THE UNIVERSITY OF CHICAGO

HEALTH CARE UTILIZATION AND 12-MONTH MORTALITY FOLLOWING A NONFATAL OPIOID OVERDOSE AMONG NONELDERLY INDIVIDUALS DUALLY ENROLLED IN MEDICARE AND MEDICAID, 2014-2016

A DISSERTATION SUBMITTED TO
THE FACULTY OF THE CROWN FAMILY SCHOOL
OF SOCIAL WORK, POLICY, AND PRACTICE
IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

BY

ALLISON L. PAULSON

CHICAGO, ILLINOIS

AUGUST 2023

This dissertation is dedicated to my sisters.

Table of Contents

List of Tables

Paper 1. 12-Month Mortality among Nonelderly Duals Following Nonfatal Opioid Overdose

Appendix Tables for Paper 1

Paper 2. Medication for Opioid Use Disorder and 12-Month Mortality among Nonelderly Dually Eligible Medicare and Medicaid Beneficiaries

Appendix Tables for Paper 2

Paper 3. Health Care Utilization and 12-Month Mortality Following Nonfatal Opioid Overdose among Nonelderly Duals by Sex and Diagnosis of Schizophrenia

Appendix Tables for Paper 3

List of Figures

Acknowledgements

First and foremost, I would like to thank my dissertation committee: Drs. Harold Pollack, Jeanne Marsh, and Prachi Sanghavi. I was incredibly fortunate to have brilliant, supportive mentors with a wealth of knowledge about Medicare and Medicaid, the opioid epidemic, and health services. Harold, I cannot overstate how much I appreciate the time and energy you committed to my dissertation. I always knew I could count on you to ask the important questions, remind me of my overarching focus, and provide invaluable feedback on drafts. There is no one I would have rather had teach me. Jeanne, your belief in my ability and enthusiasm for my work carried me through the hardest periods of the last few years. I left our meetings with buoyed spirits and optimism about my progress, even when an hour previously I had felt I was getting nowhere. Thank you for always being in my corner. Prachi, thank you for being my data and methods guru these last few years. I feel like I got a second PhD in Medicare & Medicaid data management, and I could not have done it without your guidance.

I would also like to thank Dr. Colleen Grogan for encouraging me to apply to the program back when I was a public health student. I never would have thought a school of social work would turn out to be the perfect fit for me! Thank you, Drs. Saria Awadalla, Kristin Rankin, and Ron Hershow at the University of Illinois at Chicago, for teaching me the nuts and bolts of epidemiology.

Thank you to my friends and family for supporting me all these years. I appreciate everything you did to keep me laughing and living a well-rounded life when school threatened to consume me. And finally, thank you to my husband, Adam. I could not have done this without you.

Abstract

Nearly 100,000 deaths every year in the United States are now wholly or in part attributed to opioid overdose. Innumerable people have died from the indirect effects of opioids, such as heart disease exacerbated by long-term opioid misuse, and the degradation of protective social supports. Dual-eligible Medicare and Medicaid beneficiaries under the age of 65 (nonelderly duals) comprise a population with serious risk factors for premature death following a nonfatal overdose. By definition, they have disabling conditions but cannot afford their health care. Nonelderly duals also may have beneficial relationships with health care providers as a result of managing their comorbidities. These relationships may provide opportunities to initiate medication for opioid use disorder outside emergency department encounters. The goal of this dissertation is to describe the relationship between nonfatal opioid overdose, health care utilization, and 12-month mortality in this population. I used Medicare and Medicaid claims data to examine these associations among nonelderly duals who survived an opioid overdose between 2014-2016. Data from 2013-2017 were used to capture health care utilization and diagnoses prior to and following the index overdose.

Paper 1 describes the epidemiology of nonfatal opioid overdose and 12-month mortality among nonelderly duals who overdosed in the study period. Nearly 1 in 9 nonelderly duals who experience nonfatal opioid overdose died in the following year. Sex and some observed comorbidities were predictive of post-overdose mortality. Medication for opioid use disorder (MOUD) was associated with reduced mortality, but was rarely indicated in this population. Among those who died, the average time to death was 5 months, and most beneficiaries visited health care providers prior to death, suggesting there may be opportunities following the overdose to prevent death.

Paper 2 reports associations between MOUD and 12-month mortality among nonelderly duals as assessed using propensity score methods. Associations were described for the overall population as well as by sex and general level of health. Active MOUD at the time of the nonfatal overdose was associated with lower rates of 12-month mortality among men and healthier beneficiaries only. These findings underscore the importance of addressing differences in subpopulations that may affect access to and effectiveness of MOUD.

Paper 3 describes health care utilization and its association with 12-month mortality by sex and diagnosis of schizophrenia. Men without schizophrenia had higher mortality rates than other groups in this study, despite having the highest rate of indicated MOUD use. Additionally, women had more indicators of serious chronic illnesses. Emergency department visits were not associated with death within 12 months, and inpatient visits were only associated with mortality among beneficiaries with schizophrenia. Certain physical conditions, such as congestive heart failure, were associated with 12-month mortality only among beneficiaries without schizophrenia, suggesting that physical comorbidities have differential effects between groups. On average, beneficiaries in all groups saw outpatient health care providers on 24 or more days in the year prior to the OD. These visits to health care providers in familiar settings may provide opportunities to initiate MOUD other than at the index overdose event.

Introduction to Dissertation

People with disabilities face unique challenges in the American health care system. They must endure the particular stigmas associated with their conditions in addition to navigating an administratively complex, expensive, and restrictive health insurance system. They suffer disproportionately high levels of severe physical and mental comorbidities. Not surprisingly, they also experience disproportionately high rates of premature mortality.

In any population, the risk of adverse health outcomes, including premature mortality, is heightened by opioid misuse. The effects of opioid misuse among individuals with disabilities can be catastrophic. For example, one potential side effect of opioid misuse is depressed function of the heart muscle.[1] This is dangerous for all people, but more so for individuals who are disabled by conditions such as chronic obstructive pulmonary disease, which also impairs the heart muscle.[2] Alarmingly, individuals with disabilities misuse opioids more than their peers without disabilities.

Over 4 million disabled individuals under the age of 65 who are not able to afford their health care are dually enrolled in Medicare and Medicaid each year.[3] Although these individuals have relatively comprehensive health insurance, they also face unique challenges in coordinating their complex medical care and financing between federal and state payers. These factors may limit interactions with health care providers and increase their susceptibility to premature mortality.[4] Despite this, less is known about these individuals than other Medicare and Medicaid beneficiaries.

The government generates millions of health insurance claims for Medicare and Medicaid beneficiaries. These claims tell stories of hospitalizations, emergency encounters, mental health care, and day-to-day physical ailments. Of course, health insurance claims only reflect part of the health care experience, as they cannot express patients' subjective experiences or the needs for

which care was not sought. Nor do these data express clinical insights available through electronic health records and related provider-generated data. Yet, despite its limitations, a large, rich, longitudinal administrative dataset such as that provided by the Centers for Medicare and Medicaid provides a unique opportunity to understand the health care needs of people who have complex, multidimensional illnesses, but may be excluded from other studies.

Many premature deaths following a nonfatal opioid overdose may be prevented with proper access to health care. Knowledge about when and where vulnerable individuals access health care, and their health outcomes, can help social service providers better understand and advocate for the needs of their clients. Understanding the epidemiology of health care utilization and premature mortality among those dually enrolled Medicaid and Medicare may help physicians identify which patients may be most in need of an intervention. This knowledge may provide key insight into the best allocation of public health resources and points of intervention to improve health care utilization and prevent premature death.

MEDICARE & MEDICAID

With the passage of the Social Security Amendments in 1965, the 89th United States Congress officially committed the government to providing health insurance to a portion of the American population. Originally, Medicare, which is designed and fully funded by the federal government, provided hospital and medical insurance to individuals over the age of 65. The program has expanded since 1965 to insure more people, including those under the age of 65 with certain qualifying disabilities, and provide more benefits, such as prescription drug coverage. In contrast, Medicaid programs are designed, implemented, and administered by each state. They are jointly funded by the federal and state government, and as such there are general guidelines from the federal government to which each state must adhere. Designed originally to provide health

insurance for people who receive cash assistance from the state, Medicaid now covers low-income pregnant women, people of all ages with disabilities, and individuals who need long-term care. In certain circumstances, people are eligible for dual Medicare and Medicaid coverage. Substance use disorder (SUD) is not itself a qualifying disability for federal disability programs; however, many people with SUD qualify for benefits based on other co-occurring conditions (such as serious mental illness).

Dually Eligible Medicare & Medicaid Beneficiaries

Workers in the U.S. contribute a portion of each paycheck to Social Security Disability Insurance (SSDI) and Medicare. Individuals under the age of 65 who have worked a specific number of years (which is determined by age) may be eligible to receive SSDI and Medicare if they become disabled or chronically ill and are unable to return to the work force. The amount of SSDI a person is entitled to is determined by the amount the person has contributed to Social Security (which reflects the number of years of employment and the wages or salary a person earns). An individual who has not contributed (or has contributed below the qualifying amount) to Social Security is not eligible for SSDI. There is a waiting period of 5 months after a person becomes disabled before they are eligible for SSDI, and 24 months after that before the person is eligible for Medicare.

Individuals who did not contribute enough to cover living expenses after becoming disabled may be eligible for additional cash assistance through federal and state Supplemental Security Income (SSI). In most states, this automatically qualifies an individual for Medicaid. Individuals may also qualify for Medicaid through other pathways. They may have poverty-related eligibility without SSI, or high medical costs, or they may require long-term services and supports not provided by Medicare. Individuals who qualify for both Medicare and Medicaid are known as

dual-eligible beneficiaries. Each year, there are over 4 million individuals under the age of 65 who are dually eligible for Medicare and Medicaid (nonelderly duals).[3]

Nonelderly duals differ from the rest of the U.S. population, as well as Medicare- and Medicaid-only beneficiaries. In 2013, nonelderly duals were 48% female and 61% white/non-Hispanic, and 74% lived in an urban area.[3] At the time of the 2010 US Census, the U.S. population was 50.8% female and 72.4% white, and 80.7% lived in an urban area.[5,6] Nonelderly duals are more likely not to have received a high school diploma or equivalent than the national average (approximately 30% of nonelderly duals vs. 12% nationally in 2015[3,7]). Compared to their Medicare-only counterparts, nonelderly duals are younger, have more medical and behavioral health conditions, and more likely to be of minority race/ethnicity.[3] The presence of disabilities and high prevalence of serious comorbidities distinguishes nonelderly duals from their Medicaid-only counterparts.

The government determines the extent of Medicaid assistance available to a nonelderly dual based on their federal income and assets. Over 70% of nonelderly duals have full Medicaid benefits, which means Medicaid pays for Medicare premiums, deductibles, coinsurance, and some copayments for services. The federal income and countable asset limits for full dual eligibility are extremely low: in 2017, the federal income limit varied, but was 225% or less of the federal poverty limit for an individual, and the asset limit for a couple was $3,000.

The state may choose to only pay for Medicare services that are covered by Medicaid (e.g., if a substance use treatment is covered by Medicare, but not by the Medicaid program in a state, the state may elect not to pay for the coinsurance). The state also pays for all Medicaid-covered services that are not covered by Medicare (e.g., transportation). Facilities and providers submit claims to Medicare and Medicaid for reimbursement. Unlike health records, which include

unbilled services and provide more detailed information about a visit, claims are generated solely for the purpose of payment. A 2019 National Bureau of Economic Research working paper found that medical providers were likely to report a higher-cost secondary diagnosis in the top billing code.[8] For instance, Medicare does not reimburse facilities for health care-associated infections, and as such, electronic health records have been found to provide a more credible estimate of the prevalence of sepsis.[9] Medicare and Medicaid claims data should be interpreted with the knowledge that conditions may be underreported.

The landscape of health insurance plans offered and selected by nonelderly duals has been changing over the last decade as managed care plans have risen in popularity. Between 2013 and 2019, the proportion of beneficiaries enrolled exclusively in fee-for-service plans decreased for both Medicare and Medicaid. Almost 80% of nonelderly duals were enrolled exclusively in fee-for-service Medicare plans in 2013, but only 53% in 2020. Over 50% were enrolled exclusively in fee-for-service Medicaid plans in 2013, but only 40% in 2019.[3,10] Medicare beneficiaries with managed care plans, which are offered through private insurers and are known as Medicare Advantage, differ from their counterparts with traditional Medicare benefits in demographic characteristics—for instance, a greater proportion of Medicare Advantage beneficiaries are Black or Hispanic and are generally healthier than traditional Medicare beneficiaries.[11]

OPIOID OVERDOSE

The number of opioid-involved overdose deaths rose from less than 10,000 in 1999 to 21,089 in 2010 to over 80,000 people in 2021.[12] Prescription opioids and then heroin drove the opioid epidemic in its early years. In 2015, synthetic opioids became the most common contributor to substance overdose deaths.[13] The number of overdose deaths per year involving prescription opioids has remained between 14,000-17,000 since 2016.[12] The danger of the opioid epidemic has

risen and evolved as increasingly, unknown quantities and quality fentanyl is blended with opioids prior to misuse.

Mortality after Opioid Overdose

The possible repercussions of not providing opioid use disorder (OUD) treatment to an individual following a nonfatal overdose are severe. Depending on the demographic and clinical composition, between 5-9% of individuals of all ages die within 12 months of a nonfatal overdose.[14-16] A significant proportion of deaths following nonfatal opioid overdose are attributed to fatal overdoses. As could be expected, research has shown that nonfatal opioid overdoses are predictive of fatal overdoses.[17,18] It has been reported that people who were treated in an emergency department for an opioid overdose died of a subsequent overdose at a rate 100 times that of a demographically matched population.[19]

It is possible that the number of subsequent fatal overdoses is underreported because the specific drugs leading to death may be missing even when an overdose is identified.[20] Additionally, long-term opioid misuse impairs many vital systems, and indirectly leads to many deaths through immediate mechanisms other than overdose. Studies in which researchers distinguished between subsequent overdose deaths and all-cause mortality report a wide range of opioid deaths; the proportion of post-overdose deaths that are designated as related to opioids range from one-third to almost three-quarters of deaths.[14,16] Regardless, although caution must be applied in interpreting the cause of death, the fact that the underlying cause of overdose death cannot always be unequivocally determined does not negate the high post-overdose mortality rates. Motivation, also, cannot usually be determined easily: overdose may reflect bad quality of drugs, lack of experience, or suicidal intentions, among other issues.

Opioid mortality outcomes vary by gender and psychiatric disorders. Men have consistently had more overdose deaths than women, and overdose deaths among men have increased at a higher rate in the past decade than among women.[12] Male sex has consistently been found to be associated with drug overdose deaths after accounting for other factors.[14,21,22] There is a need for sex-specific analyses, as predictors for opioid overdose and mortality differ by gender. Researchers have found that women with OUD were more likely than men with OUD to have 2 or more psychiatric disorders (depression, bipolar disorder, anxiety, post-traumatic stress disorder, or panic disorder) and men were more likely to have polysubstance use, including alcohol, cannabis, and cocaine use.[23] The same study found comparable rates of sedative use disorder between men and women, but when other authors analyzed post-overdose mortality, they found that women with comorbid sedative diagnoses had higher risk of subsequent fatal overdose than men.[21] Regardless of gender, diagnoses of psychiatric disorders are associated with higher rates of fatal opioid overdoses compared with those without disorders.[22,24]

Opioid Overdose among Medicare & Medicaid Beneficiaries

Medicare and Medicaid beneficiaries comprise a significant proportion of opioid overdoses that result in an emergency department visit or hospitalization. Medicare is the primary payer for 39% of all opioid overdoses that result in hospitalization, and 11% of opioid overdoses that result in emergency department visits.[13] The prevalence of overdose is particularly high among nonelderly individuals. Medicare-disability beneficiaries account for as much as 24.5% of opioid overdose hospitalizations among those under 65 in the U.S.[25]

This pattern may reflect the high use of prescription opioids among Medicare beneficiaries. Those who misuse opioids often begin their trajectory into misuse through legitimate prescriptions. In the general U.S. population, as many as 58% of those who misuse prescription opioids use their

own prescribed opioids, and cite pain relief as the most common reason for misuse.[26] Individuals with disabilities, regardless of insurance status, may be particularly vulnerable to addiction when they have conditions that generate chronic pain. In one study on nonelderly Medicare beneficiaries, nearly 6 times as many individuals with a diagnosed substance use disorder (SUD) had comorbidities related to pain than their matched controls.[27] In another study pertinent to the study period, more than 50% of heroin and fentanyl deaths had an opioid prescription within 3 months of death.[28]

Medicaid beneficiaries also experience high rates of opioid use and overdose. Haider et al.,[29] using data from the National Survey on Drug Use and Health, found that Medicaid beneficiaries had 5 times the odds of reporting OUD compared to those with private insurance. Medicaid is the primary payer for 30% of all opioid overdoses that result in hospitalization, and 41% of emergency department visits for opioid overdoses.[13] Medicaid beneficiaries are disproportionately out of the labor force, and have low incomes and educational attainment, which are common risk factors for opioid use disorder.

There is limited research that focuses on opioid misuse among duals specifically. Opioid misuse is the use of an opioid medication or street drug for non-medical purposes or for purposes other than those indicated by a prescribing health care provider. In a study of opioid use among nonelderly Medicare beneficiaries, researchers found that 74% of opioid users were duals, but this was reported as a demographic characteristic, not a point of analysis.[30] In a study of nonelderly Medicare beneficiaries and opioid overdose deaths, although duals comprised 58% of the study population who died, dual status was not associated with opioid overdose deaths after adjustment for other risk factors.[31] Statistically controlling for dual status, rather than allowing for the population-specific protective and risk factors, may result in overly generalized conclusions about

duals. Other studies exclude duals from their analyses of opioid use disorder. This has occurred because the authors could not capture their complete medication use,[32] the study population was too small,[33] the authors did not have disability information,[34] or no reason was given.[35,36] The characteristics that set duals apart from Medicare- and Medicaid-only beneficiaries (namely, the unique combination of physical comorbidities and socioeconomic risk factors) may mean they need targeted interventions specific to their needs.

Medication for Opioid Use Disorder

Medication for opioid use disorder (MOUD: methadone, buprenorphine, and naltrexone) is considered to be the standard of care for treating opioid use disorder. Methadone and buprenorphine have both been found to be associated with lower hazards all-cause and opioid-related mortality.[37] A meta-analysis found that all-cause mortality and overdose mortality were 2.56 times and 8.10 times higher, respectively, among untreated individuals with OUD compared to those receiving MOUD.[38] Psychosocial treatment options, e.g., rehabilitation centers, do not address the physical dependence aspect of opioid use disorders, and consequently, are not recommended without accompanying MOUD. Access to MOUD, despite its acceptance in medical literature, is limited among individuals with OUD.

Receipt of MOUD following a nonfatal opioid overdose remains rare: one study reported a peak buprenorphine rate of 3% in the 12 months following the overdose.[39] Disconcertingly, although outpatient buprenorphine prescriptions have increased in the last decade, Hispanic, Medicaid-beneficiaries, those with co-occurring psychiatric conditions, or substance use disorders are less likely to obtain MOUD prescriptions.[40] Risk of discontinuation also looms large: If terminated too early, MOUD can be dangerous because substance tolerance decreases over the course of treatment. Longer duration of buprenorphine treatment has been found to be associated

with fewer deaths,[38] and Medicaid beneficiaries retained on buprenorphine for 15-18 months have been found to have lower odds of emergency department visits, inpatient hospitalizations, and filling opioid prescriptions in the 6 months following discontinuation than those retained on buprenorphine for 6-9 months.[41] However, other authors found that individuals whose treatment involved MOUD were more likely to die during treatment than those without MOUD, possibly because of decreased client engagement and supervision.[42] It is criterial to continue psychosocial services in conjunction with MOUD.

Treatment in the form of MOUD and psychosocial measures has disparate delivery by sex and mental health status. In a national study, it was found that less than 40% of those with a dual mental health diagnosis received MOUD.[43] A significant proportion of individuals with serious mental illness and opioid use disorder do not receive mental health or substance use disorder treatment; they have reported affordability, access, stigma, and a lack of readiness to stop using as barriers to seeking care.[44] There are mixed reports on the engagement of women with SUD treatment services. One study found that women are less likely to enter substance use treatment services, citing mental health, perceiving stigma, family responsibilities, and relational factors as barriers to treatment.[45] Other authors have found that women wait more days before initiating OUD treatment, but stayed in treatment longer than men.[46,47]

Policies around SUD treatment and MOUD specifically are quickly changing in the U.S. It is important to study the baseline of opioid overdose and treatment among nonelderly duals in the 2010s to evaluate the policies of the 2020s.

Medicare & Medicaid Opioid Treatment Policy

Medicare and Medicaid have implemented several policies aimed at the opioid epidemic over the years. Medicare is the first payer of health services. Medicaid substance use treatment

wraps around Medicare—it covers services not offered by Medicare and also pays coinsurance charges. Medicare has covered buprenorphine and naltrexone since prior to the years of this study (2014-2016) in office-based settings. Medicare did not cover opioid treatment programs (OTPs) during the study years. Crucially, OTPs are the only outpatient settings in which methadone can be administered, and, although required in OTPs, behavioral therapy is not required when medication is provided in office-based settings. The U.S. Food & Drug Administration (FDA) recommends all 3 medications be available as treatment options for individuals with OUD, as individuals have different needs and reactions to medications.[48]

The Affordable Care Act (ACA) of 2010 directed that states with expanded Medicaid programs had to offer alternative benefit plans that had addiction treatment benefits that were no more restrictive than those placed on other medical services. Standard Medicaid plans, i.e., those available to nonelderly duals, did not have to comply by these regulations. However, even without this requirement, the number of state Medicaid plans that covered methadone increased from 33 states in 2014 to 40 states in 2017.[49] The percent of standard plans with utilization controls, such as preauthorization requirements and annual limits, on addiction treatment services and MOUD decreased over this period.

There are additional logistical barriers to accessing MOUD. The presence of an adequate number of providers and facilities in an area affects how many people can access MOUD. While two-thirds of eligible outpatient buprenorphine prescribers for Medicare beneficiaries were family medicine and internal medicine practitioners, they constituted the lowest proportion of active buprenorphine prescribers.[50] As an additional barrier to treatment, not all substance use treatment facilities that deliver MOUD accept Medicaid. In 2016, MOUD was available at about 40% of outpatient substance use treatment facilities that accepted Medicaid or Medicare.[51] The geographic

distribution of facilities is not always reflective of need. Some states, such as Kentucky and New Mexico, have higher opioid overdose death rates and fewer facilities that offer MOUD relative to other states.[51] Nationally, about 40% of U.S. counties do not have an outpatient SUD facility that accepts Medicaid and can deliver MOUD.[52]

HEALTH CARE UTILIZATION

Individuals with OUD are at high risk of emergency department visits and hospital readmissions.[53,54] Cardiovascular, respiratory, and liver diseases are often direct effects of opioid use, and ailments such as skin and soft tissue infections are common among those who inject heroin. Individuals with OUD may avoid health services because of prior experiences with stigma from providers and fear of withdrawal symptoms.[55] Exacerbating the situation, the most frequent users of emergency departments have been found to have nonadherence to essential chronic medications, particularly among those with more than 4 opioid medication fills in the previous 6 months, more unique prescribers, and younger individuals.[56]

SMI is a common comorbidity to OUD. There is mixed evidence about whether individuals with SMI have higher health utilization rates. One population survey found that 21% of individuals with SMI and SUD did not receive any behavioral health treatment.[44] Care for physical comorbidities may also be low: It has also been found that individuals with SMI are less likely to be up to date on cardiovascular preventive care.[57] This may be related to the fact that some physicians believe that patients with mental illnesses care less about preventive care than the general population, or that these patients are less likely to adhere to recommendations for care.[58] Others have found that patients with serious mental illness receive preventive care at rates at least equal to those without mental illness, possibly because metabolic screenings are recommended for patients taking antipsychotics.[59] Although studies have tried to create a comprehensive picture of

health care utilization among individuals with SMI, this goal may not be feasible, and moreover, may obscure different needs of subpopulations.

Health Care Utilization among Medicare and Medicaid Beneficiaries

Medicare and Medicaid beneficiaries with OUD and SMI may have different utilization patterns than people with private insurance. Burns et al. (2016)[60] found that individuals with serious mental illness and substance use disorder used health care services more after they transitioned from Medicaid-only to dual status. Service utilization did not only increase in areas specifically related to their substance use or mental illness; they also sought more outpatient care services for other conditions. This is likely related to their high number of comorbidities: It has been estimated that nearly 80% of duals with behavioral disorders have 4 or more comorbid conditions.[61]

Hospitalizations are more common among duals under 65 with mental disorders than those without mental disorders. One study found that in a given year, 25% of duals under 65 with a mental disorder were hospitalized, compared with 14% of duals under 65 without a mental disorder.[62] Many of these hospitalizations are for causes unrelated to their mental illness, including those that reflect other severe health conditions that are not being effectively managed.

Having dual eligibility status may improve health outcomes among individuals with SMI who use substances compared to those with a single source of benefits. Medicare typically provides higher reimbursements than Medicaid, and is accepted by significantly more physicians.[63] However, Medicaid covers vital services excluded in Medicare, such as case management, residential care, and psychosocial rehabilitation services. Thus, individuals with SMI who use substances who are eligible for dual benefits may be more likely to have their diverse needs met.

SOCIAL WORK SIGNIFICANCE

Understanding the social factors that influence OUD, health care utilization, and mortality is important to the social workers who provide care beyond the office of a physician. Social workers play a unique and important role in the fight against the opioid epidemic in the U.S. Unlike other stakeholders, who may only be physically present in one place (e.g., a physician or paramedic) or not at all (e.g., policymakers), social workers work with their clients in multiple settings, including hospitals, mental health clinics, rehabilitation centers, and community outreach centers. Such is their importance that the National Association of Social Workers (NASW) published standards to define the scope of services that social workers provide to clients with substance use disorders and their families in 2013. More recently, Substance Abuse and Mental Health Services Administration (SAMHSA) awarded the Council on Social Work Education (CSWE) a $500,000 grant to create a high-quality, standardized SUD curriculum. The *Practitioner Education in Substance Use and Misuse: Competency-Based Resources*[65] guide that resulted from this grant provides a pilot social work curriculum that integrates substance use and misuse content. In addition to their general social work training, social workers can undergo additional training to become a Certified Clinical Alcohol, Tobacco & Other Drugs Social Worker.

The factors that directly cause premature mortality are easy enough to detect in a clinical setting: a person with liver disease, for instance, is an easily identified focus for interventions that aim to manage SUD. However, flagging individuals who have comorbidities that are directly associated with mortality may overlook individuals at high risk of death based on other factors. Creating predictive instead of causal statistical models is one way to overcome this limitation. Predictive models, particularly those that include variables beyond the presence of a disease and its severity, allow for the identification of risk factors and noncausal correlates that may be otherwise overlooked in a clinical setting focused on causal determinants.

Nonelderly duals, who by definition are low-income individuals with complex medical needs, suffer disproportionately high levels of adverse health outcomes. Social theories, such as fundamental cause theory and life course theory, may provide valuable insight to social workers who strive to understand and address factors that influence wellbeing beyond treatment for physical comorbidities.

Fundamental Cause Theory

Fundamental cause theory suggests that socioeconomic status (SES) causes multiple disease outcomes via several direct and indirect mechanisms.[66] Once ill, high SES individuals have greater access to resources that are associated with better health outcomes than their lower SES counterparts. For instance, powerful social connections may link people to the most proficient doctors. High SES individuals are more likely to have the money to afford expensive treatment. Access to treatment is also based on the physical location and number of providers, as well as whether a person has the transportation required to see the provider. These are key factors in a person's health outcomes. Regardless of an individual's physical susceptibility to an illness, if she is not able to coordinate her health care needs with an appropriate provider in a timely fashion, she will likely suffer poor health outcomes. Her ability to coordinate her care with a provider is greatly influenced by her financial status.

Medicare is accepted by almost all providers in the U.S., but Medicaid, which offers lower reimbursement rates, is accepted by significantly fewer providers. In an attempt to boost the number of providers who accept Medicaid, the ACA required states to raise Medicaid payment rates for some services. Yet even after the payment bump, Medicaid acceptance remains low.[67] Medicare is the primary payer for services provided to nonelderly duals—but this only pertains to services that Medicare covers. Nonelderly duals often require services not covered by Medicare,

such as long-term services and supports, and in these instances, are limited to providers that accept Medicaid. There are downstream effects of disparate access to care. Adverse health outcomes (such as higher rates of intensive care unit admission and later post-surgery mobilization) in specialty care are more common among Medicaid patients than their privately insured peers, even after controlling for clinical and sociodemographic factors.[68]

There is a psychological component to health care that disproportionately affects low SES patients. Patients on Medicaid may be less likely to advocate for themselves or their children, in part based on how their physician treats them. Providers may not value the communication style patients used by patients of low SES status, or believe the patient is serious or educated about treating her condition.[69] Consequently, patients may not adhere to treatment recommendations, or even may terminate care prematurely. This may perpetuate a physician's attitudes toward low-income patients; some physicians even refuse to see patients with substance use disorders based on their negative stereotypes.[70] The relationship between the provider and the patient is just as important in social work practice. In a systematic review, Marsh et al. (2012)[71] found a robust association between the client-provider relationship and retention in substance misuse and mental health treatment.

Life Course Theory

According to life course theory, the developmental antecedents and consequences of life transitions, events, and behavior patterns vary according to timing in a life course.[72] Qualifying disabilities have a range in onset, progression, and severity. For instance, individuals may become incapacitated if they experience a spinal injury that results in paralysis—an event that may occur at any point in the life course from infancy on. Other qualifying conditions, such as schizophrenia or depressive disorder, may only reach a point where they are considered functionally debilitating

after several years, but may have begun in while an individual was in her 20s. At the other end of the spectrum, diagnoses such as early-onset Alzheimer's disease are more likely to occur when an individual is closer to retirement age. The timing of onset may affect the psychological component of being disabled. Individuals who leave the work force later may experience a loss of identity that formed over the course of a career. On the other hand, a person who becomes disabled later in life may have a partner who provides emotional support, as well as logistical support in tasks like setting and getting to appointments. The social networks that a person has earlier in life may be drastically different than those later in life

Duals who were Medicaid beneficiaries, whether in childhood or as adults, prior to disability may have different qualifying disabling conditions. This could in part be due to the disparate effects of financial strains at different times of life. Individuals who do not report childhood financial strain but strain in adulthood are more likely to be disabled than those who do not report financial strain at any time.[73] Disabling conditions may be associated with specific types of events in childhood. Conditions associated with chronic pain, for instance, have been found to be correlated to adverse childhood events, such as being institutionalized as a child.[74]

Life course theory provides a framework to understanding how physical comorbidities may lead to mental comorbidities. Many of the qualifying conditions for early Medicare generate chronic pain, which is commonly associated with depression. The number of chronic conditions an individual has is highly correlated to dramatically increased odds of major depression. Individuals with one chronic medical condition have over twice the odds of experiencing major depression compared to those without any chronic conditions; those with 3 or more chronic medical conditions have over 6 times the odds.[75] This may be key to understanding both substance use and health care utilization, as one's mental state may affect whether they seek and maintain

vital health care. Life course theory brings to prominence the importance of the timing and duration of physical and mental disorders, Medicare eligibility, and OUD.

DISSERTATION OVERVIEW

This dissertation seeks to describe the impact of nonfatal opioid overdoses on nonelderly duals and explore health services use prior to and following a nonfatal overdose. The predictive models in this dissertation used variables to explore risk factors and correlates beyond clinical diagnoses. Specifically informed by fundamental cause theory, I included variables that reflect the socioeconomic status of each beneficiary at a zip-code level. As states vary in the availability of services, demographic characteristics, and the prevalence of OUD, I theorized that geographic location may be an important variable in these analyses. Fundamental cause theory would suggest that a person who lives in a low SES zip code and in a state with fewer providers would be more likely to die in the months following a nonfatal OD.

Life course theory also was incorporated in this dissertation through the inclusion of variables reflecting the timing of comorbidities and Medicare eligibility. Although the Medicare data available indicated solely when the beneficiary became eligible for Medicare based on his or her own disability, and did not reflect the physical or mental health of the person prior to Medicare eligibility, this was a realistic estimate for the onset of severe disability. The health care utilization analysis in this dissertation considered the duration of Medicare coverage as well as the duration of diagnosed OUD and other conditions.

Paper 1 of this dissertation is a descriptive study of nonelderly duals who survived a nonfatal opioid overdose between 2014-2016. This paper assessed the association between physical and mental comorbidities and 12-month mortality. It provides predicted probabilities for mortality based on age group and comorbidity to distinguish the effect of overdose on mortality. Finally, this paper explored causes of death among those who died within 12 months of nonfatal

overdose, and described characteristics of those indicated to have died from fatal opioid overdoses and those indicated to have died from other causes.

Paper 2 is a quasi-experimental analysis using propensity score methods to assess the association between MOUD and 12-month mortality following a nonfatal opioid overdose. Nonelderly duals were stratified by sex and general level of health.

Paper 3 of this dissertation is a comprehensive exploration of health services utilization in the 12 months prior to and following a nonfatal opioid overdose, stratified by sex and the presence of schizophrenia. This paper describes inpatient and outpatient health care utilization behaviors of nonelderly duals in this study cohort prior to and following nonfatal overdose. I used predicted probabilities and logistic regression to assess the association between health care utilization and mortality.

These analyses are pertinent to social workers because nonelderly duals likely have different risk factors for mortality and patterns of utilization than their peers with other types of insurance or who are uninsured. Furthermore, nonelderly duals may be accessing health care services for their disabilities at primary care offices. Many substance use disorder interventions are placed in emergency departments and treatment facilities, but this study may reveal other locations that may be appropriate delivery sites for interventions. This information will help social workers develop targeted interventions for nonelderly duals at high risk of fatal overdose and other adverse outcomes.

These analyses are relevant to public health professionals and clinicians because the opioid epidemic is still accelerating in the US. There are over 4 million nonelderly duals and they are a high-risk but understudied population, with existing relationships to health care providers who may be able to modify risk factors to improve health outcomes.

Finally, these analyses are important to policymakers. Nonelderly duals are entirely dependent on Medicare and Medicaid for their health care. It is well-known that they have poorer health outcomes than their Medicare- and Medicaid-only peers, but the government spends more on their care. Understanding nonelderly duals as a distinct population, and not statistically controlling for dual status in studies, may provide vital information on improving access to preventive health care services, thus reducing expensive and dangerous emergency care.

Paper 1. 12-Month Mortality among Nonelderly Duals Following Nonfatal Opioid Overdose

ABSTRACT

Objectives. To describe the epidemiology of nonfatal opioid overdose among dually enrolled Medicare & Medicaid beneficiaries under age 65 (nonelderly duals), and to examine associations with 12-month post-overdose mortality.

Methods. This retrospective observational study uses 100% nationwide Medicare claims data to identify nonelderly duals who survived an opioid overdose between 2014-2016, and to examine associations between beneficiary characteristics and 12-month mortality from subsequent fatal overdose and other causes.

Results. A total of 1,561 (10.8%) of nonelderly duals who survived an opioid overdose died within 12 months. Associations with 12-month mortality included heroin involvement in the index overdose (aOR = 1.25; 95% CI = 1.07, 1.47), chronic pain (aOR = 1.23; 95% CI = 1.05,1.44), and male sex (aOR = 1.28; 95% CI = 1.13,1.45). Medication for opioid use disorder (MOUD) was associated with reduced mortality (aOR = 0.75; 95% CI = 0.62, 0.90), but was rarely indicated in this population.

Conclusions. Nearly 1 in 9 nonelderly duals who experience opioid overdose died in the following year. Sex and some observed comorbidities were predictive of post-overdose mortality.

Policy implications. Increased MOUD engagement and post-overdose interventions that serve this high-risk population are important priorities to address the opioid overdose epidemic.

