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Original Investigation | Substance Use and Addiction

Office-Based Addiction Treatment Retention and Mortality Among People Experiencing Homelessness

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Background

- **The opioid crisis has disproportionately affected those who experience homelessness.**
- **Multifaceted approach has been used to support this population including outreach and barrier free access to treatment.**

Methods

- Retrospective cohort study of individuals who accessed office-based addiction treatment programming with the Boston Health Care for the Homeless Program (BHCHP) between Jan 1 and Dec 31, 2018

Program description:

- Nurse case managers play a central role.
- OAT prescribed in the first visit.
- Behavioral management conducted by behavioral therapists.
- The primary outcome was all-cause mortality, identified by cross-linking the BHCHP cohort with the Massachusetts Department of Public Health's Registry of Vital Records and Statistics.

Methods

- Matched based on a record linkage tool (LinkPlus)
- National Death Index criteria: (1) social security number, (2) first and last name, with month and year of birth (±1 year), or (3) first and last name with month and day of birth
- The 2 investigators achieved perfect concordance and interrater reliability (κ = 1.00)

Used a Cascade of Care Model:

- (1) OBAT program retention (based on program attendance via in-person visits with a BHCHP OBAT physician, nurse care manager, or behavioral health care professional independent of buprenorphine prescriptions);
- (2) buprenorphine initiation (based on the first buprenorphine prescription during the study period), continuation (defined as having subsequent buprenorphine prescriptions), and adherence (defined as having a positive buprenorphine urine toxicologic screen); and
- (3) opioid abstinence (defined as having no detectable opioids on urine toxicologic testing).

Methods

COVARIATES:

- Covariates were selected a priori and abstracted from the electronic health record using automated methods. Sociodemographic characteristics included age, sex, race/ethnicity, insurance status, and housing status as recorded in the baseline clinical encounter,
- dichotomized into literal homelessness (shelter or street) vs other living situations.
- Clinical characteristics included comorbid conditions, medications, and addiction treatment–related characteristics
- Time-varying addiction treatment–related characteristics included OBAT program attendance, buprenorphine adherence, and opioid abstinence, as previously defined and measured on a monthly basis.

Methods Continued

Statistical Analysis:

- Tabulated all-cause mortality rates and leading causes of death.
- Multivariable Cox proportional hazards regression analyses to identify baseline and time-varying characteristics associated with mortality, reporting hazard ratios (HRs) and 95% Cis
- Excluded variables that were highly collinear and variables with a limited number of outcomes because we would not be able to establish associations
- Assess addiction treatment–related outcomes at 1, 3, 6, 9, and 12 months
- Sum and percentage of positive buprenorphine toxicologic tests and the sum and percentage of negative opioid toxicologic tests for each individual.
- Multivariable logistic regression to identify baseline characteristics independently associated with OBAT retention at 1 month, reporting odds ratios (ORs) and 95% CIs.

Results

- A total of 193 individuals (13.2%) died, with an all-cause mortality rate of 29.0 per 1000 person-years
- The leading cause was drug overdose, accounting for 87 (51.8%) of these deaths
- Opioids were present in 100% of the drug overdose deaths
- Age (adjusted HR [aHR], 1.34 per 10-year increment; 95% CI, 1.16-1.54) and a Charlson comorbidity index score of 2 or higher (aHR, 1.55; 95% CI, 1.10-2.18) were independently associated with increased hazard of all-cause mortality
- Past-month OBAT program attendance remained protective against all-cause mortality (aHR, 0.43; 95% CI, 0.24-0.78
- Past-month opioid abstinence (aHR, 0.37; 95% CI, 0.18-0.78) was independently associated with decreased hazard of all-cause mortality

Table 1. Characteristics of People Experiencing Homelessness Who Engaged in an OBAT Program, 2008-2018

