaths. Additionally, state-level differences in manufacturing decline during this time period account for a considerable amount of the geographic variation in drug overdose deaths.

Policymakers and clinicians alike may benefit from understanding the extent to which drug overdose deaths have social and economic determinants which impact the structure of opportunities available to U. S. workers. While it is most likely unfeasible to rebuild the country's manufacturing base back to mid-20th century levels, the findings of the present study would suggest that improvements in wages, benefits, and job stability for workers in low-wage service positions might decrease economic uncertainty and therefore provide a pathway towards reducing drug and opioid overdose mortality. Future research should further investigate and test specific mechanisms through which deteriorating economic conditions and employment prospects impact health and mortality.

Author statement

I am the sole author of this study.

Ethical statement

The data used in this analysis are state-level and county-level aggregated data (mortality rates) from the National Center for Health Statistics. The data have been used in accordance with the Data Use Agreement (DUA) for Vital Statistics Data Files drafted by the National Center for Health Statistics and signed by the author. The author declares no conflicts of interest, and all funding sources are listed in the

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2020.100679.

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