INTRODUCTION

More than 4 million Americans under the age of 65 are dually eligible for Medicare and Medicaid (nonelderly duals).[3] Dual eligibility hinges on fulfilling standards for each program. Most nonelderly duals qualify for Medicare because they are disabled (many with conditions that induce chronic pain) and for Medicaid because they are low income. An important subpopulation of nonelderly duals faces synergistic risks for opioid overdose (OD) and premature death. Many studies have found that opioid OD and premature death are higher among Medicare beneficiaries under 65, as well as Medicaid beneficiaries, than in the general population.[25,31,76,77] However, dual status was not included as a characteristic in many of these studies.[24,34,35] In the notable exceptions that specifically identified nonelderly duals, the unique characteristics of this population were not the focus.[31,33,77] Nonelderly duals differ significantly from their Medicare- and Medicaid-only peers. Most Medicaid-only beneficiaries are not disabled, and compared with their Medicare-only peers, nonelderly duals are more racially diverse (57% vs. 84% White), have fewer years of education (65% vs. 43% with no more than a high school degree), and live below the poverty line.[3]

Rates of fatal overdose and deaths from other causes are elevated in the 12 months following a nonfatal opioid OD among nonelderly Medicaid beneficiaries and the general public.[14,16,76] Opioid OD deaths are also likely underreported. Medical examiners and coroners often fail to identify specific substances involved in an overdose.[20] Causes of death among individuals with substance use disorders (SUD) can be difficult to disentangle, as prolonged opioid misuse can damage multiple body systems. In identifying opportunities for clinical or public health intervention, prior overdose may thus be a marker in conjunction with other chronic risk factors and immediate vulnerabilities.

This study seeks to describe mortality patterns and causes of death among nonelderly duals in the 12 months following nonfatal opioid OD. Nonelderly duals who experience nonfatal opioid OD may be uniquely positioned for focused intervention. They have rather comprehensive public health insurance coverage. Most experience comorbidities that occasion regular contact with health care providers. Knowledge about the scope of the epidemic in this population, as well as regarding risk factors and comorbidities associated with subsequent mortality, may provide life-saving information for health care and social service providers, and for public policymakers.

METHODS

Use of these data was approved by the Centers for Medicare and Medicaid Services. The University of Chicago Institutional Review Board determined this research was exempt from informed consent.

Data Sources

I used 2014-2016 100% nationwide Medicare claims data to identify eligible overdose events and diagnoses, and describe demographic characteristics of the study population at the time of the overdose. The Medicare Provider Analysis and Review (MedPAR) file and outpatient claims files were used to identify opioid overdoses and other health care utilization. The Master Beneficiary Summary File (MBSF) and its chronic conditions and other chronic conditions supplements were used to determine eligibility. The National Death Index supplement to the MBSF provided cause of death information of beneficiaries who died in 2015 and 2016.

MedPAR, outpatient, and MBSF data from 2013 and 2017 were used to describe 6-month eligibility and health care utilization for overdoses that occurred before July 1, 2014, and 12-month follow-up for overdoses that occurred after January 1, 2016.

Local availability of selected medications for opioid use disorder (MOUD) was approximated by the Automation of Reports and Consolidated Orders System (ARCOS) Retail Drug Summary Reports for 2014-2016. These annual Drug Enforcement Administration reports disclose the amount of buprenorphine distributed to geographic locations at a 3-digit zip code level.[78]

The U.S. Department of Agriculture rural-urban continuum codes were used to categorize the county of residence as metro or non-metro.[79]

Study Population

I used the 2014-2016 MBSF to select Medicare beneficiaries ages 21-64. I identified nonfatal opioid OD among these beneficiaries using MedPAR and outpatient claims files. Codes to capture nonfatal opioid OD prior to October 1, 2015, were drawn from the *International Statistical Classification of Diseases and Related Health Problems, Ninth Revision, Clinical Modification (ICD-9-CM):* codes 965.00-965.02, 965.09, E85.00-E85.02, and E93.50-E93.52. CMS switched to ICD-10-CM on October 1, 2015. Thus, ICD-10-CM codes T40.0-T40.4, and T40.6 were used to identify nonfatal opioid OD on or after this date. These overdose codes include poisonings from opiates and related narcotics, heroin, and methadone. The study index event was the discharge date of the first nonfatal opioid OD that occurred in the study period.

I used the MBSF and its supplements to identify eligible nonelderly duals. Inclusion criteria included: 1) Fee-for-service, full dual coverage, with no HMO coverage, with continuous full dual status for at least 6 months prior to and 12 months following the index OD (or until death) and 2) originally entitled to Medicare because of a disability. Exclusion criteria included: 1) diagnosis of end-stage renal disease; 2) cancer diagnosis in the year of the opioid OD; 3) residence outside the

United States at time of opioid OD; 4) death at the health care facility during the overdose event or on the day of the event.

Finally, I created a comparison population of beneficiaries who fulfilled all study criteria on January 1, 2015, but did not overdose during the study period. Twelve-month mortality for these beneficiaries was determined as death during the 2015 calendar year.

Variables

My primary study outcomes were 12-month mortality and fatal opioid OD. ICD-10-CM causes of death were provided in the NDI supplement to the MBSF. Opioid overdose deaths were identified those coded X40-X44, X60-X64, X85, or Y10-Y14, in conjunction with T40.0-T40.4, or T40.6, as immediate causes of death.

Fundamental cause theory and life course theory contributed to the conceptualization of other potentially significant risk and protective factors. Fundamental cause theory suggests that socioeconomic status (SES) causes multiple disease outcomes via several direct and indirect mechanisms theories. According to life course theory, the timing of life transitions and events affects outcomes. The MBSF was used to extract characteristics related to these theories. Beneficiaries were classified by race/ethnicity (Hispanic, Black or African American, non-Hispanic White, Other), sex, age, and years under disability insurance. These characteristics have been found to be associated with poor access to substance use disorder treatment facilities and poor health outcomes.[30,52,74,80]

The MBSF and its supplements were used to identify the presence of chronic conditions as defined by the Chronic Conditions Data Warehouse (CCW). In the CCW definition, beneficiaries with claims for buprenorphine, naltrexone, or methadone within the previous 2 years are flagged as having utilized MOUD.

Overdose variables were determined using the Outpatient and MedPAR files: number of opioid ODs in 6 months prior to index opioid OD; heroin involvement in the index event; facility type (inpatient vs. outpatient); and discharge status (transferred to different department or facility; discharged to home; other discharge).

I used van Walraven weighted Elixhauser scores to indicate overall health status, with higher scores indicating greater comorbidity.[81] Scores were determined using the ICD-9-CM or ICD-10-CM codes present on the index opioid OD claim and all inpatient and outpatient facility claims in the 180 days prior to the index opioid OD. ICD-9-CM codes were used for utilization prior to October 1, 2015, and ICD-10-CM codes thereafter.

Health care utilization was measured by 1) continuously, by the number of discharge days on which the beneficiary saw a health care provider (inpatient or outpatient), and 2) categorically by grouping the number of claims into groups of 0, 1-4, or 5 or more.

Geographic variables included the amount of buprenorphine delivered to the geographic region (measured continuously); rural or urban county (using the rural-urban continuum codes); state, and U.S. census region (identified in the MBSF).

Statistical Analysis

I calculated descriptive statistics for 12-month mortality following the index OD. Pearson's Chi-squared Test and Student's t-Test were used to assess associations between the mortality outcome and each characteristic and comorbidity.

Given the large study cohort, statistically significant differences in means and associations may not be clinically meaningful. I thus estimated predicted probabilities for 12-month mortality to examine associations between comorbidities common among individuals with opioid OD (e.g., chronic kidney disease) and mortality. I assigned beneficiaries mean characteristics except for the

comorbidity in question, and assessed 12-month mortality for nonelderly duals with these comorbidities across age groups within the cohort.

I used logistic regression to describe associations between beneficiary characteristics and 12-month mortality. Fixed and random effects of state were assessed. Descriptive statistics for nonelderly duals whose death certificates indicated subsequent fatal opioid OD were compared to those whose death certificates indicated all other causes. Finally, I conducted a secondary analysis allowing for clustered standard errors to account for the effect of living in each state. I compared this to a fixed effects model that included all states. Six states (Delaware, Hawaii, Montana, North Dakota, South Dakota, and Wyoming) and the District of Columbia each had fewer than 50 beneficiaries who fulfilled my study criteria; these states were grouped together as one state for the analysis.

Analyses were conducted in the R programming language version 4.1.1.

RESULTS

The opioid overdose cohort comprised 14,469 nonelderly duals who survived an opioid OD that was reported on a 2014-2016 MedPAR or outpatient claim. A flow diagram of the creation of the study cohort is available in Appendix 1 (Figure A1.1). 10.8% (n=1,561) died within 12 months of hospital or outpatient facility discharge. Of these beneficiaries, National Death Index were available for the 1,006 beneficiaries who died between 2015-2016. Opioid ODs were indicated as the primary cause of death for 21.8% (n=219) of these beneficiaries. A total of 1,839,920 nonelderly duals fulfilled the study criteria in 2015 and did not fulfill the overdose population criteria. Among these comparison beneficiaries, 1.9% died in 2015. This group was used to describe overall mortality and the prevalence of comorbidities among nonelderly duals. A

table comparing deceased nonelderly duals who overdosed with their deceased peers who did not overdose is available in Appendix 2 (Table A2.1).

Risk Factors for 12-Month Mortality after Nonfatal Opioid Overdose

Table 1 describes characteristics and comorbidities of survivors and those who died within 12 months following nonfatal opioid OD (summary table in text; a complete version can be found in Appendix 2, Table A2.2). On average, those who died within 12 months were older (51.1 vs 48.0 years) and less likely to have heroin indicated on the index overdose claim (21.3% vs. 23.5%). Only 10.4% of nonelderly duals who died following opioid OD had MOUD indicated within the preceding 2 years, compared with 14.2% of the survivors.

Table 1. Characteristics and Comorbidities of Nonelderly Dual Beneficiaries Who Survived an Opioid Overdose

Characteristic	Survived 12 months (n=12908)	Died within 12 months (n=1561)	*P* Value
Age (years), Mean (SD)	48.0 (10.5)	51.1 (9.80)	<0.001
Male sex, No. (%)	5209 (40.4)	727 (46.6)	<0.001
Race, No. (%)			
Non-Hispanic White	9799 (75.9)	1211 (77.6)	0.48
Black or African American	1666 (12.9)	182 (11.7)	
Hispanic	1019 (7.9)	120 (7.7)	
Other	424 (3.3)	48 (3.1)	
Census region, No. (%)			
Midwest	3241 (25.1)	389 (24.9)	0.02
Northeast	3833 (29.7)	414 (26.5)	
South	3421 (26.5)	465 (29.8)	
West	2413 (18.7)	293 (18.8)	
Number of opioid overdoses in previous 6 months, Mean (SD)	0.01 (0.11)	0.02 (0.17)	0.01
Index overdose involved heroin, No. (%)	3038 (23.5)	332 (21.3)	0.05
Elixhauser score >= 0, No. (%)	9214 (71.4)	1219 (78.1)	<0.001
Days with claims (before OD), Mean (SD)	7.37 (7.59)	8.46 (8.16)	<0.001

Table 1 continued			
One or more inpatient claims prior to OD, No. (%)	5397 (41.8)	932 (59.7)	<0.001
One or more outpatient claims prior to OD, No. (%)	11414 (88.4)	1410 (90.3)	0.05
Substance use diagnoses, No. (%)			
Alcohol use disorder	3903 (30.2)	509 (32.6)	0.06
Drug use disorder	11009 (85.3)	1415 (90.6)	<0.001
Medication for Opioid Use Disorder (MOUD)	1839 (14.2)	163 (10.4)	<0.001
Opioid use diagnosis or procedure	10154 (78.7)	1368 (87.6)	<0.001
Opioid use emergency department or hospitalization	12565 (97.3)	NA[1]	<0.001
Tobacco use disorders	9131 (70.7)	1169 (74.9)	<0.001
Mental Health Diagnoses, No. (%)			
Attention Deficit Hyperactivity Disorder (ADHD) and other conduct disorders	1651 (12.8)	132 (8.5)	<0.001
Anxiety	9765 (75.7)	1205 (77.2)	0.19
Bipolar	5983 (46.4)	696 (44.6)	0.20
Depression	10420 (80.7)	1279 (81.9)	0.27
Personality disorders	2206 (17.1)	239 (15.3)	0.08
Post-traumatic stress disorder	2806 (21.7)	261 (16.7)	<0.001
Schizophrenia and other psychotic disorders	3542 (27.4)	454 (29.1)	0.18
Pain Diagnoses, No. (%)			
Fibromyalgia, chronic pain, fatigue	9539 (73.9)	1272 (81.5)	<0.001
Migraine	2568 (19.9)	253 (16.2)	<0.001
Chronic Conditions, No. (%)			
Acute myocardial infarction	177 (1.4)	54 (3.5)	<0.001
Atrial fibrillation	359 (2.8)	79 (5.1)	<0.001
Chronic kidney disease	4358 (33.8)	825 (52.9)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	4568 (35.4)	812 (52.0)	<0.001
Congestive heart failure	2514 (19.5)	578 (37.0)	<0.001
Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS)	399 (3.1)	76 (4.9)	<0.001
Hypertension	7687 (59.6)	1080 (69.2)	<0.001
Ischemic heart disease	3701 (28.7)	689 (44.1)	<0.001
Liver disease	1977 (15.3)	423 (27.1)	<0.001
Rheumatoid arthritis / osteoarthritis	6634 (51.4)	809 (51.8)	0.77
Viral hepatitis	2959 (22.9)	464 (29.7)	<0.001

Table 1 continued			
Other Developmental Delays			
Cystic fibrosis and other metabolic developmental disorders	286 (2.2)	71 (4.5)	<0.001

[1] Cells with values less than 11 suppressed in accordance with CMS policy to protect confidentiality of beneficiaries.

Those who died following nonfatal opioid OD displayed higher comorbidity, reflected in higher prevalence of Elixhauser scores over 1 (78.1% vs. 71.4%). Several serious comorbidities were more common among those who died, including chronic kidney disease (52.9% vs. 33.8%), chronic obstructive pulmonary disease (COPD; 52.0% vs. 35.4%), and congestive heart failure (37.0% vs. 19.5%). Over half of the beneficiaries who overdosed, regardless of mortality outcome, had 5 or more outpatient facility claims in the 6 months prior to the index opioid OD. A greater proportion of those who died had at least 1 inpatient claim prior to index opioid OD (59.7% vs. 41.8%). Yet in the 6 months prior to index overdose, most beneficiaries saw health care providers in either setting between 7-8 times prior to opioid OD.

Among nonelderly duals with atrial fibrillation, chronic kidney disease, congestive heart failure, COPD, hypertension, ischemic heart disease, liver disease, and stroke, those who had survived opioid OD had markedly higher 12-month mortality than those who did not overdose (Figure 1). Among nonelderly duals assigned mean characteristics, the predicted probabilities for 12-month mortality for beneficiaries who survived an opioid OD ranged from almost 4 times higher (60-64-year-olds with congestive heart failure; 14% vs. 4%) to over 9 times higher than those who did not overdose (30-39-year-olds with liver disease, chronic kidney disease, or congestive heart failure; each over 9% vs. 1%). With all characteristics assigned mean value, I found a predicted probability of 8.8% of dying within 12 months of nonfatal opioid OD—fully 8

times the 1.0% predicted probability of dying within 12 months for a nonelderly dual assigned mean characteristics who did not overdose.

Figure 1. Predicted probabilities of 12-month mortality among nonelderly duals by opioid overdose status, age (10 years), mean characteristics, and selected conditions

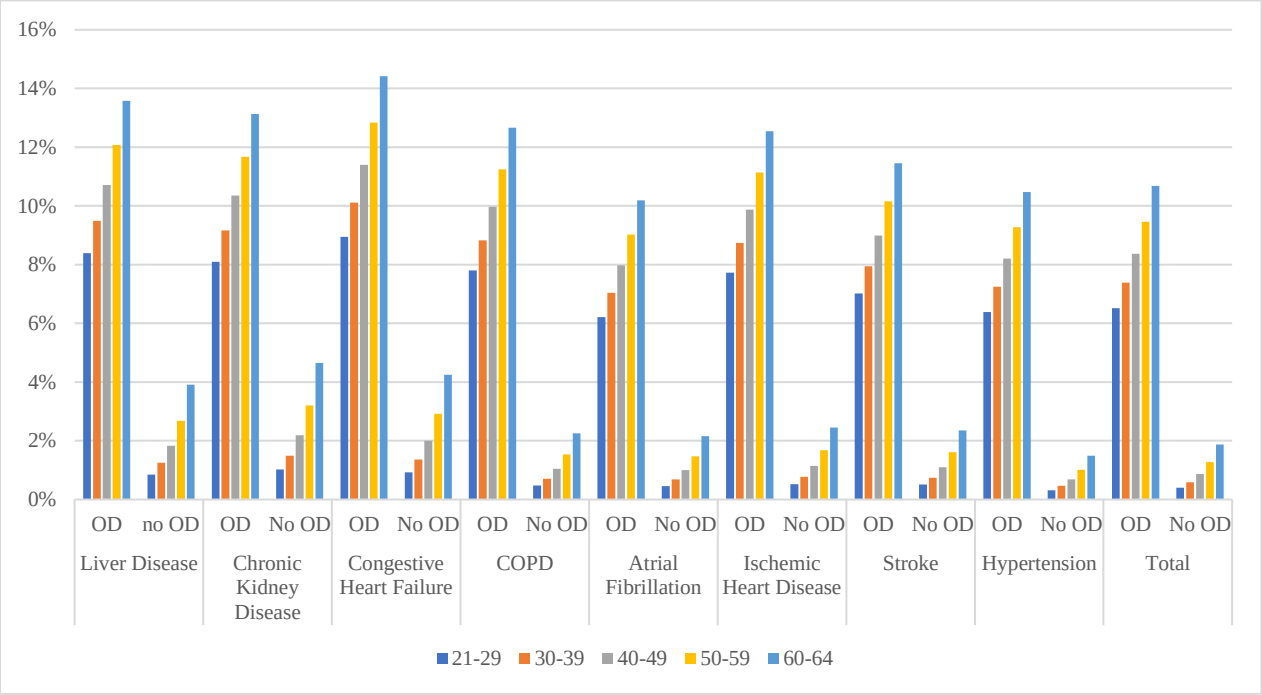


Table 2 presents logistic regression results estimating death within 12 months of a nonfatal opioid OD among nonelderly duals (summary table in text; a complete version can be found in Appendix 2, Table A2.3). Variables associated with 12-month all-cause mortality included discharge to a facility instead of home (aOR= 1.21; 95% Confidence Interval = 1.04,1.42), years-of-age (aOR = 1.02; 95% CI = 1.01,1.03), male sex (aOR = 1.28; 95% CI = 1.13,1.45, heroin involvement in index overdose (aOR = 1.25; 95% CI = 1.07,1.47), and chronic kidney disease (aOR = 1.37; 95% CI = 1.20,1.56). Medication for opioid use disorder treatment (MOUD) in past 2 years was associated with reduced mortality (aOR = 0.75; 95% CI = 0.62,0.90). Anxiety, bipolar disorder, depression, and schizophrenia and other psychotic disorders were not associated with increased odds of 12-month mortality. The area under the curve (AUC) for this model was 0.70.

Table 2. Characteristics Associated with 12-Month All-Cause Mortality

Characteristic	Unadjusted Odds Ratio (95% Confidence Interval)	*P* Value	Adjusted Odds Ratio (95% Confidence Interval)	*P* Value
Age (Years)	1.03(1.03,1.04)	<0.001	1.02(1.01,1.03)	<0.001
Sex (Ref: Female)	1.29(1.16,1.43)	<0.001	1.28(1.13,1.45)	<0.001
Black or African American Race (Ref: Non-Hispanic White)	0.88(0.75,1.04)	0.14	0.82(0.68,0.98)	0.03
Number of opioid overdoses in previous 6 months	1.86(1.31,2.59)	<0.001	1.53(1.06,2.16)	0.02
Index overdose involved heroin	0.88(0.77,1.00)	0.05	1.25(1.07,1.47)	0.01
Elixhauser score	1.06(1.05,1.07)	<0.001	1.02(1.02,1.03)	<0.001
Number of inpatient claims prior to OD (Ref: 0 visits)				
1-4 Visits	1.90(1.70,2.12)	<0.001	1.47(1.30,1.67)	<0.001
5+ Visits	3.39(2.80,4.08)	<0.001	2.09(1.67,2.61)	<0.001
Number of outpatient claims prior to OD (Ref: 0 visits)				
1-4 Visits	1.18(0.98,1.43)	0.09	1.07(0.88,1.30)	0.52
5+ Visits	1.25(1.05,1.51)	0.02	0.94(0.77,1.15)	0.53
Discharge group (Ref: discharged to home)				
Discharged to another facility	1.71(1.48,1.97)	<0.001	1.21(1.04,1.42)	0.02
Discharge - other	1.64(1.43,1.88)	<0.001	1.33(1.15,1.53)	<0.001
Substance use diagnoses				
Alcohol use disorder	1.12(1.00,1.25)	0.06	0.91(0.79,1.03)	0.13
Drug use disorder	1.67(1.41,2.00)	<0.001	0.76(0.57,1.02)	0.06
Medication for Opioid Use Disorder (MOUD)	0.70(0.59,0.83)	<0.001	0.75(0.62,0.90)	0.003
Opioid use diagnosis or procedure	1.92(1.65,2.25)	<0.001	1.69(1.32,2.20)	<0.001
Tobacco use disorders	1.23(1.09,1.39)	<0.001	1.03(0.90,1.18)	0.68
Pain diagnoses				
Fibromyalgia, chronic pain, fatigue	1.55(1.36,1.78)	<0.001	1.23(1.05,1.44)	0.01
Migraine	0.78(0.67,0.90)	0.001	0.83(0.71,0.96)	0.02
Chronic conditions				
Acute myocardial infarction	2.58(1.88,3.49)	<0.001	1.32(0.94,1.84)	0.10

Table 2 continued				
Atrial fibrillation	1.86(1.44,2.38)	<0.001	0.86(0.65,1.13)	0.28
Congestive heart failure	2.43(2.17,2.72)	<0.001	1.43(1.24,1.65)	<0.001
Chronic kidney disease	2.20(1.98,2.44)	<0.001	1.37(1.20,1.56)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	1.98(1.78,2.20)	<0.001	1.32(1.16,1.51)	<0.001
Viral hepatitis	1.42(1.27,1.60)	<0.001	1.06(0.92,1.22)	0.40
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	1.60(1.24,2.05)	<0.001	1.24(0.94,1.62)	0.12
Ischemic heart disease	1.97(1.77,2.19)	<0.001	1.27(1.11,1.45)	<0.001
Liver disease	2.06(1.82,2.32)	<0.001	1.33(1.15,1.52)	<0.001
Osteoporosis	1.23(0.99,1.52)	0.05	0.94(0.74,1.17)	0.57
Rheumatoid arthritis / osteoarthritis	1.02(0.92,1.13)	0.75	0.74(0.65,0.84)	<0.001

Fatal Opioid Overdose and All-Cause Mortality

Table 3 shows characteristics of the subpopulation of the beneficiaries who died in 2015 or 2016 who had NDI data (summary table in text; a complete version can be found in Appendix 2, Table A2.4). See Appendix 2, Table A2.5 for comparisons of beneficiaries with listed and unknown causes of death. Among those with death certificates, nonelderly duals whose death certificates indicated fatal opioid OD were younger than those who died of other causes (46.7 years old vs. 52.7 years old). The average days to death following index overdose for all beneficiaries who died, regardless of indicated cause, was about 5 months (148 days for fatal opioid OD; 155 days for other causes). Figures 2 and 3 summarize the distribution of deaths across the year for those who die of opioid overdose and other causes.

Figure 2. Days until Death among Beneficiaries Who Died from Causes Other Than Opioid Overdose

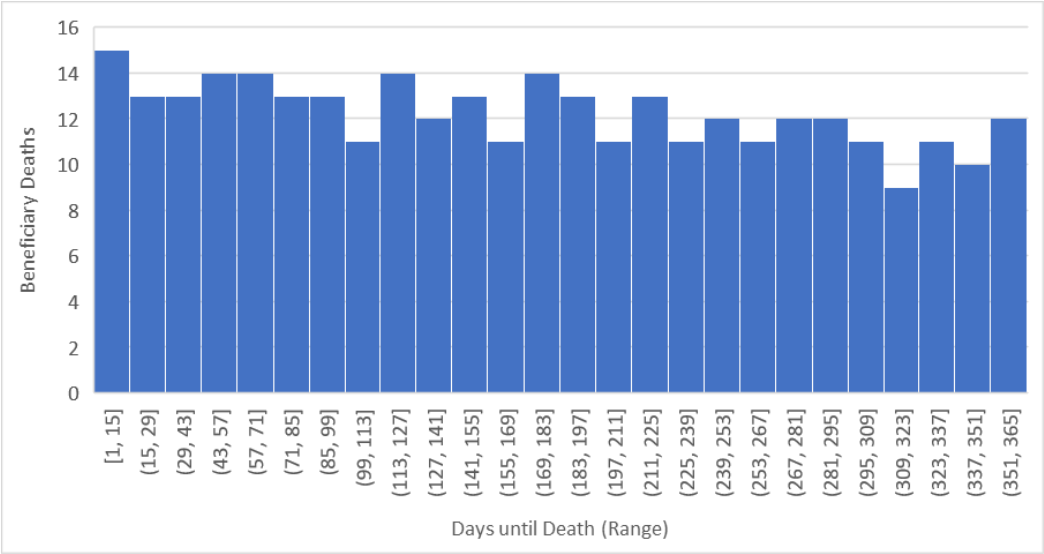


Figure 3. Days until Death among Beneficiaries Who Died from Opioid Overdose

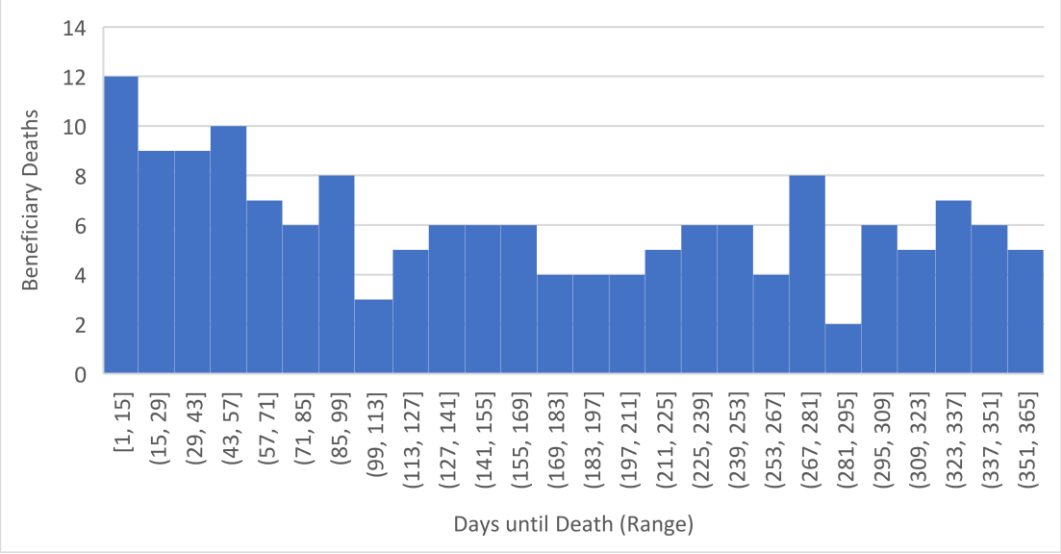


Table 3. Characteristics of Nonelderly Duals Indicated to have Died from Opioid Overdoses and Other Causes

Characteristic	Fatal Opioid OD (N = 219)	Other Causes (N = 787)	*P* value
Days to death, Mean (SD)	148 (115)	155 (107)	0.42
Age (years), Mean (SD)	46.0 (10.0)	52.7 (9.0)	<0.001
Male sex, No. (%)	118 (53.9)	427 (54.3)	0.98
Race, No. (%)			
Non-Hispanic White	172 (78.5)	615 (78.1)	0.13
Black or African American	20 (9.1)	94 (11.9)	
Hispanic	16 (7.3)	60 (7.6)	
Other	11 (5.0)	18 (2.3)	
Buprenorphine distributed (3-digit zip code level) , No. (%)			
First quartile (Least)	22 (10.0)	105 (13.3)	<0.001
Second quartile	46 (21.0)	201 (25.5)	
Third quartile	51 (23.3)	237 (30.1)	
Fourth quartile (Most)	100 (45.7)	244 (31.0)	
Prior opioid overdoses, Mean (SD)	0.0594 (0.347)	0.0178 (0.142)	0.08
Subsequent opioid overdoses, Mean (SD)	0.329 (0.615)	0.202 (0.551)	0.006
Index overdose involved heroin, No. (%)	104 (47.5)	115 (14.6)	<0.001
Elixhauser score, No. (%)			
<0	86 (39.3)	139 (17.7)	<0.001
0	76 (34.7)	218 (27.7)	
1-4	25 (11.4)	94 (11.9)	
>=5	32 (14.6)	336 (42.7)	
Number of days with claim prior to OD, Mean (SD)	7.00 (6.53)	8.67 (7.80)	0.001
Substance use diagnoses, No. (%)			
Alcohol use disorder	90 (41.1)	237 (30.1)	0.003
Drug use disorder	208 (95.0)	712 (90.5)	0.05
Medication for Opioid Use Disorder (MOUD)	50 (22.8)	62 (7.9)	<0.001
Opioid use diagnosis or procedure	202 (92.2)	692 (87.9)	0.10

Table 3 continued			
Tobacco use disorders	175 (79.9)	581 (73.8)	0.08
Mental health diagnoses, No. (%)			
ADHD and other conduct disorders	30 (13.7)	54 (6.9)	0.002
Anxiety	174 (79.5)	614 (78.0)	0.72
Bipolar	128 (58.4)	332 (42.2)	<0.001
Depression	172 (78.5)	659 (83.7)	0.09
Personality disorders	46 (21.0)	104 (13.2)	0.006
Post-traumatic stress disorder	55 (25.1)	108 (13.7)	<0.001
Schizophrenia and other psychotic disorders	62 (28.3)	234 (29.7)	0.75
Pain diagnoses, No. (%)			
Fibromyalgia, chronic pain, fatigue	159 (72.6)	671 (85.3)	<0.001
Migraine	41 (18.7)	117 (14.9)	0.20
Chronic Conditions, No. (%)			
Chronic kidney disease	76 (34.7)	477 (60.6)	<0.001
Congestive heart failure	34 (15.5)	350 (44.5)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	70 (32.0)	457 (58.1)	<0.001
Hypertension	117 (53.4)	588 (74.7)	<0.001
Ischemic heart disease	57 (26.0)	408 (51.8)	<0.001
Liver disease	42 (19.2)	237 (30.1)	0.002
Rheumatoid arthritis / osteoarthritis	87 (39.7)	430 (54.6)	<0.001
Viral hepatitis	74 (33.8)	237 (30.1)	0.34

A greater proportion of beneficiaries who died from listed causes other than opioid OD had diagnoses of chronic kidney disease (60.6% vs. 34.7%), COPD (58.1% vs. 32.0%), and congestive heart failure (44.5% vs. 15.5%). Compared with those who died of other causes, those who died of opioid OD had a greater prevalence of some psychiatric conditions, including bipolar disorder (58.4% vs. 42.2%), post-traumatic stress disorder (25.1% vs. 13.7%), and personality disorders (21.0% vs. 13.2%). I did not observe statistically significant differences in the prevalence of schizophrenia and other psychotic disorders, anxiety, or depression.

Individual states were statistically insignificant in the fixed effect model that included each state. The estimates of the model that allowed for clustered standard errors by state did not change the qualitative results (Table A2.6).

DISCUSSION

Nearly 11% of nonelderly duals in this study cohort who survived an index opioid overdose died within 12 months. This is about twice as high as has been found in other populations, in which 12-month mortality following nonfatal opioid OD has been found to be around 5%.[14,16] This is more than 5 times higher than the 12-month mortality rate observed among members of my comparison cohort who did not overdose. It is unsurprising that premature mortality is higher among nonelderly duals following an overdose than was found in these population-based studies; by definition, nonelderly duals have more disabilities than the general population, and opioid use disorder compounds the effects of many disorders. Even though individuals in other populations who overdose tend to have more illnesses than their counterparts who do not overdose,[76] the duration of the diseases and severity of the conditions among nonelderly duals sets them apart.

As many as 58% of Americans who misuse prescription opioids use their own prescribed opioids, citing pain relief as the most common reason for misuse.[26] Almost 80% of nonelderly duals in this study who overdosed have diagnosed fibromyalgia, chronic pain, or fatigue. In the adjusted logistic regression model, these diagnoses were associated with 23% higher odds of 12-month post-OD mortality. Diagnosis of a migraine disorder, another common pain diagnosis that affected 19% of the population, was associated with reduced post-overdose mortality. Serious mental illnesses are also known to be closely related to substance misuse in the general population. The vast majority of the study cohort who overdosed had at least one diagnosed mental illness: depression (80%), anxiety (76%), and bipolar disorder (46%) were particularly common.

Nonelderly duals who overdosed were more likely than other nonelderly duals to have chronic kidney disease (35.8% vs. 12.2%), congestive heart failure (21.4% vs. 8.3%) and liver disease (16.6% vs. 5.3%). Compared with their counterparts who do not overdose but had these conditions, the predicted probabilities of 12-month mortality among beneficiaries assigned mean characteristics for other variables is 8-9% vs. 1% in the youngest age group (21-29) and 16-17% vs. 4-5% in the oldest age group (60-64). Thus, the presence or duration of these illnesses alone does not appear responsible for the high mortality rate among nonelderly duals who overdose.

From a policy perspective, reducing barriers to MOUD treatment is a critical measure to reduce mortality in this population.[37,38,82] In this study cohort, receipt of treatment was associated with reduced post-OD mortality, yet only 14% of individuals who experienced opioid OD received MOUD in the preceding 2 years. Beneficiaries in this study visited health care providers on average between 7 and 8 days in the 6 months prior to the overdose, suggesting there are existing relationships with health care providers who may prescribe MOUD themselves or refer patients to those who can.

Previous research has demonstrated that individuals who survive an opioid overdose are at high risk of a subsequent nonfatal and fatal opioid overdoses.[15,19,24,39] Roughly 20% of those whose death certificates indicated fatal opioid OD had claims for MOUD in the preceding 2 years. MOUD would likely decrease the risk of fatal overdose, alongside other important benefits for physical health, social function, and personal well-being. Given the probability that many of the deaths in this study are misattributed to causes other than opioid overdose, an increase in the availability of MOUD would likely reduce mortality directly and indirectly caused by opioid misuse.

The NDI data used in this study in conjunction with the Medicare claims further illuminates the lack of clarity in causes of post-overdose death. I found that 44.5% of nonelderly duals whose death certificates do not indicate fatal opioid OD had a diagnosis of congestive heart failure, compared with 15.5% among those with fatal opioid OD indicated. It is possible that a known severity of a condition motivates it to be put on a death certificate, perhaps because of the uncertainty of overdose or the stigma associated with overdose death.

It is critical to offer MOUD and other interventions shortly after nonfatal opioid OD. Further, MOUD and other interventions should be as accessible as possible, available at a variety of locations, and free or affordable. Regardless of whether a beneficiary was recorded as having died of a fatal opioid overdose or another cause, the average time to death was roughly 5 months. Most individuals in my dataset had inpatient or outpatient encounters with health care providers prior to death. Larochelle and colleagues[37] identified "touchpoints" (i.e., locations such as pharmacies, detoxification facilities, or emergency departments at which interventions might be strategically placed to prevent fatal opioid overdose). These authors suggest that up to 50% of opioid overdose deaths in their study population could have been prevented had successful interventions been initiated at the touchpoint. Barriers to care must be considered in intervention design, as many people who live with serious mental illness and opioid use disorder do not receive behavioral health care, reporting access challenges and stigma, which may reinforce lack of readiness to stop using.[44]

STRENGTHS AND LIMITATIONS

Where many other studies of risk factors for overdose have been limited with regional data,[15,39] this study considers risk factors using nationwide data. This allowed me to create a study cohort large enough to analyze multiple conditions within a multivariate model.