Patient characteristic	All patients (N = 1467)
Sociodemographic characteristic	
Age, mean (SD)	42.2 (10.6)
Sex, No. (%)	
Male	1046 (71.3)
Female	421 (28.7)
Race/ethnicity, No. (%)	
Non-Hispanic White	731 (49.8)
Non-Hispanic Black	183 (12.5)
Hispanic	442 (30.1)
Other/unknown	111 (7.6)
Insurance type, No. (%)	
Private	15 (1.0)
Public	1266 (86.3)
Dual	130 (8.9)
Uninsured	56 (3.8)
Housing status, No. (%)	
Shelter/street	719 (49.0)
Other[a]	748 (51.0)
Clinical characteristics	
Charlson comorbidity index, median (IQR)	0 (0-1)
Serious bacterial infection, No. (%)[b]	19 (1.3)
Other substance use disorders, No. (%)	
Alcohol use disorder	275 (18.8)
Other drug use disorder	1202 (81.9)
Serious mental illness, No. (%)[c]	189 (12.9)
Cold-related injury, No. (%)[d]	31 (2.1)
Medication prescriptions, No. (%)	
Benzodiazepine	25 (1.7)
Opioid[e]	17 (1.2)
Antidepressant	71 (4.8)
Antipsychotic	37 (2.5)
Other sedating medications[f]	23 (1.6)
Naloxone	7 (0.5)
Addiction treatment-related characteristics	
Year of first OBAT encounter, No. (%)	
2008-2013	449 (30.6)
2014-018	1018 (69.4)
Site of first OBAT encounter, No. (%)	
Clinic	1181 (80.5)
Shelter/outreach	286 (19.5)
No. of OBAT encounters, median (IQR)	4 (0-17)
Positive buprenorphine toxicologic tests, median (IQR), %	100 (80-100)
Negative opioid toxicologic tests, median (IQR), %	61 (20-100)

Table 2. Cause of Death Among 168 People Experiencing Homelessness Who Engaged in an OBAT Program[a]

Underlying cause of death	No. (%) of patients
External causes	
Drug overdose	87 (51.8)
Opioid	87 (100)
Alcohol	32 (36.8)
Benzodiazepine	17 (19.5)
Cocaine	15 (17.2)
Suicide	4 (2.4)
Accidents (unintentional injuries)	3 (1.8)
Homicide	2 (1.2)
Alcohol poisoning	1 (0.6)
Other accidents (nonpoisoning)	1 (0.6)
Natural causes	
Heart disease	15 (8.9)
Psychoactive substance use disorder	12 (7.1)
HIV disease	10 (6.0)
Cancer	6 (3.6)
Liver disease	6 (3.6)
Ill-defined conditions	5 (3.0)
Cerebrovascular disease	3 (1.8)
Anoxic brain injury	2 (1.2)
Sepsis	2 (1.2)
Viral hepatitis	2 (1.2)
Other diseases of the nervous system	2 (1.2)
Chronic lower respiratory diseases	1 (0.6)
Congenital malformations of the heart	1 (0.6)
Diabetes	1 (0.6)
Other diseases of the respiratory system	1 (0.6)
Nephritis, nephrotic syndrome, and nephrosis	1 (0.6)

Results

Figure. Continuous Addiction Treatment-Related Outcomes Over 12 Months Among People Experiencing Homelessness Who Engaged in an Office-Based Addiction Treatment (OBAT) Program

