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Social isolation proxy variables and prescription opioid and benzodiazepine misuse among older adults in the U.S.: A cross-sectional analysis of data from the National Survey on Drug Use and Health, 2015–2017

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ABSTRACT

Background: Prescription drug misuse in older adults is a growing public health problem. It is important to understand factors which predispose older adults to misuse prescription drugs, and social isolation may play an important role. In this study, we examined the association between social isolation proxy variables (living alone, being unmarried, and not attending religious services) and prescription opioid/benzodiazepine misuse in older adults.

Methods: With pooled cross-sectional data from the National Survey on Drug Use and Health (2015–2017), we used multinomial multiple logistic regression models to analyze the association between each social isolation proxy variable and past-year prescription opioid/benzodiazepine misuse. We controlled for potentially confounding variables including sociodemographic, physical/mental health, and substance use variables.

Results: Being unmarried was associated with approximately three times increased odds of combined opioid and benzodiazepine misuse (OR 2.98, 95% CI 1.75, 5.08), a finding that persisted after adjusting for multiple potential confounders. Further analysis showed this finding persisted for divorced/separated and never married individuals, but not widowed. Not attending religious services was also associated with prescription opioid/benzodiazepine misuse, but only in unadjusted analyses. There was no association between living alone and opioid/benzodiazepine misuse.

Conclusion: Increased odds of combined opioid and benzodiazepine prescription drug misuse was observed among unmarried older adults. Given the susceptibility of older adults to the harms of these medications, further exploration of the role of marital relationships and other forms of social connectedness in prescription drug misuse in this vulnerable population is indicated.

1. Introduction

Prescription drug misuse among older adults is an underappreciated (Center for Substance Abuse Treatment, 1998; Maree et al., 2016) but increasingly important public health concern (Schepis and McCabe, 2016). Although older adults are less likely to use illicit drugs compared to their younger counterparts (Culberson and Ziska, 2008), they are more likely to be prescribed psychoactive medications with abuse potential (Center for Substance Abuse Treatment, 1998; Simoni-Wastila et al., 2005; Simoni-Wastila and Yang, 2006), with an estimated 1 in 4 older adults using such medications (Simoni-Wastila and Yang, 2006; Substance Abuse and Mental Health Services Administration, 2015). This exposure places them at risk for prescription drug misuse, which is taking a medication in a manner other than as directed or indicated (Webster, 2017). Recent studies suggest that prescription drug misuse rates among older adults are increasing (Schepis and McCabe, 2016; Substance Abuse and Mental Health Services Administration, 2017; West et al., 2015; West and Dart, 2016) with prevalence estimates reaching 3.6% in 2015–2016 (McCabe et al., 2019). This is concerning because older adults are particularly susceptible to the harms of prescription drug misuse. Multiple factors contribute to this increased risk, including comorbid conditions, polypharmacy, frailty, cognitive impairment, and age-related changes in body physiology which can alter medication metabolism and increase side effects (Simoni-Wastila and Yang, 2006; Substance Abuse and Mental Health Services Administration, 2015; Wu and Blazer, 2011).

Opioids and benzodiazepines are two of the most commonly prescribed psychoactive medications in older adults (Simoni-Wastila et al.,

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2005). Although they can be used safely and effectively to treat conditions that commonly affect this population (e.g. chronic pain, anxiety), they are also among the prescription medications most commonly misused by older adults (Blazer and Wu, 2009; Schepis and McCabe, 2016; Wu and Blazer, 2011). Studies show that older adults who take opioids are at increased risk for sedation, impaired cognition and physical function, falls, injuries, and fractures (Buckeridge et al., 2010; Maree et al., 2016; Rolita et al., 2013; Simoni-Wastila and Yang, 2006; Spector et al., 2007). Compared to younger individuals, older adults who misuse opioids are also at increased risk for serious medical outcomes including death (West et al., 2015; West and Dart, 2016). Benzodiazepines can have similar harms in older adults (impaired cognition, falls, accidents) as well as other side effects such as paradoxical reactions, suicidality, and respiratory distress (Airagnes et al., 2016; Maree et al., 2016). Finally, opioids and benzodiazepines in combination are particularly dangerous and frequently implicated in overdose deaths (Airagnes et al., 2016).