Opioid overdoses are often underreported in death certificate data. It is often difficult to determine cause of death for an individual, particularly someone with multiple comorbidities and chronic substance misuse. Although it is important to know the incidence of fatal opioid overdoses, by including all-cause mortality in this analysis I allowed for studying the possibly more relevant outcome of 12-month mortality.

To my knowledge, this is the first study of 12-month post-OD mortality among nonelderly duals. The beneficiaries in this study are at high risk for both overdose and premature mortality. Understanding their unique risk factors may help in the development of effective, targeted interventions.

Despite these strengths, these results may not be generalizable to other nonelderly duals or other populations. Because I needed comprehensive fee-for-service data to account for health care utilization, I excluded nonelderly duals with coverage from health maintenance organizations and those who were partial duals or did not have dual status at any time in the study period. I also excluded beneficiaries who qualified for Medicare because of end-stage renal disease. As they are not entitled to HMO care, they would have been disproportionately represented in the cohort. I excluded beneficiaries who had a cancer diagnosis on their claims because I expected their health care to differ significantly from those without cancer. I may be underreporting outpatient visits due to my use of outpatient fee-for-service facility claims without provider (carrier) claims; however, my conclusion that most beneficiaries seek outpatient care prior to and following the overdose would not change if the visits were undercounted.

The calculation of the Elixhauser score is based on the index overdose claim and claims for the preceding 6 months. Medicare transitioned from ICD-9-CM to ICD-10-CM on October 1, 2015, and the codes do not map onto each other. Therefore, for those who overdosed after October

1, 2015, and before April 1, 2016, any claims prior to October 1, 2015, were excluded from the calculation of the Elixhauser scores. Additionally, condition severity was not determined for conditions that are not included in the calculation of the Elixhauser score but are included in the MBSF supplemental files.

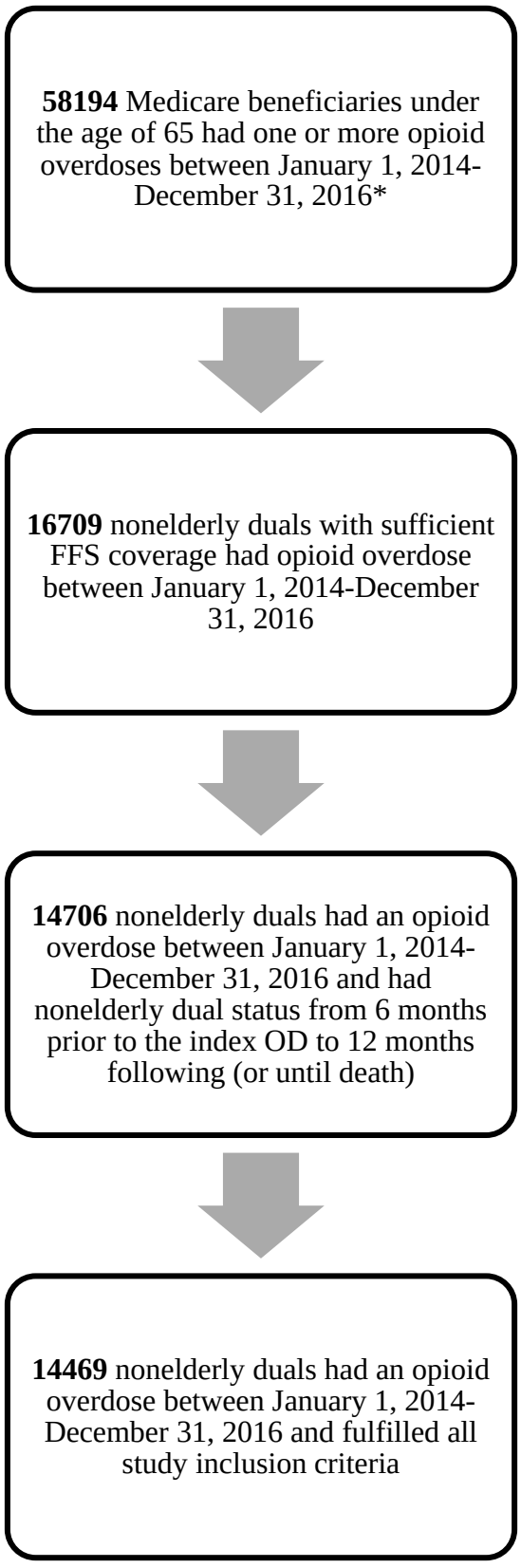
Finally, I suspect that there are effects of state that I was not able to detect in either the fixed effects model or when I allowed for the clustering of standard errors by state. I believe that I may not have detected these differences based on the disparate populations between states, or perhaps because MOUD policies and the opioid epidemic both evolved dramatically in the study years.

Accompanying Part D Medicare claims data would deeply enrich this analysis as it would allow me to better examine MOUD and prescription use. I hope to incorporate such data in future work.

SOCIAL WORK IMPLICATIONS

Almost 11% of nonelderly duals who experience nonfatal opioid OD are predicted to die in the subsequent year. Given the acute health care needs experienced by these individuals, and frequent encounters many of these individuals experience with our health care delivery system, more effective strategies for focused interventions to engage nonelderly duals must be a priority. Social workers often provide assistance in navigating relationships with the health care system, as well as provide counseling for individuals with OUD. They are uniquely situated to help clients address the multifaceted issues that prevent initation and continuation of MOUD.

Appendix 1. A Flow Diagram of the Creation of the Study Cohort



41485 beneficiaries excluded because they did not have sufficient full dual FFS coverage or had HMO care in the 6 months prior to OD or 12 months following (or until death)

971 beneficiaries excluded because they had end-stage renal disease; **974** beneficiaries excluded because they had a cancer diagnosis in the year of the OD (specifically: breast cancer, lung cancer, colorectal cancer, endometrial cancer, lung cancer, prostate cancer, or leukemia); **58** beneficiaries excluded because they were not originally entitled to Medicare because of a disability; **0** beneficiaries excluded because they did not live in 50 US states or DC at time of OD

220 beneficiaries were excluded because they died during the index event, **1** beneficiary was excluded because the claim occurred 111 days after the death date and **16** beneficiaries were excluded because they died on the date of discharge from care.

Appendix 2. Supplemental Tables for Paper 1

Table A2.1 Characteristics and Comorbidities of Nonelderly Dual Beneficiaries by Overdose Status and Mortality Outcome

	Survived at least 12 months		Died within 12 months	
	Nonfatal Opioid Overdose (N=12908)	No Overdose (N=1803790)	Nonfatal Opioid Overdose (N=1561)	No Overdose (N=36129)
Age (years)				
Mean (SD)	48.0 (10.5)	47.5 (11.4)	51.1 (9.80)	53.6 (9.06)
Median [Min, Max]	50.0 [21.0, 64.0]	50.0 [21.0, 64.0]	53.0 [21.0, 64.0]	56.0 [21.0, 64.0]
Age (10 years), No. (%)				
21-29	794 (6.2)	162414 (9.0)	50 (3.2)	905 (2.5)
30-39	2326 (18.0)	310884 (17.2)	185 (11.9)	2458 (6.8)
40-49	2998 (23.2)	411960 (22.8)	306 (19.6)	5716 (15.8)
50-59	5022 (38.9)	630012 (34.9)	694 (44.5)	15909 (44.0)
60-64	1768 (13.7)	288520 (16.0)	326 (20.9)	11141 (30.8)
Sex, No. (%)				
Female	7699 (59.6)	925044 (51.3)	834 (53.4)	16571 (45.9)
Male	5209 (40.4)	878746 (48.7)	727 (46.6)	19558 (54.1)
Race, No. (%)				
Non-Hispanic White	9799 (75.9)	1165345 (64.6)	1211 (77.6)	25691 (71.1)
Black or African American	1666 (12.9)	376267 (20.9)	182 (11.7)	6798 (18.8)
Hispanic	1019 (7.9)	179549 (10.0)	120 (7.7)	2422 (6.7)
Other	424 (3.3)	82629 (4.6)	48 (3.1)	1218 (3.4)
Census Region, No. (%)				
Midwest	3241 (25.1)	458155 (25.4)	389 (24.9)	9542 (26.4)
Northeast	3833 (29.7)	447814 (24.8)	414 (26.5)	7753 (21.5)
South	3421 (26.5)	560226 (31.1)	465 (29.8)	13453 (37.2)

Table A2.1 continued				
West	2413 (18.7)	337595 (18.7)	293 (18.8)	5381 (14.9)
County description, No. (%)				
Metro	10086 (78.1)	1373430 (76.1)	1211 (77.6)	27133 (75.1)
Urban	2456 (19.0)	385818 (21.4)	310 (19.9)	8019 (22.2)
Rural	280 (2.2)	43885 (2.4)	27 (1.7)	964 (2.7)
Missing	86 (0.7)	657 (0.0)	13 (0.8)	13 (0.0)
Buprenorphine distributed (3-digit zip code level) , No. (%)				
First quartile	1932 (15.0)	349052 (19.4)	216 (13.8)	6754 (18.7)
Second quartile	2903 (22.5)	466388 (25.9)	368 (23.6)	9514 (26.3)
Third quartile	3584 (27.8)	488013 (27.1)	445 (28.5)	10096 (27.9)
Fourth quartile	4489 (34.8)	500337 (27.7)	532 (34.1)	9765 (27.0)
Years under disability insurance (years)				
Mean (SD)	10.1 (7.42)	11.5 (9.47)	10.2 (7.58)	13.4 (10.8)
Median [Min, Max]	8.30 [0.496, 42.1]	9.01 [0, 41.5]	8.59 [0.507, 41.8]	10.6 [0, 41.5]
Substance use diagnoses, No. (%)				
Alcohol use disorder	3903 (30.2)	111358 (6.2)	509 (32.6)	5496 (15.2)
Drug use disorder	11009 (85.3)	192376 (10.7)	1415 (90.6)	6251 (17.3)
Medication for Opioid Use Disorder (MOUD)	1839 (14.2)	25833 (1.4)	163 (10.4)	500 (1.4)
Opioid use disorder (moud, dx, or ED)	12663 (98.1)	99513 (5.5)	NA	3500 (9.7)
Opioid use diagnosis or procedure	10154 (78.7)	84802 (4.7)	1368 (87.6)	3118 (8.6)
Opioid use emergency department or hospitalization	12565 (97.3)	46786 (2.6)	NA	2650 (7.3)
Tobacco use disorders	9131 (70.7)	443050 (24.6)	1169 (74.9)	12997 (36.0)

Table A2.1 continued				
Mental health diagnoses, No. (%)				
ADHD and other conduct disorders	1651 (12.8)	117083 (6.5)	132 (8.5)	1913 (5.3)
Anxiety	9765 (75.7)	551031 (30.5)	1205 (77.2)	15373 (42.6)
Autism	74 (0.6)	46757 (2.6)	NA	435 (1.2)
Bipolar	5983 (46.4)	315400 (17.5)	696 (44.6)	6968 (19.3)
Depression	10420 (80.7)	695950 (38.6)	1279 (81.9)	18255 (50.5)
Personality disorders	2206 (17.1)	75147 (4.2)	239 (15.3)	1562 (4.3)
Post-traumatic stress disorder	2806 (21.7)	98487 (5.5)	261 (16.7)	1507 (4.2)
Schizophrenia and other psychotic disorders	3542 (27.4)	294650 (16.3)	454 (29.1)	7831 (21.7)
Disability-related conditions, No. (%)				
Cerebral palsy	112 (0.9)	68949 (3.8)	11 (0.7)	1973 (5.5)
Epilepsy	2339 (18.1)	198571 (11.0)	313 (20.1)	8405 (23.3)
Mobility Impairments	1189 (9.2)	99256 (5.5)	182 (11.7)	6513 (18.0)
Multiple sclerosis and transverse myelitis	379 (2.9)	29732 (1.6)	37 (2.4)	1309 (3.6)
Muscular dystrophy	49 (0.4)	5306 (0.3)	NA	331 (0.9)
Sensory - deafness and hearing impairment	434 (3.4)	67650 (3.8)	67 (4.3)	1557 (4.3)
Sensory - blindness and visual impairment	202 (1.6)	21019 (1.2)	31 (2.0)	1137 (3.1)
Spina bifida and other congenital anomalies of the nervous system	104 (0.8)	16615 (0.9)	NA	554 (1.5)
Spinal cord injury	377 (2.9)	16341 (0.9)	64 (4.1)	858 (2.4)
Traumatic brain injury and nonpsychotic mental disorders due to brain damage	264 (2.0)	20149 (1.1)	27 (1.7)	829 (2.3)
Pain diagnoses, No. (%)				
Fibromyalgia, chronic pain, fatigue	9539 (73.9)	419415 (23.3)	1272 (81.5)	12603 (34.9)
Migraine	2568 (19.9)	117744 (6.5)	253 (16.2)	1850 (5.1)

Table A2.1 continued				
Chronic conditions, No. (%)				
Acquired hypothyroidism	2201 (17.1)	212032 (11.8)	306 (19.6)	5742 (15.9)
Acute myocardial infarction	177 (1.4)	6157 (0.3)	54 (3.5)	1069 (3.0)
Alzheimer's disease and related disorders or senile dementia	1074 (8.3)	89211 (4.9)	222 (14.2)	7505 (20.8)
Anemia	4650 (36.0)[1]	324102 (18.0)	761 (48.8)	15907 (44.0)
Asthma	3394 (26.3)	184229 (10.2)	416 (26.6)	4376 (12.1)
Atrial fibrillation	359 (2.8)	26977 (1.5)	79 (5.1)	2372 (6.6)
Benign prostatic hyperplasia	458 (3.5)	40245 (2.2)	87 (5.6)	1528 (4.2)
Cataract	803 (6.2)	133296 (7.4)	104 (6.7)	2111 (5.8)
Chronic kidney disease	4358 (33.8)	207641 (11.5)	825 (52.9)	16465 (45.6)
COPD	4568 (35.4)	219246 (12.2)	812 (52.0)	10439 (28.9)
Congestive heart failure	2514 (19.5)	139920 (7.8)	578 (37.0)	13093 (36.2)
Diabetes	4093 (31.7)	450325 (25.0)	618 (39.6)	14976 (41.5)
Glaucoma	324 (2.5)	75634 (4.2)	29 (1.9)	814 (2.3)
Hip/Pelvic Fracture	101 (0.8)	3674 (0.2)	21 (1.3)	358 (1.0)
HIV/AIDS	399 (3.1)	34192 (1.9)	76 (4.9)	966 (2.7)
Hyperlipidemia	4786 (37.1)	542025 (30.0)	600 (38.4)	10765 (29.8)
Hypertension	7687 (59.6)	691042 (38.3)	1080 (69.2)	19321 (53.5)
Ischemic heart disease	3701 (28.7)	235634 (13.1)	689 (44.1)	12821 (35.5)
Liver disease	1977 (15.3)	90337 (5.0)	423 (27.1)	7400 (20.5)
Obesity	4361 (33.8)	394829 (21.9)	560 (35.9)	10069 (27.9)
Osteoporosis	699 (5.4)	50179 (2.8)	103 (6.6)	1757 (4.9)
Peripheral vascular disease	1481 (11.5)	136331 (7.6)	314 (20.1)	7778 (21.5)
Pressure ulcers and chronic ulcers	1442 (11.2)	84863 (4.7)	355 (22.7)	8891 (24.6)

Table A2.1 continued				
Rheumatoid arthritis / osteoarthritis	6634 (51.4)	425101 (23.6)	809 (51.8)	10012 (27.7)
Stroke / transient ischemic attack	768 (5.9)	44740 (2.5)	132 (8.5)	3260 (9.0)
Viral hepatitis	2959 (22.9)	72817 (4.0)	464 (29.7)	3982 (11.0)
Other developmental delays, No. (%)				
Cystic fibrosis and other metabolic developmental disorders	286 (2.2)	18049 (1.0)	71 (4.5)	1227 (3.4)
Intellectual disabilities and related conditions	240 (1.9)	225659 (12.5)	20 (1.3)	5779 (16.0)
Learning disabilities	85 (0.7)	13019 (0.7)	NA	279 (0.8)
Other developmental delays	96 (0.7)	26884 (1.5)	NA	937 (2.6)

Table A2.2 Complete Characteristics and Comorbidities of Nonelderly Dual Beneficiaries Who Survived an Opioid Overdose

	Survived 12 months (N=12908)	**Died within 12 months (N=1561)**	***P* value**
Age (years)			
Mean (SD)	48.0 (10.5)	51.1 (9.8)	<0.001
Median [Min, Max]	50.0 [21.0, 64.0]	53.0 [21.0, 64.0]	
Age (10-year), No. (%)			
21-29	794 (6.2)	50 (3.2)	<0.001
30-39	2326 (18.0)	185 (11.9)	
40-49	2998 (23.2)	306 (19.6)	
50-59	5022 (38.9)	694 (44.5)	
60-64	1768 (13.7)	326 (20.9)	
Sex, No. (%)			
Female	7699 (59.6)	834 (53.4)	<0.001
Male	5209 (40.4)	727 (46.6)	
Race, No. (%)			
Non-Hispanic White	9799 (75.9)	1211 (77.6)	0.48
Black or African American	1666 (12.9)	182 (11.7)	
Hispanic	1019 (7.9)	120 (7.7)	
Other	424 (3.3)	48 (3.1)	
Census region, No. (%)			
Midwest	3241 (25.1)	389 (24.9)	0.02

Table A2.2 continued			
Northeast	3833 (29.7)	414 (26.5)	
South	3421 (26.5)	465 (29.8)	
West	2413 (18.7)	293 (18.8)	
County Description, No. (%)			
Metro	10086 (78.1)	1211 (77.6)	0.50
Urban	2456 (19.0)	310 (19.9)	
Rural	280 (2.2)	27 (1.7)	
Missing	86 (0.7)	13 (0.8)	
Buprenorphine distributed (3-digit zip code level), No. (%)			
First quartile	1932 (15.0)	216 (13.8)	0.50
Second quartile	2903 (22.5)	368 (23.6)	
Third quartile	3584 (27.8)	445 (28.5)	
Fourth quartile	4489 (34.8)	532 (34.1)	
Number of opioid overdoses in previous 6 months			
Mean (SD)	0.00875 (0.105)	0.0205 (0.174)	0.009
Median [Min, Max]	0 [0, 4]	0 [0, 3]	
Heroin indicated in index OD, No. (%)	3038 (23.5)	332 (21.3)	0.05
Years under disability insurance (years)			
Mean (SD)	10.1 (7.42)	10.2 (7.58)	0.46
Median [Min, Max]	8.30 [0.496, 42.1]	8.59 [0.507, 41.8]	
Elixhauser score, No. (%)			
<0	3694 (28.6)	342 (21.9)	<0.001
0	4857 (37.6)	443 (28.4)	
1-4	1471 (11.4)	200 (12.8)	
>=5	2886 (22.4)	576 (36.9)	
Days with claims (before OD)			
Mean (SD)	7.37 (7.59)	8.46 (8.16)	<0.001
Median [Min, Max]	5.00 [0, 145]	6.00 [0, 105]	
Number of inpatient claims prior to OD, No. (%)			
0	7511 (58.2)	629 (40.3)	<0.001
1-4	4794 (37.1)	761 (48.8)	
5+	603 (4.7)	171 (11.0)	
Number of outpatient claims prior to OD, No. (%)			
0	1494 (11.6)	151 (9.7)	0.05
1-4	4839 (37.5)	577 (37.0)	

Table A2.2 continued			
5+	6575 (50.9)	833 (53.4)	
Substance use diagnoses, No. (%)			
Alcohol use disorder	3903 (30.2)	509 (32.6)	0.06
Drug use disorder	11009 (85.3)	1415 (90.6)	<0.001
Medication for Opioid Use Disorder (MOUD)	1839 (14.2)	163 (10.4)	<0.001
Opioid use disorder (MOUD, Diagnosis, or ED)	12663 (98.1)	NA[1]	<0.001
Opioid use diagnosis or procedure	10154 (78.7)	1368 (87.6)	<0.001
Opioid use emergency department or hospitalization	12565 (97.3)	NA[1]	<0.001
Tobacco use disorders	9131 (70.7)	1169 (74.9)	<0.001
Mental health diagnoses, No. (%)			
Attention Deficit Hyperactivity Disorder (ADHD) and other conduct disorders	1651 (12.8)	132 (8.5)	<0.001
Anxiety	9765 (75.7)	1205 (77.2)	0.19
Autism	74 (0.6)	NA[1]	0.27
Bipolar	5983 (46.4)	696 (44.6)	0.20
Depressive disorders	10420 (80.7)	1279 (81.9)	0.27
Personality disorders	2206 (17.1)	239 (15.3)	0.08
Post-traumatic stress disorder	2806 (21.7)	261 (16.7)	<0.001
Schizophrenia and other psychotic disorders	3542 (27.4)	454 (29.1)	0.18
Disability-related conditions, No. (%)			
Cerebral palsy	112 (0.9)	11 (0.7)	0.61
Epilepsy	2339 (18.1)	313 (20.1)	0.07
Mobility impairments	1189 (9.2)	182 (11.7)	0.002
Multiple sclerosis and transverse myelitis	379 (2.9)	37 (2.4)	0.23
Muscular dystrophy	49 (0.4)	NA[1]	0.56
Sensory - deafness and hearing impairment	434 (3.4)	67 (4.3)	0.07
Sensory - blindness and visual impairment	202 (1.6)	31 (2.0)	0.25
Spina bifida and other congenital anomalies of the nervous system	104 (0.8)	NA[1]	0.59
Spinal cord injury	377 (2.9)	64 (4.1)	0.01
Traumatic brain injury and nonpsychotic mental disorders due to brain damage	264 (2.0)	27 (1.7)	0.46
Pain diagnoses, No. (%)			
Fibromyalgia, chronic pain, fatigue	9539 (73.9)	1272 (81.5)	<0.001
Migraine	2568 (19.9)	253 (16.2)	<0.001

Table A2.2 continued			
Chronic conditions, No. (%)			
Acquired hypothyroidism	2201 (17.1)	306 (19.6)	0.01
Acute myocardial infarction	177 (1.4)	54 (3.5)	<0.001
Alzheimer's disease and related disorders or senile dementia	1074 (8.3)	222 (14.2)	<0.001
Anemia	4650 (36.0)	761 (48.8)	<0.001
Asthma	3394 (26.3)	416 (26.6)	0.79
Atrial fibrillation	359 (2.8)	79 (5.1)	<0.001
Benign prostatic hyperplasia	458 (3.5)	87 (5.6)	<0.001
Cataract	803 (6.2)	104 (6.7)	0.53
Chronic kidney disease	4358 (33.8)	825 (52.9)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	4568 (35.4)	812 (52.0)	<0.001
Congestive heart failure	2514 (19.5)	578 (37.0)	<0.001
Diabetes	4093 (31.7)	618 (39.6)	<0.001
Glaucoma	324 (2.5)	29 (1.9)	0.14
Hip/pelvic fracture	101 (0.8)	21 (1.3)	0.03
Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS)	399 (3.1)	76 (4.9)	<0.001
Hyperlipidemia	4786 (37.1)	600 (38.4)	0.31
Hypertension	7687 (59.6)	1080 (69.2)	<0.001
Ischemic heart disease	3701 (28.7)	689 (44.1)	<0.001
Liver disease	1977 (15.3)	423 (27.1)	<0.001
Obesity	4361 (33.8)	560 (35.9)	0.11
Osteoporosis	699 (5.4)	103 (6.6)	0.06
Peripheral vascular disease	1481 (11.5)	314 (20.1)	<0.001
Pressure ulcers and chronic ulcers	1442 (11.2)	355 (22.7)	<0.001
Rheumatoid arthritis / osteoarthritis	6634 (51.4)	809 (51.8)	0.77
Stroke / transient ischemic attack	768 (5.9)	132 (8.5)	<0.001
Viral hepatitis	2959 (22.9)	464 (29.7)	<0.001
Other developmental delays, No. (%)			
Cystic fibrosis and other metabolic developmental disorders	286 (2.2)	71 (4.5)	<0.001
Intellectual disabilities and related conditions	240 (1.9)	20 (1.3)	0.13
Learning disabilities	85 (0.7)	NA[1]	0.26
Other developmental delays	96 (0.7)	NA[1]	0.25

[1] Cells with values less than 11 suppressed in accordance with CMS policy to protect confidentiality of beneficiaries.

Table A2.3. Complete Characteristics Associated with 12-Month All-Cause Mortality among Nonelderly Duals Following a Nonfatal Opioid Overdose

Characteristic	Unadjusted Odds Ratio (95% Confidence Interval)	*P* Value	Adjusted Odds Ratio (95% Confidence Interval)	*P* Value
Age (Years)	1.03(1.03,1.04)	<0.001	1.02(1.01,1.03)	<0.001
Sex (Ref: Female)	1.29(1.16,1.43)	<0.001	1.28(1.13,1.45)	<0.001
Race (Ref: Non-Hispanic White)				
Black or African American	0.88(0.75,1.04)	0.14	0.82(0.68,0.98)	0.03
Hispanic	0.95(0.78,1.16)	0.63	0.99(0.80,1.21)	0.91
Other	0.92(0.67,1.23)	0.57	0.96(0.69,1.30)	0.78
Census Region (Ref: West)				
Midwest	0.99(0.84,1.16)	0.89		
Northeast	0.89(0.76,1.04)	0.15		
South	1.12(0.96,1.31)	0.15		
Number of opioid overdoses in previous 6 months	1.86(1.31,2.59)	<0.001	1.53(1.06,2.16)	0.02
Heroin indicated in index OD	0.88(0.77,1.00)	0.05	1.25(1.07,1.47)	0.01
Years under disability insurance (Years)	1.00(1.00,1.01)	0.46	0.98(0.98,0.99)	<0.001
Elixhauser score	1.06(1.05,1.07)	<0.001	1.02(1.02,1.03)	<0.001
Number of inpatient claims prior to OD (Ref: 0 Visits)				
1-4 Visits	1.90(1.70,2.12)	<0.001	1.47(1.30,1.67)	<0.001
5+ Visits	3.39(2.80,4.08)	<0.001	2.09(1.67,2.61)	<0.001
Number of outpatient claims prior to OD (Ref: 0 visits)				
1-4 Visits	1.18(0.98,1.43)	0.09	1.07(0.88,1.30)	0.52
5+ Visits	1.25(1.05,1.51)	0.02	0.94(0.77,1.15)	0.53
Emergency department type (Ref: Outpatient)	1.75(1.57,1.94)	<0.001		
Discharge Group (Ref: Discharged to home)				
Discharged to another facility	1.71(1.48,1.97)	<0.001	1.21(1.04,1.42)	0.02
Discharge - other	1.64(1.43,1.88)	<0.001	1.33(1.15,1.53)	<0.001
Substance use diagnoses				
Alcohol use disorder	1.12(1.00,1.25)	0.05	0.91(0.79,1.03)	0.13

Table A2.3 continued				
Drug use disorder	1.67(1.41,2.00)	<0.001	0.76(0.57,1.02)	0.06
Medication for Opioid Use Disorder (MOUD)	0.70(0.59,0.83)	<0.001	0.75(0.62,0.90)	0.003
Opioid use diagnosis or procedure	1.92(1.65,2.25)	<0.001	1.69(1.32,2.20)	<0.001
Tobacco use disorders	1.23(1.09,1.39)	<0.001	1.03(0.90,1.18)	0.68
Mental health diagnoses				
ADHD and other conduct disorders	0.63(0.52,0.76)	<0.001		
Anxiety	1.09(0.96,1.24)	0.18		
Autism	0.56(0.20,1.25)	0.21		
Bipolar	0.93(0.84,1.03)	0.19		
Depressive disorders	1.08(0.95,1.24)	0.25		
Personality disorders	0.72(0.63,0.83)	<0.001		
Post-traumatic stress disorder	0.88(0.76,1.01)	0.08		
Schizophrenia and other psychotic disorders	1.08(0.97,1.22)	0.17		
Disability-related conditions				
Cerebral palsy	0.81(0.41,1.44)	0.51		
Epilepsy	1.13(0.99,1.29)	0.06		
Sensory - deafness and hearing impairment	1.29(0.98,1.66)	0.06		
Mobility impairments	1.30(1.10,1.53)	0.002		
Multiple sclerosis and transverse myelitis	0.80(0.56,1.11)	0.21		
Muscular dystrophy	1.35(0.59,2.70)	0.43		
Spina bifida and other congenital anomalies of the nervous system	0.79(0.39,1.45)	0.49		
Spinal cord injury	1.42(1.08,1.85)	0.01		
Sensory - blindness and visual impairment	1.27(0.85,1.84)	0.21		
Traumatic brain injury and nonpsychotic mental disorders due to brain damage	0.84(0.55,1.23)	0.40		
Pain diagnoses				
Fibromyalgia, chronic pain, fatigue	1.55(1.36,1.78)	<0.001	1.23(1.05,1.44)	0.01
Migraine	0.78(0.67,0.90)	0.001	0.83(0.71,0.96)	0.02
Chronic conditions				

Table A2.3 continued				
Alzheimer's disease and related disorders or senile dementia	1.83(1.56,2.13)	<0.001	1.16(0.97,1.37)	0.09
Acute myocardial infarction	2.58(1.88,3.49)	<0.001	1.32(0.94,1.84)	0.10
Anemia	1.69(1.52,1.88)	<0.001	1.04(0.91,1.18)	0.56
Asthma	1.02(0.90,1.15)	0.76	0.88(0.77,1.00)	0.05
Atrial fibrillation	1.86(1.44,2.38)	<0.001	0.86(0.65,1.13)	0.28
Cataract	1.08(0.87,1.32)	0.50	0.80(0.64,1.00)	0.05
Congestive heart failure	2.43(2.17,2.72)	<0.001	1.43(1.24,1.65)	<0.001
Chronic kidney disease	2.20(1.98,2.44)	<0.001	1.37(1.20,1.56)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	1.98(1.78,2.20)	<0.001	1.32(1.16,1.51)	<0.001
Diabetes	1.41(1.27,1.57)	<0.001	0.95(0.83,1.09)	0.49
Glaucoma	0.74(0.49,1.06)	0.12	0.73(0.48,1.07)	0.12
Viral hepatitis	1.42(1.27,1.60)	<0.001	1.06(0.92,1.22)	0.40
Hip/pelvic fracture	1.73(1.05,2.72)	0.02	0.96(0.57,1.55)	0.88
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	1.60(1.24,2.05)	<0.001	1.24(0.94,1.62)	0.12
Hyperlipidemia	1.06(0.95,1.18)	0.29	0.66(0.58,0.76)	<0.001
Benign prostatic hyperplasia	1.60(1.26,2.02)	<0.001	0.94(0.72,1.22)	0.66
Hypertension	1.53(1.36,1.71)	<0.001	0.91(0.79,1.06)	0.22
Acquired hypothyroidism	1.19(1.04,1.35)	0.01	1.05(0.90,1.21)	0.55
Ischemic heart disease	1.97(1.77,2.19)	<0.001	1.27(1.11,1.45)	<0.001
Liver disease	2.06(1.82,2.32)	<0.001	1.33(1.15,1.52)	<0.001
Obesity	1.10(0.98,1.22)	0.10	0.92(0.81,1.04)	0.20
Osteoporosis	1.23(0.99,1.52)	0.05	0.94(0.74,1.17)	0.57
Peripheral vascular disease	1.94(1.70,2.22)	<0.001	1.04(0.88,1.22)	0.64
Rheumatoid arthritis / osteoarthritis	1.02(0.92,1.13)	0.75	0.74(0.65,0.84)	<0.001
Stroke / transient ischemic attack	1.46(1.20,1.76)	<0.001	1.01(0.82,1.24)	0.93
Pressure ulcers and chronic ulcers	2.34(2.05,2.66)	<0.001	1.37(1.18,1.60)	<0.001
Developmental disorders				
Cystic fibrosis	2.10(1.60,2.73)	<0.001		
Intellectual disabilities and related conditions	0.69(0.42,1.06)	0.11		
Learning disabilities	0.58(0.23,1.22)	0.20		
Other developmental delays	0.60(0.25,1.20)	0.19		

Tale A2.4. Characteristics of Nonelderly Duals Who Died from Opioid Overdoses and Other Causes

Characteristic	Fatal Opioid OD (N = 219)	Other Causes (N = 787)	*P* value
Days to death			
Mean (SD)	148 (115)	155 (107)	0.42
Median [Min, Max]	125 [1.00, 365]	145 [1.00, 364]	
Age (Years)			
Mean (SD)	46.0 (9.95)	52.7 (9.00)	<0.001
Median [Min, Max]	47.0 [22.0, 64.0]	55.0 [21.0, 64.0]	
Male sex, No. (%)	118 (53.9)	427 (54.3)	0.98
Race, No. (%)			
Non-Hispanic White	172 (78.5)	615 (78.1)	0.13
Black or African American	20 (9.1)	94 (11.9)	
Hispanic	16 (7.3)	60 (7.6)	
Other	11 (5.0)	18 (2.3)	
Census region, No. (%)			
Midwest	38 (17.4)	209 (26.6)	<0.001
Northeast	99 (45.2)	177 (22.5)	
South	48 (21.9)	247 (31.4)	
West	34 (15.5)	154 (19.6)	
Buprenorphine distributed (3-digit zip code level) , No. (%)			
First quartile (least)	22 (10.0)	105 (13.3)	<0.001
Second quartile	46 (21.0)	201 (25.5)	
Third quartile	51 (23.3)	237 (30.1)	
Fourth quartile (most)	100 (45.7)	244 (31.0)	
Prior opioid overdoses			
Mean (SD)	0.0594 (0.347)	0.0178 (0.142)	0.08
Median [Min, Max]	0 [0, 3.00]	0 [0, 2.00]	
Subsequent opioid overdoses			
Mean (SD)	0.329 (0.615)	0.202 (0.551)	0.006
Median [Min, Max]	0 [0, 4.00]	0 [0, 4.00]	
Heroin indicated in index OD, No. (%)	104 (47.5)	115 (14.6)	<0.001
Years under disability insurance			
Mean (SD)	8.69 (6.35)	10.4 (7.70)	<0.001
Median [Min, Max]	7.20 [0.510, 31.3]	8.76 [0.521, 40.0]	
Elixhauser score, No. (%)			
<0	86 (39.3)	139 (17.7)	<0.001

Table A2.4 continued			
0	76 (34.7)	218 (27.7)	
1-4	25 (11.4)	94 (11.9)	
>=5	32 (14.6)	336 (42.7)	
Number of days with insurance claim prior to OD			
Mean (SD)	7.00 (6.53)	8.67 (7.80)	0.001
Median [Min, Max]	5.00 [0, 36.0]	7.00 [0, 63.0]	
Number of inpatient claims prior to OD, No. (%)			
0 Visits	106 (48.4)	287 (36.5)	0.004
1-4 Visits	96 (43.8)	406 (51.6)	
5+ Visits	17 (7.8)	94 (11.9)	
Number of outpatient claims prior to OD, No. (%)			
0 Visits	16 (7.3)	70 (8.9)	0.01
1-4 Visits	105 (47.9)	289 (36.7)	
5+ Visits	98 (44.7)	428 (54.4)	
Substance use diagnoses, No. (%)			
Alcohol use disorder	90 (41.1)	237 (30.1)	0.002
Drug use disorder	208 (95.0)	712 (90.5)	0.05
Medication for Opioid Use Disorder (MOUD)	50 (22.8)	62 (7.9)	<0.001
Opioid use diagnosis or procedure	202 (92.2)	692 (87.9)	0.09
Tobacco use disorders	175 (79.9)	581 (73.8)	0.08
Mental health diagnoses, No. (%)			
ADHD and other conduct disorders	30 (13.7)	54 (6.9)	0.002
Anxiety	174 (79.5)	614 (78.0)	0.72
Bipolar	128 (58.4)	332 (42.2)	<0.001
Depressive disorders	172 (78.5)	659 (83.7)	0.09
Personality disorders	46 (21.0)	104 (13.2)	0.001
Post-traumatic stress disorder	55 (25.1)	108 (13.7)	<0.001
Schizophrenia and other psychotic disorders	62 (28.3)	234 (29.7)	0.74
Disability-related conditions, No. (%)			
Epilepsy	33 (15.1)	173 (22.0)	0.03
Mobility impairments	11 (5.0)	99 (12.6)	0.002
Pain diagnoses, No. (%)			
Fibromyalgia, chronic pain, fatigue	159 (72.6)	671 (85.3)	<0.001
Migraine	41 (18.7)	117 (14.9)	0.20
Chronic conditions, No. (%)			