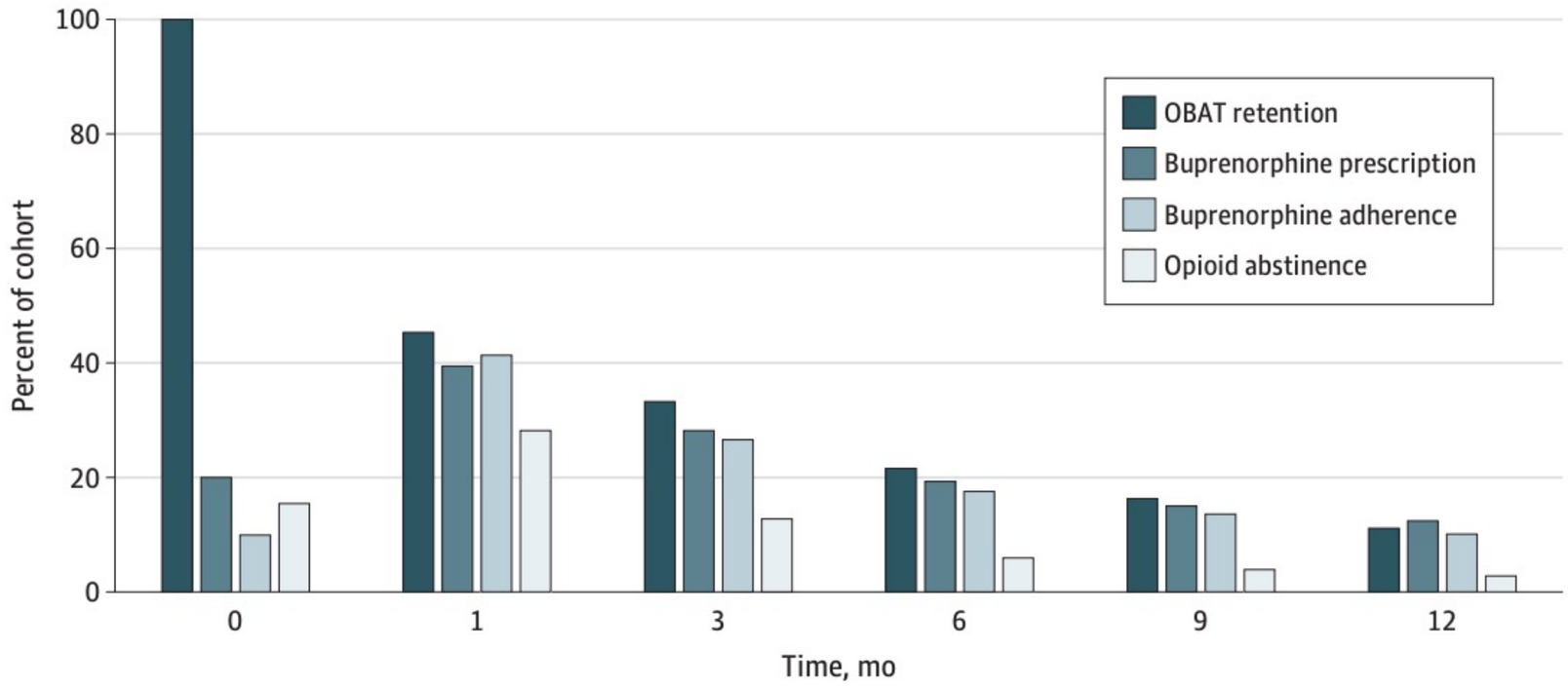

Table 4. Baseline Characteristics Associated With One-Month Addiction Treatment Retention Among People Experiencing Homelessness Who Engaged in an OBAT Program[a]

Patient characteristic	Adjusted odds ratio (95% CI)	*P* value
Sociodemographic characteristics		
Age (per 10-y increment)	1.00 (0.99-1.01)	.48
Sex		
Female	1 [Reference]	[Reference]
Male	1.21 (0.95-1.54)	.12
Race/ethnicity		
White	1 [Reference]	[Reference]
Non-Hispanic Black	0.83 (0.59-1.17)	.29
Hispanic	1.56 (1.22-2.01)	<.001
Other/unknown	0.80 (0.52-1.22)	.30
Housing status		
Other[b]	1 [Reference]	[Reference]
Shelter/street	0.79 (0.64-0.98)	.04
Clinical characteristics		
Charlson comorbidity index		
0-1	1 [Reference]	[Reference]
≥2	0.91 (0.67-1.22)	.52
Alcohol use disorder	0.93 (0.70-1.23)	.61
Other drug use disorder	1.97 (1.47-2.66)	<.001
Serious mental illness[c]	0.71 (0.51-0.98)	.04
Medication prescriptions		
Benzodiazepine	1.41 (0.73-2.72)	.30
Opioid[d]	0.56 (0.31-0.98)	.05
Antidepressant	1.22 (0.90-1.67)	.21
Antipsychotic	0.94 (0.61-1.44)	.78
Other sedating medications[e]	1.45 (0.85-2.48)	.17
Naloxone	1.11 (0.67-1.83)	.67
Addiction treatment-related characteristics		
Year of first OBAT encounter		
2008-2013	1 [Reference]	[Reference]
2014-2018	0.67 (0.53-0.86)	<.001
Site of first OBAT encounter		
Clinic	1 [Reference]	[Reference]
Shelter/outreach	1.30 (0.99-1.72)	.06

Discussion

Individuals who experienced homelessness and engaged with OBAT experienced the following:

- High mortality rates
- Substantially high numbers dying from overdoses.
- OBAT program attendance was associated with decreased mortality despite complete opioid abstinence being uncommon.
- Continuous retention in addiction care was low, with considerable loss to follow-up within the first month of care
- all-cause mortality in this cohort was 12-fold higher than in a similarly aged general population
- 2-fold higher than in a similarly aged homeless population
- program attendance remained protective independent of buprenorphine adherence and opioid abstinence
- a low-threshold harm reduction approach that prioritizes engagement in addiction care whenever possible regardless of lapses in previous attendance or ongoing illicit drug use
- Patients who were living in a shelter or on the street were less likely than housed individuals to be retained in OBAT care at 1 month but also less likely to die during follow-up

