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RESEARCH ARTICLE

Buprenorphine After Nonfatal Opioid Overdose: Reduced Mortality Risk in Medicare Disability Beneficiaries

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Introduction: Opioid-involved overdose mortality is a persistent public health challenge, yet limited evidence exists on the relationship between opioid use disorder treatment after a nonfatal overdose and subsequent overdose death.

Methods: National Medicare data were used to identify adult (aged 18−64 years) disability beneficiaries who received inpatient or emergency treatment for nonfatal opioid-involved overdose in 2008−2016. *Opioid use disorder treatment* was defined as (1) buprenorphine, measured using medication days' supply, and (2) psychosocial services, measured as 30-day exposures from and including each service date. Opioid-involved overdose fatalities were identified in the year after nonfatal overdose using linked National Death Index data. Cox proportional hazards models estimated the associations between time-varying treatment exposures and overdose death. Analyses were conducted in 2022.

Results: The sample (N=81,616) was mostly female (57.3%), aged ≥50 years (58.8%), and White (80.9%), with a significantly elevated overdose mortality rate, compared with the general U.S. population (standardized mortality ratio=132.4, 95% CI=129.9, 135.0). Only 6.5% of the sample (*n*=5,329) had opioid use disorder treatment after the index overdose. Buprenorphine (*n*=3,774, 4.6%) was associated with a significantly lower risk of opioid-involved overdose death (adjusted hazard ratio=0.38, 95% CI=0.23, 0.64), but opioid use disorder−related psychosocial treatment (*n*=2,405, 2.9%) was not associated with risk of death (adjusted hazard ratio=1.18, 95% CI=0.71, 1.95).

Conclusions: Buprenorphine treatment after nonfatal opioid-involved overdose was associated with a 62% reduction in the risk of opioid-involved overdose death. However, fewer than 1 in 20 individuals received buprenorphine in the subsequent year, highlighting a need to strengthen care connections after critical opioid-related events, particularly for vulnerable groups.

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INTRODUCTION

Drug overdose mortality remains an urgent health concern in the U.S., surpassing 105,000 deaths in 2021, largely attributed to opioids.[1] Opioid-involved overdose deaths are preventable with medication for opioid use disorder (MOUD), which has a well-established association with reduced mortality risk during treatment.[2,3] Nonfatal opioid-involved overdoses represent critical opportunities to initiate potentially life-saving interventions because these events are strong risk factors for subsequent overdose and death.[4−10]

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Current evidence on opioid use disorder (OUD) treatment after opioid-involved overdose consistently shows low MOUD uptake.[11−21] The literature on nonmedication services is more limited, indicating a very low uptake of residential treatment for OUD.[21] However, general services are more common, such as healthcare encounters with OUD[11] or substance use disorder diagnoses[17] and mental health counseling visits.[15] Evidence connecting OUD-specific treatment with the risk of subsequent mortality is lacking.

Single-state research to date has found a reduced risk of opioid-involved overdose mortality for buprenorphine medication[20,21] but not for residential OUD treatment.[21] Both studies measured medication dispensing at monthly intervals that do not account for briefer gaps in supply when mortality risk is elevated.[2,3] In addition, wide variation in state epidemiologic and health system contexts underscores a need for national data to inform tertiary prevention and treatment efforts, particularly for high-risk groups.

Individuals with disabilities have a nearly threefold higher risk of opioid-involved overdose death than those without functional limitations.[22] As the primary source of insurance coverage for adults receiving federal disability benefits owing to long-term (>1 year) or terminal conditions causing inability to work,[23] Medicare disability beneficiaries (MDBs) constitute a key U.S. healthcare population in the management of chronic illness. MDBs have elevated rates of chronic pain,[24,25] long-term and high-dosage prescription opioid use,[25,26] and OUD.[27] Although only 14% of enrollees are MDBs,[28] they comprise a growing share of opioid-involved overdose hospitalizations[29,30] and account for over 80% of opioid-involved overdose deaths in the Medicare population.[31]

This study examined the associations of buprenorphine and OUD-related psychosocial services with the risk of opioid-involved overdose death in the year after nonfatal opioid-involved overdose, focusing on the MDB population to generate national-level U.S. data in a priority group for interventions to address the ongoing opioid overdose crisis.