Social isolation is an emerging public health concern (Holt-Lunstad, 2017) which may play a role in prescription drug misuse in older adults. The term "social isolation" refers to a deficit in the structure or function of social connections in one's life (Valtorta et al., 2016) and has been studied using specific scales (e.g. UCLA Loneliness Scale) as well as less specific indicators or proxy variables (e.g. being unmarried or living alone) (Cornwell and Waite, 2009; Valtorta et al., 2016). Recent studies show that social isolation is associated with numerous adverse health outcomes including depression, cognitive decline, dementia, decreased medication adherence, and even premature mortality (Holt-Lunstad, 2017). Social isolation has been described as a factor associated with substance abuse in older adults (Simoni-Wastila and Yang, 2006), but there are relative few studies regarding prescription drug misuse in older adults. In a small study of older adults with chronic pain (n = 163), using a specific scale for social support (the ENRICH Social Support Instrument) a suggestive association between reduced social support and increased risk of prescription opioid misuse was identified, but the finding did not reach statistical significance (p = 0.07) (Park and Lavin, 2010). Another small study of older adults found no significant association between living alone and prescription drug misuse (Chang, 2018). Several studies have shown increased odds of prescription drug misuse for unmarried individuals, although findings are not specific to older adults (Ford et al., 2018; Ford and Perna, 2015; Simoni-Wastila and Strickler, 2004). Finally, attendance at religious services has not been associated with increased odds of prescription drug misuse, but these findings are either not representative of or specific to older adults (Burdette et al., 2018; Ford et al., 2018). Given the paucity of data on social isolation and prescription drug misuse among older adults, and the potential for such findings to inform public health action, we decided to investigate further.

We evaluated the association between social isolation and prescription drug misuse in older adults using cross-sectional data from the National Survey on Drug Use and Health (NSDUH). More specifically, we assessed the association between three different social isolation proxy variables (lives alone, unmarried, and no religious services) and opioid/benzodiazepine misuse in adults aged 50 and older. We also assessed whether the association between each social isolation proxy variable and opioid/benzodiazepine misuse differed according to age group (50–64 years old vs. 65 +) and sex (male vs. female). We hypothesized that there would be a positive association between each social isolation proxy variable and opioid/benzodiazepine misuse, with those having the social isolation proxy variable (e.g. lives alone) having increased odds of opioid/benzodiazepine misuse compared to those without the proxy variable (e.g. does not live alone). Because baby boomers are more likely than older generations to have used psychoactive drugs (Johnson and Gerstein, 1998), we hypothesized that this association would be stronger for those aged 50–64 versus 65 and older. Since women may be more likely to be socially connected compared to men (Cornwell and Waite, 2009), we hypothesized that this association would be stronger for men than for women.

2. Methods

2.1. Study design and population

This study is a cross-sectional analysis of pooled data from the National Survey on Drug Use and Health (NSDUH) for years 2015–2017 (United States Department of Health and Human Services et al., 2017, 2016, 2015). The NSDUH is a nationally-representative survey conducted annually by RTI International and funded by the Substance Abuse and Mental Health Services Administration (SAMHSA). It serves as a major source of epidemiologic data on the use of illicit drugs, alcohol, tobacco, and mental health issues in the U.S. The target population for the survey is U.S. civilian, non-institutionalized individuals aged 12 and older (Center for Behavioral Health Statistics and Quality, 2018a). In 2015, the NSDUH underwent a partial redesign, which lead to a break in trend for certain variables from earlier survey years (Center for Behavioral Health Statistics and Quality, 2018b). For this reason, we pooled data starting from this "trend break" year through the most recently available year.

The NSDUH utilizes a multistage area probability sample for each of the 50 states and the District of Columbia. Data collection methods include a combination of computer-assisted personal interviewing and computer-assisted self-interviewing (Center for Behavioral Health Statistics and Quality, 2018a). The total national target sample size each year was 67,507 and the achieved sample size was 68,073, 67,942, and 68,032, for years 2015, 2016, and 2017, respectively. Due to application of a statistical disclosure limitation method to the full file, public use files include sample sizes of 57,146, 56,897, and 56,276, for each year in the analysis, respectively (Center for Behavioral Health Statistics and Quality, 2018b, 2018c, 2018a). For this study, we further restricted public use file samples to older individuals only (aged 50 and older), resulting in analytic sample sizes of 8,755, 8,853, and 8,714, for each year in the analysis, respectively, and a final analytic sample size of 26,322 for all years combined. Weighted screening response rates for each of the original samples was 81.9%, 77.9%, 75.1%, respectively. Weighted interview response rates for the original samples were 71.2%, 68.4%, 67.1%, respectively (Center for Behavioral Health Statistics and Quality, 2018b, 2018c, 2018a).