Table A2.4 continued			
Acquired hypothyroidism	34 (15.5)	171 (21.7)	0.05
Anemia	63 (28.8)	436 (55.4)	<0.001
Asthma	55 (25.1)	208 (26.4)	0.76
Chronic kidney disease	76 (34.7)	477 (60.6)	<0.001
Congestive heart failure	34 (15.5)	350 (44.5)	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	70 (32.0)	457 (58.1)	<0.001
Diabetes	53 (24.2)	361 (45.9)	<0.001
Hyperlipidemia	57 (26.0)	339 (43.1)	<0.001
Hypertension	117 (53.4)	588 (74.7)	<0.001
Ischemic heart disease	57 (26.0)	408 (51.8)	<0.001
Liver disease	42 (19.2)	237 (30.1)	0.002
Obesity	65 (29.7)	306 (38.9)	0.02
Peripheral vascular disease	18 (8.2)	189 (24.0)	<0.001
Pressure ulcers and chronic ulcers	16 (7.3)	212 (26.9)	<0.001
Rheumatoid arthritis / osteoarthritis	87 (39.7)	430 (54.6)	<0.001
Viral hepatitis	74 (33.8)	237 (30.1)	0.34

Table A2.5. Nonelderly Duals with Known vs. Unknown Causes of Death among Those Who Died within 12 Months of Opioid Overdose

	Known Cause of Death (N=1006)	**Unknown Cause of Death (N=555)**	***P* value**
Age (Years)			
Mean (SD)	51.2 (9.62)	50.9 (10.1)	0.56
Median [Min, Max]	53.0 [21.0, 64.0]	53.0 [22.0, 64.0]	
Male sex, No. (%)	461 (45.8)	266 (47.9)	0.46
Race, No. (%)			
Non-Hispanic White	787 (78.2)	424 (76.4)	0.85
Black or African American	114 (11.3)	68 (12.3)	
Hispanic	76 (7.6)	44 (7.9)	
Other	29 (2.9)	19 (3.4)	
Census region, No. (%)			
Midwest	247 (24.6)	142 (25.6)	0.74
Northeast	276 (27.4)	138 (24.9)	
South	295 (29.3)	170 (30.6)	
West	188 (18.7)	105 (18.9)	
County description, No. (%)			
Metro	801 (79.6)	410 (73.9)	0.02

Table A2.5 continued			
Urban	182 (18.1)	128 (23.1)	
Rural or missing	23 (2.29)	17 (3.06)	
Buprenorphine distributed (3-digit zip code level), No. (%)			
First quartile	127 (12.6)	89 (16.0)	0.24
Second quartile	247 (24.6)	121 (21.8)	
Third quartile	288 (28.6)	157 (28.3)	
Fourth quartile	344 (34.2)	188 (33.9)	
Number of opioid overdoses in previous 6 months			
Mean (SD)	0.0268 (0.205)	0.00901 (0.0946)	0.02
Median [Min, Max]	0 [0, 3.00]	0 [0, 1.00]	
Subsequent opioid overdoses			
Mean (SD)	0.230 (0.568)	0.207 (0.533)	0.44
Median [Min, Max]	0 [0, 4.00]	0 [0, 5.00]	
Heroin indicated in index OD, No. (%)	219 (21.8)	113 (20.4)	0.56
Years under disability insurance			
Mean (SD)	10.0 (7.46)	10.6 (7.79)	0.20
Median [Min, Max]	8.33 [0.510, 40.0]	9.02 [0.507, 41.8]	
Elixhauser score, No. (%)			
<0	225 (22.4)	117 (21.1)	0.36
0	294 (29.2)	149 (26.8)	
1-4	119 (11.8)	81 (14.6)	
>=5	368 (36.6)	208 (37.5)	
Number of days with insurance claim prior to OD			
Mean (SD)	8.31 (7.57)	8.74 (9.14)	0.34
Median [Min, Max]	6.00 [0, 63.0]	6.00 [0, 105]	
Number of inpatient claims prior to OD, No. (%)			
0	393 (39.1)	236 (42.5)	0.40
1-4	502 (49.9)	259 (46.7)	
5+	111 (11.0)	60 (10.8)	
Number of outpatient claims prior to OD, No. (%)			
0	86 (8.5)	65 (11.7)	0.02
1-4	394 (39.2)	183 (33.0)	
5+	526 (52.3)	307 (55.3)	
Substance use diagnoses, No. (%)			

Table A2.5 continued			
Alcohol use disorder	327 (32.5)	182 (32.8)	0.95
Drug use disorder	920 (91.5)	495 (89.2)	0.17
Medication for Opioid Use Disorder (MOUD)	112 (11.1)	51 (9.2)	0.27
Opioid use disorder (MAT, Dx, or ED)	NA[1]	NA[1]	0.50
Opioid use diagnosis or procedure	894 (88.9)	474 (85.4)	0.06
Opioid use emergency department or hospitalization	NA[1]	NA[1]	0.75
Tobacco use disorders	756 (75.1)	413 (74.4)	0.80
Mental health diagnoses, No. (%)			
ADHD and other conduct disorders	84 (8.4)	48 (8.6)	0.91
Anxiety	788 (78.3)	417 (75.1)	0.17
Autism	NA[1]	NA[1]	1
Bipolar	460 (45.7)	236 (42.5)	0.24
Depressive disorders	831 (82.6)	448 (80.7)	0.39
Personality disorders	150 (14.9)	89 (16.0)	0.61
Post-traumatic stress disorder	163 (16.2)	98 (17.7)	0.51
Schizophrenia and other psychotic disorders	296 (29.4)	158 (28.5)	0.73
Disability-Related Conditions, No. (%)			
Cerebral palsy	NA[1]	NA[1]	1
Epilepsy	206 (20.5)	107 (19.3)	0.62
Mobility impairments	110 (10.9)	72 (13.0)	0.26
Multiple sclerosis and transverse myelitis	19 (1.9)	18 (3.2)	0.13
Muscular dystrophy	NA[1]	NA[1]	1
Sensory - deafness and hearing impairment	41 (4.1)	26 (4.7)	0.66
Sensory - blindness and visual impairment	21 (2.1)	NA[1]	0.84
Spina bifida and other congenital anomalies of the nervous system	NA[1]	NA[1]	1
Spinal cord injury	45 (4.5)	19 (3.4)	0.39
Traumatic brain injury and nonpsychotic mental disorders due to brain damage	19 (1.9)	NA[1]	0.66
Pain diagnoses, No. (%)			

Table A2.5 continued			
Fibromyalgia, chronic pain, fatigue	830 (82.5)	442 (79.6)	0.18
Migraine	158 (15.7)	95 (17.1)	0.51
Chronic conditions, No. (%)			
Acquired hypothyroidism	205 (20.4)	101 (18.2)	0.33
Acute myocardial infarction	34 (3.4)	20 (3.6)	0.93
Alzheimer's disease and related disorders or senile dementia	151 (15.0)	71 (12.8)	0.26
Anemia	499 (49.6)	262 (47.2)	0.39
Asthma	263 (26.1)	153 (27.6)	0.58
Atrial fibrillation	60 (6.0)	19 (3.4)	0.04
Benign prostatic hyperplasia	55 (5.5)	32 (5.8)	0.90
Cataract	71 (7.1)	33 (5.9)	0.46
Chronic kidney disease	553 (55.0)	272 (49.0)	0.03
COPD	527 (52.4)	285 (51.4)	0.74
Congestive heart failure	384 (38.2)	194 (35.0)	0.23
Diabetes	414 (41.2)	204 (36.8)	0.10
Glaucoma	17 (1.7)	12 (2.2)	0.64
Hip/pelvic fracture	14 (1.4)	NA[1]	1
HIV	51 (5.1)	25 (4.5)	0.71
Hyperlipidemia	396 (39.4)	204 (36.8)	0.34
Hypertension	705 (70.1)	375 (67.6)	0.33
Ischemic heart disease	465 (46.2)	224 (40.4)	0.03
Liver disease	279 (27.7)	144 (25.9)	0.48
Obesity	371 (36.9)	189 (34.1)	0.29
Osteoporosis	64 (6.4)	39 (7.0)	0.69
Peripheral vascular disease	207 (20.6)	107 (19.3)	0.59
Pressure ulcers	228 (22.7)	127 (22.9)	0.97
Rheumatoid arthritis	517 (51.4)	292 (52.6)	0.68
Stroke / transient ischemic attack	89 (8.8)	43 (7.7)	0.51
Viral hepatitis	311 (30.9)	153 (27.6)	0.18
Other developmental delays, No. (%)			
Cystic fibrosis; other metabolic developmental disorders	48 (4.8)	23 (4.1)	0.66
Intellectual disabilities; related conditions	NA[1]	11 (2.0)	0.11
Learning disabilities	NA[1]	NA[1]	0.59
Other developmental delays	NA[1]	NA[1]	0.99

[1] Cells with values less than 11 suppressed in accordance with CMS policy to protect confidentiality of beneficiaries.

Table A2.6. Complete Characteristics Associated with 12-Month All-Cause Mortality among Nonelderly Duals Following a Nonfatal Opioid Overdose, Fixed Effects of State vs. Clustered Standard Error

	Fixed Effects of State			Clustered Standard Errors by State		
Characteristic	Point Estimate	Std. Error	*P* Value	Point Estimate	Std. Error	*P* Value
Age (Years)	0.021	0.004	<0.001	0.020	0.004	<0.001
Sex (Ref: Female)	0.243	0.066	<0.001	0.237	0.064	<0.001
Race (Ref: Non-Hispanic White)						
Black or African American	-0.246	0.094	0.009	-0.231	0.081	0.004
Hispanic	-0.005	0.110	0.966	-0.028	0.087	0.749
Other	0.024	0.166	0.883	-0.053	0.158	0.736
Number of opioid overdoses in previous 6 months	0.441	0.181	0.015	0.438	0.189	0.021
Heroin indicated in index OD	0.224	0.085	0.008	0.234	0.074	0.002
Years under disability insurance (Years)	-0.015	0.004	<0.001	-0.015	0.004	<0.001
Elixhauser score	0.022	0.005	<0.001	0.023	0.004	<0.001
Number of inpatient claims prior to OD (Ref: 0 Visits)						
1-4 Visits	0.410	0.066	<0.001	0.410	0.062	<0.001
5+ Visits	0.790	0.116	<0.001	0.787	0.092	<0.001
Number of outpatient claims prior to OD (Ref: 0 visits)						
1-4 Visits	0.070	0.101	0.490	0.075	0.109	0.494
5+ Visits	-0.028	0.103	0.784	-0.033	0.122	0.787
Emergency department type (Ref: Outpatient)	0.073	0.068	0.283	0.080	0.058	0.169
Discharge Group (Ref: Discharged to home)						
Discharged to another facility	0.187	0.083	0.024	0.188	0.096	0.052
Discharge - other	0.286	0.074	<0.001	0.277	0.062	<0.001
Substance use diagnoses						
Alcohol use disorder	-0.063	0.068	0.354	-0.076	0.085	0.373

Table A2.6 continued						
Drug use disorder	-0.262	0.149	0.079	-0.276	0.136	0.042
Medication for Opioid Use Disorder (MOUD)	-0.261	0.098	0.008	-0.251	0.082	0.002
Opioid use diagnosis or procedure	0.500	0.135	<0.001	0.499	0.117	<0.001
Tobacco use disorders	0.037	0.071	0.599	0.039	0.067	0.559
Mental health diagnoses						
ADHD and other conduct disorders	-0.330	0.103	0.001	-0.337	0.099	0.001
Anxiety	0.012	0.077	0.874	0.022	0.050	0.661
Bipolar	0.064	0.066	0.331	0.068	0.062	0.275
Depressive disorders	-0.102	0.082	0.214	-0.101	0.087	0.245
Personality disorders	-0.008	0.086	0.929	-0.018	0.105	0.864
Post-traumatic stress disorder	-0.130	0.082	0.112	-0.138	0.085	0.107
Schizophrenia and other psychotic disorders	-0.019	0.069	0.789	-0.014	0.076	0.857
Pain diagnoses						
Fibromyalgia, chronic pain, fatigue	0.203	0.082	0.014	0.209	0.081	0.009
Migraine	-0.175	0.079	0.026	-0.174	0.070	0.013
Chronic conditions						
Alzheimer's disease and related disorders or senile dementia	0.162	0.088	0.067	0.158	0.087	0.069
Acute myocardial infarction	0.266	0.173	0.124	0.273	0.147	0.064
Anemia	0.038	0.065	0.557	0.030	0.070	0.673
Asthma	-0.132	0.068	0.053	-0.131	0.063	0.037
Atrial fibrillation	-0.165	0.140	0.238	-0.154	0.174	0.374
Cataract	-0.206	0.115	0.073	-0.224	0.147	0.128
Congestive heart failure	0.352	0.073	<0.001	0.355	0.070	<0.001
Chronic kidney disease	0.309	0.067	<0.001	0.300	0.066	<0.001
Chronic Obstructive Pulmonary Disease (COPD)	0.258	0.069	<0.001	0.270	0.069	<0.001
Diabetes	-0.057	0.069	0.406	-0.052	0.066	0.430
Viral hepatitis	0.073	0.071	0.300	0.074	0.068	0.277
Hip/pelvic fracture	-0.038	0.255	0.883	-0.019	0.247	0.938
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	0.229	0.140	0.102	0.210	0.162	0.195

Table A2.6 continued						
Hyperlipidemia	-0.415	0.069	<0.001	-0.411	0.060	<0.001
Benign prostatic hyperplasia	-0.038	0.134	0.779	-0.054	0.168	0.747
Hypertension	-0.097	0.074	0.187	-0.088	0.069	0.205
Acquired hypothyroidism	0.055	0.076	0.469	0.047	0.072	0.514
Ischemic heart disease	0.229	0.068	0.001	0.235	0.066	<0.001
Liver disease	0.276	0.072	<0.001	0.276	0.063	<0.001
Obesity	-0.076	0.067	0.257	-0.083	0.055	0.134
Osteoporosis	-0.055	0.118	0.639	-0.074	0.101	0.459
Peripheral vascular disease	0.040	0.083	0.633	0.040	0.075	0.594
Rheumatoid arthritis / osteoarthritis	-0.305	0.065	<0.001	-0.297	0.068	<0.001
Stroke / transient ischemic attack	0.005	0.107	0.966	0.001	0.073	0.985
Pressure ulcers and chronic ulcers	0.320	0.079	<0.001	0.318	0.066	<0.001
State						
Alaska	-0.415	0.548	0.449			
Arizona	0.149	0.394	0.705			
Arkansas	0.835	0.379	0.028			
California	-0.191	0.269	0.478			
Colorado	-0.052	0.343	0.878			
Connecticut	0.009	0.352	0.980			
Florida	-0.234	0.304	0.441			
Georgia	-0.288	0.367	0.433			
Idaho	-0.048	0.411	0.908			
Illinois	-0.100	0.294	0.735			
Indiana	0.199	0.297	0.503			
Iowa	-0.441	0.401	0.271			
Kansas	-0.154	0.402	0.702			
Kentucky	-0.229	0.345	0.507			
Louisiana	-0.618	0.399	0.121			
Maine	-0.432	0.381	0.258			
Maryland	-0.006	0.313	0.985			
Massachusetts	-0.104	0.273	0.702			
Michigan	0.033	0.276	0.906			
Minnesota	-0.457	0.345	0.185			
Mississippi	0.293	0.371	0.429			
Missouri	-0.185	0.304	0.544			
Nebraska	0.273	0.403	0.498			
Nevada	0.034	0.497	0.945			
New Hampshire	-0.585	0.537	0.276			
New Jersey	-0.167	0.304	0.584			

Table A2.6 continued						
New Mexico	-0.008	0.408	0.985			
New York	-0.173	0.285	0.542			
NorthCarolina	0.087	0.282	0.758			
Ohio	0.209	0.306	0.495			
Oklahoma	-0.300	0.305	0.326			
Oregon	-0.108	0.402	0.788			
Pennsylvania	-0.042	0.280	0.880			
RhodeIsland	0.198	0.410	0.629			
SouthCarolina	0.092	0.318	0.772			
SuperState	-0.381	0.368	0.301			
Tennessee	-0.095	0.310	0.760			
Texas	0.006	0.317	0.985			
Utah	-0.280	0.429	0.514			
Vermont	-0.092	0.469	0.845			
Virginia	0.236	0.342	0.491			
Washington	-0.174	0.329	0.597			
WestVirginia	-0.047	0.375	0.900			
Wisconsin	-0.297	0.319	0.352			

Paper 2. Medication for Opioid Use Disorder and 12-Month Mortality among Nonelderly Dually Eligible Medicare and Medicaid Beneficiaries

ABSTRACT

Objective. To compare the 12-month post-overdose mortality rates of dually eligible Medicare and Medicaid beneficiaries under the age of 65 who have received medication for opioid use disorder (MOUD) in the 12 months prior to a nonfatal opioid overdose (OD) with those who have either no history of MOUD treatment or evidence of treatment only more than 12 months prior to OD.

Methods. I linked Medicare and Medicaid claims data from 2013-2017 in this observational cohort study to identify nonfatal opioid overdoses, MOUD treatment, and deaths within 12 months. I used propensity score methods to adjust for numerous characteristics, and to compare 12-month mortality rates by use of MOUD and stratified by sex and health status.

Results. Of the 14,420 beneficiaries in this study cohort, 14.5% (n = 2,095) had used MOUD in the 12 months prior to the OD. Active MOUD was associated with lower rates of 12-month mortality among men (13.2% vs. 8.0% among active MOUD; 5.2 [95% CI: 2.2, 8.0] percentage points). Mortality rates were not significantly different between MOUD groups among women (aHR: 1.27; 95% CI: 0.95,1.59) and sicker beneficiaries (aHR: 1.26; 95% CI: 0.90,1.62).

Conclusions. Active MOUD, a well-established standard of care for opioid use disorder, was rarely used by beneficiaries in this study cohort. I found mixed results on the association between active MOUD and mortality by sex and level of health.

Policy implications. Engagement strategies and post-overdose care need to take into consideration differences between groups that influence receipt, acceptance, and effectiveness of care.

INTRODUCTION

In 2016, Medicare and Medicaid were the primary payers for over 50% of the almost two hundred thousand emergency department visits for opioid overdoses in the United States.[13] The significant subpopulation of beneficiaries under the age of 65 who are eligible for both Medicare and Medicaid (nonelderly duals) have many risk factors for opioid overdose and death. Medicare is available to individuals prior to the usual age of eligibility (65) who have certain qualifying disabilities that prevent them from working but have 24 months of work history, or who have end-stage renal disease. Qualifying conditions include disabilities that cause chronic pain (e.g., back injuries and severe arthritis) and severe mental health disorders (e.g., major depressive disorder), well-known risk factors for opioid misuse. Medicare beneficiaries under the age of 65 may also be eligible for Medicaid benefits if they need assistance paying the monthly premium for Medicare (or other cost-sharing responsibilities) or if they need care beyond what is covered by Medicare (such as long-term services and supports). Nonelderly duals are an extremely vulnerable population: many have complicated medical needs but they cannot afford their care.

Unlike many others who experience opioid overdose (OD), nonelderly duals have comprehensive health insurance that may facilitate their access to medication to opioid use disorder (MOUD; methadone, buprenorphine, or naltrexone), widely considered to be the standard of care for opioid use disorder (OUD). Prescription drug coverage is part of regular coverage for Medicaid beneficiaries, and nonelderly duals may also have Medicare Part D coverage. MOUD may be delivered as an inpatient or outpatient procedure. All state Medicaid programs cover at least one medication, and Medicare covers all three. Despite this promise of comprehensive treatment for OUD, previous studies have found that Medicare and Medicaid beneficiaries do not have adequate access to MOUD, nor is it of sufficient duration when prescribed.[83-85]

Nonelderly duals face barriers to MOUD related to both their physical health and socioeconomic status. Health care providers may be reluctant to prescribe MOUD to nonelderly duals, who often have multiple chronic conditions. Among nonelderly duals, OUD is often a secondary diagnosis, a distinction that is associated with lower chances of being treated with MOUD.[86] A physician may choose to prioritize treatment for another condition because it is clinically dominant, such as heart failure, or is highly symptomatic, such as fibromyalgia. Or, as OUD is not an eligible qualifying disability for SSI and SSDI, treatment may be prioritized for the qualifying disability. Additionally, physicians may be unwilling to risk drug interactions between MOUD and heart medications, antiretrovirals, antidepressants, and others.[87] They may have biases about medication adherence, which they may believe would be low due to co-occurring mental illness or other substance use disorders.[70] Compared to their Medicare-only peers, nonelderly duals are a more racially diverse and less educated population.[3] Barriers to MOUD related to socioeconomic status may also include racial discrimination, travel burden, and stigma.[88,89]

People with OUD are at risk of death both from overdose and death from other causes, in part because long-term opioid misuse damages many organ systems. The 12 months following an opioid overdose are a time of particularly high risk of death from subsequent opioid overdose and other causes.[14,16,90] Nonelderly duals face unique risk factors to both opioid overdose and subsequent mortality, but are an understudied population. I seek to compare the 12-month post-overdose mortality rates of beneficiaries who have received MOUD in the 12 months prior to the overdose, and thus have evidence of recent MOUD treatment, with those who have either no history of MOUD treatment or evidence of treatment only more than 12 months prior to OD. I expect to find that nonelderly duals with active MOUD engagement in the 12 months prior to the OD will have better mortality outcomes than those with inactive MOUD. The factors that influence

use of MOUD, such as the severity of comorbidities, may result in biased results in analyses of effectiveness of MOUD among nonelderly duals. Therefore, I use propensity score methods to minimize confounding that arises from these differences in observable characteristics.

METHODS

Use of these data was approved by the Centers for Medicare and Medicaid Services. The University of Chicago Institutional Review Board determined this research was exempt from informed consent.

Data sources

I linked Medicare and Medicaid data from 2013-2017 in this study to identify eligible beneficiaries, opioid overdoses, diagnoses, MOUD, and health care utilization in the 12 months prior to overdose. From Medicare, I used data from the Master Beneficiary Summary File, Chronic Conditions File, Other Chronic Conditions File, Medicare Provider Analysis and Review (MedPAR) and Outpatient Fee-for-Service (FFS) Files (all years: nationwide, 100%). From Medicaid, I used the Other Services Files and Prescription Files (2013: 28 states, 100%; 2014: 17 states, 100%; 2015-2017: nationwide, 100%). All Medicaid files for 2013 and 2014 were Medicaid Analytic eXtract (MAX) data. In 2015, 28 states were MAX data and the rest were Transformed Medicaid Statistical Information System Analytic Files (TAF), and in 2016, all were TAF.

I approximated local accessibility of buprenorphine using the Automation of Reports and Consolidated Orders System (ARCOS) Retail Drug Summary Reports for 2014-2016. These annual Drug Enforcement Administration reports disclose the amount of buprenorphine distributed to geographic locations at a 3-digit zip code level.[91]

Participants

Nonelderly duals eligible for this study survived a nonfatal opioid overdose between January 1, 2014 and December 31, 2016. Codes to capture nonfatal opioid overdose prior to October 1, 2015, were drawn from the *International Statistical Classification of Diseases and Related Health Problems, Ninth Revision, Clinical Modification* (ICD-9-CM): 965.00-965.02, 965.09, E85.00-E85.02, and E93.50-E93.52. CMS switched to ICD-10-CM on October 1, 2015. Thus, ICD-10-CM codes T40.0-T40.4, and T40.6 were used to identify opioid overdoses on or after this date. These overdose codes include poisonings from opiates and related narcotics, heroin, and methadone. The study index date was the discharge date of the first opioid overdose that occurred in the study period.

I excluded beneficiaries under 21 or over 64, those who did not qualify for Medicare based on disability, and those with cancer diagnoses in the year of the overdose. I removed nonelderly duals who did not live in the 50 states or DC at the time of the overdose. I excluded those who were not full duals with fee-for-service only coverage (i.e., those with health maintenance organization plans) for the 12 months prior to the overdose and 12 months following (or until death). I excluded beneficiaries who died within 2 days of discharge from the index overdose event.

Outcome

Death within 12 months of the index overdose date was the primary dependent variable in this study. I determined days to death using the validated date of death in the Master Beneficiary Summary File and the discharge date for the index overdose date.

Study variables

Beneficiaries were classified as having active MOUD if they had any claims with codes for MOUD in the 12 months prior to the index overdose. I classified procedures and prescriptions

as MOUD using the algorithm provided by the Chronic Conditions Warehouse (Appendix 3) in the MedPAR and Outpatient FFS claims data (Medicare) and the Prescription and Other Services Files (Medicaid). I also identified beneficiaries as having active MOUD if the date of first diagnosis was within 12 months of the index date, or if the beneficiary had an indicator for active MOUD (both variables found in the Medicare Other Chronic Conditions File). Beneficiaries with MOUD activity indicated prior to or following the study period only, or with no MOUD activity indicated ever, were classified as having inactive MOUD.

I used the R package "comorbidity" to calculate Van Walraven weighted Elixhauser scores for each beneficiary.[92] Elixhauser scores have been found to have good predictive validity of short-term mortality.[93,94] Higher Elixhauser scores indicate greater comorbidity.

Propensity scores and weights were created based on characteristics present at the time of the overdose. I classified the 816 "crossover" beneficiaries, i.e., those who initiated MOUD in the 12 months following the overdose, with those had active MOUD at the time of the overdose, and censored them in survival analyses at the time of MOUD initiation. I conducted several sensitivity analyses (described below) to examine the possible bias introduced by this decision.

Propensity score analysis

I used propensity score methods to balance the study population prior to analyzing mortality rates to control for the significant differences in observable characteristics between the active MOUD and inactive MOUD beneficiaries. Propensity score weights allow a quasi-experimental approach to observational data because they balance the distribution of covariates between the treatment groups, thus mimicking randomization.

I chose propensity score weights over including the score in a regression model or matching or stratifying based on the score because it allows the inclusion of all beneficiaries in the analysis.

Further, using weights instead of including the propensity score in the regression model allowed a check of the balance of the groups.

I used 38 variables (those in Table 1, with the exclusion of time to OUD prior to OD) in a logistic regression model to model the probability of having active MOUD in the 12 months prior to the overdose, i.e., to create a propensity score (*P*). Variables in this model included age, sex, race, Elixhauser score, known prior opioid overdoses, and several preexisting conditions. I used the propensity score to derive individual overlap weights, a method of weighting in which each beneficiary with inactive MOUD received a weight of 1, and each beneficiary with active MOUD received a weight of 1 – *P*. I used overlap weights because the groups had large differences in covariates, and standard propensity score weighting predicted extreme weights. Overlap weights have also been found to be robust in small populations,[95] and receipt of MOUD was rare. Beneficiaries near the maximum overlap (weights approaching 1) are rewarded, and those with an extreme propensity score at the boundaries (weights approaching 0) are penalize. The advantage of this approach is stability and low variance of the overlap weights.

I determined unweighted and weighted 12-month mortality rates by MOUD status. I also compared 12-month mortality rates by MOUD status using Cox proportional hazards survival analyses. I checked for proportional hazards using the unweighted data, as the test is not available using weights. I censored crossover beneficiaries at the time of MOUD initiation. Finally, I completed these analyses stratified by Elixhauser score (high score, i.e., sicker beneficiaries, and low score, e.g., healthier beneficiaries) and sex.

Life course theory and fundamental cause theory contributed to the choice of propensity score methods as well as the groups for stratification. Specifically, according to life course theory, the timing of life transitions and events affects outcomes. Therefore, the physical and mental

conditions that a person has indicated at the time of the overdose may provide key insight into the classification of a person as active or inactive MOUD. The ability to access and maintain MOUD may be influenced by socioeconomic factors, such as having access to providers and overcoming racial and gender biases.

I computed the E-value using the "EValue" R package.[96] This parameter describes the degree of unmeasured confounding that would be necessary to explain the association between MOUD and mortality. E-values are evaluated based on the magnitude of other covariates in a regression model. An E-value that is higher than the adjusted covariates indicate a more robust association between the exposure and outcome, as it suggests that a significant amount of confounding would need to be included to subvert the results.

Sensitivity analyses

In the primary analysis, I classified beneficiaries who initiated MOUD within 12 months following the overdose (crossover beneficiaries) as having active MOUD when I calculated the propensity score. Because propensity scores and weights were determined based on characteristics present at the time of the overdose, this may have introduced bias, as a beneficiary may have different diagnoses at the time of initiating MOUD. I compared the crossover beneficiaries with the active MOUD and inactive MOUD groups, and determined crossover beneficiaries were more similar to the active MOUD than inactive MOUD group (Appendix 4, Tables A4.1 and A4.2). I assessed the sensitivity to the classification of crossover beneficiaries by completing two additional analyses: in one, I assigned half of the beneficiaries to the active MOUD group and half to the inactive MOUD group, and in the second, I excluded all crossover beneficiaries. For each assessment, I determined unweighted 12-month mortality rates and compared results to the primary analysis.

To assess the sensitivity of this propensity score method, I used the "PSweight" package in R to create inverse probability of treatment weights, matching weights, and entropy weights[97] and assessed balance with these weights. Finally, I used the "MatchIt" package in R to estimate 12-month mortality rates using datasets that were matched on propensity scores with 1:1 Nearest Neighbor and full matching.Ho, Imai, King, Stuart [98] I determined 12-month mortality rates and hazard ratios for the overall study cohort and stratified by sex and Elixhauser score using both methods of propensity score matching for each group. Groups were evaluated on the standardized mean difference, and considered balanced if the difference between covariates was less than 0.1.[99]

RESULTS

Of the 14,420 beneficiaries in this study cohort, 14.5% (n = 2,095) had used MOUD in the 12 months prior to the OD, and an additional 5.7% (n = 816) initiated MOUD within 12 months following the OD. In total, 20.2% (n = 2,911) beneficiaries were classified as having active MOUD in the creation of propensity scores and weights.

Beneficiary characteristics

Beneficiaries who had active MOUD differed in many regards from their inactive MOUD peers (Table 4). Active MOUD beneficiaries were younger on average (43.4 vs. 49.6 years old), and did not have as many indicators of serious comorbidities. Less than 25% of beneficiaries who had active MOUD had Elixhauser scores over 1, compared with almost 40% among those who did not have active MOUD. Serious physical comorbidities, including chronic obstructive pulmonary disorder, congestive heart failure, and chronic kidney disease, were more common among those who did not have active MOUD than those who did (40.1% vs. 25.7%, 23.9% vs. 11.2%, and 38.7% vs. 24.3%, respectively).

More active MOUD beneficiaries had indicators of a history of substance misuse: almost 17% of Active MOUD beneficiaries had known prior opioid overdoses, compared with 10% in the Inactive MOUD group. About 50% of those who had active MOUD had been diagnosed with alcohol use disorder, versus 26% among those with inactive MOUD. Most beneficiaries had an OUD diagnosis prior to the index event: 88.6% of active MOUD and 55.1% of Inactive MOUD beneficiaries had diagnoses prior to the OD, and for each group, beneficiaries had been diagnosed on average more than 4 years prior to the event (4.73 years for the active MOUD group and 4.24 years for the inactive MOUD group).

Table 4. Differences in Characteristics and Comorbidities of Nonelderly Duals by MOUD Status at the Time of Nonfatal Opioid Overdose

	Unweighted		**Weighted**	
	Active MOUD (n=2911)	**Inactive MOUD (n=11509)**	**Active MOUD (n=2911)**	**Inactive MOUD (n=11509)**
Age, mean, years	43.4	49.6	45.5	45.5
Female (%)	49.9	61.3	52.3	52.3
Race/ethnicity (%)				
Non-Hispanic White	78.6	75.5	77.3	77.3
Black or African American	9.8	13.5	11.6	11.6
Other	11.6	11.0	11.1	11.1
Census region (%)				
West	13.7	20.0	16.4	16.4
Midwest	19.3	26.5	22.4	22.4
Northeast	50.5	24.0	41.0	41.0
South	16.5	29.5	20.2	20.2
Time under disability insurance, mean, years	8.6	10.5	9.2	9.2
Elixhauser score (%)				
<0	49.5	22.4	40.4	40.4
0	27.5	39.0	32.0	32.0
1-4	9.7	12.0	10.6	10.6
>=5	13.4	26.6	17.0	17.0
Any known prior opioid OD (%)	16.5	10.1	14.5	14.5

Table 4 continued				
Known opioid OD in 6 months prior (%)	2.1	1.2	1.8	1.8
Time to OUD diagnosis prior to OD, mean, years[a]	-4.73	-4.24		
No diagnosis prior to OD (%)	11.4	44.9		
Buprenorphine distributed, 3-digit zip code level (%)				
First Quartile (Lowest)	7.8	16.6	10.0	10.0
Second Quartile	16.8	24.1	20.0	20.0
Third Quartile	22.2	29.3	24.5	24.5
Fourth Quartile (Highest)	53.2	30.0	45.5	45.5
No inpatient claims 6 months prior to OD (%)	52.0	57.4	55.0	55.0
Number of serious chronic conditions[b] (%)				
0-1	59.6	39.9	53.2	53.2
2-4	34.7	46.5	39.2	39.2
5-8	5.7	13.6	7.6	7.6
Substance use diagnoses (%)				
Alcohol use disorder	48.4	26.0	41.7	41.7
Drug use disorder	96.6	83.2	95.1	95.1
Tobacco use disorder	82.1	68.4	79.0	79.0
Number of mental health diagnoses prior to OD, median[c]	2.5	2.2	2.4	2.4
Mental health diagnoses (%)				
ADHD and other conduct disorders	22.0	9.9	17.4	17.4
Anxiety	81.3	74.5	78.6	78.6
Bipolar	60.2	42.6	54.4	54.4
Major depressive disorder	75.5	73.6	74.2	74.2
Personality disorders	23.9	15.2	21.8	21.8
Schizophrenia and other psychotic conditions	31.4	26.7	29.9	29.9
Schizophrenia	17.8	15.8		
Post-traumatic stress disorder	33.8	18.0	27.3	27.3
Pain diagnoses (%)				
Fibromyalgia, chronic pain, fatigue, or migraine	64.5	79.9	70.6	70.6
Chronic conditions (%)				
Atrial fibrillation	1.8	3.4	2.2	2.2
Congestive heart failure	11.2	23.9	14.2	14.2
Chronic kidney disease	24.3	38.7	28.6	28.6

Table 4 continued				
Chronic obstructive pulmonary disease	25.7	40.1	30.3	30.3
Diabetes	20.2	35.7	24.4	24.4
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	4.4	3.0	4.3	4.3
Ischemic heart disease	20.6	32.8	24.1	24.1
Obesity	25.2	36.2	28.0	28.0
Osteoporosis	2.8	6.3	3.7	3.7
Rheumatoid arthritis/Osteoarthritis	34.0	55.9	41.0	41.0
Viral hepatitis	42.0	19.0	33.8	33.8

[a] Missing data (those with no diagnosis at time of OD) precludes inclusion in propensity score matching
[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.
[c] Major depressive disorder, bipolar, anxiety, and/or schizophrenia and other psychotic conditions.

Fewer beneficiaries in this study cohort were males (39.3%), yet 50.1% of Active MOUD beneficiaries were male. Many mental health disorders were common among both MOUD groups, including major depressive disorder, anxiety disorders, and bipolar disorder. Most beneficiaries in both groups had at least 2 serious mental illnesses. Once adjusted with overlap weights created using propensity scores, the 2 MOUD groups had the same distribution of characteristics on average.