METHODS

This longitudinal, retrospective cohort study used a 20% random sample of national Medicare Part D (prescription drug) beneficiaries.[32] Data comprised all prescription drugs; outpatient, inpatient, and emergency department (ED) services; and demographic, enrollment, and eligibility information. Medicare data were linked to National Death Index data with dates and causes of death. This study was approved by the Rutgers IRB. Reporting follows the STROBE guidelines.

Study Sample

The cohort included adults aged 18−64 years with Medicare eligibility on the basis of disability with a nonfatal opioid-involved overdose treated in inpatient or in ED settings during 2008−2016. Enrollees with any other basis of eligibility (i.e., seniors aged ≥65 years) were excluded. The sample was restricted to individuals with continuous fee-for-service and Part D enrollment throughout the 180-day baseline period preceding the index opioid-involved overdose and 365-day follow-up period (in the absence of death or censoring) to ensure full availability of treatment data. Index events resulting in death were excluded (Appendix Figure 1, available online).

Measures

Nonfatal opioid-involved overdoses were identified using diagnosis codes from the International Classification of Diseases, Ninth and Tenth (ICD-10) Revisions, Clinical Modification (Appendix Table 1, available online).[33,34] The first qualifying event per person was analyzed, including consecutive days with opioid-involved poisoning diagnoses in the index event. The follow-up period began on the first date with no opioid-involved poisoning code. Additional index characteristics included the involvement of heroin or synthetic opioids other than methadone (e.g., fentanyl), involvement of benzodiazepines, and indicators of medical severity (i.e., hospitalization, mechanical ventilation),[4,35] measured using diagnosis, revenue, and procedure codes (Appendix Table 2, available online).

To estimate the associations between follow-up OUD treatment and subsequent opioid-involved overdose mortality, time-varying measures were created for buprenorphine medication and psychosocial services across the study period. Buprenorphine was identified using National Drug Codes on prescription claims, excluding drugs approved only for pain management (Appendix Table 3, available online), with daily medication availability based on days' supply. Psychosocial services were identified using procedure codes[36,37] selected from the Healthcare Effectiveness Data and Information Set measure for substance use treatment initiation and engagement (Appendix Table 3, available online)[38] and restricted to services with OUD diagnoses to capture treatment specifically for opioid addiction. The time-varying indicator for each psychosocial service remained positive for up to 30 days to account for the intermittent nature of this treatment modality. The primary outcome was opioid-involved overdose death, identified using ICD-10 cause of death codes in linked National Death Index data following Centers for Disease

Table 1. Baseline Sample Characteristics, Stratified by Opioid Overdose Death in the Year After Nonfatal Overdose