2.2. Measures

Three separate exposure variables were used as proxies for social isolation in the main analysis: lives alone (yes, no), unmarried (yes, no), and no religious services (yes, no). Individuals were identified as living alone if they reported living with no other individuals. Individuals were unmarried if they were widowed, divorced, separated, or never married. Individuals were identified as attending no religious services if they reported attending zero religious services in the past year. For an additional analysis, we also evaluated the exposure variable marital status (married, widowed, divorced or separated, never been married).

The main outcome variable was past-year opioid/benzodiazepine misuse and had four levels: opioid misuse alone, benzodiazepine misuse alone, combined opioid and benzodiazepine misuse, and no opioid or benzodiazepine misuse. Since 2015, NSDUH has identified prescription drug misuse by asking participants to report use of the drug in question in any way a doctor did not direct them to use it, including: 1) use without one's own prescription, 2) use in greater amounts, more often, or longer than they were told to take it, or 3) use in any other way a doctor did not direct them to take it (Center for Behavioral Health Statistics and Quality, 2018b, 2018c, 2018a).

The covariates were grouped into three categories: sociodemographic, physical/mental health, and substance use. The sociodemographic variables included: age (50–64 years old, 65 or older), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic,

Other), sex (male, female), total family income (less than $20,000, $20,000 to $49,999, $50,000 to $74,999, $75,000 or more), education (less than high school, high school graduate, some college/Associate Degree, College graduate), employment (employed full time, employed part time, unemployed, other), poverty level (living in poverty, income up to two times the federal poverty threshold, income more than two times the federal poverty threshold), health insurance (private only, Medicare only, Medicaid only, Medicare and Medicaid only, Medicare and private only, other, none), and urbanicity (large metro, small metro, nonmetro). Physical/mental health variables included: self-reported overall health (fair/poor, not fair/poor), activities of daily living (ADL) disability (yes, no), instrumental activities of daily living (IADL) disability (yes, no), past-year suicidal thoughts (yes, no), and past-year major depressive episode (yes, no). ADL disability was considered present for individuals who reported having a condition which caused serious difficulty either a) concentrating, remembering, or making decisions, b) walking or climbing stairs, or c) dressing or bathing. IADL disability was considered present for individuals who reported having a condition which caused difficulty doing errands alone. Substance use variables included: smoking recency (within the past 30 days, more than 30 days ago but within the past year, more than one year ago but within the past 3 years, more than 3 years ago, never smoked cigarettes), past-month binge drinking (yes, no), and past-year marijuana use (yes, no). Although the NSDUH datasets include a variable for past-year illicit drug use other than marijuana, it could not be considered in this analysis because all individuals with past-year prescription opioid/benzodiazepine misuse also had a history of past-year other illicit drug use. Therefore, past-year other illicit drug use was not included in the models to avoid issues of collinearity. Finally, person level weights were adjusted by dividing by number of years in the analysis (three).

2.3. Statistical analysis

Preliminary analyses evaluated the distribution and frequency of variables of interest. Univariate sample characteristics were evaluated with application of weighting and nesting variables. We examined unadjusted associations between the exposures and the outcome using multinomial logistic regression. We also tested for interaction by age or sex by addition of interaction terms to the unadjusted model. Since there was no evidence for interaction in the preliminary stage, we did not explore further potential for interaction in later analyses.

Using prior knowledge from our literature review, we selected variables for our analysis and constructed a causal diagram to graph the causal assumptions underlying our analysis. We then employed a confounder selection criterion referred to as “disjunctive cause criterion,” which offers a conservative method for selecting confounders for control when causal relationships are complex or unknown (VanderWeele and Shpitser, 2011). Each of the covariates met the disjunctive cause criterion as potential confounders. We then used Chi-square tests to evaluate bivariate associations between the covariates and the exposure variables, and also between the covariates and the outcome variable. We decided *a priori* to include all covariates that met disjunctive cause criterion and were associated with any of the three main exposure variables and the outcome variable (at a significance level of $p < 0.10$). Because each of the covariates met disjunctive cause criterion and was significantly associated with at least one exposure variable and the outcome variable, all the covariates were considered potential confounders.