Limitations

LIMITATIONS:

- Adults who received care in BHCHP's OBAT program, so the findings may not be generalizable to homeless individuals who avoid care or to homeless adults in other cities.
- Observational nature of the study introduces the possibility of confounding by unmeasured variables, such as the severity of addiction, periods of incarceration, and social supports

Our Discussion

Association Between Benzodiazepine or Z-Drug Prescriptions and Drug-Related Poisonings Among Patients Receiving Buprenorphine Maintenance: A Case-Crossover Analysis

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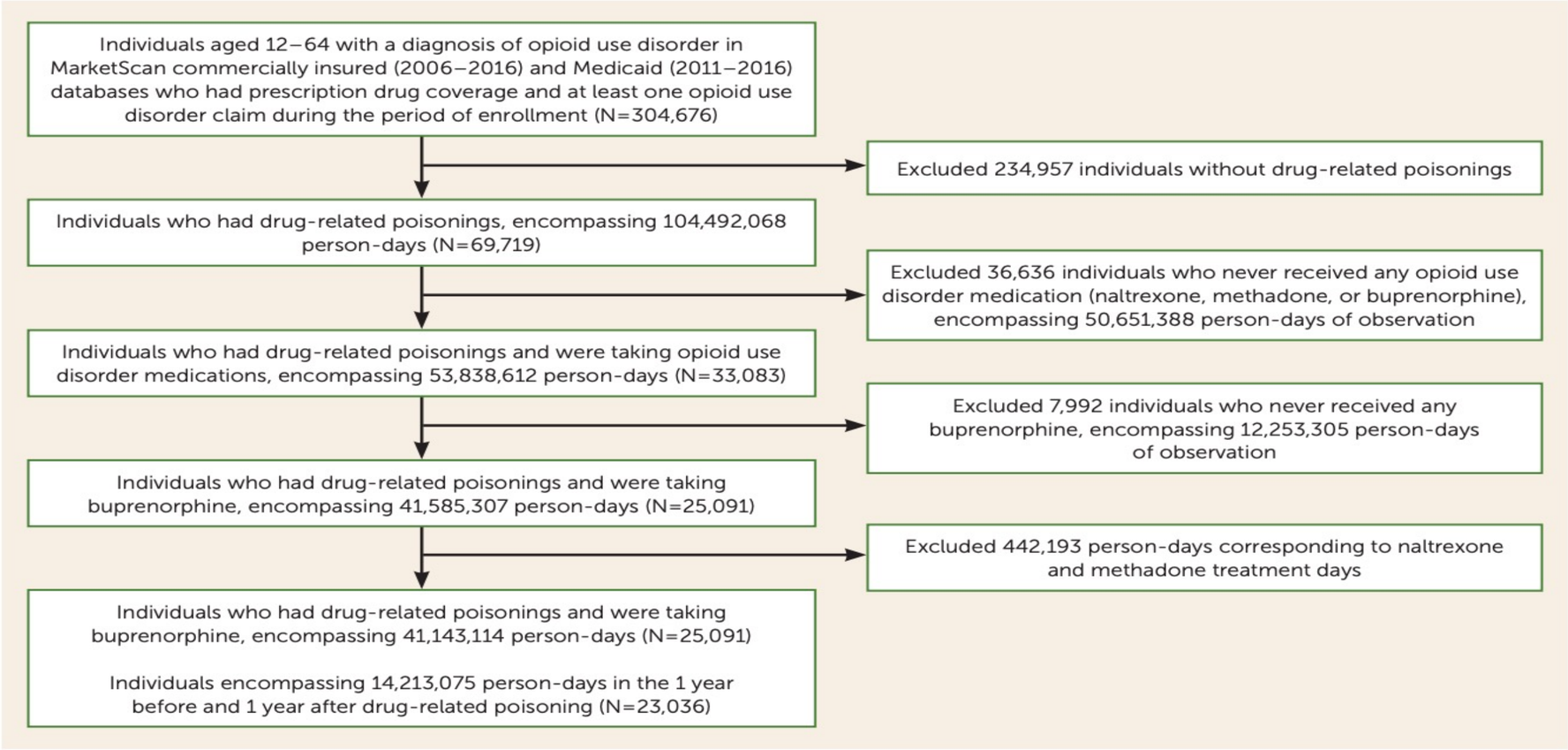
Background

- Buprenorphine is used to treat OUD
- Up to 30% of this population may be using concurrent Benzos which put them at high risk of overdose.
- Some findings suggest that benzodiazepines may enhance retention in buprenorphine maintenance treatment
- Benzodiazepines have also been associated with:
  - Increases in drug-related poisonings
  - All-cause mortality
  - Non-overdose deaths
  - Decreased retention in treatment
  - Accidental injury-related emergency department visit
  - Limited studies on the interaction between benzos and buprenorphine.