Baseline sample characteristics	Total (N=81,616)	No overdose death (*n*=80,104)	Overdose death (*n*=1,512)	*p*-value[a]
Sociodemographic characteristics, *n* (%)				
Sex				
Male	34,868 (42.7)	34,074 (42.5)	794 (52.5)	**<0.001**
Female	46,748 (57.3)	46,030 (57.5)	718 (47.5)	
Age				
18–29	3,154 (3.9)	3,087 (3.9)	67 (4.4)	**<0.001**
30–39	10,180 (12.5)	9,944 (12.4)	236 (15.6)	
40–49	20,254 (24.8)	19,767 (24.7)	487 (32.2)	
50–59	34,049 (41.7)	33,474 (41.8)	575 (38.0)	
60–64	13,979 (17.1)	13,832 (17.3)	147 (9.7)	
Race/ethnicity				
White	65,991 (80.9)	64,682 (80.7)	1,309 (86.6)	**<0.001**
Black	8,602 (10.5)	8,509 (10.6)	93 (6.2)	
Hispanic	4,840 (5.9)	4,762 (5.9)	78 (5.2)	
Other[b]	2,183 (2.7)	2,151 (2.7)	32 (2.1)	
Region				
Northeast	14,844 (18.2)	14,500 (18.1)	344 (22.8)	**<0.001**
Midwest	17,749 (21.7)	17,430 (21.8)	319 (21.1)	
South	34,876 (42.7)	34,298 (42.8)	578 (38.2)	
West	14,147 (17.3)	13,876 (17.3)	271 (17.9)	
Dual Medicaid eligibility	62,853 (77.0)	61,721 (77.1)	1,132 (74.9)	**0.05**
Clinical characteristics, *n* (%)				
Substance use disorder				
Opioids	16,496 (20.2)	16,038 (20.0)	458 (30.3)	**<0.001**
Alcohol	10,961 (13.4)	10,692 (13.3)	269 (17.8)	**<0.001**
Sedatives	3,338 (4.1)	3,229 (4.0)	109 (7.2)	**<0.001**
Cannabis	4,125 (5.1)	4,026 (5.0)	99 (6.5)	**0.01**
Mental health comorbidities				
Depression	15,934 (19.5)	15,610 (19.5)	324 (21.4)	0.06
Anxiety	26,403 (32.4)	25,858 (32.3)	545 (36.0)	**0.002**
Bipolar disorder	14,583 (17.9)	14,244 (17.8)	339 (22.4)	**<0.001**
Schizophrenia	4,857 (6.0)	4,737 (5.9)	120 (7.9)	**<0.001**
Personality disorder	2,695 (3.3)	2,627 (3.3)	68 (4.5)	**0.01**
Other mental disorder	33,797 (41.4)	33,105 (41.3)	692 (45.8)	**<0.001**
Medical comorbidities				
Chronic pain	47,027 (57.6)	46,183 (57.7)	844 (55.8)	0.15
Asthma	10,444 (12.8)	10,240 (12.8)	204 (13.5)	0.41
Cerebrovascular disease	6,654 (8.2)	6,567 (8.2)	87 (5.8)	**<0.001**
COPD	9,181 (11.2)	9,036 (11.3)	145 (9.6)	**0.04**
Diabetes	18,445 (22.6)	18,174 (22.7)	271 (17.9)	**<0.001**
Heart failure	7,901 (9.7)	7,786 (9.7)	115 (7.6)	**0.01**
Hepatitis C	7,879 (9.7)	7,691 (9.6)	188 (12.4)	**<0.001**
HIV	1,452 (1.8)	1,421 (1.8)	31 (2.1)	0.42
Hypertension	31,797 (39.0)	31,239 (39.0)	558 (36.9)	0.10

(*continued on next page*)

Table 1. Baseline Sample Characteristics, Stratified by Opioid Overdose Death in the Year After Nonfatal Overdose (*continued*)

Baseline sample characteristics	Total (N=81,616)	No overdose death (*n*=80,104)	Overdose death (*n*=1,512)	*p*-value[a]
Pneumonia	9,794 (12.0)	9,575 (12.0)	219 (14.5)	**0.003**
Sleep apnea	7,601 (9.3)	7,495 (9.4)	106 (7.0)	**0.002**
Health care utilization				
Inpatient	19,020 (23.3)	18,617 (23.2)	403 (26.7)	**0.002**
Emergency department	31,354 (38.4)	30,742 (38.4)	612 (40.5)	0.10
OUD-related psychosocial services	1,164 (1.4)	1,131 (1.4)	33 (2.2)	**0.01**
Prescription drugs				
Buprenorphine	2,230 (2.7)	2,164 (2.7)	66 (4.4)	**<0.001**
Opioids	45,131 (55.3)	44,329 (55.3)	802 (53.0)	0.89
Antidepressants	37,602 (46.1)	36,908 (46.1)	694 (45.9)	0.89
Antipsychotics	18,092 (22.2)	17,687 (22.1)	405 (26.8)	**<0.001**
Mood stabilizers	25,731 (31.5)	25,224 (31.5)	507 (33.5)	0.09
Sedatives	12,225 (15.0)	11,990 (15.0)	235 (15.5)	0.54
Index overdose characteristics, *n* (%)				
Involved heroin or synthetic opioids	9,484 (11.6)	9,156 (11.4)	328 (21.7)	**<0.001**
Involved benzodiazepines	19,700 (24.1)	19,291 (24.1)	409 (27.1)	**0.01**
Required mechanical ventilation	12,382 (15.2)	12,077 (15.1)	305 (20.2)	**<0.001**
Required inpatient hospitalization	60,531 (74.2)	59,411 (74.2)	1,120 (74.1)	0.93
Fatal overdose characteristics, *n* (%)				
Involved heroin or synthetic opioids			598 (39.6)	

Note: Boldface indicates statistical significance ($p<0.05$).
COPD, chronic obstructive pulmonary disease; OUD, opioid use disorder.
[a]*p*-Values represent chi-square comparisons of each baseline characteristic category.
[b]Other race/ethnicity represents combined statistics for American Indian/Alaska Native, Asian/Pacific Islander, and other/unknown groups in compliance with the Centers for Medicare and Medicaid Services confidentiality requirements to suppress cell sizes 1–10 and any cells that could be used to derive a value of 1 to 10.