Once stratified by gender and adjusted by propensity scores for MOUD, a greater proportion of men than women had alcohol use disorder (47.1% vs. 36.7%), schizophrenia (22.3% vs. 13.8%), HIV/AIDS (5.4% vs. 3.2%), and viral hepatitis (38.3% vs. 29.4%). A greater proportion of women than men had other mental illnesses, including anxiety, bipolar disorder, major depressive disorder, personality disorders, and post-traumatic stress disorder. Pain

diagnoses were also more common among women than men. The balance of Elixhauser scores and the number of serious chronic conditions, measures of overall health, was similar between groups.

Once stratified by Elixhauser scores and adjusted by propensity scores, a greater proportion of sicker beneficiaries (those with Elixhauser scores greater than 0) than healthier beneficiaries were women (55.0% vs. 51.1%) and had a recorded opioid OD in the 6 months prior to the index event (2.5% vs. 1.6%). Most sicker beneficiaries had 2-4 serious chronic conditions (51.9%), compared with healthier beneficiaries, of whom the most had 0-1 serious chronic conditions (61.0%). Many beneficiaries in both groups had diagnoses of other substance use disorders: around 40% had alcohol use disorder and almost 80% had tobacco use disorder.

Appendix tables A5.1-A5.4 show the complete distribution of characteristics of the stratified groups prior to and following propensity score weighting.

Differences in 12-month mortality

The unadjusted 12-month mortality rate (Table 5) for the inactive MOUD group was 4.2 (95% CI: 3.1, 5.3) percentage points higher than that of the active MOUD group (11.3% vs. 7.1% for active MOUD group). This did not change significantly after propensity score adjustment: the mortality rate for those with no MOUD was 3.9 (95% confidence interval [CI]: 2.0, 5.8) percentage points (pp) higher than that of the active MOUD group (11.3% vs. 7.4% for active MOUD group).

Percentage point differences between the inactive MOUD and active MOUD groups also did not change significantly after propensity score adjustment in the stratified analyses. For each group, after adjustment, differences in mortality ranged from 3.4 to 5.2 percentage points. The difference between the inactive and active MOUD groups was highest among men (5.2 pp, 95% CI: 2.2, 8.0). Although the difference was also great among the high Elixhauser group after adjustment (4.8 pp, 95% CI: 0.6, 9.1), the overlapping confidence intervals between the inactive

and active MOUD groups suggests MOUD may not do much to improve 12-month mortality among the sickest beneficiaries. To a lesser extent, the 95% confidence intervals between the active and inactive MOUD groups also overlapped among women, and the 95% lower limit was close to 0 (3.4 pp, 95% CI: 0.7, 5.9).

Even among beneficiaries with low Elixhauser scores and women, who had the lowest mortality rates, mortality was still high: over 6% of those with active MOUD, and 10% of those with inactive MOUD, died within a year.

Table 5. 12-Month Mortality Following Nonfatal Opioid Overdose by Active MOUD Status and Stratified by Level of Health and Sex.

		% (95% CI)		
		Inactive MOUD	Active MOUD	Percentage Point Difference
Overall (N = 14420)	Unadjusted 12-month mortality rate	11.3 (10.8, 11.9)	7.1 (6.2, 8.1)	4.2 (3.1, 5.3)
	Adjusted 12-month mortality rate	11.3 (9.8, 12.8)	7.4 (6.2, 8.6)	3.9 (2.0, 5.8)
Women (N =8504)	Unadjusted 12-month mortality rate	10.1 (9.4, 10.8)	6.5 (5.3, 7.8)	3.6 (2.1, 5.0)
	Adjusted 12-month mortality rate	10.2 (8.2, 12.1)	6.8 (5.1, 8.4)	3.4 (0.7, 5.9)
Men (N = 5916)	Unadjusted 12-month mortality rate	13.3 (12.3, 14.3)	7.8 (6.4, 9.1)	5.5 (3.9, 7.0)
	Adjusted 12-month mortality rate	13.2 (10.8, 15.4)	8.0 (6.1, 9.8)	5.2 (2.2, 8.0)
Elixhauser: Low (N = 9309)	Unadjusted 12-month mortality rate	8.8 (8.1, 9.4)	6.2 (5.2, 7.2)	2.6 (1.4, 3.8)

Table 5 continued				
Elixhauser: Low (N = 9309)	Adjusted 12-month mortality rate	10.1 (8.4, 11.7)	6.2 (4.8, 7.5)	3.9 (1.8, 6.0)
Elixhauser: High (N = 5111)	Unadjusted 12-month mortality rate	15.4 (14.3, 16.5)	10.4 (8.3, 12.8)	5.0 (2.4, 7.5)
	Adjusted 12-month mortality rate	15.4 (12.1, 18.6)	10.6 (7.8, 13.2)	4.8 (0.6, 9.1)

The p-value for the proportional hazards test for the unweighted data was 0.15, but this test could not be run with the weighted data. After propensity score adjustment, inactive MOUD in the year prior to OD was a significant risk factor for 12-month mortality among all beneficiaries (Table 6), although to varying degrees. Overall, and in the stratified analyses of men and the low Elixhauser group, inactive MOUD was a significant risk factor for 12-month mortality (adjusted hazard ratio [aHR]: 1.31, 95% CI: 1.09, 1.53, p = 0.001; aHR: 1.42, 95% CI: 1.12, 1.72, p = 0.002; and HR: 1.68, 95% CI: 1.40, 1.96, p < 0.001, respectively). Women and the high Elixhauser group showed weaker associations between inactive MOUD and 12-month mortality (aHR: 1.27, 95% CI: 0.95, 1.59, p = 0.05; aHR: 1.26, 95% CI: 0.90, 1.61, p = 0.12).

Table 6. Propensity Score Adjusted Association between Use of MOUD prior to Nonfatal Opioid Overdose and 12-Month Mortality

Cohort	Hazard ratio (95% CI)	*P* value	E-value (lower CI)
Entire cohort	1.31 (1.09,1.53)	0.001	1.94 (1.40)
Women only	1.27 (0.95,1.59)	0.05	1.85 (1.00)
Men only	1.42 (1.12,1.72)	0.002	2.19 (1.48)
Low Elixhauser score	1.68 (1.40,1.96)	<0.001	2.74 (2.14)
High Elixhauser score	1.26 (0.90,1.62)	0.12	1.82 (1.00)

The E-values of active MOUD for the overall cohort, men, and the low Elixhauser groups were 1.94 (lower CI limit: 1.40), 2.19 (lower CI limit: 1.48), and 2.74 (lower CI limit 2.14). These

E-values are relatively larger than the HRs for these groups, suggesting that a significant amount of unmeasured confounding would need to be present to subvert these results. Among women and the high Elixhauser groups, although the E-values were higher than the HRs, the lower CI limits were 1.0 for both groups. This indicates there may be factors influencing 12-month mortality that are not captured in observable characteristics, and that unmeasured confounding may be present.

Sensitivity analysis results

Appendix 6 shows the results of the sensitivity analyses. Whether I grouped 50% of the crossover beneficiaries in each MOUD group or excluded them, the percentage point difference in mortality rates for each population (total and stratified by sex and Elixhauser score) decreased, and the conclusion of the analyses did not change from when 100% of crossover beneficiaries were grouped with the Active MOUD beneficiaries (Table A6.1).

Finally, I used the "MatchIt" package in R to estimate 12-month mortality rates. I created datasets for each population that were matched on propensity scores with 1:1 Nearest Neighbor and full matching (Table A6.2). Each of the datasets was balanced with standardized mean differences between groups less than 0.10. The 12-month mortality rates and hazard ratios for the inactive and active MOUD groups were similar to those found using overlap weights.

DISCUSSION

Medicare and Medicaid coverage includes MOUD, generally considered the standard of care for OUD, yet only 14.5% of the 14,420 nonelderly duals in this study had active MOUD at the time of the index overdose, with an additional 5.7% initiating MOUD in the 12 months following the OD. The index overdose was not the first sign of OUD for most beneficiaries in this study cohort: the majority were first diagnosed with OUD more than 4 years prior to the OD, and, on average, had been covered by Medicare for over 8 years.

As has been found in other studies,[37] beneficiaries in this cohort who used MOUD had better health outcomes—in this case, 12-month mortality—than those who did not use it. The unadjusted 12-month mortality rate of nonelderly duals in the active MOUD group was over 4 percentage points lower than the inactive MOUD group. Beneficiaries with active MOUD were younger, with fewer serious physical comorbidities, and had a greater presence of other substance use disorders than those with inactive MOUD. Additionally, men were disproportionately represented in the active MOUD group. Thus, I used propensity score methods to create balanced groups to account for the differences in observable characteristics that may have influenced receipt of MOUD and biased mortality results.

After propensity score adjustments, the 4-percentage-point difference in mortality rates between the active and inactive MOUD groups remained. In the stratified analyses, I found mixed evidence of the benefit of MOUD. Among men, there was a 5.2 percentage point difference in adjusted mortality rates between the MOUD groups. Other studies have found male sex has been found to be a significant risk factor for mortality following overdose.[14,24] Notably, although active MOUD was associated with lower mortality among men, rates were still high: 8% of men with active MOUD died within 12 months of the nonfatal overdose. The healthier beneficiaries in the study—those with low Elixhauser scores—also seemed to benefit from active MOUD. Around 6% of beneficiaries with active MOUD died within 12 months, 4 percentage points lower than the inactive MOUD group. Thus, although MOUD is associated with lower mortality among men and healthier nonelderly duals, it is not panacea. This likely reflects the long period of OUD prior to the index OD as well as the physical comorbidities present.

Among women and the sicker beneficiaries (high Elixhauser scores), adjusted 12-month mortality rates between the MOUD groups had overlapping confidence intervals, and thus a less

clear association between active MOUD and lower mortality. With the sicker beneficiaries, this is not an unexpected finding; some people, such as those with congestive heart failure, are likely to die regardless of any treatment, MOUD or otherwise, they receive.

The finding with women did not have a clear explanation. I found in Study 1 of this dissertation that just half (51.2%) of all nonelderly duals in the control population (those who fulfilled all study criteria *except* did not survive an opioid overdose) were women. Women comprise 59.6% of the study cohort who overdosed, yet male sex is associated with increased odds of dying within 12 months. Slightly more men than women in the study cohort have a history of opioid OD (18% versus 15%), and of those who were diagnosed with OUD prior to the index OD, on average, men in both the inactive and active MOUD groups had been diagnosed for longer than women in either group prior to the index OD (4.5 years versus 4.1 years among active MOUD, and 3.1 years versus 2.8 years among inactive MOUD). The overrepresentation of men in the study cohort who received MOUD, therefore, may reflect longer known history of opioid misuse. However, this does not explain why active MOUD would not be associated with lower 12-month mortality rates among women. The male and female propensity-score-adjusted groups were similar on indicators of disease severity and serious comorbidities. As I did not study treatment retention, it is possible that there were differences in the length of engagement that affected mortality. Other studies have found differences between women and men in MOUD initiation and retention. Marsh, Amaro, Kong, Khachikian, Guerrero [46] found that compared to men, women spent longer on waitlists for outpatient methadone clinics, but were more likely to stay in treatment.

The E-value for the hazard ratio for mortality rates among women has a lower confidence interval of 1.0, suggesting there may be unmeasured confounders that are affecting these findings. Given the high prevalence of pain diagnoses among women in this study, as well evidence from

as other studies examining gender differences,[100] I hypothesize that women in this study cohort may be using misusing medical prescription opioids and men may be misusing heroin. In the general U.S. population, as many as 58% of those who misuse prescription opioids use their own prescribed opioids, and cite pain relief as the most common reason for misuse.[26]

In a national study, it was found that less than 40% of those with a dual mental health diagnosis received MOUD.[43] In this study, over 80% of nonelderly duals in both groups had depression, which, if treated with antidepressants, holds risk of dangerous interactions with MOUD.[87] Almost 5% of nonelderly duals who used MOUD had HIV/AIDS, even though antivirals also are known to interact with MOUD. This suggests concerns about drug interaction may be overridden by other factors. For instance, about 17% of nonelderly duals with active MOUD had a known prior OD, compared with 10% of those with inactive MOUD. This may reflect a sense of urgency on the part of physicians in encouraging beneficiaries with overdose histories to use MOUD.

Over 50% of beneficiaries with active MOUD live in the Northeast Region. Receipt of MOUD may reflect acceptability in a geographic location, which may reduce stigma and increase beneficiary motivation. A study placed in Massachusetts found that 26% of the population had received MOUD in the 12 months prior to nonfatal OD, and 30% received MOUD following the overdose.[37]

STRENGTHS AND LIMITATIONS

To my knowledge, this study is the first to study the use of MOUD and its associations with mortality among nonelderly duals. I used multiple years of Medicare and Medicaid claims data to determine the use of MOUD, ensuring that I had a complete picture of MOUD use even when there were different payers. Additionally, I studied claims from hospital and clinics to

identify procedure claims for MOUD instead of relying solely on drug codes. Finally, I used propensity score methods to make the MOUD groups comparable in observable characteristics, a strategy that reduced bias in this analysis.

However, although I was able to use multiple years of Medicare and Medicaid data, I did not have access to Medicaid data from all states for 2013 and 2014. I do not have Medicaid data for the 4,514 beneficiaries in 2013 or the 8,729 beneficiaries in 2014 who lived in 1 of the states without complete data. The number of beneficiaries with active MOUD at the time of the OD is likely greater than reported, as I also did not have Medicare Part D data. However, this study cohort was similar to the Medicare MBSF Other Chronic Conditions supplement, which indicates MOUD in any Medicare file. This study cohort differed because I looked for recent (1 year) indicators of MOUD instead of 2 years as in the Other Chronic Conditions supplement.

These results must be interpreted cautiously, as a significant limitation of propensity score methods is that they are based on observable characteristics. In this study, we are limited to characteristics and conditions as described in claims, rather than possibly more accurate and informative health records. Health records include information about diagnostic tests and unbilled services, as well as the severity of conditions. Accuracy is also more important in health records, which are generated for treatment, than in claims, which are generated for payment. Finally, the groups who used MOUD may have differences from those who did not, including barriers to care that also may affect mortality, such as safe, stable housing and social support, that would not be apparent in any administrative record.

I was not able to check for proportional hazards in my Cox proportional hazards model because I used overlap weights. However, the R package used in estimating hazard ratios in this study provides unbaised average hazard ratio estimates regardless of whether the hazards are

proportional or non-proportional.[101] The unweighted data had proportional hazards between MOUD groups. Given the differences between the groups, however, these results must be interpreted cautiously. I hope to conduct a more comprehensive time-varying model in the future that would include timing of MOUD delivery.

Finally, without Part D data, I was unable to ascertain detailed prescription data for beneficiaries. I used other Medicare files to determine use of MOUD and general timelines, but was not able to analyze outpatient prescriptions.

CONCLUSION

Nonelderly duals are a medically complex, vulnerable population, and the effects of opioid misuse and overdose among nonelderly duals are even worse than among other populations. Fewer than 1 in 4 nonelderly duals in this study had evidence of MOUD at the time of or within 12 months of nonfatal opioid overdose, despite having MOUD covered by Medicare and Medicaid. Barriers to care must be explored in future work: it cannot be determined from this study whether provider reluctance, stigma, unfamiliarity with MOUD, or other factors accounted for the low number of beneficiaries who received treatment. Futher research also needs to explore the disparities indicated in the effectiveness of MOUD between populations. In particular, the difference in effectiveness by sex must be examined to increase access. Existing relationships with providers who care for nonelderly duals in other capacities may provide opportunities to initiate more nonelderly duals with OUD to treatment.

Appendix 3. Chronic Conditions Warehouse Codes for Identifying Receipt of Medication for Opioid Use Disorder

HCPCS codes for MOUD: G2067, G2068, G2069, G2070, G2071, G2072, G2073, G2078, G2079, H0020, J0571, J0572, J0573, J0574, J0575, J0592, J1230, J2315, S0109

NDCs for Buprenorphine: 00054017613, 00054017713, 00054018813, 00054018913, 00093537856, 00093537956, 00093572056, 00093572156, 00228315303, 00228315403, 00228315473, 00228315503, 00228315567, 00228315573, 00228315603, 00378092393, 00378092493, 00378876716, 00378876793, 00378876816, 00378876893, 00406192303, 00406192403, 00406800503, 00406802003, 00490005100, 00490005130, 00490005160, 00490005190, 00781721606, 00781721664, 00781722706, 00781722764, 00781723806, 00781723864, 00781724906, 00781724964, 12496010001, 12496010002, 12496010005, 12496030001, 12496030002, 12496030005, 12496120201, 12496120203, 12496120401, 12496120403, 12496120801, 12496120803, 12496121201, 12496121203, 12496127802, 12496128302, 12496130602, 12496131002, 16590066605, 16590066630, 16590066705, 16590066730, 16590066790, 23490927003, 23490927006, 23490927009, 35356000407, 35356000430, 35356055530, 35356055630, 42291017430, 42291017530, 42858050103, 42858050203, 43063018407, 43063018430, 43063066706, 43063075306, 43598057901, 43598057930, 43598058001, 43598058030, 43598058101, 43598058130, 43598058201, 43598058230, 47781035503, 47781035511, 47781035603, 47781035611, 47781035703, 47781035711, 47781035803, 47781035811, 49999039507, 49999039515, 49999039530, 49999063830, 49999063930, 50090292400, 50268014411, 50268014415, 50268014511, 50268014515, 50383028793, 50383029493, 50383092493, 50383093093, 52427069203, 52427069211, 52427069403, 52427069411, 52427069803, 52427069811, 52427071203, 52427071211, 52440010014, 52959030430, 52959074930, 53217013830, 53217024630, 54123011430, 54123090730, 54123091430, 54123092930, 54123095730, 54123098630, 54569549600, 54569573900, 54569573901, 54569573902, 54569639900, 54569640800, 54569657800, 54868570700, 54868570701, 54868570702, 54868570703, 54868570704, 54868575000, 55045378403, 55700014730, 55700018430, 55700030230, 55700030330, 58284010014, 59385001201, 59385001230, 59385001401, 59385001430, 59385001601, 59385001630, 60429058611, 60429058630, 60429058633, 60429058711, 60429058730, 60429058733, 60687048111, 60687048121, 60687049211, 60687049221, 62175045232, 62175045832, 62756045983, 62756046083, 62756096983, 62756097083, 63629402801, 63629403401, 63629403402, 63629403403, 63629409201, 63874108403, 63874108503, 63874117303, 65162041503, 65162041603, 66336001630, 68071138003, 68071151003, 68258299103, 68258299903, 68308020230, 68308020830, 71335115403

NDCs for Naltrexone (see exclusion criteria, below): 00056001122, 00056001130, 00056001170, 00056007950, 00056008050, 00185003901, 00185003930, 00406009201, 00406009203, 00406117001, 00406117003, 00555090201, 00555090202, 00904703604, 16729008101, 16729008110, 42291063230, 43063059115, 47335032683, 47335032688, 50090286600, 50436010501, 51224020630, 51224020650, 51285027501, 51285027502, 52152010502,

52152010504, 52152010530, 54868557400, 63459030042, 63629104601, 63629104701, 65694010003, 65694010010, 65757030001, 65757030202, 68084029111, 68084029121, 68094085362, 68115068030;

Exclude beneficiaries with NDC for Naltrexone, if the CCW alcohol use disorder indicator = Yes and opioid use disorder DX indicator (from measure #2 OUD using diagnoses) = No; or CCW drug use disorder indicator = Yes and opioid use DX disorder = No

Appendix 4. Characteristics and Comorbidities of Active MOUD, Inactive MOUD, and Crossover MOUD Nonelderly Duals at the Time of Nonfatal Opioid Overdose.

Table A4.1. Characteristics and Comorbidities of Active MOUD and Crossover MOUD Nonelderly Duals at the Time of Nonfatal Opioid Overdose

	Active MOUD (N=2095)	Crossover MOUD (N=816)	*P* value
Age (years), Mean (SD)	43.3 (10.8)	43.9 (10.8)	0.17
Race, No. (%)			
Black or African American	211 (10.1)	75 (9.2)	0.50
Non-Hispanic White	1635 (78.0)	653 (80.0)	
Other	249 (11.9)	88 (10.8)	
Male sex, No. (%)	1068 (51.0)	389 (47.7)	0.12
Census region, No. (%)			
West	300 (14.3)	98 (12.0)	0.01
Midwest	380 (18.1)	182 (22.3)	
Northeast	1084 (51.7)	386 (47.3)	
South	331 (15.8)	150 (18.4)	
Time under disability insurance (years), Mean (SD)	8.63 (6.38)	8.46 (6.97)	0.53
Any known prior opioid OD, No. (%)	375 (17.9)	105 (12.9)	0.001
Known opioid OD in 6 months prior, No. (%)	44 (2.1)	17 (2.1)	1
Time to OUD diagnosis prior to OD (years), Mean (SD)	-4.94 (4.23)	-4.07 (4.24)	<0.001
No diagnosis at time of OD	129 (6.2)	204 (25.0)	<0.001
Buprenorphine distribution area, 3-digit zip code level, No. (%)			
First quartile	174 (8.3)	52 (6.4)	0.04
Second quartile	348 (16.6)	141 (17.3)	
Third quartile	442 (21.1)	205 (25.1)	
Fourth quartile	1131 (54.0)	418 (51.2)	
Sum of mental health diagnoses[a], Mean (SD)	2.55 (1.17)	2.32 (1.21)	<0.001
Number of serious chronic conditions[b], No. (%)			
0-1 Major chronic conditions	1259 (60.1)	477 (58.5)	0.71
2-4 Major chronic conditions	717 (34.2)	292 (35.8)	
5-8 Major chronic conditions	119 (5.7)	47 (5.8)	
Elixhauser score, No. (%)			
<0	1118 (53.4)	323 (39.6)	<0.001
0	508 (24.2)	292 (35.8)	
1-4	197 (9.4)	84 (10.3)	

Table A4.1 continued			
>=5	272 (13.0)	117 (14.3)	
Fibromyalgia, chronic pain, fatigue, or migraine, No. (%)	1310 (62.5)	567 (69.5)	<0.001
Number of inpatient claims prior to OD, No. (%)			
0	1034 (49.4)	479 (58.7)	<0.001
1-4	906 (43.2)	300 (36.8)	
5+	155 (7.4)	37 (4.5)	
Number of outpatient claims prior to OD, No. (%)			
0	235 (11.2)	107 (13.1)	<0.001
1-4	818 (39.0)	366 (44.9)	
5+	1042 (49.7)	343 (42.0)	
Chronic conditions, No. (%)			
ADHD and other conduct disorders	505 (24.1)	135 (16.5)	<0.001
Alcohol use disorder	1063 (50.7)	345 (42.3)	<0.001
Anxiety	1736 (82.9)	631 (77.3)	<0.001
Asthma	545 (26.0)	183 (22.4)	0.05
Atrial fibrillation	36 (1.7)	15 (1.8)	0.95
Bipolar disorder	1316 (62.8)	437 (53.6)	<0.001
Chronic kidney disease	485 (23.2)	221 (27.1)	0.03
Chronic obstructive pulmonary disease	534 (25.5)	214 (26.2)	0.72
Congestive heart failure	237 (11.3)	90 (11.0)	0.88
Major depressive affective disorder	1609 (76.8)	590 (72.3)	0.01
Diabetes	414 (19.8)	174 (21.3)	0.37
Drug use disorder	2044 (97.6)	769 (94.2)	<0.001
Epilepsy	385 (18.4)	125 (15.3)	0.06
Fibromyalgia, chronic pain, or fatigue	1252 (59.8)	552 (67.6)	<0.001
Hearing impairment	50 (2.4)	16 (2.0)	0.58
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	97 (4.6)	32 (3.9)	0.46
Hyperlipidemia	426 (20.3)	204 (25.0)	0.01
Hyperplasia	53 (2.5)	28 (3.4)	0.23
Hypertension	928 (44.3)	395 (48.4)	0.05
Hypothyroidism	221 (10.5)	93 (11.4)	0.56
Ischemic heart disease	433 (20.7)	166 (20.3)	0.89
Liver disease	340 (16.2)	124 (15.2)	0.53
Migraine	304 (14.5)	149 (18.3)	0.01
Mobility impairment	72 (3.4)	29 (3.6)	0.97
Obesity	531 (25.3)	204 (25.0)	0.88
Osteoporosis	57 (2.7)	24 (2.9)	0.84

Table A4.1 continued			
OUD diagnosis	2028 (96.8)	747 (91.5)	<0.001
Peripheral vascular disease	114 (5.4)	38 (4.7)	0.45
Personality disorders	512 (24.4)	183 (22.4)	0.27
Post-traumatic stress disorder	753 (35.9)	230 (28.2)	<0.001
Rheumatoid arthritis/Osteoarthritis	657 (31.4)	334 (40.9)	<0.001
Schizophrenia and other psychotic disorders	679 (32.4)	236 (28.9)	0.08
Spinal injury	21 (1.0)	15 (1.8)	0.10
Stroke	68 (3.2)	23 (2.8)	0.63
Tobacco use disorder	1745 (83.3)	646 (79.2)	0.01
Traumatic brain injury	44 (2.1)	15 (1.8)	0.76
Ulcers	140 (6.7)	56 (6.9)	0.93
Viral hepatitis	963 (46.0)	261 (32.0)	<0.001

[a] Schizophrenia and other psychotic disorders, major depressive disorder, bipolar disorder, and/or anxiety.
[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.

Table A4.2. Characteristics and Comorbidities of Inactive MOUD and Crossover MOUD Nonelderly Duals at the Time of Nonfatal Opioid Overdose

	Inactive MOUD (N=11509)	**Crossover MOUD (N=816)**	***P* value**
Age (years), Mean (SD)	49.6 (10.0)	43.9 (10.8)	<0.001
Race, No. (%)			
Black or African American	1562 (13.5)	75 (9.2)	0.002
Non-Hispanic White	8715 (75.5)	653 (80.0)	
Other	1273 (11.0)	88 (10.8)	
Male sex, No. (%)	4433 (38.7)	389 (47.7)	<0.001
Census region, No. (%)			
West	2308 (20.0)	98 (12.0)	<0.001
Midwest	3065 (26.5)	182 (22.3)	
Northeast	2772 (24.0)	386 (47.3)	
South	3405 (29.5)	150 (18.4)	
Time under disability insurance (years), Mean (SD)	10.5 (7.59)	8.46 (6.97)	<0.001
Any known prior opioid OD, No. (%)	1163 (10.1)	105 (12.9)	0.02
Known opioid OD in prior 6 months, No. (%)	135 (1.2)	17 (2.1)	0.03
Time to OUD diagnosis (years), Mean (SD)	-4.24 (4.25)	-4.07 (4.24)	0.37

Table A4.2 continued			
No diagnosis at time of OD	5182 (44.9)	204 (25.0)	<0.001
Buprenorphine distribution area, 3-digit zip code level, No. (%)			
First quartile	1922 (16.6)	52 (6.4)	<0.001
Second quartile	2781 (24.1)	141 (17.3)	
Third quartile	3381 (29.3)	205 (25.1)	
Fourth quartile	3466 (30.0)	418 (51.2)	
Number of mental health diagnoses[a], No. (%)			
0	1041 (9.0)	71 (8.7)	<0.001
1	1844 (16.0)	107 (13.1)	
2	3757 (32.5)	228 (27.9)	
3	3117 (27.0)	247 (30.3)	
4	1791 (15.5)	163 (20.0)	
Number of serious chronic conditions[b], No. (%)			
0-1 Major Chronic Conditions	4603 (39.9)	477 (58.5)	<0.001
2-4 Major Chronic Conditions	5374 (46.5)	292 (35.8)	
5-8 Major Chronic Conditions	1573 (13.6)	47 (5.8)	
Elixhauser score, No. (%)			
<0	2591 (22.4)	323 (39.6)	<0.001
0	4499 (39.0)	292 (35.8)	
1-4	1388 (12.0)	84 (10.3)	
>=5	3072 (26.6)	117 (14.3)	
Fibromyalgia, chronic pain, fatigue, or migraine	9228 (79.9)	567 (69.5)	<0.001
Number of inpatient claims prior to OD, No. (%)			
0	6623 (57.3)	479 (58.7)	0.69
1-4	4346 (37.6)	300 (36.8)	
5+	581 (5.0)	37 (4.5)	
Number of outpatient claims prior to OD, No. (%)			
0	1303 (11.3)	107 (13.1)	<0.001
1-4	4229 (36.6)	366 (44.9)	
5+	6018 (52.1)	343 (42.0)	
Chronic conditions, No. (%)			
ADHD and other conduct disorders	135 (16.5)	1140 (9.9)	<0.001
Alcohol use disorder	345 (42.3)	2993 (26.0)	<0.001
Anxiety	631 (77.3)	8571 (74.5)	0.08
Asthma	183 (22.4)	3075 (26.7)	0.01
Atrial fibrillation	15 (1.8)	387 (3.4)	0.02
Bipolar disorder	437 (53.6)	4908 (42.6)	<0.001

Table A4.2 continued			
Chronic kidney disease	221 (27.1)	4451 (38.7)	<0.001
Chronic obstructive pulmonary disease	214 (26.2)	4612 (40.1)	<0.001
Congestive heart failure	90 (11.0)	2748 (23.9)	<0.001
Major depressive affective disorder	590 (72.3)	8468 (73.6)	0.45
Diabetes	174 (21.3)	4105 (35.7)	<0.001
Drug use disorder	769 (94.2)	9575 (83.2)	<0.001
Epilepsy	125 (15.3)	2134 (18.5)	0.02
Fibromyalgia, chronic pain, or fatigue	552 (67.6)	8974 (78.0)	<0.001
Hearing impairment	16 (2.0)	434 (3.8)	0.01
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	32 (3.9)	346 (3.0)	0.17
Hyperlipidemia	204 (25.0)	4738 (41.2)	<0.001
Hyperplasia	28 (3.4)	463 (4.0)	0.46
Hypertension	395 (48.4)	7415 (64.4)	<0.001
Hypothyroidism	93 (11.4)	2186 (19.0)	<0.001
Ischemic heart disease	166 (20.3)	3771 (32.8)	<0.001
Liver disease	124 (15.2)	1924 (16.7)	0.28
Migraine	149 (18.3)	2364 (20.5)	0.13
Mobility impairment	29 (3.6)	1268 (11.0)	<0.001
Obesity	204 (25.0)	4165 (36.2)	<0.001
Osteoporosis	24 (2.9)	720 (6.3)	<0.001
OUD diagnosis	747 (91.5)	8714 (75.7)	<0.001
Peripheral vascular disease	38 (4.7)	1635 (14.2)	<0.001
Personality disorders	183 (22.4)	1747 (15.2)	<0.001
Post-traumatic stress disorder	230 (28.2)	2076 (18.0)	<0.001
Rheumatoid arthritis/Osteoarthritis	334 (40.9)	6428 (55.9)	<0.001
Schizophrenia and other psychotic disorders	236 (28.9)	3072 (26.7)	0.18
Spinal injury	15 (1.8)	405 (3.5)	0.01
Stroke	23 (2.8)	805 (7.0)	<0.001
Tobacco use disorder	646 (79.2)	7875 (68.4)	<0.001
Traumatic brain injury	15 (1.8)	231 (2.0)	0.84
Ulcers	56 (6.9)	1591 (13.8)	<0.001
Viral hepatitis	261 (32.0)	2185 (19.0)	<0.001

[a] Schizophrenia and other psychotic disorders, major depressive disorder, bipolar disorder, and/or anxiety.
[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.

Appendix 5. Differences in Characteristics and Comorbidities of Nonelderly Duals by MOUD Status at the Time of Nonfatal Opioid Overdose, Stratified by Sex and Level of Health

Table A5.1. Differences in Characteristics and Comorbidities of Female Nonelderly Duals by MOUD Status at the Time of Nonfatal Opioid Overdose, 2014-2016

	Unweighted		**Weighted**	
	Active MOUD (N= 1454)	Inactive MOUD (N= 7050)	Active MOUD (N= 1454)	Inactive MOUD (N= 7050)
Age (years), Mean	43.4	50.2	45.8	45.8
Race/ethnicity, %				
Non-Hispanic White	81	77	80	80
Black or African American	9	13	11	11
Other	9	10	9	9
Census region, %				
West	14	20	16	16
Midwest	22	28	25	25
Northeast	48	21	38	38
South	17	32	21	21
Time under disability insurance (years), Mean	8.3	10.1	8.8	8.8
Elixhauser Score, %				
<0	47	22	39	39
0	28	38	32	32
1-4	10	13	11	11
>=5	15	27	18	18
Any known prior opioid OD, %	15	10	14	14
Known opioid OD in prior 6 months, %	2	1	2	2
Time to OUD diagnosis prior to OD, mean, years[a]	4.1	2.8		
No diagnosis prior to OD, %	4	24		
Buprenorphine distributed, 3-digit zip code level, %				
First Quartile (Lowest)	8	17	10	10
Second Quartile	18	26	21	21
Third Quartile	23	30	25	25
Fourth Quartile (Highest)	51	28	44	44
No inpatient claims 6 months prior to OD, %	52	57	55	55

Table A5.1 continued				
Number of serious chronic conditions[b], %				
0-1	61	38	54	54
2-4	34	48	39	39
5-8	5	14	7	7
Substance use diagnoses, %				
Alcohol use disorder	44	20	37	37
Drug use disorder	97	83	96	96
Tobacco use disorder	83	68	79	79
Number of mental health diagnoses prior to OD, mean[c]	2.6	2.3	2.5	2.5
Mental health diagnoses, %				
ADHD and other conduct disorders	22	9	17	17
Anxiety	86	80	85	85
Bipolar	64	46	58	58
Major depressive disorder	80	79	80	80
Personality disorders	27	17	25	25
Schizophrenia	13	14	14	14
Schizophrenia and other psychotic conditions	28	25	27	27
Post-traumatic stress disorder	41	22	33	33
Pain diagnoses, %				
Fibromyalgia, chronic pain, fatigue, or migraine	70	86	77	77
Chronic conditions, %				
Atrial fibrillation	1	3	2	2
Congestive heart failure	11	25	15	15
Chronic kidney disease	23	39	27	27
Chronic obstructive pulmonary disease	28	44	33	33
Diabetes	20	38	25	25
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	4	2	3	3
Ischemic heart disease	20	33	24	24
Obesity	30	42	33	33
Osteoporosis	5	9	6	6
Rheumatoid arthritis/Osteoarthritis	39	63	47	47
Viral hepatitis	38	16	29	29

Table A5.1 continued
[a] Missing data (those with no diagnosis at time of OD) precludes inclusion in propensity score matching [b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension. [c] Major depressive disorder, bipolar, anxiety, and/or schizophrenia and other psychotic conditions.

Table A5.2. Differences in Characteristics and Comorbidities of Male Nonelderly Duals by MOUD Status at the Time of Nonfatal Opioid Overdose

	Unweighted		**Weighted**	
	Active MOUD (N= 1457)	Inactive MOUD (N= 4459)	Active MOUD (N= 1457)	Inactive MOUD (N= 4459)
Age (years), Mean	43.4	48.6	45.3	45.3
Race/ethnicity, %				
Non-Hispanic White	76	73	74	74
Black or African American	10	14	12	12
Other	14	13	13	13
Census region, %				
West	14	20	17	17
Midwest	17	25	20	20
Northeast	53	29	44	44
South	16	26	19	19
Time under disability insurance (years), Mean	8.9	11.0	9.6	9.6
Elixhauser Score, %				
<0	52	23	42	42
0	27	40	32	32
1-4	9	10	10	10
>=5	12	26	16	16
Any known prior opioid OD, %	18	10	15	15
Known opioid OD in prior 6 months, %	3	1	2	2
Time to OUD diagnosis prior to OD (years), Mean	4.5	3.1		
No diagnosis prior to OD, %	5	26		
Buprenorphine distributed, 3-digit zip code level, %				
First Quartile (Lowest)	8	17	11	11
Second Quartile	16	22	19	19

Table A5.2 continued				
Third Quartile	22	28	24	24
Fourth Quartile (Highest)	55	33	47	47
No inpatient claims 6 months prior to OD, %	52	59	55	55
Number of serious chronic conditions[b], %				
0-1	59	43	53	53
2-4	35	45	39	39
5-8	6	13	8	8
Substance use diagnoses, %				
Alcohol use disorder	53	36	47	47
Drug use disorder	96	83	94	94
Tobacco use disorder	82	70	79	79
Number of mental health diagnoses prior to OD, mean[c]	2.4	2.0	2.2	2.2
Mental health diagnoses, %				
ADHD and other conduct disorders	22	12	18	18
Anxiety	76	65	72	72
Bipolar	57	38	50	50
Major depressive disorder	71	65	68	68
Personality disorders	21	12	18	18
Schizophrenia	23	19	22	22
Schizophrenia and other psychotic conditions	35	29	33	33
Post-traumatic stress disorder	27	12	20	20
Pain diagnoses, %				
Fibromyalgia, chronic pain, fatigue, or migraine	59	71	64	64
Chronic conditions, %				
Atrial fibrillation	2	4	3	3
Congestive heart failure	11	22	14	14
Chronic kidney disease	26	38	30	30
Chronic obstructive pulmonary disease	24	34	27	27
Diabetes	20	33	24	24
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	5	5	5	5
Ischemic heart disease	21	33	25	25
Obesity	21	27	22	22

Table A5.2 continued				
Osteoporosis	1	2	1	1
Rheumatoid arthritis/Osteoarthritis	29	45	35	35
Viral hepatitis	46	25	38	38

[a] Missing data (those with no diagnosis at time of OD) precludes inclusion in propensity score matching
[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.
[c] Major depressive disorder, bipolar, anxiety, and/or schizophrenia and other psychotic conditions.