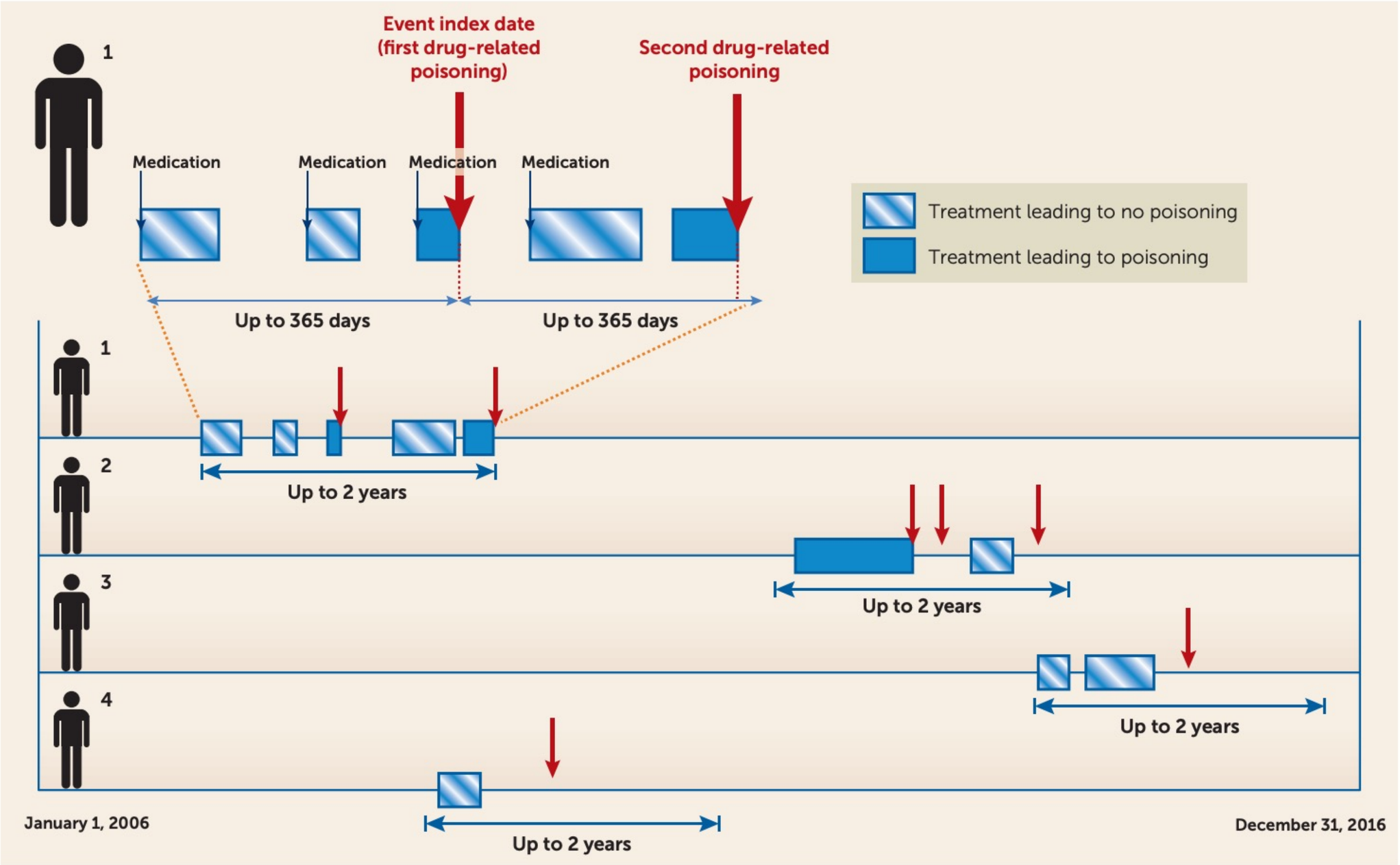
Methods

FIGURE 1. Derivation of the analytic sample during follow-up of patients with opioid use disorder with a drug-related poisoning