Control and Prevention methods (Appendix Table 1, available online).

Sociodemographics and clinical covariates were measured in the 180-day baseline period. Sociodemographics included sex (male, female), age (18–29, 30–39, 40–49, 50–59, 60–64 years), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, American Indian/Alaska Native, Asian/Pacific Islander, other/unknown), U.S. Census region of residence (Northeast, Midwest, South, West), and dual Medicaid eligibility.

Clinical characteristics included baseline comorbidities and health services. Mental health diagnoses included major depressive disorder, anxiety disorders, bipolar disorder, schizophrenia, personality disorder, and any other mental illness (Appendix Table 2, available online). Substance use indicators included diagnoses for opioid, alcohol, cannabis, and sedative use disorders. Medical conditions included diagnoses of asthma, cerebrovascular disease, chronic pain, chronic obstructive pulmonary disease, diabetes, heart failure, hepatitis C, HIV, hypertension, pneumonia, and sleep apnea. Health service indicators included inpatient, ED, and OUD-related psychosocial services described earlier. Prescription drugs included buprenorphine, opioids, antidepressants, antipsychotics, mood stabilizers, and sedatives. For buprenorphine and opioids, total days with medication supply were calculated to account for the full extent of baseline use. Benzodiazepines were not measured owing to changes in Medicare reimbursement during the study period[32] that precluded benzodiazepine coverage before 2013. In the follow-up period, daily indicators of prescription opioid availability and inpatient hospitalizations were used to account for these exposures in estimates of mortality risk.

Statistical Analysis

Unadjusted descriptive statistics with chi-square tests compared groups with opioid-involved overdose death with those without in the follow-up year. Descriptive statistics for OUD treatment characterized time-varying follow-up exposures.

Table 2. Opioid Overdose Mortality Rates in the Year After Nonfatal Opioid Overdose, Stratified by Demographics

	Index opioid overdose	Person-years of follow-up	Opioid overdose deaths	Crude mortality rate Per 100,000 person-years	Expected deaths	Standardized mortality ratio,[a]
	N	*n*	*n*		*n*	SMR (95% CI)
Total	81,616	69,531.3	1512	2,174.6	11.4	132.4 (129.9, 135.0)
Demographics						
Sex						
Male	34,868	29,295.9	794	2,710.3	6.2	127.1 (135.5, 139.7)
Female	46,748	40,235.5	718	1,784.5	5.2	138.8 (135.7, 141.9)
Age						
18–29	3,154	2,793.6	67	2,398.3	0.4	166.4 (163.8, 169.2)
30–39	10,180	8,863.8	236	2,662.5	1.8	128.5 (126.5, 130.6)
40–49	20,254	17,732.6	487	2,746.4	3.4	143.7 (141.3, 146.1)
50–59	34,049	28,730.4	575	2,001.4	4.8	119.4 (117.2, 121.6)
60–64	13,979	11,411.0	147	1,288.2	1.0	150.8 (144.5, 157.4)
Race/ethnicity						
White	65,991	56,406.3	1309	2,320.7	10.1	129.4 (127.6, 131.3)
Black	8,602	7,149.1	93	1,300.9	0.8	113.2 (108.2, 118.6)
Hispanic	4,840	4,122.1	78	1,892.2	0.3	256.5 (244.1, 270.1)
American Indian/ Alaska Native	1,064	910.3	12	1,318.2	0.2	68.3 (60.2, 78.4)
Asian/ Pacific Islander	406	346.9	NR	NR	NR	910.7 (754.6, 1,115.2)

The Centers for Medicare and Medicaid Services require the suppression of cell sizes 1–10 and any cells that could be used to derive a value of 1–10 to protect confidentiality.
CDC, Centers for Disease Control and Prevention; NR, not reportable.
[a]SMR is the ratio of observed to expected deaths in the study sample. The number of expected deaths in each group was calculated using CDC WONDER mortality data, standardized by sex, age, and race/ethnicity. Population rates were obtained for 2008–2016 using CDC definition of opioid overdose deaths.