For our final analysis we added the potential confounders to the unadjusted multinomial logistic regression models for each exposure. We added potential confounders by categories of similar variables (sociodemographics, physical/mental health, and substance use) to see the relative influence of each set of related variables. We employed this process for each of our three main exposure variables (lives alone, unmarried, no religious services) as well as our additional analysis exposure variable (marital status). Significance for regression model estimates was determined using Wald confidence limits and Wald chi-square tests with a significance level of 0.05.

Lastly, we performed a supplemental analysis to evaluate the main reason for last opioid misuse and last tranquilizer misuse (including benzodiazepine tranquilizers) among married versus unmarried older adults.

All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC). Results were generated using survey procedures (i.e. SURVEYFREQ, SURVEYLOGISTIC) with incorporation of survey weights and nesting variables.

2.4. Ethics

This analysis was deemed exempt from Institutional Review Board review at the University of Maryland since it involved use of publicly available datasets from which individual subjects cannot be identified.

3. Results

3.1. Sample characteristics

There were 26,322 individuals aged 50 and older in the combined dataset for years 2015–2017, representing a weighted sample size of 110,622,733 (Table 1).

Regarding the main exposure variables, the majority of individuals lived with others (80.7%), were married (61.8%), and/or attended at least one religious service in the past year (62.5%). Regarding the outcome variable, 3.1% misused either opioids alone, benzodiazepines alone, or both opioids and benzodiazepines in the past year (2.1%, 0.7%, and 0.3%, respectively).

Concerning the covariates, the majority of individuals were aged 50–64 (56.4%), and there were more females than males (53.2% vs. 46.8%, respectively). The sample was majority Non-Hispanic White (72.9%), with Non-Hispanic Blacks and Hispanics being the next two largest racial/ethnic groups represented (10.4% and 10.4%, respectively). Regarding socioeconomic variables, the majority of individuals had a total family income greater than $50,000, at least some college education or Associate degree, and had an employment status of ‘other’ (which includes retired or disabled). About 20% rated their overall health as fair/poor and a similar proportion also reported an ADL disability. Less than 5% had experienced a major depressive episode in the past year and 2.5% reported past-year suicidal thoughts. For substance use, almost two-thirds had a history of smoking, more than 1 in 6 reported binge drinking in the past 30 days, and about 7% reported past-year marijuana use.

3.2. Unadjusted analyses

Table 2 shows both unadjusted (Model 1) and adjusted (Models 2–4) multinomial logistic regression models for the association between each main exposure variable (lives alone, unmarried, and no religious services) and past-year prescription opioid/benzodiazepine misuse. Living alone was not associated with past-year prescription opioid/benzodiazepine misuse for any of the categories of misuse. Conversely, being unmarried was significantly associated with increased odds of past-year prescription opioid/benzodiazepine misuse for each category of misuse, with the strongest association for combined opioid and benzodiazepine misuse (OR 3.72, 95% CI 2.10, 6.59). Further analysis of marital status (Table 3) showed a similarly increased odds of combined opioid and benzodiazepine misuse for divorced/separated and never married, but not widowed individuals. No attendance at religious services (Table 2) was significantly associated with increased odds of opioid misuse alone and combined opioid and benzodiazepine misuse, but not benzodiazepine misuse alone. There was no evidence for interaction (global p-value < 0.05) in any of the unadjusted models with testing for interaction by age (50–64 vs. 65 +) or sex (male vs. female).

Table 1
Sample characteristics, Adults aged 50 and older, National Survey on Drug Use and Health, 2015–2017 (weighted sample n = 110622733).