Table A5.3. Differences in Characteristics and Comorbidities of Nonelderly Duals with Elixhauser scores below 1 by MOUD Status at the Time of Nonfatal Opioid Overdose

	Unweighted		**Weighted**	
	Active MOUD (N=2241)	Inactive MOUD (N=7068)	Active MOUD (N=2241)	Inactive MOUD (N=7068)
Age (years), Mean	42.3	48.4	44.5	44.5
Race/ethnicity, %				
Non-Hispanic White	78.9	74.2	77.0	77.0
Black or African American	9.5	13.9	11.6	11.6
Other	11.6	11.9	11.4	11.4
Male sex, %	51.0	40.2	48.9	48.9
Census region, %				
West	12.7	19.7	15.4	15.4
Midwest	18.5	25.2	21.8	21.8
Northeast	52.3	26.5	42.5	42.5
South	16.6	28.6	20.3	20.3
Time under disability insurance (years), Mean	8.233	10.186	8.832	8.832
Any known prior opioid OD, %	16.2	9.3	13.6	13.6
Known opioid OD in prior 6 months, %	1.9	1.0	1.6	1.6
Time to OUD diagnosis prior to OD (years), Mean[a]	4.2	2.9		
No diagnosis prior to OD, %	4.9	26.8		
Buprenorphine distributed, 3-digit zip code level, %				
First Quartile (Lowest)	7.4	16.0	9.7	9.7
Second Quartile	16.2	24.1	19.8	19.8
Third Quartile	22.1	28.8	24.4	24.4

Table A5.3 continued				
Fourth Quartile (Highest)	54.3	31.1	46.1	46.1
No inpatient claims 6 months prior to OD, %	5.5	67.6	60.4	60.4
Number of serious chronic conditions[b], %				
0-1	66.2	50.7	61.0	61.0
2-4	30.3	42.0	34.4	34.4
5-8	3.6	7.3	4.6	4.6
Substance use diagnoses, %				
Alcohol use disorder	49.1	26.2	42.0	42.0
Drug use disorder	96.5	81.6	94.7	94.7
Tobacco use disorder	82.3	67.2	78.6	78.6
Number of mental health diagnoses prior to OD, mean[c]	2.5	2.1	2.4	2.4
Mental health diagnoses, %				
ADHD and other conduct disorders	22.5	11.2	17.7	17.7
Anxiety	80.7	72.1	77.2	77.2
Bipolar	60.7	43.8	54.5	54.5
Major depressive disorder	74.7	70.5	72.7	72.7
Personality disorders	24.0	15.3	21.6	21.6
Schizophrenia	18.1	16.5	18.7	18.7
Schizophrenia and other psychotic conditions	32.1	26.2	30.5	30.5
Post-traumatic stress disorder	34.6	19.0	27.7	27.7
Pain diagnoses, %				
Fibromyalgia, chronic pain, fatigue, or migraine	61.7	75.6	67.6	67.6
Chronic conditions, %				
Atrial fibrillation	1.1	1.6	1.1	1.1
Congestive heart failure	8.1	15.4	9.9	9.9
Chronic kidney disease	20.5	31.0	24.0	24.0
Chronic obstructive pulmonary disease	20.4	30.8	24.1	24.1
Diabetes	17.4	30.1	21.2	21.2
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	4.0	3.0	4.0	4.0
Ischemic heart disease	17.4	26.3	20.4	20.4
Obesity	22.8	32.7	25.3	25.3

Table A5.3 continued				
Osteoporosis	2.1	4.9	3.0	3.0
Rheumatoid arthritis/Osteoarthritis	30.3	52.0	37.2	37.2
Viral hepatitis	40.2	17.1	31.0	31.0

[a] Missing data (those with no diagnosis at time of OD) precludes inclusion in propensity score matching
[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.
[c] Major depressive disorder, bipolar, anxiety, and/or schizophrenia and other psychotic conditions.

Table A5.4. Differences in Characteristics and Comorbidities of Nonelderly Duals with Elixhauser scores 1 or higher by MOUD Status at the Time of Nonfatal Opioid Overdose

	Unweighted		**Weighted**	
	Active MOUD (N=670)	Inactive MOUD (N=4441)	Active MOUD (N=670)	Inactive MOUD (N=4441)
Age (years), Mean	47.3	51.4	48.4	48.4
Race/ethnicity, %				
Non-Hispanic White	78	78	78	78
Black or African American	11	13	12	12
Other	12	10	10	10
Male sex, %	47	36	45	45
Census region, %				
West	17	21	19	19
Midwest	22	29	24	24
Northeast	45	20	37	37
South	16	31	19	19
Time under disability insurance (years), Mean	9.7	11.0	10.1	10.1
Any known prior opioid OD, Ever, %	18	11	17	17
Known opioid OD in prior 6 months, %	3	1	3	3
Time to OUD diagnosis prior to OD (years), Mean[a]	4.7	2.8		
No diagnosis prior to OD, %	4	20		
Buprenorphine distributed, 3-digit zip code level, %				
First Quartile (Lowest)	9	18	11	11

Table A5.4 continued				
Second Quartile	19	24	21	21
Third Quartile	23	30	25	25
Fourth Quartile (Highest)	50	28	44	44
No inpatient claims 6 months prior to OD, %	40	41	40	40
Number of serious chronic conditions[b], %				
0-1	38	23	33	33
2-4	49	54	52	52
5-8	13	24	15	15
Substance use diagnoses, %				
Alcohol use disorder	46	26	41	41
Drug use disorder	97	86	96	96
Tobacco use disorder	82	70	80	80
Number of mental health diagnoses prior to OD, mean[c]	2.5	2.3	2.4	2.4
Mental health diagnoses, %				
ADHD and other conduct disorders	20	8	16	16
Anxiety	83	78	82	82
Bipolar	59	41	54	54
Major depressive disorder	78	79	78	78
Personality disorders	24	15	23	23
Schizophrenia and other psychotic conditions	29	28	28	28
Schizophrenia	17	15	16	16
Post-traumatic stress disorder	29	28	26	26
Pain diagnoses, %				
Fibromyalgia, chronic pain, fatigue, or migraine	74	87	79	79
Chronic conditions, %				
Atrial fibrillation	4	6	5	5
Congestive heart failure	22	37	25	25
Chronic kidney disease	37	51	41	41
Chronic obstructive pulmonary disease	43	55	46	46
Diabetes	30	45	33	33
Human Immunodeficiency Virus and/or Acquired Immunodeficiency Syndrome (HIV/AIDS)	6	3	5	5

Table A5.4 continued				
Ischemic heart disease	31	43	34	34
Obesity	33	42	35	35
Osteoporosis	5	8	6	6
Rheumatoid arthritis/Osteoarthritis	46	62	51	51
Viral hepatitis	48	22	41	41

[a] Missing data (those with no diagnosis at time of OD) precludes inclusion in propensity score matching

[b] Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.

[c] Major depressive disorder, bipolar, anxiety, and/or schizophrenia and other psychotic conditions.

Appendix 6. Sensitivity Analyses for Crossover Beneficiaries and Propensity Score Methods

Table A6.1. Sensitivity analysis of unadjusted 12-month mortality rates comparing results grouping 100% crossover beneficiaries with active MOUD group, grouping 50% crossover beneficiaries with active MOUD, and excluding crossover beneficiaries.

			Unadjusted % (95% CI)		
	Grouping method	**No. (%) of beneficiaries in group with Active MOUD**	**Inactive MOUD**	**Active MOUD**	**Percentage Point Difference**
Overall	100% crossover beneficiaries with active MOUD	2911 (20.2)	11.3 (10.8, 11.9)	7.1 (6.2, 8.1)	4.2 (3.1, 5.3)
	50% crossover beneficiaries with active MOUD	2503 (17.4)	11.1 (10.5, 11.7)	7.6 (6.5, 8.6)	3.5 (2.4, 4.7)
	Excluding crossover beneficiaries	2095 (15.4)	11.3 (10.8, 11.9)	8.4 (7.1, 9.5)	2.9 (1.7, 4.3)
Women	100% crossover beneficiaries with active MOUD	1454 (17.1)	10.1 (9.4, 10.8)	6.5 (5.3, 7.8)	3.6 (2.1, 5.0)
	50% crossover beneficiaries with active MOUD	1243 (14.6)	9.9 (9.2, 10.6)	6.8 (5.4, 8.2)	3.1 (1.5, 4.6)
	Excluding crossover beneficiaries	1027 (12.7)	10.1 (9.4, 10.8)	7.4 (5.8, 9.0)	2.7 (0.9, 4.4)
Men	100% crossover beneficiaries with active MOUD	1457 (24.6)	13.3 (12.3, 14.3)	7.8 (6.4, 9.1)	5.5 (3.9, 7.0)

Table A6.1 continued					
Men	50% crossover beneficiaries with active MOUD	1260 (21.3)	13.0 (12.0, 13.9)	8.3 (6.7, 9.8)	4.7 (2.9, 6.5)
	Excluding crossover beneficiaries	1068 (19.3)	13.3 (12.3, 14.3)	9.3 (7.5, 11.0)	4.0 (2.0, 6.1)
Low Elixhauser Group	100% crossover beneficiaries with active MOUD	2241 (24.1)	8.8 (8.1, 9.4)	6.2 (5.2, 7.2)	2.6 (1.4, 3.8)
	50% crossover beneficiaries with active MOUD	1926 (20.7)	8.6 (8.0, 9.2)	6.4 (5.3, 7.5)	2.2 (1.0, 3.5)
	Excluding crossover beneficiaries	1626 (18.7)	8.8 (8.1, 9.4)	7.2 (5.9, 8.5)	1.6 (0.2, 3.0)
High Elixhauser Group	100% crossover beneficiaries with active MOUD	670 (13.1)	15.4 (14.3, 16.5)	10.4 (8.3, 12.8)	5.0 (2.4, 7.5)
	50% crossover beneficiaries with active MOUD	577 (11.3)	15.2 (14.1, 16.2)	11.4 (8.8, 14.0)	3.8 (0.9, 6.5)
	Excluding crossover beneficiaries	469 (9.6)	15.4 (14.3, 16.5)	12.4 (9.4, 15.3)	3.0 (0.0, 6.2)

Table A6.2. 12-month mortality following nonfatal opioid overdose by Active MOUD status adjusted for propensity score matching and stratified by level of health and sex.

		% (95% CI)			
		Inactive MOUD	Active MOUD	Pearson's X^2 p	HR (95% CI)*
Overall (N = 14420)	1:1 Nearest neighbor (N = 4767)	10.4	7.1	< 0.001	1.27 (1.07,1.46)*

Table A6.2 continued					
Overall (N = 14420)	Full matching (N = 14420)	10.7	7.1	< 0.001	1.29 (1.14,1.44)*
Women (N =8504)	1:1 Nearest neighbor (N = 2422)	10.1	7.4	0.006	1.12 (0.88,1.36)
	Full matching (N = 8504)	9.4	6.5	< 0.001	1.24 (1.02,1.45)
Men (N = 5916)	1:1 Nearest neighbor (N = 2346)	12.1	7.8	< 0.001	1.46 (1.21,1.7)*
	Full matching (N = 5916)	12.7	7.8	< 0.001	1.44 (1.24,1.64)*
Elixhauser: Low (N = 9309)	1:1 Nearest neighbor (N = 3615)	9.5	6.2	< 0.001	1.58 (1.35,1.82)*
	Full matching (N = 9309)	10.4	6.2	< 0.001	1.74 (1.55,1.92)*
Elixhauser: High (N = 5111)	1:1 Nearest neighbor (N = 1180)	13.3	10.4	0.138	1.12 (0.78,1.45)
	Full matching (N = 5111)	13.3	10.4	0.037	1.13 (0.88,1.37)
* Statistically significant at $p < 0.05$					

Paper 3. Health Care Utilization and 12-Month Mortality Following Nonfatal Opioid Overdose among Nonelderly Duals by Sex and Diagnosis of Schizophrenia

ABSTRACT

Objectives. I aim to 1) determine 12-month mortality among nonelderly duals by sex and diagnosed schizophrenia; 2) identify predictors of mortality by sex and diagnosed schizophrenia; and 3) examine patterns of health care utilization among nonelderly duals.

Methods. I used nationwide Medicare claims data from 2013-2017 to identify nonfatal opioid overdoses, health care utilization, and 12-month mortality. I described inpatient, emergency department, and outpatient care for the 12 months prior to and following nonfatal OD, and associations with 12-month mortality.

Results. Men without schizophrenia had higher mortality rates (12.7%) than other groups in this study, but women had more indicators of serious chronic illnesses. Men also were more likely than women to have medication for opioid use disorder (MOUD) indicated within two years of the OD. Beneficiaries with schizophrenia accessed health care more than those without schizophrenia: Over 70% had inpatient stays prior to the OD. Emergency department visits were high among all groups, and not predictive of 12-month mortality.

Conclusions. Beneficiaries in this study accessed health care services frequently in the year prior to and following nonfatal OD. Health care utilization and mortality rates differ by sex and the presence of schizophrenia.

Policy Implications. As the range of prescribers for MOUD broadens, existing relationships that nonelderly duals have with health care providers should be leveraged to increase access to MOUD.

BACKGROUND

It has been widely established that opioid use disorder (OUD) frequently co-occurs with serious mental illness (bipolar disorder, depression, or schizophrenia).[102] More than 10% of individuals with a mental illness misuse opioids, compared with less than 3% of those without a mental illness.[102] Independently, opioid use disorder and serious mental illness have been established to be strongly associated with premature mortality, and those with both conditions often have the worst health outcomes.[24,103] Dually eligible Medicare and Medicaid beneficiaries under the age of 65 (nonelderly duals) have high rates of diagnosed OUD and serious mental illness, but are unlike other populations with dual diagnoses in many significant respects. For instance, Novak, Feder, Ali, Chen [44] found in a national survey that among individuals with OUD, there was an unmet need for mental health treatment among 30% of those with co-occurring mild serious mental illness and 60% of those with co-occurring moderate serious mental illness. The most prevalent barrier to treatment was affordability. This is not a barrier among nonelderly duals, as Medicaid pays for premiums and copayments. Nonelderly duals also have a different distribution of risk factors than the general population. Significant direct and indirect risk factors for premature mortality are common among nonelderly duals, including those with clear causal relationships (e.g., high rates of heart disease) and social determinants of health (e.g., low education).

In general, Medicare and Medicaid beneficiaries with mental illness have higher rates of fatal opioid overdose than those without mental illness.[24,31] Earlier in this dissertation, I found that 12-month mortality rates following an opioid overdose were dramatically different between men and women, and those with and without a diagnosed serious mental illness. Notably, although a

greater proportion of nonelderly duals who survived a nonfatal opioid overdose were women, men were more likely to die within 12 months.

The Centers for Medicare & Medicaid identifies beneficiaries as having chronic conditions based on the presence of diagnosis codes on inpatient and outpatient claims. Specifically, for depression, bipolar, and schizophrenia, the presence of an *International Statistical Classification of Diseases and Related Health Problems, Ninth Revision, Clinical Modification (ICD-9-CM)*[104] or *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Clinical Modification (ICD-10-CM)*[104] code in any position on either 1 inpatient claim or 2 outpatient claims within the previous 2 years fulfills the requirements for having 1 of the conditions.[105] By definition, therefore, any nonelderly dual with a serious mental illness diagnosis has been treated for the condition. As such, the prevalence of serious mental illness may not be accurately captured by this measure. Depression is underdiagnosed for many reasons, including the fact that clinicians may not regularly screen for depression.[106] Bipolar disorder, on the other hand, may be underdiagnosed when clinicians misdiagnosis the disorder as depression.[107] Treatment for physical comorbidities may also be prioritized over depression or bipolar disorder.[108] On the contrary, schizophrenia presents with overt symptoms such as delusions, hallucinations or disorganized speech. Thus, the prevalence of schizophrenia is more accurately captured than for depression and bipolar when health insurance claims are the basis for estimates.

Riecher-Rössler, Butler, Kulkarni [109] noted, in a review of studies about sex and schizophrenia, that it is generally accepted that the incidence of schizophrenia is higher among men than women. However, there are not differences in the prevalence of schizophrenia by sex, possibly reflecting better treatment adherence among women. Overall, this review concludes,

women have a better course of illness in terms of acute episodes and chronic symptoms and cognitive impairments between episodes.

This study seeks to understand relationship between sex, schizophrenia, and premature mortality following a nonfatal overdose. The disparate rates of 12-month mortality by gender may reflect a difference in treatment for substance use or mental health issues. Specifically, this study addresses health care utilization, which may have a protective effect against mortality that would explain the difference in mortality rates among women and men with schizophrenia. I aim to 1) determine 12-month mortality among nonelderly duals by sex and diagnosed schizophrenia; 2) identify predictors of mortality by sex and diagnosed schizophrenia; and 3) examine patterns of health care utilization among nonelderly duals.

Knowledge of the health care utilization behaviors of nonelderly duals prior to and following a nonfatal opioid overdose has the potential to better understand 1) the extent to which beneficiaries are using emergency and acute care services; 2) whether those with schizophrenia are engaging in behavioral or substance use treatment; and 3) the relationships with health care providers that may be protective against premature mortality. If beneficiaries are not accessing health care providers regularly, or are treated mostly in emergency departments, this knowledge may identify beneficiaries for whom engagement strategies may need to be different. Treating mental illness and OUD improves mortality outcomes both directly and indirectly, and should be an ultimate goal for health care providers. Identifying gender differences in accessing care, schizophrenia, and OUD patterns may influence how best to target populations who would benefit from treatment, but are not engaged with a provider.

METHODS

Use of these data was approved by the Centers for Medicare and Medicaid Services. The University of Chicago Institutional Review Board determined this research was exempt from informed consent. All analyses were conducted using R programming language 4.1.1.

Study Data and Cohort

I used Medicare beneficiary and claims data from 2013-2017 in this study to identify eligible beneficiaries, opioid overdoses, diagnoses, and health care utilization in the 12 months prior to overdose. I determined beneficiary eligibility, demographic characteristics, and comorbidities using the Master Beneficiary Summary File (MBSF), Chronic Conditions File, and Other Chronic Conditions File. Beneficiaries in this study cohort were between the ages of 21-64 and were continuously enrolled as full duals for 12 months prior to a nonfatal opioid overdose and 12 months following the event (or until death). I excluded beneficiaries who had cancer diagnoses, were eligible because of end-stage renal disease, and did not live in the 50 U.S. states or Washington, DC. I identified the index nonfatal opioid overdose using the Medicare Provider Analysis and Review (MedPAR) and Outpatient (OP) Fee-for-Service Files (all years: nationwide, 100%). More details about the qualifying nonfatal opioid overdose event can be found in Paper 1 of this dissertation.

I identified hospitalizations and characteristics of hospitalizations using MedPAR claims. ED visits were identified in the OP and MedPAR files. I used OP and carrier files (20% random sample of beneficiaries) to identify outpatient health care utilization, including substance use treatment and behavioral health treatment. As I did not have 100% of claims for outpatient care, these study data comprised a secondary cohort analysis.

Independent Variables

Sex and diagnosed schizophrenia were the 2 primary stratifications of interest in this study. Sex (male or female) was identified in the MBSF base; schizophrenia was identified in the other chronic conditions file.[105]

Covariates

Race/ethnicity were identified using the CMS research triangle race/ethnicity variable (Non-Hispanic White, Black or African American, Other Race). Age at the time of the OD was included as a continuous variable.

I used the "comorbidity" package in R to create the Elixhauser score for each beneficiary.[92] The Elixhauser score was calculated using MedPAR and Medicare outpatient claims for 180 days prior to the index overdose. I used the Elixhauser index to group beneficiaries by scores in the descriptive analysis (<0, 0, 1-4, 5 or more) and used the score as a continuous measure in the statistical models. Elixhauser scores have been found to have good predictive validity of short-term mortality.[93,94] Higher Elixhauser scores indicate greater comorbidity. I created an index for the number of serious chronic conditions (liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension). Beneficiaries were grouped by the number of conditions (0-1, 2-4, 5-8).

The number of opioid overdoses that occurred in an emergency department following the index OD was included this in analyses as a dichotomous variable ("Any subsequent OD" vs. "No subsequent OD"). The involvement of heroin in the index OD was identified by the presence of *ICD-9* codes 965.01, E85.00, and E935.0, and *ICD-10* code T40.1*.

I categorized the reason for the visit (mental health, substance use, other) based on the primary diagnosis code present on the claim. The codes for mental health and substance use visits are included in Appendix 7.

Outcome Variables

Days hospitalized were identified using MedPAR claims. Claims that extended beyond the 365 days prior to or following the overdose were not excluded. I counted all days a beneficiary was hospitalized within the range. I distinguished between hospital stays in 1) acute care facilities; 2) psychiatric hospitals or the psychiatric wing of an acute care hospital; and 3) and long-term, rehab hospital, and skilled nursing facilities. Visits were further categorized by the primary diagnosis code present on the claims as mental health visit, SUD visit, or other visit. Finally, I determined whether the beneficiary was admitted to the hospital following an emergency department (either at the hospital or at an outpatient facility). I included hospitalization as 'Any Visit' or 'No Visit' prior to or following the overdose in the statistical models. The MedPAR variables used to describe facility characteristics are available in Appendix 8 (Table A8.1).

I used the MedPar and OP files to identify and count days with emergency department visits (OP revenue center codes 0450–0459 or 0981; or a MedPAR claim with an emergency room charge > $0). Claims for OP emergency department visits that either had discharge codes indicating a transfer to a hospital (2, 3, 4, 5, 9, 30, 43, 50, 51, or 70), or that occurred on the same date as admission to a hospital (linked with MedPAR), were not included in the count of days with ED visits. Beneficiaries could only have 1 ED visit per day.

I classified outpatient ED visits by primary diagnosis as MH emergency, SUD emergency, or other emergency visit. I included emergency department visits as a categorical variable in the descriptive analysis (0, 1-3, 4 or more) and a continuous variable in the statistical model.

I used a 20% sample of outpatient facility and provider claims to study outpatient health care utilization. I defined a visit as mental health care and substance use care if it had a primary diagnosis code either condition, or as other if another diagnosis code was present. Visits were

included if they occurred in community mental health clinics, homeless shelters, and rural health clinics, among other locations (Appendix 8, Table A8.2). I counted the number of days with a claim for mental health, substance use, or other care. Beneficiaries could have more than 1 type of outpatient visit on a day, but multiple visits on a single day were counted as 1 visit for that category. Visits that occurred on days when the beneficiary was hospitalized were excluded.

Statistical Analyses

For both the full study cohort and 20% random sample, descriptive statistics were determined for health care utilization following nonfatal opioid overdose by sex and diagnosed schizophrenia. I used Pearson's Chi-squared Test and Student's t-Test to assess associations with utilization by group. Person-years were used in analyses of utilization following OD to account for the reduced time available for visits among those who died. I used the "tableone" package in R to create the descriptive tables.[110]

I counted days hospitalized and days with outpatient ED visits per person year in the primary analysis. I used predicted probabilities to assess the association between hospitalization (any vs. none) and premature mortality by sex and schizophrenia, and ED visits (0; 1-3; 4 or more) and 12-month mortality by sex and schizophrenia. I assigned beneficiaries mean characteristics with health care utilization, and assessed associations by sex and schizophrenia group. In the secondary analysis with 20% outpatient claims, I counted days with outpatient mental health and substance use treatment visits. I also used predicted probabilities to assess the association between the rate of outpatient visits (quartiles: <14 visits; 14-23 visits; 24-37 visits; 38 or more visits) and 12-month mortality by sex and schizophrenia among the 20% sample.

Finally, for the full study cohort only, I used logistic regression to describe associations between beneficiary characteristics and health care utilization and 12-month mortality by group.

RESULTS

More than 20% of the 5,936 male nonelderly duals in this study cohort were diagnosed with schizophrenia, and about 13% of the 8,533 female nonelderly duals in this study cohort were diagnosed with schizophrenia (Table 7). Among women, those with schizophrenia had slightly higher 12-month mortality rates (10.5% vs. 9.7%). Among men, those with schizophrenia had lower mortality rates (10.6% vs. 12.7%). Over 70% of beneficiaries with schizophrenia had comorbid bipolar disorder or depression. They were also common among those without schizophrenia: over 30% of men and 40% of women were diagnosed with bipolar disorder, and over 64% of men and 78% of women were diagnosed with depression. Over a third of beneficiaries in all groups had chronic kidney disease and 15-20% of all beneficiaries had liver disease. A greater proportion of women than men had congestive obstructive pulmonary disorder (COPD) and congestive heart failure (46.0% vs. 34.3% and 25.6% vs. 18.2%, respectively, among those with schizophrenia; similar rates were found among those without schizophrenia). Over 80% of beneficiaries in each group had been diagnosed with OUD prior to the index OD, and on average, diagnoses were around 3 years prior to the OD. Between 14-16% of beneficiaries in all groups had subsequent opioid overdoses in the 12 months following the index OD.

Table 7. Characteristics of Nonelderly Duals by Sex and Schizophrenia Diagnosis

	Female		Male		
	Schizophrenia Diagnosis (N=1137)	**No Schizophrenia Diagnosis (N=7396)**	**Schizophrenia Diagnosis (N=1200)**	**No Schizophrenia Diagnosis (N=4736)**	***P* Value**
12-Month Mortality	119 (10.5)	715 (9.7)	127 (10.6)	600 (12.7)	<0.001
Age, years, Mean (SD)	47.9 (10.2)	49.2 (10.1)	45.2 (11.0)	47.9 (10.8)	<0.001
Race/Ethnicity, No. (%)					<0.001
Non-Hispanic White	826 (72.6)	5806 (78.5)	846 (70.5)	3532 (74.6)	
Black or African American	185 (16.3)	876 (11.8)	181 (15.1)	606 (12.8)	
Other	126 (11.1)	714 (9.7)	173 (14.4)	598 (12.6)	
Elixhauser score, No. (%)					<0.001
<0	367 (32.3)	1871 (25.3)	481 (40.1)	1317 (27.8)	
0	350 (30.8)	2754 (37.2)	374 (31.2)	1822 (38.5)	
1-4	144 (12.7)	935 (12.6)	124 (10.3)	468 (9.9)	
>=5	276 (24.3)	1836 (24.8)	221 (18.4)	1129 (23.8)	
Years on Medicare, No. (%)					<0.001
<= 4	178 (15.7)	1815 (24.5)	224 (18.7)	1201 (25.4)	
5-8	243 (21.4)	1874 (25.3)	278 (23.2)	1180 (24.9)	
9-14	332 (29.2)	2013 (27.2)	288 (24.0)	1079 (22.8)	
>=15	384 (33.8)	1694 (22.9)	410 (34.2)	1276 (26.9)	
Years with diagnosed opioid use disorder prior to index overdose, Mean (SD)	-3.75 (4.25)	-2.92 (3.92)	-4.11 (4.55)	-3.36 (4.29)	<0.001
No diagnosis prior to OD, No. (%)	167 (14.7)	1230 (16.6)	146 (12.2)	827 (17.5)	
Any opioid overdose in 12 months following index overdose, No. (%)	187 (16.4)	1033 (14.0)	192 (16.0)	772 (16.3)	0.002
Mental Disorders, No. (%)					
Bipolar	926 (81.4)	3242 (43.8)	862 (71.8)	1649 (34.8)	<0.001

Table 7 continued					
Major depressive affective disorder	976 (85.8)	5789 (78.3)	909 (75.8)	3028 (63.9)	<0.001
Attention deficit hyperactivity disorder (ADHD) and other conduct disorders	175 (15.4)	767 (10.4)	268 (22.3)	573 (12.1)	<0.001
Anxiety	1012 (89.0)	5935 (80.2)	942 (78.5)	3081 (65.1)	<0.001
Personality disorders	409 (36.0)	1188 (16.1)	359 (29.9)	489 (10.3)	<0.001
Post-traumatic stress disorder	440 (38.7)	1696 (22.9)	252 (21.0)	679 (14.3)	<0.001
Substance Use Disorders, No. (%)					
Alcohol use disorder	379 (33.3)	1677 (22.7)	637 (53.1)	1719 (36.3)	<0.001
Opioid use disorder	930 (81.8)	5877 (79.5)	1002 (83.5)	3713 (78.4)	<0.001
Medication for opioid use disorder	114 (10.0)	882 (11.9)	236 (19.7)	770 (16.3)	<0.001
Tobacco use disorder	906 (79.7)	5079 (68.7)	1023 (85.3)	3292 (69.5)	<0.001
Other Chronic Conditions, No. (%)					
Chronic kidney disease	432 (38.0)	2681 (36.2)	412 (34.3)	1658 (35.0)	0.14
Chronic obstructive pulmonary disease (COPD)	523 (46.0)	3002 (40.6)	411 (34.3)	1444 (30.5)	<0.001
Congestive heart failure	291 (25.6)	1654 (22.4)	218 (18.2)	929 (19.6)	<0.001
Liver disease	188 (16.5)	1180 (16.0)	230 (19.2)	802 (16.9)	0.04
Number of serious chronic conditions*, No. (%)					<0.001
0-1	414 (36.4)	3170 (42.9)	558 (46.5)	2201 (46.5)	
2-4	570 (50.1)	3293 (44.5)	516 (43.0)	2008 (42.4)	
5-8	153 (13.5)	933 (12.6)	126 (10.5)	527 (11.1)	

*Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.

Overall, beneficiaries with schizophrenia had greater health care utilization rates than those without schizophrenia, although women and men in each group had a very high rate of visits (Tables 8 and 9). Compared to those without a schizophrenia diagnosis, a greater proportion of those with schizophrenia had at least 1 hospitalization prior to OD (72.8% vs. 55.3% among women and 70.3% vs. 52.9% among men). A greater proportion of men than women, regardless of schizophrenia diagnosis, had hospitalizations prior to OD with a primary substance use diagnosis indicated (17.8% of men vs. 9.9% of women, among those with schizophrenia; 11.1% of men vs. 6.8% of women, among those without schizophrenia; rates were similar to primary diagnoses for ED claims). Most beneficiaries—over 85%—of beneficiaries who were hospitalized in either period were admitted through the emergency department. All beneficiaries had high rates of emergency department visits prior to and following the overdose: over 75% of all groups had at least 1 visit prior to the overdose. Of those with ED visits, more than half had at least 5 visits in the year prior to the overdose.

Table 8. Hospitalizations and Emergency Department Visits prior to Nonfatal Opioid OD (100% of Study Cohort) by Sex and Schizophrenia Diagnosis

	Female		Male		
	Schizophrenia Diagnosis (N=1137)	**No Schizophrenia Diagnosis (N=7396)**	**Schizophrenia Diagnosis (N=1200)**	**No Schizophrenia Diagnosis (N=4736)**	
ALL BENEFICIARIES					
Outcome 1: Inpatient Admissions					
Any inpatient admission, %	72.8	55.3	70.3	52.9	
Any inpatient mental health admission[a], %	41.1	12.9	46.5	14.1	
Any inpatient substance use disorder admission, %	9.9	7.3	15.3	11.0	
Outcome 2: Emergency Department Visits					
Any ED visit, %	84.3	78.3	81.8	73.8	
Any ED visit for mental health emergency[a], %	27.5	12.2	33.1	12.1	
Any ED visit for substance use disorder emergency, %	9.9	6.8	17.8	11.1	
	Female		**Male**		
Outcome 1: Inpatient Admissions	**Schizophrenia Diagnosis (N = 828)**	**No Schizophrenia Diagnosis (N = 4089)**	**Schizophrenia Diagnosis (N = 843)**	**No Schizophrenia Diagnosis (N = 2503)**	***P* Value**
BENEFICIARIES ADMITTED TO HOSPITAL					
Any visit in facility type, No. (%)					

Table 8 continued					
Inpatient psychiatric facility	396 (47.8)	799 (19.5)	479 (56.8)	592 (23.7)	<0.001
Acute care	713 (86.1)	3780 (92.4)	673 (79.8)	2291 (91.5)	<0.001
Long-term care/rehabilitation/skilled nursing facility	158 (19.1)	695 (17.0)	135 (16.0)	452 (18.1)	0.27
Number of short-stay visits, mean (SD)	3.09 (3.16)	2.47 (2.44)	3.24 (3.44)	2.63 (2.78)	<0.001
Number of days hospitalized in short-stay facility, mean (SD)	16.31 (19.89)	12.09 (15.75)	19.85 (25.24)	13.28 (17.94)	<0.001
Any emergency department admission, No. (%)	763 (92.1)	3580 (87.6)	781 (92.6)	2185 (87.3)	<0.001
Any primary diagnosis for condition, No. (%)					
Mental health[a]	467 (56.4)	957 (23.4)	558 (66.2)	669 (26.7)	<0.001
Substance use	112 (13.5)	541 (13.2)	183 (21.7)	519 (20.7)	<0.001
	Female		**Male**		
Outcome 2: Emergency Department Visits	**Schizophrenia Diagnosis (N = 958)**	**No Schizophrenia Diagnosis (N = 5792)**	**Schizophrenia Diagnosis (N = 981)**	**No Schizophrenia Diagnosis (N = 3493)**	***P* Value**
BENEFICIARIES WITH EMERGENCY DEPARTMENT VISITS					
Number of ED visits, mean (SD)	8.14 (11.32)	5.24 (7.60)	7.73 (13.78)	5.16 (7.57)	<0.001
Any primary diagnosis for condition, No. (%)					
Mental health[a]	313 (32.7)	903 (15.6)	397 (40.5)	574 (16.4)	<0.001
Substance use	112 (11.7)	503 (8.7)	213 (21.7)	524 (15.0)	<0.001

[a] Mental Health treatment refers to visits for any mental health condition (schizophrenia, depression, anxiety, personality disorder, etc.)