Crude and standardized mortality rates were calculated by sex, age, and race/ethnicity and, separately, by follow-up OUD treatment. To minimize bias in mortality rates stratified by OUD treatment, the time between the index event and treatment initiation was classified as unexposed.[39] Crude mortality rates represent the observed number of deaths per 100,000 person-years of follow-up. Standardized mortality ratios (SMRs) represent the ratio of observed to expected deaths in the sample. Expected deaths were calculated using Centers for Disease Control and Prevention Wide-ranging ONline Data for Epidemiologic Research (WONDER) [40] mortality rates for opioid-involved overdoses defined using cause of death codes described earlier; limited to the study years; and standardized by sex, age, and race/ethnicity.

Cox proportional hazards regression estimated the time to fatal opioid-involved overdose during follow-up, with time-varying indicators for buprenorphine and psychosocial treatment exposures (Appendix Table 4, available online). Individuals contributed person-time to analyses until the death date or *censoring date*, defined as the last date of the 365-day follow-up period, last date of the study period, or date of death because of other causes. Individuals were also censored on the first naltrexone fill date (n=610, 0.7%) given low use in national MOUD treatment samples (<1%).[41] Estimates were adjusted for all baseline characteristics and the index year to account for trends over time in opioid-involved overdose mortality. Data management and statistical analyses were performed in 2022 using SAS Enterprise Guide 8.3 and Stata 17, respectively.

To ensure the robustness of findings, multiple sensitivity analyses were conducted using alternate exposure (i.e., stratified by treatment modality, restricted to incident treatment in follow-up) or outcome (i.e., excluding deaths early in follow-up) measures and calculating *E*-values for unmeasured confounding[42] (Appendix Methods, available online, and Appendix Tables 5–8, available online).

Table 3. OUD Treatment Characteristics and Opioid Overdose Mortality in the Year After Non-fatal Opioid Overdose

	OUD treatment receipt in the year after nonfatal opioid overdose			
	None	Any	Buprenorphine	Psychosocial
n, %	76,287 (93.5)	5,329 (6.5)	3,774 (4.6)	2,405 (2.9)
Treatment characteristics				
Time to exposure, mean (SD)	—	88.8 (103.9)	92.8 (105.9)	97.6 (105.2)
Median	—	40.0	45.0	55.0
1–30 days, *n* (%)	—	2,464 (46.2)	1,687 (44.7)	975 (40.5)
31–90 days, *n* (%)	—	937 (17.6)	658 (17.4)	463 (19.3)
91–180 days, *n* (%)	—	849 (15.9)	616 (16.3)	429 (17.8)
181–365 days, *n* (%)	—	1,079 (20.2)	813 (21.5)	538 (22.4)
Days treated, mean (SD)	—	51.4% (35.4)	55.0% (35.8)	41.4% (32.8)
>0–25%, *n* (%)	—	1,841 (34.5)	1,148 (30.4)	1,093 (45.4)
>25–50%, *n* (%)	—	928 (17.4)	611 (16.2)	494 (20.5)
>50–75%, *n* (%)	—	703 (13.2)	506 (13.4)	292 (12.1)
>75%, n (%)	—	1,857 (34.8)	1,509 (40.0)	526 (21.9)
Any gap >30-days, *n* (%)	—	3,599 (67.5)	2,228 (59.0)	1,838 (76.4)
Mortality rates				
Person-years[a]	64,790.4	3,444.6	2,425.2	1,491.9
Opioid overdose deaths	1431	81	54	38
CMR[b]	2,208.7	2,351.5	2,226.6	2,547.1
SMR[c] (95% CI)	135.3 (132.7, 138.0)	96.2 (94.7, 97.8)	89.7 (88.3, 91.2)	100.1 (98.5, 101.8)
Hazard ratio (95% CI)[d]	—	—	0.38 (0.23, 0.64)	1.18 (0.71, 1.95)