Category	Variable	Values	Unweighted Frequency[1] (n = 26322)	Weighted Percent[2]	SE of Percent
Exposures (Main Analysis)	Lives alone	Yes	5774	19.3	0.30
		No	20548	80.7	0.30
	Unmarried	Yes	10683	38.2	0.41
		No	15639	61.8	0.41
	No religious services	Yes	10088	37.5	0.41
		No	15994	62.5	0.41
Exposure (Additional Analysis)	Marital status	Married	15639	61.8	0.41
		Widowed	3243	12.0	0.27
		Divorced or separated	5127	18.3	0.34
		Never been married	2313	7.8	0.20
Outcome	Past-year opioid/benzodiazepine misuse	Opioid misuse alone	547	2.1	0.09
		Benzodiazepine misuse alone	169	0.7	0.06
		Combined opioid and benzodiazepine misuse	97	0.3	0.05
		No opioid or benzodiazepine misuse	25509	96.9	0.12
Sociodemographic	Age	50-64 years old	15395	56.4	0.37
		65 or older	10927	43.6	0.37
	Race/ethnicity	Non-Hispanic White	19200	72.9	0.40
		Non-Hispanic Black	2849	10.4	0.26
		Hispanic	2509	10.4	0.32
		Other	1764	6.3	0.21
	Sex	Male	12041	46.8	0.45
		Female	14281	53.2	0.45
	Total family income	Less than $20,000	4559	15.8	0.36
		$20,000 - $49,999	8316	30.2	0.37
		$50,000 - $74,999	4348	16.7	0.27
		$75,000 or more	9099	37.3	0.47
	Education	Less than high school	3813	14.1	0.33
		High school graduate	7381	26.8	0.34
		Some college/Associate Degree	7357	27.5	0.33
		College graduate	7771	31.6	0.50
	Employment	Employed full time	9525	36.2	0.39
		Employed part time	3020	11.1	0.22
		Unemployed	686	2.4	0.11
		Other	13091	50.2	0.38
	Poverty level	Living in poverty	2858	10.1	0.31
		Income up to 2X federal poverty threshold	5270	19.1	0.31
		Income more than 2X federal poverty threshold	18194	70.8	0.42
	Health insurance	Private only	10433	39.4	0.37
		Medicare only	2634	10.4	0.22
		Medicaid only	1459	4.8	0.19
		Medicare and Medicaid only	1214	4.4	0.23
		Medicare and private only	6512	25.9	0.32
		Other	2904	10.6	0.28
		None (uninsured)	1166	4.5	0.14
	Urbanicity	Large metro	11146	52.8	0.48
		Small metro	9138	30.9	0.52
		Nonmetro	6038	16.3	0.34
Physical/Mental Health	Self-reported overall health	Fair or poor	5334	19.6	0.39
		Not fair or poor	20983	80.4	0.39
	Activities of daily living (ADL) disability	Yes	5445	20.2	0.30
		No	20746	79.8	0.30
	Instrumental activities of daily living (IADL) disability	Yes	1900	7.1	0.22
		No	24313	92.9	0.22
	Past-year suicidal thoughts	Yes	689	2.5	0.10
		No	25633	97.5	0.10
	Past-year major depressive episode	Yes	1304	4.7	0.14
		No	25018	95.3	0.14
Substance use	Smoking recency	≤ 30 days	4347	15.3	0.29
		> 30 days but ≤ 1 year	440	1.6	0.10
		> 1 year but ≤ 3 years	530	2.0	0.12
		> 3 years	11732	45.2	0.34
		Never	9273	36.0	0.37
	Past-month binge drinking	Yes	4690	17.6	0.30
		No	21632	82.4	0.30
	Past-year marijuana use	Yes	1865	6.7	0.21
		No	24457	93.3	0.21

Abbreviations: standard error (SE).
[1] Counts for some covariates do not add to final sample size due to missing data.
[2] Some column percentages do not add to 100% due to rounding error.

Table 2
Multinomial logistic regression models for association between social isolation proxy variables and past-year prescription opioid/benzodiazepine misuse, Adults aged 50 and older, National Survey on Drug Use and Health, 2015–2017.