Methods Continued

- Individuals ages 12 to 64 with insurance claims indicating an opioid use disorder diagnosis, at least one buprenorphine prescription, and at least one nonfatal drug-related poisoning were included for analysis.
- Buprenorphine use was characterized in terms of strength, quantity, and days of supply in order to calculate a daily milligram dose.
- Stratified into daily buprenorphine doses >12 mg and <12mg
- Case crossover study design was used.
- Units of observation were person-days, denoting days during which patients were enrolled in a health insurance plan.
- Case periods were days when a patient experienced nonfatal drug related poisonings
- Control periods were nearby days without poisoning events
- Person-day of observation by the presence or absence of benzodiazepine or Z-drug treatment and the presence or absence of buprenorphine treatment
- Individuals with fewer observation days on either side of the index event were included with missing days treated as censored.
- selective serotonin reuptake inhibitors (SSRIs) (sertraline, fluoxetine, escitalopram, and citalopram) were included in our conditional logistic models as an active comparator analysis


Event index date
(first drug-related
poisoning)
Second drug-related
poisoning
1
Medication
Medication
Medication
Medication
Treatment leading to no poisoning
Treatment leading to poisoning
Up to 365 days
Up to 365 days
1
2
Up to 2 years
3
Up to 2 years
4
Up to 2 years
Up to 2 years
January 1, 2006
December 31, 2016

Methods Continued

- Ascertainment of Outcomes and Exposures:
  benzodiazepine, Z-drug, and buprenorphine prescriptions were evaluated on strength, quantity dispensed, and days of supply
- Strength of each benzodiazepine or Z-drug in terms of total diazepam-equivalent milligrams
- Daily diazepam-equivalent dose by multiplying the number supplied by strength (in diazepam-equivalent milligrams) and dividing by days of supply
- Benzodiazepine and Z-drug dosage was stratified into high-dose (diazepam-equivalent-mg dose .30 mg) and lowdose (#30 mg)
- Benzodiazepine exposure was categorized by the duration of action, namely, short-acting (half-life #24 hours) or longacting (half-life .24 hours)

Methods Continued

Statistical Analysis:

- SAS
- logistic regression models stratified by subject and modeled the risk of poisoning as a function of drug exposure by days with or without treatment.
- additive or interactive effects of benzodiazepines or Z-drugs and buprenorphine in association with drug-related poisonings.
- SSRIs were included in our models as an active comparator analysis
- Subgroup analyses were conducted to assess the effect of buprenorphine treatment days, compared with days without treatment, on drug-related poisoning among patients who received benzodiazepine or Z-drug prescriptions and those who did not

Characteristic	N	%
Buprenorphine use	16,451	71.41
Low-dose (≤12 mg daily)	9,469	41.11
High-dose (>12 mg daily)	11,690	50.75
Benzodiazepine or Z-drug use	12,890	55.96
Benzodiazepine use excluding Z-drugs	11,839	51.39
Low-dose (≤30 diazepam-equivalent mg daily)	10,356	44.96
High-dose (>30 diazepam-equivalent mg daily)	5,227	22.69
Short-acting benzodiazepine use	9,292	40.34
Alprazolam	6,210	26.96
Lorazepam	4,433	19.24
Oxazepam	130	0.56
Triazolam	248	1.08
Estazolam	19	0.08
Temazepam	1,127	4.89
Midazolam	47	0.2
Long-acting benzodiazepine use	6,660	28.91
Clonazepam	3,885	16.86
Diazepam	3,612	15.68
Chlordiazepoxide	206	0.89
Clobazam	1	0
Flurazepam	33	0.14
Quazepam	2	0.01
Z-drug use	5,068	22
Zolpidem	4,640	20.14
Eszopiclone	1,025	4.45
Zaleplon	216	0.94
Methadone use	420	1.82
Naltrexone use	1,449	6.29
Naltrexone extended-release use	746	3.24
Selective serotonin reuptake inhibitor use	10,286	44.65

	Mean	SD
Age (years)	30.05	12.15
Year of birth	1980	
Days of observation	298.73	107.88
	N	%
Male	11,713	50.85
Relationship of patient to primary beneficiary		
Employee	4,345	28.30
Spouse	3,746	24.40
Child or other	7,263	47.30
Medicaid	7,682	33.35

TABLE 2. Opioid use disorder treatment characteristics at the person-days level among individuals with a drug-related poisoning (N=23,036)[a]