CDC, Centers for Disease Control and Prevention; CMR, crude mortality rate; OUD, opioid use disorder; SMR, standardized mortality rate ratio.
[a]Person-years were calculated on the basis of exposed follow-up time after initiating treatment, excluding time between the index event and treatment initiation to minimize bias in mortality rates.
[b]CMR represents the rate per 100,000 person-years.
[c]SMR is the ratio of observed to expected deaths in the study sample. The number of expected deaths in each group was calculated using CDC WONDER mortality data, standardized by sex, age, and race/ethnicity. Population rates were obtained for 2008–2016 using CDC definition of opioid overdose deaths.
[d]Results of multivariable Cox proportional hazards models adjusted for all baseline sociodemographic and clinical characteristics (Appendix Table 4, available online, for full model results).

RESULTS

The sample included 81,616 MDBs with at least 1 nonfatal opioid-involved overdose (Table 1). The sample was mostly female (57.3%), aged ≥50 years (58.8%), White (80.9%), living in the South (42.7%), and dually eligible for Medicaid at the time of the index overdose (77.0%).

Over one tenth of individuals died during follow-up (*n*=9,439; 11.6%) (Appendix Figure 2, available online). One quarter of deaths was drug related (*n*=2,430; 25.7%), and nearly two thirds of drug-related deaths involved opioid poisoning (*n*=1,512; 62.2%). Most opioid-involved overdose deaths were unintentional (*n*=1,413; 93.5%), and 40% involved heroin or synthetic opioids other than methadone (*n*=598).

There were significant differences in unadjusted baseline characteristics between groups with and without subsequent opioid-involved overdose death (Table 1). A greater proportion of those who died were male ($p<0.001$), aged <50 years ($p<0.001$), and White ($p<0.001$). Those who died had more substance use disorder and mental health diagnoses (all $p<0.01$), except depression ($p=0.06$). Those who died also had higher rates of hepatitis C ($p<0.001$) and pneumonia ($p=0.003$) but lower rates of cerebrovascular disease ($p<0.001$), chronic obstructive pulmonary disease ($p=0.04$), diabetes ($p<0.001$), heart failure ($p=0.01$), and sleep apnea ($p=0.002$). Those who died had higher rates of baseline buprenorphine use ($p<0.001$). Hospitalization rates during the index event were comparable ($p=0.93$), but index events requiring mechanical ventilation ($p<0.001$), involving heroin or synthetic opioids ($p<0.001$), or involving benzodiazepines ($p=0.01$) were more common among those who died.

The overall unadjusted crude mortality rate was 2,174.6 opioid-involved overdose deaths per 100,000 person-years (Table 2). After accounting for the distribution of sex, age, and race/ethnicity, this translated into a mortality rate over 130 times higher than that of the demographically standardized general U.S. population during the same period (SMR=132.4, 95% CI=129.9, 135.0).

SMRs were similar for males (SMR=127.1, 95% CI=135.5, 139.7) and females (SMR=138.8, 95% CI=135.7, 141.9). Young adults aged 18−29 years comprised the smallest proportion of opioid-involved overdose deaths but had a significantly higher SMR than all other age groups (SMR=166.4, 95% CI=163.8, 169.2). SMRs were significantly lower for Black (SMR=113.2, 95% CI=108.2, 118.6) and American Indian/Alaska Native (SMR=68.3, 95% CI=60.2, 78.4) groups than for their White counterparts (SMR=129.4, 95% CI=127.6, 131.3) but significantly higher for Hispanic (SMR=265.5, 95% CI=244.1, 270.1) and Asian/Pacific Islander (SMR=910.7, 95% CI=754.6, 1,115.2) groups.

In adjusted Cox model estimates, male sex (adjusted hazard ratio [AHR]=1.35, 95% CI=1.21, 1.50) and younger age were associated with a higher risk of opioid-involved overdose death than females and ages 60−64 years, respectively (Appendix Table 4, available online). Black (AHR=0.59, 95% CI=0.48, 0.74) and Hispanic (AHR=0.72, 95% CI=0.57, 0.91) groups had a lower risk of death than White race/ethnicity. A minority of MDBs had any OUD treatment after the index event (n=5,329, 6.5%), with most receiving buprenorphine (n=3,774, 70.8%) and less than half (n=2,405, 45.1%) receiving psychosocial services (Table 3).