Social isolation proxy variables		Opioid misuse alone		Benzodiazepine misuse alone		Combined opioid and benzodiazepine misuse		No misuse	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Lives alone	Model 1	0.84	(0.64, 1.10)	1.23	(0.79, 1.93)	1.43	(0.88, 2.33)	1	Ref
	Model 2	0.78	(0.57, 1.07)	1.23	(0.76, 2.01)	1.34	(0.74, 2.40)	1	Ref
	Model 3	0.78	(0.58, 1.05)	1.20	(0.74, 1.96)	1.42	(0.78, 2.57)	1	Ref
	Model 4	0.75	(0.55, 1.02)	1.14	(0.70, 1.88)	1.29	(0.70, 2.38)	1	Ref
Unmarried	Model 1	1.29*	(1.04, 1.60)	1.46*	(1.02, 2.10)	3.72***	(2.10, 6.59)	1	Ref
	Model 2	1.10	(0.85, 1.43)	1.56*	(1.00, 2.44)	3.56***	(1.93, 6.59)	1	Ref
	Model 3	1.06	(0.81, 1.40)	1.48	(0.94, 2.35)	3.95***	(2.33, 6.70)	1	Ref
	Model 4	0.94	(0.71, 1.25)	1.35	(0.85, 2.13)	2.98***	(1.75, 5.08)	1	Ref
No religious services	Model 1	1.53***	(1.23, 1.90)	1.12	(0.80, 1.56)	1.64*	(1.07, 2.51)	1	Ref
	Model 2	1.36**	(1.08, 1.71)	1.06	(0.76, 1.48)	1.17	(0.74, 1.87)	1	Ref
	Model 3	1.35**	(1.08, 1.70)	1.06	(0.75, 1.48)	1.12	(0.71, 1.77)	1	Ref
	Model 4	1.16	(0.93, 1.46)	0.90	(0.64, 1.26)	0.81	(0.52, 1.25)	1	Ref

Abbreviations: odds ratio (OR), confidence interval (CI), reference (Ref).
Model 1: unadjusted.
Model 2: adjusted for sociodemographic variables.
Model 3: adjusted for sociodemographic + physical/mental health variables.
Model 4: adjusted for sociodemographic + physical/mental health + substance use variables.
* Significant at $p < 0.05$.
** Significant at $p < 0.01$.
*** Significant at $p < 0.001$.

3.3. Adjusted analyses

Similar to the unadjusted model, in each of the adjusted models there was no significant association between living alone and past-year prescription opioid/benzodiazepine misuse for any of the categories of misuse. After adjusting for sociodemographic variables, the association between being unmarried and opioid misuse alone became non-significant. Similarly, after adjusting for sociodemographic and physical/mental health variables, the association between being unmarried and benzodiazepine misuse alone became non-significant. However, after adjusting for all covariates (sociodemographic, physical/mental health, and substance use variables), the association for combined opioid and benzodiazepine misuse remained strongly significant (OR 2.98, 95% CI 1.75, 5.08; $p < 0.0001$). Further analysis of marital status (Table 3) again showed significantly increased odds of combined opioid and benzodiazepine misuse for both divorced/separated (OR 2.86, 95% CI 1.61, 5.06) and never married (OR 3.78, 95% CI 1.80, 7.92), but not widowed individuals (OR 2.44, 95% CI 0.90, 6.59). Adjusted analyses for marital status also revealed a significantly increased odds of benzodiazepine misuse alone for never married individuals (OR 2.02, 95% CI 1.03, 3.96), a finding which was not seen in the fully adjusted model for unmarried. The associations between attendance at religious services and opioid misuse either alone or combined with benzodiazepine misuse became non-significant after adjusting for confounders (Table 2).

Less than 2% of observations were excluded from the final regression models due to missingness in the variables of interest. Final sample sizes for each model were as follows: 26,169 for lives alone, unmarried,

Table 3
Multinomial logistic regression models for association between marital status and past-year prescription opioid/benzodiazepine misuse, Adults aged 50 and older, National Survey on Drug Use and Health, 2015–2017.

Marital status[1]		Opioid misuse alone		Benzodiazepine misuse alone		Combined opioid and benzodiazepine misuse		No misuse	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Widowed	Model 1	0.93	(0.65, 1.34)	0.83	(0.53, 1.31)	1.43	(0.54, 3.80)	1	Ref
	Model 2	1.17	(0.77, 1.76)	1.01	(0.61, 1.64)	2.22	(0.75, 6.55)	1	Ref
	Model 3	1.17	(0.77, 1.76)	0.97	(0.58, 1.61)	2.82*	(1.08, 7.35)	1	Ref
	Model 4	1.13	(0.75, 1.70)	0.95	(0.57, 1.58)	2.44	(0.90, 6.59)	1	Ref
Divorced or separated	Model 1	1.48***	(1.19, 1.85)	1.57	(0.95, 2.60)	4.47***	(2.47, 8.10)	1	Ref
	Model 2	1.16	(0.89, 1.51)	1.62	(0.92, 2.85)	3.78***	(2.05, 6.98)	1	Ref
	Model 3	1.07	(0.81, 1.41)	1.49	(0.84, 2.67)	3.98***	(2.29, 6.94)	1	Ref
	Model 4	0.91	(0.68, 1.22)	1.31	(0.72, 2.36)	2.86***	(1.61, 5.06)	1	Ref
Never married	Model 1	1.39	(0.94, 2.06)	2.12**	(1.29, 3.71)	5.34***	(2.60, 11.77)	1	Ref
	Model 2	0.92	(0.60, 1.41)	2.19*	(1.14, 4.21)	4.31***	(2.02, 9.17)	1	Ref
	Model 3	0.94	(0.62, 1.43)	2.17*	(1.12, 4.18)	4.86***	(2.39, 9.88)	1	Ref
	Model 4	0.83	(0.53, 1.30)	2.02*	(1.03, 3.96)	3.78***	(1.80, 7.92)	1	Ref