Characteristic	N	%
Treatment days marked by drug-related poisoning	26,243	0.18
Days treated with buprenorphine	2,210,927	15.56
Dose (mean±SD)	15.44	7.31
Low-dose (≤12 mg daily)	758,261	5.33
High-dose (>12 mg daily)	1,367,893	9.62
Days treated with selective serotonin reuptake inhibitors	1,715,489	12.07
Days treated with benzodiazepines or Z-drugs	2,493,800	17.55
Dose (diazepam-equivalent mg daily) (mean±SD)	23.39	25.88
Days treated with benzodiazepines excluding Z-drugs	1,968,944	13.85
Dose (diazepam-equivalent mg daily) (mean±SD)	27.58	26.98
Low-dose (≤30 diazepam-equivalent mg daily)	1,453,110	10.22
High-dose (>30 diazepam-equivalent mg daily)	515,834	3.63
Days treated with short-acting benzodiazepines	1,584,424	11.15
Dose (diazepam-equivalent mg daily)	25.33	20.53
Days treated with long-acting benzodiazepines	452,820	3.19
Dose (diazepam-equivalent mg daily)	31.28	38.10
Days treated with Z-drugs	825,610	5.81
Dose (diazepam-equivalent mg daily) (mean±SD)	4.88	1.24
Concurrent use of buprenorphine or benzodiazepines or Z-drugs		
Days without buprenorphine or benzodiazepine or Z-drug treatment	9,982,529	70.23
Days treated with benzodiazepines or Z-drugs only	2,019,619	14.21
Days treated with buprenorphine only	1,736,746	12.22
Days treated with concurrent buprenorphine and benzodiazepines or Z-drugs	474,181	3.34

[a] Data are presented as Ns and percentages except as otherwise noted. Among all individuals with a history of drug-related poisoning during the study's observation window (1 year before and 1 year after the index poisoning event), the number of person-days for which insurance claims were filed for medication treatment was calculated. Because the data in this table do not represent the individual subject level, it was possible for an individual subject to contribute multiple person-days.

Results

- Excluded individuals without drug-related poisonings, individuals who never received medication for opioid use disorder, and individuals without days of naltrexone and methadone treatment and days of observation outside a maximum of a 1-year period before and after the index poisoning

- 1,968,944 person-days (13.9%) entailed claims for benzodiazepines or Z-drugs, of which 474,181 person-days entailed concurrent buprenorphine treatment

- mean daily dose of any benzodiazepine or Z-drug to be 23.4 diazepam-milligram equivalents and the mean daily dose for short-acting benzodiazepines, long-acting benzodiazepines, and Z-drugs to be 25.3, 31.3, and 4.9 diazepam-milligram equivalents

- Buprenorphine and Benzo-Z drug poisonings:

- Buprenorphine treatment days were associated with 37% lower odds of drug-related poisoning (95% CI=0.60, 0.66) compared with nontreatment days
- Odds of poisoning increased 81% on days when patients were treated with benzodiazepines or Z-drugs (95% CI=1.73, 1.91; model 1)

- Z-drug treatment days were associated with increased odds of poisoning events (odds ratio=1.29, 95% CI=1.19, 1.39), but this was notably lower than the odds associated with benzodiazepine treatment days (odds ratio=1.88, 95% CI=1.78, 1.98; model 2)
- No association between SSRI treatment days and drug-related poisonings (odds ratio=0.95, 95% CI=0.90, 1.00; model 3)
- No difference in magnitude of protective effect against poisoning conferred by buprenorphine treatment days when conducting stratified analyses of patients who used benzodiazepines or Z-drugs (odds ratio=0.64, 95% CI=0.60, 0.69, model 4) and those who never used benzodiazepines or Z-drugs during the study's observation period (odds ratio=0.64, 95% CI=0.59, 0.69; model 5).

Results

- Similarly elevated odds of drug-related poisoning for short acting benzodiazepine treatment days (odds ratio=1.86, 95% CI=1.75, 1.97; model 6) and long-acting benzodiazepine treatment days (odds ratio=1.68, 95% CI=1.54, 1.83; model 6)

- Similar patterns to overdose were noted between z-drugs and benzos stratified into low dose and high dose.