Table 9. Hospitalizations and Emergency Department Visits Following Nonfatal Opioid OD (100% of Study Cohort) by Sex and Schizophrenia Diagnosis

	Female		Male		
	Schizophrenia Diagnosis (N=1137)	**No Schizophrenia Diagnosis (N=7396)**	**Schizophrenia Diagnosis (N=1200)**	**No Schizophrenia Diagnosis (N=4736)**	
ALL BENEFICIARIES					
Outcome 1: Inpatient Admissions					
Any inpatient admission (%)	74.1	60.8	71.7	55.5	
Any inpatient mental health admission[a] (%)	44.6	20.9	50.1	20.2	
Any inpatient substance use disorder admission (%)	10.8	9.8	13.9	11.2	
Outcome 2: Emergency Department Visits					
Any ED visit (%)	82.7	74.9	76.8	70.8	
Any ED visit for mental health emergency[a] (%)	25.4	14.2	34.2	16.2	
Any ED visit for substance use disorder emergency (%)	11.6	9.1	16.6	14.9	
Outcome 1: Inpatient Admissions	**Female**		**Male**		
BENEFICIARIES ADMITTED TO HOSPITAL	**Schizophrenia Diagnosis (N = 842)**	**No Schizophrenia Diagnosis (N = 4496)**	**Schizophrenia Diagnosis (N = 860)**	**No Schizophrenia Diagnosis (N = 2629)**	***P* Value**
Any visit in facility type, No. (%)					
Inpatient psychiatric facility	438 (52.0)	1273 (28.3)	511 (59.4)	749 (28.5)	<0.001
Acute care	693 (82.3)	3890 (86.5)	663 (77.1)	2313 (88.0)	<0.001

Table 9 continued					
Long-term care/rehabilitation/skilled nursing facility	178 (21.1)	882 (19.6)	155 (18.0)	520 (19.8)	0.40
Number of short-stay visits, Mean (SD)	3.46 (3.85)	3.02 (7.28)	3.87 (6.54)	3.69 (8.26)	<0.001
Number of days hospitalized in short-stay facility, Mean (SD)	20.07 (27.64)	15.50 (27.74)	23.88 (37.22)	18.75 (33.80)	<0.001
Any emergency department admission, No. (%)	755 (89.7)	3811 (84.8)	772 (89.8)	2283 (86.8)	<0.001
Any primary diagnosis for condition, No. (%)					
Mental health[a]	507 (60.2)	1547 (34.4)	601 (69.9)	955 (36.3)	<0.001
Substance use	123 (14.6)	724 (16.1)	167 (19.4)	529 (20.1)	<0.001
Outcome 2: Emergency Department Visits	**Female**		**Male**		
BENEFICIARIES WITH EMERGENCY DEPARTMENT VISITS	**Schizophrenia Diagnosis (N = 940)**	**No Schizophrenia Diagnosis (N = 5538)**	**Schizophrenia Diagnosis (N = 921)**	**No Schizophrenia Diagnosis (N = 3352)**	***P* Value**
Number of ED visits, Mean (SD)	9.00 (17.48)	5.79 (11.40)	8.52 (14.06)	6.26 (16.94)	<0.001
Any primary diagnosis for condition, No. (%)					
Mental health[a]	289 (30.7)	1047 (18.9)	410 (44.5)	769 (22.9)	<0.001
Substance use	132 (14.0)	675 (12.2)	199 (21.6)	704 (21.0)	<0.001

[a] Mental Health treatment refers to visits for any mental health condition (schizophrenia, depression, anxiety, personality disorder, etc.)

Table 10 shows the results of the predicted probabilities. Regardless of whether beneficiaries were diagnosed with schizophrenia, mortality rates for those with any hospitalization prior to OD were higher than those with no hospitalization (9-10% of women who were hospitalized vs. 6-7% of women who were not hospitalized; 12% of men who were hospitalized vs. 8% who were not hospitalized). These differences were similar by gender in each schizophrenia group. No gradient effect was detected for the number of ED visits prior to OD either by sex or schizophrenia diagnosis.

Table 10. Predicted Probabilities of 12-Month Mortality Following Nonfatal Opioid Overdose by Sex and Schizophrenia Diagnosis

	Female		**Male**	
	Schizophrenia	**No Schizophrenia**	**Schizophrenia**	**No Schizophrenia**
Any hospitalization prior to OD	9%	10%	12%	12%
No hospitalization prior to OD	6%	7%	8%	8%
No ED visits prior to OD	8%	8%	10%	11%
1-3 ED visits prior to OD	8%	8%	10%	10%
4 or more ED visits prior to OD	8%	8%	9%	10%

Table 11 presents the risk factors associated with 12-month mortality by sex and the presence of schizophrenia. Age was associated with 12-month mortality among women and men without schizophrenia only [aOR(95% CI): 1.02(1.01,1.04), $p<0.0001$; aOR(95% CI): 1.02(1.01,1.03), $p< 0.0001$]. Race was not associated with 12-month mortality for any group except men without schizophrenia, among whom Black men had lower odds of 12-month mortality than white men [aOR(95% CI): 1.40(1.06,1.89), $p<0.05$] or those of other races [aOR(95% CI):

1.53(1.06,2.22), $p<0.05$]. Subsequent opioid overdose in the 12 months following the index OD was not associated with 12-month mortality.

Table 11. Characteristics Associated with 12-Month All-Cause Mortality by Sex and Schizophrenia Diagnosis

	Women with Schizophrenia		Women without Schizophrenia		Men with Schizophrenia		Men without Schizophrenia	
	aOR (95% CI)	***P* Value**	**aOR (95% CI)**	***P* Value**	**aOR (95% CI)**	***P* Value**	**aOR (95% CI)**	***P* Value**
Age	1.02 (1.00,1.05)	0.08	1.02 (1.01,1.03)	0.00	1.00 (0.98,1.02)	0.84	1.02 (1.01,1.03)	0.00
Race/Ethnicity [ref: Black or African American]								
Non-Hispanic White	0.77 (0.46,1.33)	0.33	1.11 (0.87,1.44)	0.40	1.78 (1.00,3.40)	0.06	1.40 (1.06,1.89)	0.02
Other	0.79 (0.35,1.67)	0.54	1.04 (0.73,1.49)	0.82	1.72 (0.82,3.68)	0.16	1.53 (1.06,2.22)	0.02
Elixhauser score	0.98 (0.95,1.01)	0.27	1.03 (1.02,1.05)	0.00	1.04 (1.01,1.07)	0.02	1.03 (1.01,1.04)	0.00
Index overdose with heroin indicated	*	*	1.44 (1.12,1.84)	0.00	1.11 (0.71,1.74)	0.64	1.25 (1.00,1.56)	0.05
Any inpatient stays within 12 months prior to OD	1.22 (0.75,2.06)	0.44	1.55 (1.29,1.87)	0.00	1.49 (0.92,2.48)	0.11	1.53 (1.25,1.88)	0.00
Substance use disorders								
Alcohol use disorder	1.07 (0.69,1.65)	0.76	0.91 (0.75,1.12)	0.38	*	*	*	*
Any drug user disorder	1.12 (0.55,2.54)	0.76	1.30 (1.00,1.73)	0.06	0.93 (0.45,2.13)	0.86	1.38 (1.03,1.87)	0.03
Medication for opioid Use disorder	*	*	0.87 (0.65,1.16)	0.35	0.83 (0.48,1.39)	0.49	0.70 (0.52,0.94)	0.02
Tobacco use disorder	2.30 (1.26,4.52)	0.01	1.13 (0.93,1.38)	0.21	*	*	*	*
Other chronic conditions								
Chronic kidney disease	1.43 (0.92,2.23)	0.11	1.69 (1.41,2.02)	0.00	1.86 (1.23,2.83)	0.00	1.24 (1.01,1.51)	0.04

Table 11 continued								
Chronic obstructive pulmonary disease (COPD)	0.88 (0.55,1.40)	0.59	1.29 (1.07,1.56)	0.01	1.19 (0.77,1.84)	0.43	1.40 (1.14,1.72)	0.00
Congestive heart failure	1.52 (0.95,2.43)	0.08	1.57 (1.29,1.91)	0.00	1.18 (0.70,1.94)	0.53	1.51 (1.21,1.89)	0.00
Hyperlipidemia	0.62 (0.40,0.96)	0.03	0.76 (0.64,0.91)	0.00	0.57 (0.37,0.88)	0.01	0.56 (0.45,0.69)	0.00
Liver disease	1.58 (0.94,2.59)	0.08	1.25 (1.02,1.52)	0.03	1.49 (0.93,2.36)	0.09	1.45 (1.16,1.82)	0.00
Peripheral vascular disease	1.47 (0.86,2.47)	0.15	1.13 (0.90,1.41)	0.29	0.83 (0.43,1.51)	0.56	1.35 (1.05,1.72)	0.02
Rheumatoid arthritis/osteoarthritis	1.12 (0.71,1.77)	0.64	0.67 (0.56,0.79)	0.00	*	*	*	*
Viral hepatitis	1.59 (1.00, 2.49)	0.05	1.26 (1.02,1.54)	0.03	0.91 (0.59, 1.39)	0.66	0.83 (0.67,1.03)	0.09
* These covariates were excluded from the analysis for the subgroup due to small cell sizes (i.e., either too many or too few had the condition)								

Some diseases that are worsened with long-term opioid use were statistically significant predictors of mortality only among women and men without schizophrenia, including COPD [OR(95% CI): 1.29(1.07,1.56), p<0.05; OR(95% CI): 1.40(1.14,1.72), p<0.01], congestive heart failure [OR(95% CI): 1.57(1.29,1.91), p<0.001; OR(95% CI): 1.51(1.21,1.89), p<0.001], and liver disease [OR(95% CI): 1.25(1.02,1.52), p<0.05; OR(95% CI: 1.45(1.16,1.82), p<0.01]. Having any inpatient stays prior to the index OD were associate with higher 12-month mortality rates among beneficiaries without schizophrenia only [OR(95% CI): 1.55(1.29,1.87), p<0.0001 among women; OR(95% CI): 1.53(1.25,1.88), p<0.0001 among men]. Higher Elixhauser scores were associated with higher 12-month mortality among all groups except women with schizophrenia.

Secondary Analysis

Descriptive statistics of the 20% random sample (the subset of the study cohort with complete outpatient care data) are available in Appendix 9. Beneficiaries in the sample were similar to the full cohort in all characteristics. Virtually all of the nonelderly duals in the 20% random sample had outpatient health care visits in the 12 months prior to and following the overdose (Tables 12 and 13). Women with schizophrenia had an average of 37.6 (SD: 24.74) visits prior to the OD. Men without schizophrenia had an average of 24.7 (19.9) visits prior to the OD. Visits for substance use disorder were rare: only 9.9% of women with schizophrenia had substance disorder indicated as the primary reason for an outpatient claim prior to OD. Men with schizophrenia had the most visits: 20.9% had substance use disorder indicated as the primary reason for an outpatient claim prior to OD. Among those who had any visits for substance use, women with schizophrenia had an average of 2.90 (3.53) visits, women without schizophrenia had an average of 5.33 (8.25) visits, men with schizophrenia had an average of 5.26 (9.33) visits, and men without schizophrenia had an average of 4.88 (7.13) visits. There was no statistical difference

in the mean number of visits between groups. Figure 1 shows predicated probabilities of 12-month mortality by group and number of outpatient visits in the year prior to OD. For each group, having greater number of outpatient visits is associated with higher mortality rates.

Table 12. Outpatient Utilization prior to Nonfatal Opioid OD (20% of Study Cohort) by Sex and Schizophrenia Diagnosis

	Schizophrenia (N=242)	**No Schizophrenia (N=1475)**	**Schizophrenia (N=245)**	**No Schizophrenia (N=927)**	***P Value***
Outcome 3: Outpatient Visits					
Number of All Outpatient Visits, mean(SD)	37.58 (24.74)	29.53 (20.27)	27.75 (20.60)	24.68 (19.93)	<0.001
Any primary diagnosis for condition, No. (%)					
Mental health*	200 (82.6)	877 (59.7)	190 (77.9)	445 (48.5)	<0.001
Substance use	24 (9.9)	181 (12.3)	51 (20.9)	158 (17.2)	<0.001
Other diagnosis	N/A	1439 (98.0)	215 (88.1)	859 (93.7)	<0.001
Number of outpatient mental health visits among those with a MH visit*, Mean (SD)	10.21 (13.47)	7.27 (8.52)	8.84 (8.57)	6.25 (7.08)	<0.001
Number of outpatient SUD visits among those with a SUD visit, Mean (SD)	2.90 (3.53)	5.33 (8.25)	5.26 (9.33)	4.88 (7.13)	0.538

*Mental Health treatment indicates at least one claim for any mental health condition (schizophrenia, depression, anxiety, personality disorder, etc.)].

Table 13. Outpatient Utilization Following Nonfatal Opioid OD (20% of Study Cohort) by Sex and Schizophrenia Diagnosis

	Female		Male		
	Schizophrenia (N=242)	**No Schizophrenia (N=1,475)**	**Schizophrenia (N=245)**	**No Schizophrenia (N=927)**	***P* Value**
Outcome 3: Outpatient Visits					
Number of All Outpatient Visits, Mean (SD)	42.55 (28.14)	31.24 (22.66)	28.79 (23.57)	26.10 (22.05)	<0.001
Any primary diagnosis for condition No. (%)					
Mental health*	199 (83.6)	919 (63.7)	188 (78.0)	483 (53.9)	<0.001
Substance use	17 (7.1)	133 (9.2)	26 (10.8)	113 (12.6)	0.0
Other diagnosis	226 (95.0)	1398 (96.9)	212 (88.0)	824 (92.0)	<0.001
Number of outpatient mental health visits among those with a MH visit*, Mean (SD)	11.50 (15.34)	8.22 (9.27)	9.39 (9.71)	7.70 (10.45)	<0.001
Number of outpatient SUD visits among those with a SUD visit, Mean (SD)	2.63 (2.37)	4.61 (7.02)	6.24 (7.88)	4.80 (7.01)	0.4

*Mental Health treatment indicates at least one claim for any mental health condition (schizophrenia, depression, anxiety, personality disorder, etc.)].

DISCUSSION

Men without schizophrenia had the highest 12-month mortality rates in this study at 12.7%, 2% more than men and women with schizophrenia (10.6% and 10.5%, respectively), and a full 3%

more than women without schizophrenia (9.7%). The reasons behind this disparity remain unclear, although it could be that beneficiaries with schizophrenia are more likely to receive comprehensive health care in conjunction with mental health treatment. It also could be expected that beneficiaries who are eligible for Medicare based on mental disability are in better physical health those who are eligible based on physical disability, but the findings in this study do not support this as the primary reason for the disparity. Men without schizophrenia were somewhat sicker when judged by Elixhauser score—33.7% of men without schizophrenia had Elixhauser scores of 1 or higher compared with 28.7% of men with schizophrenia. However, when looking at the number of serious chronic conditions—liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension—the prevalence of disease between groups of men did not differ. Moreover, women, regardless of whether diagnosed with schizophrenia, have more indicators of severe physical comorbidities than men without schizophrenia. Severity of physical health conditions may be less important than frequent engagement with health care providers.

Stratified analyses of mortality provide valuable insight into how the combined effects of poor physical health and overdose differ by subpopulations. In the first study of this dissertation, in which I did not stratify by any characteristic, the adjusted logistic regression model showed that having higher Elixhauser scores and the presence of many serious comorbidities (e.g., liver disease, chronic kidney disease, and congestive heart failure) were associated with 12-month mortality. In the stratified adjusted logistic regression models in this paper, I found that physical disease was not associated with mortality among all beneficiaries. Liver disease, chronic kidney disease, and congestive heart failure, among other conditions, were associated with 12-month mortality only among beneficiaries who did not have schizophrenia. Higher Elixhauser scores were

associated with mortality in all groups except women with schizophrenia, but there was not a statistically significant association between many chronic diseases and mortality. In fact, the only statistically significant association found in all groups was a protective association of hyperlipidemia. It is possible that the smaller cohort sizes of the schizophrenia groups precluded detection of statistically significant predictors of mortality, or that these chronic diseases were managed better among those who were also receiving treatment for schizophrenia. Disease, I found, was not a universal predictor of 12-month mortality.

In Paper 1 of this dissertation, I found that nonelderly duals in the study cohort with an overdose following the index event had higher 12-month mortality rates (12.3% among those who had a subsequent OD vs. 10.5% among those without a subsequent OD, $p < 0.05$). Having a subsequent opioid overdose was not statistically associated with mortality in the adjusted model with the whole study cohort. 14-16% of beneficiaries in all groups in this analysis had an overdose in year following index OD, but it was not a predictor in the stratified models in this study. Among beneficiaries without schizophrenia, many chronic conditions were associated with mortality, but it is not clear what is driving the mortality rate of beneficiaries with schizophrenia, whose 12-month mortality rate is twice as what has been found in other populations.[14,16]

It may be that higher rates of outpatient care may indicate ongoing management of chronic conditions, and be protective against subsequent mortality. On the other hand, high rates of acute care utilization (specifically, emergency department visits with and without subsequent hospitalization) may indicate greater severity or poorer management of illnesses. Overall, nonelderly duals utilize health care much more than their nonelderly Medicare- and Medicaid-only counterparts,[3] and this was true for each of the subgroups of this study cohort, as well. Over 70% of beneficiaries with schizophrenia and over 55% of those without schizophrenia had at least 1

inpatient stay in the year prior to OD. The majority of beneficiaries in all groups were seen in outpatient EDs, as well. Virtually every beneficiary in the 20% sample (those beneficiaries for whom I had complete outpatient data) had outpatient care in the 12 months prior to and following the overdose.

I assessed the association between health care utilization and 12-month mortality using predicted probabilities and a logistic regression model. Contrary to other studies,[111] the number of ED visits was not associated with higher 12-month mortality rates for any group. This may indicate that nonelderly duals use EDs for care that requires immediate attention (e.g., pain management) but do not have a high risk of death. I found that the predicted probability of 12-month mortality was higher among beneficiaries with at least 1 inpatient stay in all groups. In the adjusted logistic regression model, the number of days with an ED visit was not statistically significant. Further, having any hospitalization in the 12 months prior to OD was associated with 12-month mortality only among beneficiaries without schizophrenia. This aligned with my expectations: I had expected beneficiaries who were hospitalized and did not have schizophrenia to have higher mortality rates than those with schizophrenia, assuming that being hospitalized for reasons unrelated to mental health would indicate worse physical health. These findings must be interpreted with some caution, as I may have been unable to detect a statistically significant relationship between health care utilization and mortality among the beneficiaries with schizophrenia due to the subgroup population size.

Other populations at high risk of premature mortality following an overdose, such as uninsured individuals, may not have access to health care services beyond the initial ED visit for the OD. I did not find this with this study; the majority of nonelderly duals have health care visits in hospitals, emergency departments, and outpatient settings. As affordability and access to care is

a barrier to receiving mental health and substance use treatment,[102] I found fewer than expected visits with substance use disorders and mental health primary diagnoses. This indicates there may be missed opportunities for care among nonelderly duals who are being treated for other conditions. On the other hand, a willingness to be treated is a common barrier to substance use treatment, and a qualitative assessment of barriers to care for nonelderly duals may reveal an unwillingness to reduce opioid use, especially among beneficiaries who are using opioids to treat chronic pain.[112]

Evidence of substance misuse and treatment among nonelderly duals in this study varied by group. Compared with women, a greater proportion of men had more outpatient and acute care visits for substance use, suggesting they had more symptomatic substance use disorders. Additionally, more men than women received MOUD. It is possible that the differences in mortality rates between men and women without schizophrenia reflect disparities not captured through their health insurance claims, such as adherence to medication[113] and social support. Notably, no group in the study cohort had high receipt of MOUD: only 20% of men with schizophrenia, the group with the greatest proportion of receipt, had MOUD indicated. Disparities in MOUD utilization have been found in other studies. Pro et al. (2020)[43] found that individuals with dual mental health and OUD diagnoses have higher receipt of MOUD, and that men have higher odds of receipt of MOUD than women. In this study, receipt of MOUD only had a statistically significant protective effect among men without schizophrenia.

The receipt and effectiveness of MOUD in this population may be influenced by the physical health of a beneficiary. In Paper 2 of this dissertation, I described the use of MOUD in the study cohort, and found that less than 25% of beneficiaries with MOUD indicated had Elixhauser scores over 1. As such, the finding in this study that more men had MOUD indicated

might partially reflect that men in this study generally had better health than women. However, I also found in Paper 2 that mortality rates among beneficiaries with higher Elixhauser scores were not improved with MOUD. In the current study, I found that men without schizophrenia had higher Elixhauser scores than those with schizophrenia, yet MOUD only had a statistically significant protective association with 12-month mortality among men without schizophrenia. This study had too few beneficiaries to detect differences in these groups, but a multivariate analysis with a larger population might reveal more information about the nuances of MOUD among chronically ill people. Furthermore, more information is needed about the duration of MOUD treatment, as other studies have reported that Medicaid beneficiaries have insufficient duration of MOUD.[83]

Health care utilization following the nonfatal OD did not increase as much as expected. Beneficiaries without schizophrenia had an increase in hospital admissions, and had more visits with primary diagnoses for mental health and substance use disorder following the OD. Following the OD, men were still more likely to have care for these conditions than women. Surprisingly, outpatient utilization did not increase dramatically, despite expectations to see nonelderly duals having an increase in visits for follow-up care to the OD. It could be that health care utilization in all settings was so high prior to the OD that behavior did not have much room to change following the OD.

STRENGTHS AND LIMITATIONS

As far as I know, this study is the first of its kind to use 100% nationwide claims to study health care utilization among nonelderly duals who survived nonfatal opioid overdose. These data allowed a description all inpatient and emergency care received by nonelderly duals prior to and following the overdose. I was able to detect differences in care between groups that might not be apparent in a smaller sample. The finding that men with schizophrenia had MOUD indicated more

than other groups suggests that nonelderly duals have different patterns of treatment than their peers in the general population. However, mortality is a rare outcome, and as such, my ability to explore all the possible comorbidities associated with mortality was limited.

The findings from this study may not be generalizable to other populations. I limited the study cohort to beneficiaries who had fee-for-service coverage to capture detailed information about each visit. Nonelderly duals in this study were all full duals for the entire study period so I could ensure all visits would be included. It is possible that beneficiaries with care provided through health maintenance organizations or who are not full duals have different patterns of care and outcomes.

Finally, I used a 20% sample of claims with outpatient care. The descriptive results of care among these beneficiaries may differ from those of 100% cohort. However, I do not expect outpatient care in this sample to differ meaningfully from the full study cohort because it is the most common form of care.

CONCLUSION

16.2% of nonelderly duals in this study cohort have schizophrenia, a well-known risk factor for substance use and premature mortality. I found that beneficiaries with schizophrenia had greater use of health care services both prior to and following a nonfatal opioid overdose. Overall, men without schizophrenia had the highest 12-month mortality rate, although they had more visits for substance use disorder and fewer overall indicators of poor health than women. Existing relationships with health care providers may provide an opportunity to deliver MOUD, a potentially life-saving treatment, to more populations.

Appendix 7. ICD Codes for Mental Health and Substance Use Disorder Visits

Visits were classified as Mental Health visits if the primary diagnosis code included ICD-9 codes 290-319 and ICD-10 are F01-F99, excluding ICD-9/ICD-10 codes that were used for substance use diagnoses (below).

ICD-9 codes	**ICD-10 codes**
291.0 291.0, 291.1, 291.2, 291.3, 291.4, 291.5, 291.8, 291.81, 291.82, 291.89, 291.9, 303.00, 303.01, 303.02, 303.90, 303.91, 303.92, 305.00, 305.01, 305.02, 357.5, 425.5, 535.30, 535.31, 571.0, 571.1, 571.2, 571.3, 760.71, 980.0, V65.42, V79.1, E860.0	F10.1, F10.2, F10.9, G62.1, I42.6, K29.20, K29.21, K70.0, K70.10, K70.11, K70.2, K70.30, K70.31, K70.40, K70.41, K70.9, P04.3, Q86.0, T51.0X1A, T51.0X2A, T51.0X3A, T51.0X4A, Z13.89, Z71.41, Z71.42, Z71.51, Z71.52, Z71.6
292.0, 292.11, 292.12, 292.2, 292.81, 292.82, 292.83, 292.84, 292.85, 292.89, 292.9, 304.00, 304.01, 304.02, 304.10, 304.11, 304.12, 304.2, 304.20, 304.21, 304.22, 304.3, 304.30, 304.31, 304.32, 304.4, 304.40, 304.41, 304.42, 304.5, 304.50, 304.51, 304.52, 304.6, 304.60, 304.61, 304.62, 304.7, 304.70, 304.71, 304.72, 304.8, 304.80, 304.81, 304.82, 304.9, 304.90, 304.91, 304.92, 305.2, 305.20, 305.21, 305.22, 305.3, 305.30, 305.31, 305.32, 305.4, 305.40, 305.41, 305.42, 305.5, 305.50, 305.51, 305.52, 305.6, 305.60, 305.61, 305.62, 305.7, 305.70, 305.71, 305.72, 305.8, 305.80, 305.81, 305.82, 305.9, 305.90, 305.91, 305.92, 648.3, 648.30, 648.31, 648.32, 648.33, 648.34, 655.5, 655.50, 655.51, 655.53, 760.72, 760.73, 760.75, 779.5, 965.0, 965.00, 965.01, 965.02, 965.09, V65.42, E850.0	F11.1, F11.2, F11.9, F12.1, F12.2, F12.9, F13.1, F13.2, F13.9, F14.1, F14.2, F14.9, F15.1, F15.2, F15.9, F16.1, F16.2, F16.9, F17.203, F17.208, F17.209, F17.213, F17.218, F17.219, F17.223, F17.228, F17.229, F17.293, F17.298, F17.299, F18.1, F18.2, F18.9, F19.1, F19.2, F19.9, F55.0, F55.1, F55.2, F55.3, F55.4, F55.8, O35.5XX0, O35.5XX1, O35.5XX2, O35.5XX3, O35.5XX4, O35.5XX5, O35.5XX9, T40.691A, T40.692A, T40.693A, T40.694A, O99.320, O99.321, O99.322, O99.323, O99.324, O99.325, P04.41, P04.49, P96.1, P96.2, T40.0X1A, T40.0X2A, T40.0X3A, T40.0X4A, T40.0X5A, T40.0X5S, T40.1X1A, T40.1X2A, T40.1X3A, T40.1X4A, T40.2X1A, T40.2X2A, T40.2X3A, T40.2X4A, T40.3X1A, T40.3X2A, T40.3X3A, T40.3X4A, T40.3X5A, T40.3X5S, T40.4X1A, T40.4X2A, T40.4X3A, T40.4X4A, T40.7X1A, T40.8X1A, T40.601A, T40.602A, T40.603A, T40.604A, T40.691A, T40.692A, T40.693A, T40.694A, T40.901A, T40.991A, Z71.41, Z71.42, Z71.51, Z71.52, Z71.6

Appendix 8. Inpatient and Outpatient Facility Types

Table A8.1 Inpatient Facility Type

MedPAR Provider Number	Description
Provider Number Special Unit Code in "M" or "S"; or last 4 digits of MedPAR provider number >= 4000 and <= 4499	Inpatient psychiatric facility
Last 4 digits of MedPAR provider <= 1399	Acute care facility
Last 4 digits of MedPAR provider >= 2000 & not between 4000 and 4499	Long-term hospitals; Rehabilitation hospitals; Skilled nursing facilities

Table A8.2 Outpatient Facility Type

Place of Service Code(s)	Place of Service Name	Place of Service Description
04	Homeless Shelter	A facility or location whose primary purpose is to provide temporary housing to homeless individuals (e.g., emergency shelters, individual or family shelters). (Effective January 1, 2003)
11	Office	Location, other than a hospital, skilled nursing facility (SNF), military treatment facility, community health center, State or local public health clinic, or intermediate care facility (ICF), where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.
15	Mobile Unit	A facility/unit that moves from place-to-place equipped to provide preventive, screening, diagnostic, and/or treatment services. (Effective January 1, 2003)
17	Walk-in Retail Health Clinic	A walk-in health clinic, other than an office, urgent care facility, pharmacy or independent clinic and not described by any other Place of Service code, that is located within a retail operation and provides, on an ambulatory basis, preventive and primary care services. (This code is available for use immediately with a final effective date of May 1, 2010)

Table A8.2 continued		
19	Off Campus-Outpatient Hospital	A portion of an off-campus hospital provider based department which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization. (Effective January 1, 2016)
22	On Campus-Outpatient Hospital	A portion of a hospital's main campus which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization. (Description change effective January 1, 2016)
49	Independent Clinic	A location, not part of a hospital and not described by any other Place of Service code, that is organized and operated to provide preventive, diagnostic, therapeutic, rehabilitative, or palliative services to outpatients only. (Effective October 1, 2003)
50	Federally Qualified Health Center	A facility located in a medically underserved area that provides Medicare beneficiaries preventive primary medical care under the general direction of a physician.
52	Psychiatric Facility-Partial Hospitalization	A facility for the diagnosis and treatment of mental illness that provides a planned therapeutic program for patients who do not require full time hospitalization, but who need broader programs than are possible from outpatient visits to a hospital-based or hospital-affiliated facility.
53	Community Mental Health Center	A facility that provides the following services: outpatient services, including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the CMHC's mental health services area who have been discharged from inpatient treatment at a mental health facility; 24 hour a day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to State mental health facilities to determine the appropriateness of such admission; and consultation and education services.

Table A8.2 continued		
57	Non-residential Substance Abuse Treatment Facility	A location which provides treatment for substance (alcohol and drug) abuse on an ambulatory basis. Services include individual and group therapy and counseling, family counseling, laboratory tests, drugs and supplies, and psychological testing. (Effective October 1, 2003)
71	Public Health Clinic	A facility maintained by either State or local health departments that provides ambulatory primary medical care under the general direction of a physician.
72	Rural Health Clinic	A certified facility which is located in a rural medically underserved area that provides ambulatory primary medical care under the general direction of a physician.

Appendix 9. Characteristics of 20% Sample of Nonelderly Duals Who Survived Nonfatal Opioid Overdose by Sex and Schizophrenia Diagnosis

Table A9.1. Characteristics of 20% Sample of Nonelderly Duals Who Survived Nonfatal Opioid Overdose by Sex and Schizophrenia Diagnosis, 2014-2016

	Female		Male	
	Schizophrenia Diagnosis (N=243)	**No Schizophrenia Diagnosis (N=1477)**	**Schizophrenia Diagnosis (N=245)**	**No Schizophrenia Diagnosis (N=934)**
12-Month Mortality	8.2	10.4	11.4	12.7
Age, years, mean(SD)	47.6 (10.4)	49.3 (9.93)	44.9 (11.2)	48.3 (10.8)
Race/Ethnicity, n (%)				
Non-Hispanic White	170 (70.0)	1162 (78.7)	162 (66.1)	699 (74.8)
Black or African American	48 (19.8)	184 (12.5)	44 (18.0)	119 (12.7)
Other	25 (10.3)	131 (8.9)	39 (15.9)	116 (12.4)
Elixhauser score, n (%)				
<0	74 (30.5)	404 (27.4)	98 (40.0)	261 (27.9)
0	78 (32.1)	538 (36.4)	75 (30.6)	336 (36.0)
1-4	32 (13.2)	182 (12.3)	23 (9.4)	90 (9.6)
>=5	59 (24.3)	353 (23.9)	49 (20.0)	247 (26.4)
Years with diagnosed opioid use disorder prior to index overdose, mean(SD)	-3.73 (4.41)	-2.89 (3.89)	-3.87 (4.51)	-3.49 (4.33)
No diagnosis prior to OD	30 (12.3)	252 (17.1)	30 (12.2)	173 (18.5)
Any opioid overdose in 12 months following index overdose, n (%)	41 (16.9)	217 (14.7)	39 (15.9)	159 (17.0)
Mental disorders, n (%)				
Bipolar	196 (80.7)	648 (43.9)	171 (69.8)	346 (37.0)
Major depressive affective disorder	212 (87.2)	1158 (78.4)	184 (75.1)	600 (64.2)

Table A9.1 continued				
Attention deficit hyperactivity disorder (ADHD) and other conduct disorders	40 (16.5)	169 (11.4)	54 (22.0)	126 (13.5)
Anxiety	216 (88.9)	1167 (79.0)	196 (80.0)	612 (65.5)
Personality disorders	84 (34.6)	251 (17.0)	68 (27.8)	116 (12.4)
Post-traumatic stress disorder	88 (36.2)	354 (24.0)	53 (21.6)	138 (14.8)
Substance use disorders, n (%)				
Alcohol use disorder	75 (30.9)	370 (25.1)	132 (53.9)	323 (34.6)
Opioid use disorder	204 (84.0)	1169 (79.1)	202 (82.4)	724 (77.5)
Medication for opioid use disorder	25 (10.3)	167 (11.3)	43 (17.6)	144 (15.4)
Tobacco use disorder	187 (77.0)	996 (67.4)	209 (85.3)	649 (69.5)
Other chronic conditions, n (%)				
Chronic kidney disease	94 (38.7)	547 (37.0)	79 (32.2)	332 (35.5)
Chronic obstructive pulmonary disease (COPD)	107 (44.0)	581 (39.3)	88 (35.9)	300 (32.1)
Congestive heart failure	64 (26.3)	320 (21.7)	44 (18.0)	185 (19.8)
Liver disease	39 (16.0)	225 (15.2)	40 (16.3)	157 (16.8)
Number of serious chronic conditions*, n (%)				
0-1	90 (37.0)	633 (42.9)	121 (49.4)	418 (44.8)
2-4	118 (48.6)	681 (46.1)	99 (40.4)	412 (44.1)
5-8	35 (14.4)	163 (11.0)	25 (10.2)	104 (11.1)

*Liver disease, chronic kidney disease, congestive heart failure, congestive obstructive pulmonary disease, atrial fibrillation, ischemic heart disease, stroke, and/or hypertension.

Dissertation Conclusion

A national state of emergency was announced in October 2017 in response to a dramatic increase in opioid overdose deaths. Despite the best efforts of public health professionals, social workers, and physicians, the opioid epidemic continues to wreak havoc in America. Tens of thousands of people die every year of opioid overdoses, and even more die of opioid-related causes. The effect of the epidemic among Medicare and Medicaid beneficiaries, 2 large populations with significant risk factors for overdose and mortality, have been well documented.[25,31,36,90] To my knowledge, this dissertation is the first study to investigate the impact of the opioid epidemic among nonelderly, dually eligible Medicare and Medicaid beneficiaries, a group with unique physical and social risk factors for subsequent opioid overdose and death.

In this dissertation, I explored the impact of the opioid epidemic among nonelderly duals by asking three overarching research questions: 1) What is the epidemiology of nonfatal opioid overdose and 12-month mortality? 2) What is the association between medication for opioid use disorder and 12-month mortality? 3) What are the health care utilization behaviors prior to and following a nonfatal opioid overdose? As I hypothesized that the answers to these questions might vary between subpopulations of nonelderly duals, I investigated differences between groups in addition to studying the overall population.

I found that nearly 11% of nonelderly duals in this study cohort died within 12 months of a nonfatal opioid overdose. This is about twice as high as has been found in other populations,[14,114] and more than 5 times higher than the 12-month mortality rate observed among members of the comparison population who did not overdose. Although members of this study cohort had high rates of dangerous comorbidities—for example, more than 20% of beneficiaries who overdosed had congestive heart failure—there was a synergistic effect between having a comorbidity and

surviving an opioid overdose that amplified mortality rates in this population. The average time to death following the index event was 5 months, and virtually all beneficiaries saw health care providers in this period. However, only 14% of nonelderly duals had MOUD indicated, although all beneficiaries had coverage of buprenorphine and naltrexone through Medicare, and many had methadone covered through Medicaid. Additionally, outpatient visits to treat substance use disorder were rare. I found that more men than women received MOUD and had health care visits for SUD. On the whole, women had more indicators of poor health than men. Men, nevertheless, had higher 12-month mortality rates than women, and MOUD had a statistically significant association with lower mortality only among men. In addition to broader Medicare and Medicaid policies that would improve access to MOUD, therefore, nonelderly duals would also benefit from targeted interventions from physicians and social workers that address the issues affecting different subpopulations. These significance of the findings of these studies can best be understood in the context of the Medicare & Medicaid opioid treatment benefits in the plans during the study years and at present.

MEDICARE & MEDICAID OPIOID TREATMENT POLICY

One of the most significant findings from these studies was the low proportion of beneficiaries with insurance claims for outpatient care for substance use disorder and MOUD. Despite having buprenorphine included in the Medicare formulary during the study years, and methadone available in outpatient settings through many state's standard Medicaid programs, very few beneficiaries were treated with MOUD. In the years of this study, nonelderly duals who lived in the states without methadone covered in their state Medicaid programs did not have access to methadone through either payer. The same disparity in coverage occurred in outpatient SUD treatment services, such as counseling: nonelderly duals only had their services covered if they

lived in states with the service included in the Medicaid plan. As cost is a significant barrier to receiving care,[44] and nonelderly duals are a low-income population, it is likely out-of-pocket payments were not affordable for many beneficiaries with OUD.