Among MDBs receiving OUD treatment, the average time to exposure was 92.8 days for buprenorphine (median=45.0) and 97.6 days for psychosocial services (median=55.0). Less than half of those receiving buprenorphine (n=1,687, 44.7%) or psychosocial services (n=975, 40.5%) had treatment in the first 30 follow-up days. Over 20% had no treatment in the first 6 months of follow-up (buprenorphine n=813, 21.5%; psychosocial n=538, 22.4%).

OUD treatment exposure was inconsistent (Table 3). On average, MDBs with buprenorphine had medication supply on slightly over half of exposed follow-up days (55.0%), and most had at least 1 treatment gap >30 days (n=2,228, 59.0%). On average, those with psychosocial treatment were exposed on 41.4% of follow-up days by the 30-day definition, and most had at least 1 treatment gap >30 days (n=1,838, 76.4%).

Overall mortality rates were elevated compared with those of the standardized reference population (Table 3). However, there were differences in treatment status. MDBs with no follow-up OUD treatment had the highest SMR (SMR=135.3, 95% CI=132.7, 138.0), whereas SMRs were lower for those with any buprenorphine (SMR=89.7, 95% CI=88.3, 91.2) or any OUD-related psychosocial services (SMR=100.1, 95% CI=98.5, 101.8).

In adjusted Cox model estimates, buprenorphine had the strongest association with subsequent opioid-involved overdose mortality, with a significantly lower risk of death (AHR=0.38, 95% CI=0.23, 0.64). OUD-related psychosocial services were not significantly associated with the risk of death (AHR=1.18, 95% CI=0.71, 1.95). Sensitivity results were consistent with primary analyses, and E-values indicated robustness to unmeasured confounding (Appendix Tables 5−8, available online).

DISCUSSION

Buprenorphine was associated with a 62% reduction in the risk of opioid-involved overdose death in the year after nonfatal opioid-involved overdose, despite patterns reflecting delayed and inconsistent treatment access or use. The magnitude of this effect is similar to that of an all-payer study estimating a 69% reduction in opioid-involved overdose mortality risk during buprenorphine treatment,[21] suggesting that the effectiveness of buprenorphine for MDBs is comparable with that of the general population.

Yet, buprenorphine uptake was low and indicative of limited access to timely treatment, which could contribute to elevated opioid-involved overdose mortality given that buprenorphine is associated with a reduced risk of death.[2,3,21] For example, 2.1% of the sample received buprenorphine in the first 30 follow-up days, consistent with studies of multipayer (2.2%)[17] and veteran (1.3%)[12] samples. Because all individuals presented to acute care settings and because 1 in 5 had documented OUD diagnoses before presentation, this signals an overwhelming need to improve the health system's response to life-threatening events with life-saving treatment. Increased efforts to implement hospital-based MOUD induction and warm hand-offs to community providers[43] are potentially critical to reducing opioid-related morbidity and mortality. Despite the effectiveness of ED-initiated buprenorphine, uptake may be limited by inadequate training because few ED physicians report preparedness to treat OUD.[44,45] Formal training may facilitate readiness[44] by addressing identified gaps in knowledge,[45] but clinical decision support may not be sufficient[46] to overcome systemic barriers related to a lack of treatment and referral protocols, support staff, and other resources to address logistical challenges in acute care contexts.[44,45]

In addition to strengthening the initial connection to OUD treatment, interventions that facilitate medication continuity after induction could further reduce the risk of adverse opioid-related outcomes.[47,48] Most of the sample receiving buprenorphine had sporadic treatment (e.g., minimal follow-up days with medication,

substantial gaps in supply), which is linked with increased mortality risk.[2,3] In addition, a higher proportion of those who died had baseline buprenorphine use, possibly signaling OUD severity. Although baseline buprenorphine was not significantly associated with mortality in adjusted analyses, sporadic medication access or use could contribute to opioid-related morbidity. Assessing potential risk[49] and protective factors[50] and ensuring that adequate support services are available[51] through delivery or referral to specialty care for co-occurring medical and behavioral health problems may promote buprenorphine treatment continuity.