TABLE 3. Odds of drug-related poisoning associated with benzodiazepine use among individuals with opioid use disorder[a]

Variable	Odds Ratio	95% CI
Model 1		
Buprenorphine	0.63	0.60, 0.66
Any benzodiazepine or Z-drug	1.81	1.73, 1.91
Model 2		
Buprenorphine	0.63	0.60, 0.67
Benzodiazepines, excluding Z-drugs	1.88	1.78, 1.98
Z-drugs	1.29	1.19, 1.39
Model 3		
Buprenorphine	0.63	0.60, 0.67
Benzodiazepines, excluding Z-drugs	1.88	1.79, 1.99
Z-drugs	1.29	1.19, 1.40
Selective serotonin reuptake inhibitors	0.95	0.90, 1.00
Model 4		
Buprenorphine (among benzodiazepine or Z-drug users)	0.64	0.60, 0.69
Model 5		
Buprenorphine (among benzodiazepine or Z-drug nonusers)	0.64	0.59, 0.69
Model 6		
Buprenorphine	0.63	0.60, 0.66
Short-acting benzodiazepines	1.86	1.75, 1.97
Long-acting benzodiazepines	1.68	1.54, 1.83
Z-drugs	1.29	1.19, 1.39
Model 7		
Buprenorphine	0.63	0.60, 0.66
Low-dose benzodiazepines	1.78	1.67, 1.88
High-dose benzodiazepines	2.22	2.03, 2.43
Z-drugs	1.29	1.19, 1.39
Model 8		
Buprenorphine	0.64	0.62, 0.67
Any benzodiazepine or Z-drug, low-dose	1.86	1.77, 1.95
Any benzodiazepine or Z-drug, high-dose	2.53	2.35, 2.73
Model 9		
Low-dose buprenorphine	0.62	0.57, 0.67
High-dose buprenorphine	0.63	0.59, 0.67
Low-dose benzodiazepines	1.78	1.68, 1.88
High-dose benzodiazepines	2.22	2.03, 2.43
Z-drugs	1.29	1.19, 1.39
Model 10		
Buprenorphine only	0.61	0.58, 0.65
Benzodiazepine or Z-drug, low-dose (plus buprenorphine)	1.11	1.00, 1.23
Benzodiazepine or Z-drug, high-dose (plus buprenorphine)	1.64	1.39, 1.93

TABLE 3, *continued*

Variable	Odds Ratio	95% CI
Benzodiazepine or Z-drug, low-dose (no buprenorphine)	1.69	1.60, 1.79
Benzodiazepine or Z-drug, high-dose (no buprenorphine)	2.23	2.04, 2.45

[a] Low-dose benzodiazepines are ≤30 diazepam-equivalent milligrams daily; high-dose benzodiazepines are >30 diazepam-equivalent milligrams daily; low-dose Z-drugs are ≤30 diazepam-equivalent milligrams daily; high-dose Z-drugs are >30 diazepam-equivalent milligrams daily; low-dose buprenorphine is ≤12 mg/day; and high-dose buprenorphine is >12 mg/day.

Discussion

- Buprenorphine treatment days conferred a nearly 40% reduction in poisonings, benzodiazepine or Z-drug treatment days corresponded to a near-doubling in poisoning risk
- Individuals taking both buprenorphine and benzodiazepines or Z-drugs were at elevated risk of poisoning, they still had a lower net risk than those taking benzodiazepines or Z-drugs without buprenorphine
- Patients with opioid use disorder for whom benzodiazepine or Z-drug cessation is risky, lower doses and shorter treatment duration of sedative/hypnotics may reduce risk
- Lower risk of poisonings with long-acting benzodiazepines compared with short-acting benzodiazepines and substantially lower risk associated with Z-drugs compared with either long- or short-acting benzodiazepines
- Switching benzodiazepine users from short-acting to long-acting agents or to Z-drugs may hold promise in lowering overdose risk

Discussion

- Even though benzodiazepines and Z-drugs may increase drug-related poisonings, buprenorphine's protective effect is not eliminated by benzodiazepine or Z-drug treatment
- Dose reduction in benzos and z-drugs while maintaining buprenorphine treatment can be advantageous.

Limitations

LIMITATIONS:

- Despite active comparator and case-crossover design, we cannot exclude the possibility of residual confounding by indication.
- Unmeasured exposures, such as illicit substances and nonprescribed benzodiazepines, have commonly been noted in the opioid user population (37) and warrant further investigation
- Secular time trends in exposure and outcome may introduce confounding into case-crossover designs
- Efforts to control for temporal variation and reduce heterogeneity in observation time per person using calendar time and time from event as a covariate and restricting study subjects to a maximum of 2-year periods of observation
- limited by its focus on nonfatal drug-related poisonings as opposed to poisoning deaths

Our Discussion

Thank You For Joining Us!

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Canadian Society of Addiction Medicine

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