Even nonelderly duals who lived in states with greater treatment coverage depended on their providers having and using the waiver to prescribe buprenorphine, or having access to a methadone clinic or other treatment center. Studies with data contemporaneous to this dissertation suggest that these barriers may have contributed to the low uptake of treatment. In the study years, family medicine and internal medicine practitioners comprised two-thirds of outpatient buprenorphine prescribers for Medicare beneficiaries, yet they constituted the lowest proportion of active buprenorphine prescribers.[50]

Geographic barriers may also have affected MOUD uptake and influenced mortality. In this dissertation, I studied 12-month all-cause mortality instead of fatal opioid overdose. My limited access to data with cause of death precluded a determination of statistically significant differences between characteristics of fatal opioid overdoses and deaths from other causes. However, opioid overdose deaths are often misclassified,[20] and long-term opioid misuse indirectly causes many deaths from other causes. As such, I felt overall mortality was an appropriate outcome for this population. About 40% of U.S. counties did not have an outpatient SUD facility that accepted Medicaid and could deliver MOUD.[52] Of the 10 states with the highest proportion of counties without an outpatient SUD facility that accepted Medicaid,[52] 3 states (North Dakota, South Dakota, and Nevada) did not have enough beneficiaries in the study cohort to report 12-month mortality rates due to CMS privacy guidelines. States with the highest proportion of counties without access to an SUD facility that accepted Medicaid (in rank order) were: Arkansas (12-month all-cause mortality rate of 23.5%), Texas (12-month all-cause mortality rate of 11.9%),

Louisiana (12-month all-cause mortality rate of 6.6%), Idaho (12-month all-cause mortality rate of 11.7%), and Nebraska (12-month all-cause mortality rate of 13.4%). With the exception of Louisiana, each of these states had higher 12-month mortality rates than that of the total study cohort. Such concerning and suggestive finding, though not definitive, merit closer investigation. I cannot discern from the data how much of the all-cause mortality rate is attributable to lack of MOUD. I suspect the availability of facilities that offer MOUD is related to all-cause mortality, but it is also reflective of access to general level of health and access to all health care providers.

In 2020, Medicare, the primary payer of care for duals, adopted the Substance Use-Disorder Prevention That Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act. This Act requires Medicare plans to cover OUD treatment, including methadone and behavioral health services at opioid treatment programs (OTPs). OTPs are key to addressing the opioid epidemic, as they are required to provide adequate medical, counseling, vocational, educational, and other assessment and treatment services. Office-based care is an important aspect of Medicare plans, as OTPs are not available in every state, as described in the above section. Medicare has tried to ease the burden on buprenorphine prescribers to address the imbalance of patients and providers. In 2021, the 8-hour training requirement was lifted for physicians providing MOUD to fewer than 30 patients. Behavioral therapy is not required for office-based care, and the U.S. Office of the Inspector General (OIG) found that less than half of beneficiaries (47%) who receive office-based MOUD also received recommended behavioral therapy.[115] These findings align with this study, in which very few beneficiaries had mental health or SUD outpatient care, although almost everyone saw outpatient providers prior to and following the overdose.

The OIG reported concerns about other gaps in OUD treatment in Medicare plans after the SUPPORT Act was implemented. The OIG reported that in 2020, only 16% of beneficiaries with OUD received MOUD, and rates varied greatly substantially across the country.[115] Fifty-six percent of Medicare beneficiaries with OUD in Vermont received MOUD in 2020, whereas Florida, Texas, Kansas, and Nevada had the lowest rates of MOUD receipt in the country at less than 8% (OIG, 2021). The sex disparity I found in this study cohort was reflected in the general Medicare population in the OIG report: 13% of female and 19% of male beneficiaries received MOUD in 2020. Finally, the OIG report noted racial disparities in the receipt of MOUD, an analysis that data limitations precluded me from including. Compared with the general Medicare population, nonelderly duals are a more racially diverse population and that a greater proportion are female. As such, I suspect that the disparities I found in the study persisted after the study years, and that the racial disparities found by the OIG report are worse among nonelderly duals.

There are other concerns that Medicare has not addressed in the SUPPORT Act. In 2021, Deborah Steinberg and Ellen Weber of the Legal Action Center compared Medicare's coverage of SUD benefits to the SUD continuum of care standards that have been developed by the American Society of Addiction Medicine (ASAM).[85] These authors note several significant gaps in Medicare coverage that potentially affect the ability of nonelderly duals to access opioid use treatment. For instance, although Medicare covers office-based care and OTPs, freestanding SUD treatment facilities are not covered, nor are many licensed counselors and certified addiction counselors.

As of January 1, 2023, Medicare has covered telehealth treatment services delivered by OTPs, regardless of the location of the beneficiary (previously, only rural beneficairies were eligible for this benefit). This expansion of telehealth coverage does not extend to office-based opioid treatment. However, it is likely that many nonelderly duals will benefit from this expansion,

as barriers such as geographic proximity, transportation, and perceived stigma are reduced. Preliminary evaluations of these expanded policies show promising results: Medicare beneficiaries with access to telehealth for substance use disorder treatment and MOUD during the COVID-19 pandemic had significantly lower odds of fatal drug overdose, compared with those not receiving MOUD.[116] At the same time, beneficiaries without reliable access to the internet, or who do not have the required video function, may need extra attention to ensure equitable access to care.

Not all nonelderly duals are reliant on standard Medicare coverage for their opioid use disorder treatment. Medicaid managed care plans are subject to the 2008 Mental Health Parity and Addiction Equity Act (Parity Act), which requires health plans that offer SUD and mental health benefits to provide coverage that is on par with the medical and surgical benefits they offer. In 2020, seventy-eight percent of full duals of all ages were enrolled in some time of Medicaid managed care plans during the year.[10] Nonelderly duals who live in a state with a section 1115 demonstrations that focuses on substance use disorder may also have better access to treatment. For many ongoing evaluation metrics, states with 1115 SUD demonstrations are required to specifically calculate and report metrics for duals. Analyses such as those completed in this dissertation can provide a benchmark for access to care from the mid-2010s to today.

Even with the improvements to opioid use disorder treatment, there are disparities in access to care. Nonelderly duals who are not on managed care plans do not have the same guarantee of parity between SUD benefits and medical and surgical benefits. Those who live in states without 1115 waivers may have piecemeal access to benefits along the continuum of care, such as expanding access to residential treatment services. Beneficiaries without access to the internet may not be able to access telehealth services. There is a concerted effort within CMS to improve access to health care among duals by increasing enrollment in integrated care plans, which would help

duals who experience fragmented care, but as of 2020, only 10% of duals were enrolled in one of these plans.[117] Work still remains to address remaining gaps in care among nonelderly duals with OUD.

SOCIAL WORK IMPLICATIONS

Social workers are key stakeholders role in the fight against the opioid epidemic in the U.S. In their work with their clients in hospitals, mental health clinics, community outreach centers, and other settings, social workers have myriad roles: counselors, advocates, outreach workers, case managers, and others.

Social workers are trained to identify and contextual the micro, mezzo, and macro practice and policy issues related to substance use. I studied micro-level predictors of 12-month mortality, and described the mezzo- and macro-level factors that may have influenced utilization and mortality outcomes. This knowledge can help social workers better understand the risk factors for mortality among their nonelderly dual clients who have OUD, and strategize about how best to help them.

Some of the findings about micro-level predictors for 12-month mortality aligned with expectations: heroin involvement in the index opioid overdose, a history of opioid overdose, and having a higher Elixhauser score of disease severity. It countered expectations to discover that having alcohol use disorder, viral hepatitis, and HIV/AIDS were not associated with higher odds of mortality. These results also highlighted the synergistic effect of having certain chronic conditions in addition to surviving an opioid overdose. For social workers, these findings can help them identify which of their clients might need more help in seeking care, particularly since among nonelderly duals, OUD is often a secondary diagnosis, a distinction that is associated with lower chances of being treated with MOUD.[86] A physician may choose to prioritize treatment for another

condition because it is clinically dominant, such as heart failure, or is highly symptomatic, such as fibromyalgia.

On a mezzo-level, which considers the environment, clients may be hindered from accessing treatment if they live in a geographic location that does not have any or many substance use treatment facilities.[52] They may need help finding facilities, or arranging transportation to treatment. There may also be mezzo-level factors that make it more difficult for women than men to seek care. Social workers may be able to address some of these barriers, such as whether women need to arrange childcare. Social workers may need to employ different strategies to engage and maintain their female clients in treatment.

There are also macro-level considerations, such as Medicare and Medicaid policies on who can prescribe MOUD, and in what location they can deliver treatment. I found that beneficiaries who overdosed, on average, were diagnosed with OUD 3 years prior to their index overdose. There may have been policy-related reasons that nonelderly duals were unable to treat their OUD before it progressed to the point of overdose. Nonelderly duals also had high rates of visits to emergency departments prior to and following their overdose. Social workers are well-situated to help nonelderly duals set up and maintain vital health care. In general, clients may benefit by having someone advocate for treating their OUD in health care and treatment settings.

Knowledge of each of factors can help social workers identify the available treatments that may be available to their clients. They are uniquely placed to consider individuals in the context of their lives, and actual barriers. Physicians and other stakeholders who cannot view the individual in a holistic way may not understand why an individual cannot access or maintain care. Furthermore, they may not realize, as a social worker might, that even if an individual is not ready to stop misusing opioids, there are intermediate steps that can be undertaken to support the person.

Social workers can understand each of the micro-, mezzo-, and macro-level factors of addiction can influence treatment initiation, retention, adherence, and success. They are well-equipped to employ a person-in-environment perspective that can improve the wellbeing of their clients and the families.

FINAL NOTES

The studies presented in this dissertation are not without limitations. I studied nonelderly full duals with fee-for-service plans so I could examine health care utilization in granular detail. These studies may not be generalizable to the overall dual population. It is likely that older duals, partial duals, and duals with managed care plans differ than the duals in this study. Partial duals have similar risk factors to full duals—the income and asset requirements are still very low. I do not know how duals with managed care plans differ; it is possible they are healthier or seek health care more. The risk of opioid overdose and mortality among older duals is a study that merits independent research. Although the majority of overdoses occur in younger populations, opioid misuse is a growing problem among older Americans.

I was also limited in my data access. I had death certificate data for 2015 and 2016 only, and as such, could not study cause of death for all beneficiaries in my study who died within 12 months. I compared those with death certificate data and those without data, and determined they were statistically similar. However, the lack of complete data reduced my data to the point where I could not obtain statistically significant predictors of subsequent fatal overdose or all-cause deaths. Additionally, I had 20% of outpatient provider ("carrier") claims. This limited the depth to which I could describe outpatient utilization in my third paper, as beneficiaries in my study sought outpatient care in both facilities related to hospitals (the outpatient claims to which I had access) and the provider claims. I used the 20% sample to study outpatient care in the third paper, and

beneficiaries in the remaining 80% would have had to be drastically different to change my findings.

Finally, administrative changes occurred in Medicare and Medicaid in the years of these studies that affected my study. CMS adopted ICD-10 codes on October 1, 2015, and ICD-10 codes do not map directly onto ICD-9 codes. Because of this, I had to calculate two sets of Elixhauser scores to approximate the health of beneficiaries, and I cannot be certain that the scores from ICD-9 are equivalent to ICD-10. Additionally, Medicaid changed its claims from MAX to T-MSIS format in 2015. T-MSIS data from these years varies greatly in completeness and quality.

This dissertation explores the scope of the opioid epidemic among a vulnerable, often-overlooked population. The 4 million nonelderly duals in the U.S. need to be considered as a distinct population in research. They are at risk of opioid overdose and premature mortality, yet, as I found, they also have many interactions with the health care system. Medicare and Medicaid policies have improved since the years of this study, and we need to know: are nonelderly duals receiving the care they need to treat their OUD now? I found that on the whole, nonelderly duals who were treated with MOUD were less likely to die within 12-months, despite high rates of dangerous comorbidities. Policymakers need to ensure that Medicare and Medicaid policies will not hinder access to care, eligible physicians need to obtain waivers—and follow through with prescriptions and treatment, and social workers need to work with their clients to ensure they are able to access and maintain treatment. Only by addressing all of these issues will the health outcomes of nonelderly duals with OUD improve.

References

1. Sakhuja A, Sztajnkrycer M, Vallabhajosyula S, Cheungpasitporn W, Patch R, Jentzer J. National trends and outcomes of cardiac arrest in opioid overdose. *Resuscitation.* 2017;121:84-89.
2. de Miguel Díez J, Chancafe Morgan J, Jiménez García R. The association between COPD and heart failure risk: a review. *Int J Chron Obstruct Pulmon Dis.* 2013;8:305-312.
3. Commission MPA, Commission MaCPaA. Data Book: Beneficiaries dually eligible for Medicare and Medicaid. In. Vol CY 2013. Washington, DC: MedPAC and MACPAC; 2018.
4. Moynihan D, Herd P, Harvey H. Administrative Burden: Learning, Psychological, and Compliance Costs in Citizen-State Interactions. *Journal of Public Administration Research and Theory.* 2015;25(1):43-69.
5. Bureau USC. American fact finder. 2010; https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=CF. Accessed January 29, 2020.
6. Howden LM, Meyer JA. Age and Sex Composition: 2010. In: Commerce USDo, ed2011.
7. Ryan CL, Bauman K. Educational Attainment in the United States: 2015. In: Commerce USDo, ed: U.S. Census Bureau; 2016.
8. Gowrisankaran G, Joiner KA, Lin J. *How do Hospitals Respond to Payment Incentives?* 2019.
9. Hennessy S, Leonard CE, Freeman CP, et al. Validation of diagnostic codes for outpatient-originating sudden cardiac death and ventricular arrhythmia in Medicaid and Medicare claims data. *Pharmacoepidemiology and Drug Safety.* 2010;19(6):555-562.
10. Commission MPA, Commission MaCPaA. Data Book: Beneficiaries Dually Eligible for Medicare and Medicaid. In. Vol February 2023. Washington, DC: MedPAC and MACPAC; 2023.
11. Jacobson G, Cicchiello A, Sutton JP, Shah A. Medicare Advantage vs. Traditional Medicare: How Do Beneficiaries' Characteristics and Experiences Differ? 2021; OCTOBER 14:https://www.commonwealthfund.org/publications/issue-briefs/2021/oct/medicare-advantage-vs-traditional-medicare-beneficiaries-differ. Accessed March 15, 2023.
12. Abuse NIoD. Drug Overdose Death Rates. 2023; https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates. Accessed March 14, 2023.
13. Prevention CfDCa. 2019 Annual surveillance report of drug-related risks and outcomes--United States Surveillance Special Report. 2019; https://www.cdc.gov/drugoverdose/pdf/pubs/2019-cdc-drug-surveillance-report.pdf. Accessed May 3, 2020.
14. Leece P, Chen C, Manson H, et al. One-Year Mortality After Emergency Department Visit for Nonfatal Opioid Poisoning: A Population-Based Analysis. *Annals of emergency medicine.* 2020;75(1):20-28.
15. Boscarino JA, Kirchner HL, Pitcavage JM, et al. Factors associated with opioid overdose: a 10-year retrospective study of patients in a large integrated health care system. *Subst Abuse Rehabil.* 2016;7:131-141.

16. Weiner SG, Baker O, Bernson D, Schuur JD. One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose. *Annals of emergency medicine.* 2020;75(1):13-17.
17. Thylstrup B, Seid AK, Tjagvad C, Hesse M. Incidence and predictors of drug overdoses among a cohort of >10,000 patients treated for substance use disorder. *Drug and Alcohol Dependence.* 2020;206:107714.
18. Caudarella A, Dong H, Milloy MJ, Kerr T, Wood E, Hayashi K. Non-fatal overdose as a risk factor for subsequent fatal overdose among people who inject drugs. *Drug and Alcohol Dependence.* 2016;162:51-55.
19. Goldman-Mellor S, Olfson M, Lidon-Moyano C, Schoenbaum M. Mortality Following Nonfatal Opioid and Sedative/Hypnotic Drug Overdose. *American Journal of Preventive Medicine.* 2020;59(1):59-67.
20. Ruhm CJ. Corrected US opioid-involved drug poisoning deaths and mortality rates, 1999–2015. *Addiction.* 2018;113(7):1339-1344.
21. Brady JE, Giglio R, Keyes KM, DiMaggio C, Li G. Risk markers for fatal and non-fatal prescription drug overdose: a meta-analysis. *Injury Epidemiology.* 2017;4(1):24.
22. Suffoletto B, Zeigler A. Risk and protective factors for repeated overdose after opioid overdose survival. *Drug and Alcohol Dependence.* 2020;209:107890.
23. Rhee TG, Peltier MR, Sofuoglu M, Rosenheck RA. Do Sex Differences Among Adults With Opioid Use Disorder Reflect Sex-specific Vulnerabilities? A Study of Behavioral Health Comorbidities, Pain, and Quality of Life. *Journal of Addiction Medicine.* 2020;14(6).
24. Olfson M, Wall M, Wang S, Crystal S, Blanco C. Risks of fatal opioid overdose during the first year following nonfatal overdose. *Drug and Alcohol Dependence.* 2018;190:112-119.
25. Peters JL, Durand WM, Monteiro KA, Dumenco L, George P. Opioid Overdose Hospitalizations among Medicare-Disability Beneficiaries. *The Journal of the American Board of Family Medicine.* 2018;31(6):881.
26. Griesler PC, Hu M-C, Wall MM, Kandel DB. Medical Use and Misuse of Prescription Opioids in the US Adult Population: 2016–2017. *American Journal of Public Health.* 2019;109(9):1258-1265.
27. Roland CL, Ye X, Stevens V, Oderda GM. The Prevalence and Cost of Medicare Beneficiaries Diagnosed and At Risk for Opioid Abuse, Dependence, and Poisoning. *Journal of Managed Care & Specialty Pharmacy.* 2018;25(1):18-27.
28. Nechuta SJ, Tyndall BD, Mukhopadhyay S, McPheeters ML. Sociodemographic factors, prescription history and opioid overdose deaths: a statewide analysis using linked PDMP and mortality data. *Drug and Alcohol Dependence.* 2018;190:62-71.
29. Haider MR, Brown MJ, Gupta RD, Karim S, Olatosi B, Li X. Psycho-Social Correlates of Opioid Use Disorder among the US Adult Population: Evidence from the National Survey on Drug Use and Health, 2015-2018. *Subst Use Misuse.* 2020;55(12):2002-2010.
30. Morden NE, Munson JC, Colla CH, et al. Prescription Opioid Use Among Disabled Medicare Beneficiaries: Intensity, Trends, and Regional Variation. *Medical Care.* 2014;52(9).
31. Kuo Y-F, Raji MA, Goodwin JS. Association of Disability With Mortality From Opioid Overdose Among US Medicare Adults. *JAMA Network Open.* 2019;2(11):e1915638-e1915638.

32. Cochran G, Gordon AJ, Lo-Ciganic W-H, et al. An Examination of Claims-based Predictors of Overdose from a Large Medicaid Program. *Medical care.* 2017;55(3):291-298.
33. Fernandes JC, Campana D, Harwell TS, Helgerson SD. High mortality rate of unintentional poisoning due to prescription opioids in adults enrolled in Medicaid compared to those not enrolled in Medicaid in Montana. *Drug and Alcohol Dependence.* 2015;153:346-349.
34. Grigoras CA, Karanika S, Velmahos E, et al. Correlation of Opioid Mortality with Prescriptions and Social Determinants: A Cross-sectional Study of Medicare Enrollees. *Drugs.* 2018;78(1):111-121.
35. Swartz JA, Beltran SJ. Prescription opioid availability and opioid overdose-related mortality rates in Medicaid expansion and non-expansion states. *Addiction.* 2019;114(11):2016-2025.
36. Garg RK, Fulton-Kehoe D, Franklin GM. Patterns of Opioid Use and Risk of Opioid Overdose Death Among Medicaid Patients. *Medical Care.* 2017;55(7).
37. Larochelle MR, Bernson D, Land T, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality. *Annals of Internal Medicine.* 2018;169(3):137-145.
38. Ma J, Bao Y-P, Wang R-J, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. *Molecular Psychiatry.* 2019;24(12):1868-1883.
39. Karmali RN, Ray GT, Rubinstein AL, Sterling SA, Weisner CM, Campbell CI. The role of substance use disorders in experiencing a repeat opioid overdose, and substance use treatment patterns among patients with a non-fatal opioid overdose. *Drug and Alcohol Dependence.* 2020;209:107923.
40. Rhee TG, Rosenheck RA. Buprenorphine prescribing for opioid use disorder in medical practices: can office-based out-patient care address the opiate crisis in the United States? *Addiction.* 2019;114(11):1992-1999.
41. Williams AR, Samples H, Crystal S, Olfson M. Acute Care, Prescription Opioid Use, and Overdose Following Discontinuation of Long-Term Buprenorphine Treatment for Opioid Use Disorder. *American Journal of Psychiatry.* 2019;177(2):117-124.
42. Goldman JE, Samuels EA, Rich JD, Marshall BDL. Correlates of death during outpatient treatment for opioid use disorder: A national study. *Journal of Substance Abuse Treatment.* 2020;112:76-85.
43. Pro G, Utter J, Haberstroh S, Baldwin JA. Dual mental health diagnoses predict the receipt of medication-assisted opioid treatment: Associations moderated by state Medicaid expansion status, race/ethnicity and gender, and year. *Drug and Alcohol Dependence.* 2020;209:107952.
44. Novak P, Feder KA, Ali MM, Chen J. Behavioral health treatment utilization among individuals with co-occurring opioid use disorder and mental illness: Evidence from a national survey. *Journal of Substance Abuse Treatment.* 2019;98:47-52.
45. Agterberg S, Schubert N, Overington L, Corace K. Treatment barriers among individuals with co-occurring substance use and mental health problems: Examining gender differences. *Journal of Substance Abuse Treatment.* 2020;112:29-35.

46. Marsh JC, Amaro H, Kong Y, Khachikian T, Guerrero E. Gender disparities in access and retention in outpatient methadone treatment for opioid use disorder in low-income urban communities. *Journal of Substance Abuse Treatment.* 2021;127:108399.
47. Choi S, Adams SM, Morse SA, MacMaster S. Gender Differences in Treatment Retention Among Individuals with Co-Occurring Substance Abuse and Mental Health Disorders. *Substance Use & Misuse.* 2015;50(5):653-663.
48. Administration USFD. Information about Medication-Assisted Treatment (MAT). 2023; https://www.fda.gov/drugs/information-drug-class/information-about-medication-assisted-treatment-mat. Accessed May 11, 2023.
49. Andrews CM, Grogan CM, Smith BT, et al. Medicaid Benefits For Addiction Treatment Expanded After Implementation Of The Affordable Care Act. *Health Affairs.* 2018;37(8):1216-1222.
50. Abraham R, Wilkinson E, Jabbarpour Y, Petterson S, Bazemore A. Characteristics of Office-Based Buprenorphine Prescribers for Medicare Patients. *The Journal of the American Board of Family Medicine.* 2020;33(1):9.
51. Mojtabai R, Mauro C, Wall MM, Barry CL, Olfson M. Medication Treatment For Opioid Use Disorders In Substance Use Treatment Facilities. *Health Affairs.* 2019;38(1):14-23.
52. Cummings JR, Wen H, Ko M, Druss BG. Race/Ethnicity and Geographic Access to Medicaid Substance Use Disorder Treatment Facilities in the United States. *JAMA Psychiatry.* 2014;71(2):190-196.
53. Moreno JL, Wakeman SE, Duprey MS, Roberts RJ, Jacobson JS, Devlin JW. Predictors for 30-Day and 90-Day Hospital Readmission Among Patients With Opioid Use Disorder. *Journal of Addiction Medicine.* 2019;13(4).
54. Basu J. Multilevel Risk Factors for Hospital Readmission Among Patients With Opioid Use Disorder in Selected US States: Role of Socioeconomic Characteristics of Patients and Their Community. *Health Services Research and Managerial Epidemiology.* 2020;7:2333392820904240.
55. Summers PJ, Hellman JL, MacLean MR, Rees VW, Wilkes MS. Negative experiences of pain and withdrawal create barriers to abscess care for people who inject heroin. A mixed methods analysis. *Drug and Alcohol Dependence.* 2018;190:200-208.
56. Surbhi S, Graetz I, Wan JY, Gatwood J, Bailey JE. The Effect of Opioid Use and Mental Illness on Chronic Disease Medication Adherence in Superutilizers. *Journal of Managed Care & Specialty Pharmacy.* 2018;24(3):198-207.
57. Ukhanova MA, Tillotson CJ, Marino M, et al. Uptake of Preventive Services Among Patients With and Without Multimorbidity. *American Journal of Preventive Medicine.* 2020;59(5):621-629.
58. Stumbo SP, Yarborough BJH, Yarborough MT, Green CA. Perspectives on Providing And Receiving Preventive Health Care From Primary Care Providers and Their Patients With Mental Illnesses. *American Journal of Health Promotion.* 2018;32(8):1730-1739.
59. Yarborough BJH, Perrin NA, Stumbo SP, Muench J, Green CA. Preventive Service Use Among People With and Without Serious Mental Illnesses. *American Journal of Preventive Medicine.* 2018;54(1):1-9.
60. Burns ME, Huskamp HA, Smith JC, Madden JM, Soumerai SB. The Effects of the Transition From Medicaid to Medicare on Health Care Use for Adults With Mental Illness. *Medical Care.* 2016;54(9).

61. Thorpe K, Jain S, Joski P. Prevalence And Spending Associated With Patients Who Have A Behavioral Health Disorder And Other Conditions. *Health Affairs.* 2017;36(1):124-132.
62. Frank RG, Epstein AM. Factors Associated With High Levels Of Spending For Younger Dually Eligible Beneficiaries With Mental Disorders. *Health Affairs.* 2014;33(6):1006-1013.
63. Hing E, Decker SL, Jamoom E. Acceptance of New Patients with Public and Private Insurance by Office-based Physicians: United States, 2013. In: Services USDoHaH, ed. Hyattsville, MD: Centers for Disease Control and Prevention; 2015.
64. Raiha NK, Daley JG. Chapter 7: Medical Social Work in the U.S. Armed Forces. In: Taylor & Francis Ltd; 1999:107-121.
65. Education CoSW. *Practitioner education in substance use and misuse: Competency-based resources.* Alexandria, VA2021.
66. Link BG, Phelan J. Social Conditions As Fundamental Causes of Disease. *Journal of Health and Social Behavior.* 1995:80-94.
67. Decker SL. No Association Found Between The Medicaid Primary Care Fee Bump And Physician-Reported Participation In Medicaid. *Health Affairs.* 2018;37(7):1092-1098.
68. Ahmad TR, Chen L-m, Chapman JS, Chen L-l. Medicaid and Medicare payer status are associated with worse surgical outcomes in gynecologic oncology. *Gynecologic Oncology.* 2019;155(1):93-97.
69. Gage-Bouchard EA. Culture, Styles of Institutional Interactions, and Inequalities in Healthcare Experiences. *Journal of Health and Social Behavior.* 2017;58(2):147-165.
70. Chang J, Dubbin L, Shim J. Negotiating substance use stigma: the role of cultural health capital in provider-patient interactions. *Sociology of Health & Illness.* 2016;38(1):90-108.
71. Marsh JC, Angell B, Andrews CM, Curry A. Client-Provider Relationship and Treatment Outcome: A Systematic Review of Substance Abuse, Child Welfare, and Mental Health Services Research. *Journal of the Society for Social Work and Research.* 2012;3(4):233.
72. Elder GH. *Children of the Great Depression: Social changes in life experience.* 25th Anniversay Edition ed. Boulder, CO: Westview Press; 1999.
73. Szanton SL, Thorpe RJ, Whitfield K. Life-course financial strain and health in African–Americans. *Social Science & Medicine.* 2010;71(2):259-265.
74. Jones GT, Power C, Macfarlane GJ. Adverse events in childhood and chronic widespread pain in adult life: Results from the 1958 British Birth Cohort Study. *Pain.* 2009;143(1):92-96.
75. Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. *General Hospital Psychiatry.* 2007;29(5):409-416.
76. Olfson M, Crystal S, Wall M, Wang S, Liu S-M, Blanco C. Causes of Death After Nonfatal Opioid Overdose. *JAMA Psychiatry.* 2018;75(8):820-827.
77. Garg RK, Fulton-Kehoe D, Franklin GM. Patterns of opioid use and risk of opioid overdose death among Medicaid patients. *Medical Care.* 2017;55(7):661-668.
78. Division DC. *ARCOS Retail Drug Summary Reports.* 2014-2016.
79. Service ER, Agriculture UDo. Rural-Urban Continuum Codes. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/. Accessed January 3, 2022.

80. Furr-Holden D, Milam AJ, Wang L, Sadler R. African Americans now outpace whites in opioid-involved overdose deaths: a comparison of temporal trends from 1999 to 2018. *Addiction.* 2021;116(3):677-683.
81. Austin SR, Wong Yn Fau - Uzzo RG, Uzzo Rg Fau - Beck JR, Beck Jr Fau - Egleston BL, Egleston BL. Why Summary Comorbidity Measures Such As the Charlson Comorbidity Index and Elixhauser Score Work. (1537-1948 (Electronic)).
82. Andrews CM, Abraham AJ, Grogan CM, Westlake MA, Pollack HA, Friedmann PD. Impact of Medicaid Restrictions on Availability of Buprenorphine in Addiction Treatment Programs. *American Journal of Public Health.* 2019;109(3):434-436.
83. Samples H, Williams AR, Olfson M, Crystal S. Risk factors for discontinuation of buprenorphine treatment for opioid use disorders in a multi-state sample of Medicaid enrollees. *Journal of Substance Abuse Treatment.* 2018;95:9-17.
84. Landis RK, Levin JS, Saloner B, et al. Sociodemographic differences in quality of treatment to Medicaid enrollees receiving buprenorphine. *Substance Abuse.* 2022;43(1):1057-1071.
85. Steinberg DG, Weber EM. *Medicare Coverage of Substance Use Disorder Care: A Landscape Review of Benefit Coverage, Service Gaps and a Path to Reform.* Legal Action Center;2021.
86. Johnson K, Hills H, Ma J, Brown CH, McGovern M. Treatment for opioid use disorder in the Florida medicaid population: Using a cascade of care model to evaluate quality. *The American Journal of Drug and Alcohol Abuse.* 2021;47(2):220-228.
87. Organization WH. *Annex 5, Drug interactions involving methadone and buprenorphine.* Geneva2009.
88. Stahler GJ, Mennis J, Baron DA. Racial/ethnic disparities in the use of medications for opioid use disorder (MOUD) and their effects on residential drug treatment outcomes in the US. *Drug and Alcohol Dependence.* 2021;226:108849.
89. Saini J, Johnson B, Qato DM. Self-Reported Treatment Need and Barriers to Care for Adults With Opioid Use Disorder: The US National Survey on Drug Use and Health, 2015 to 2019. *American Journal of Public Health.* 2022;112(2):284-295.
90. Olfson M, Crystal S, Wall M, Wang S, Liu SM, Blanco C. Causes of Death After Nonfatal Opioid Overdose. *JAMA Psychiatry.* 2018;75(8):820-827.
91. Agency DE, Justice UDo. *ARCOS Retail Drug Summary Reports.* 2014-2016.
92. Gasparini. Comorbidity: An R package for computing comorbidity scores. *Journal of Open Source Software.* 2018;3(23):648.
93. Austin SR, Wong Y-N, Uzzo RG, Beck JR, Egleston BL. Why Summary Comorbidity Measures Such As the Charlson Comorbidity Index and Elixhauser Score Work. *Medical Care.* 2015;53(9).
94. Thompson NR, Fan Y, Dalton JE, et al. A New Elixhauser-based Comorbidity Summary Measure to Predict In-Hospital Mortality. *Medical Care.* 2015;53(4).
95. Mlcoch T, Hrnciarova T, Tuzil J, Zadak J, Marian M, Dolezal T. Propensity Score Weighting Using Overlap Weights: A New Method Applied to Regorafenib Clinical Data and a Cost-Effectiveness Analysis. *Value in Health.* 2019;22(12):1370-1377.
96. Mathur MB, Ding P, Riddell CA, VanderWeele TJ. Web Site and R Package for Computing E-values. *Epidemiology.* 2018;29(5).
97. Zhou T, Tong G, Li F, Thomas LE, Li F. PSweight: An R Package for Propensity Score Weighting Analysis. *The R Journal.* 2022;14(1):282-300.

98. Ho D, Imai K, King G, Stuart EA. MatchIt: Nonparametric Preprocessing for Parametric Causal Inference. *Journal of Statistical Software.* 2011;42(8):1 - 28.
99. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behavioral Research.* 2011;46(3):399-424.
100. Marsh J, Park K, Lin Y-A, Bersamira C. Gender differences in trends for heroin use and nonmedical prescription opioid use, 2007–2014. *Journal of Substance Abuse Treatment.* 2018;87:79-85.
101. Dunkler D, Heinze G, Ploner M. Package 'coxphw'. 2022; https://cran.r-project.org/web/packages/coxphw/coxphw.pdf. Accessed July 6, 2023.
102. Administration SAaMHS. Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). In. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2020.
103. Olfson M, Gerhard T, Huang C, Crystal S, Stroup TS. Premature Mortality Among Adults With Schizophrenia in the United States. *JAMA Psychiatry.* 2015;72(12):1172-1181.
104. Organization WH. International Statistical Classification of Diseases and Related Health Problems (ICD). 2022; https://www.who.int/standards/classifications/classification-of-diseases.
105. Warehouse CCD. Other Chronic Health, Mental Health, and Potentially Disabling Conditions. 2015; https://www2.ccwdata.org/web/guest/condition-categories-other.
106. Smith R, Meeks S. Screening Older Adults for Depression: Barriers Across Clinical Discipline Training. *Innovation in Aging.* 2019;3(2):igz011.
107. Smith DJ, Griffiths E, Kelly M, Hood K, Craddock N, Simpson SA. Unrecognised bipolar disorder in primary care patients with depression. *The British Journal of Psychiatry.* 2011;199(1):49-56.
108. Downey LVA, Zun LS, Burke T. Undiagnosed Mental Illness in the Emergency Department. *The Journal of Emergency Medicine.* 2012;43(5):876-882.
109. Riecher-Rössler A, Butler S, Kulkarni J. Sex and gender differences in schizophrenic psychoses—a critical review. *Archives of Women's Mental Health.* 2018;21(6):627-648.
110. Yoshida K. tableone: Create 'Table 1' to Describe Baseline Characteristics with or without Propensity Score Weights. 2022; https://cran.r-project.org/package=tableone.
111. Moe J, Kirkland S, Ospina MB, et al. Mortality, admission rates and outpatient use among frequent users of emergency departments: a systematic review. *Emergency Medicine Journal.* 2016;33(3):230.
112. Stumbo SP, Yarborough BJH, McCarty D, Weisner C, Green CA. Patient-reported pathways to opioid use disorders and pain-related barriers to treatment engagement. *Journal of Substance Abuse Treatment.* 2017;73:47-54.
113. Ochoa S, Usall J, Cobo J, Labad X, Kulkarni J. Gender Differences in Schizophrenia and First-Episode Psychosis: A Comprehensive Literature Review. *Schizophrenia Research and Treatment.* 2012;2012:916198.
114. Weiner SG, Baker O, Bernson D, Schuur JD. One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose. *Annals of emergency medicine.* 2020;75(1):13-17.

115. General OotI. Many Medicare Beneficiaries Are Not Receiving Medication to Treat Their Opioid Use Disorder. In: Services UDoHaH, ed. Washington, DC2021.
116. Jones CM, Shoff C, Blanco C, Losby JL, Ling SM, Compton WM. Association of Receipt of Opioid Use Disorder–Related Telehealth Services and Medications for Opioid Use Disorder With Fatal Drug Overdoses Among Medicare Beneficiaries Before and During the COVID-19 Pandemic. *JAMA Psychiatry.* 2023;80(5):508-514.
117. Commission MaCPaA. *Chapter 2: Integrating Care for Dually Eligible Beneficiaries: Policy Issues and Options.* Washington, DC2020.