To the authors' knowledge, this is the first study to examine the relationship of outpatient OUD-specific psychosocial services with subsequent opioid-involved overdose mortality. The low uptake of psychosocial services was concentrated among individuals without buprenorphine, reflecting a substantial gap in evidence-based treatment. Although results were inconclusive owing to low treatment exposure leading to uncertainty in estimates, psychosocial services were not significantly associated with opioid-involved overdose mortality risk, consistent with evidence that medication with psychosocial treatment is no more effective at reducing adverse opioid-related outcomes than medication alone.[52–54]

Overall, 1.9% of MDBs had fatal opioid-involved overdoses in follow-up, aligning with previous estimates for any drug overdose death (2.4%).[8] Nonetheless, rates of opioid-involved overdose mortality were markedly elevated compared with those of the general population. Although high mortality rates may be related to factors other than OUD treatment (e.g., type and severity of disability, prevalence of secondary conditions), the findings coincide with national trends.[22] Mortality risk was higher for males and younger adults and similarly high for White and American Indian/Alaska Native groups. Risk was also comparable for Asian/Pacific Islanders or other race/ethnicity, but small samples and uncertainty in estimates preclude definitive interpretations. Although Black and Hispanic groups had lower risk, these relationships may not persist over time given the recent acceleration in opioid-involved overdose mortality rates among Black Americans.[55] Continued research in large diverse samples could improve the understanding of shifting racial/ethnic disparities in overdose risk.

Limitations

Findings should be interpreted in the context of several limitations. First, although the data are generalizable to the Medicare Part D population,[32] results may not be representative of all adults with disabilities, such as those with Medicaid coverage based on nonfederal disability determinations, those who report living with a disability but do not qualify for public insurance, and those with private or no insurance. In addition, results may not generalize to nonfatal opioid-involved overdoses that are untreated or treated outside acute care settings or to individuals with no opioid-involved overdose history who could benefit from low-threshold buprenorphine treatment in community-based settings other than conventional healthcare contexts.[56]

Second, some exposures and outcomes may have been underestimated. The data do not capture treatment funded by non-Medicare sources (e.g., block grants, other public programs, self-pay, self-help, peer support), including methadone, which is a highly effective medication[57] that Medicare did not cover until 2020 but should be examined in future research. The data also preclude measurement of nonprescribed buprenorphine use, which is associated with a reduced risk of adverse opioid-related outcomes, including overdose.[50,58] Although specified drug involvement in cause-of-death codes has improved over time, opioid-involved overdose fatalities may have been misclassified as nonopioid deaths owing to data limitations.[59] Thus, findings represent conservative estimates of opioid-involved overdose mortality and the association with OUD treatment.

Alternatively, treatment need and exposures may have been overestimated. Some individuals with nonfatal opioid-involved overdose may not meet the criteria for OUD. In addition, although buprenorphine approved for pain treatment was excluded, Medicare-covered buprenorphine exposures may include off-label prescriptions for pain management,[60] which suggests that treatment rates could be lower than observed estimates. In addition, psychosocial services were defined as 30-day exposures, and the duration of treatment benefits may be shorter. Finally, although models adjusted for a range of individual and treatment characteristics, causal inferences are not possible owing to potential residual confounding by unobserved covariates.

CONCLUSIONS

Low buprenorphine treatment after nonfatal opioid-involved overdose highlights the importance of expanding MOUD induction in acute care settings. Buprenorphine substantially reduced the risk of subsequent opioid-involved overdose mortality, despite delayed and inconsistent treatment. Disproportionately high opioid-involved overdose mortality rates and low rates of OUD treatment uptake indicate that

the disability population is particularly vulnerable to opioid-related morbidity and mortality. In addition to comprising a priority group for prevention and treatment efforts, the disability population has a high concentration of socioeconomic disadvantage,[61] and efforts to increase treatment engagement and continuity in this group could help address disparities in health care and outcomes.

CREDIT AUTHOR STATEMENT

Hillary Samples: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. Molly A. Nowels: Data curation, Formal analysis, Writing – review & editing. Arthur R. Williams: Conceptualization, Writing – review & editing. Mark Olfson: Conceptualization, Methodology, Supervision, Writing – review & editing. Stephen Crystal: Conceptualization, Methodology, Supervision, Writing – review & editing.

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SUPPLEMENTAL MATERIAL

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