Abbreviations: odds ratio (OR), confidence interval (CI), reference (Ref).
Model 1: unadjusted.
Model 2: adjusted for sociodemographic variables.
Model 3: adjusted for sociodemographic + physical/mental health variables.
Model 4: adjusted for sociodemographic + physical/mental health + substance use variables.
[1] Reference group for each level of marital status shown is Married.
* Significant at $p < 0.05$.
** Significant at $p < 0.01$.
*** Significant at $p < 0.001$.

and marital status, and 25,998 for no religious services.

3.4. Supplementary analysis

Among older adults with past-year opioid misuse, most unmarried and married individuals reported their last opioid misuse was mainly *to relieve physical pain* (greater than 70% for each group) (Supplementary Figure 1). Among older adults with past-year tranquilizer benzodiazepine misuse, most unmarried and married older adults misused tranquilizers mainly *to relax or relieve tension* or *to help with sleep*, with unmarried older adults having a higher proportion in *relax or relieve tension* (46.2% vs. 38.2% in married individuals) and married older adults having a higher proportion in *help with sleep* (48.1% vs. 28.5% in unmarried individuals) (Supplementary Figure 2).

4. Discussion

4.1. Context

As the U.S. population ages, we are seeing increasing rates of prescription drug misuse among older adults (Schepis and McCabe, 2016). This is likely influenced by the entry of baby boomers into the older cohort, as the baby boomer generation is both larger and more experienced with psychoactive substances compared to prior generations (Han et al., 2009; Simoni-Wastila and Yang, 2006). This concerning trend comes as researchers now warn of increasing social isolation in the U.S. population (Holt-Lunstad, 2017). Therefore, there is an increasing need to understand factors associated with prescription drug misuse in older adults within this evolving social context. Our research addresses this research gap by evaluating the association between social isolation proxy variables and opioid/benzodiazepine misuse in older adults.

4.2. Main results

In this study, we found that being unmarried is associated with approximately three times increased odds of combined opioid and benzodiazepine misuse in the past year for older adults, a finding that persisted even after adjusting for multiple potential confounders (OR 2.98, 95% CI 1.75, 5.08). Further evaluation by marital status revealed similar findings for divorced/separated and never married, but not widowed individuals, as well as the additional finding of significantly increased odds of benzodiazepine misuse alone among never married individuals. Regarding other social isolation proxy variables, we found that not attending religious services was associated with increased odds of opioid misuse alone and combined opioid and benzodiazepine misuse. However, these findings had only modest effect sizes and they became non-significant after adjusting for confounders. Lastly, there was no association between living alone and opioid/benzodiazepine misuse in either unadjusted or adjusted analyses, suggesting that this proxy variable is not helpful for predicting older adults' tendency to misuse opioids/benzodiazepines.

4.3. Comparison to prior literature

Our results are consistent with prior studies involving adults of all ages and add to prior literature where there is a currently a paucity of data specific to older adults. Regarding unmarried status, Simoni-Wastila et al. (2004) found that for individuals aged 12 and older, in adjusted analyses, being unmarried was significantly associated with prescription opioid misuse (Simoni-Wastila and Strickler, 2004). Our study differed slightly, in that we found a significant association for unmarried older adults and combined opioid and benzodiazepine misuse, but not for opioid misuse alone. Our study was also consistent with two more recent studies by Ford et al., which showed a protective effect of being married on general prescription drug misuse in adults of all ages (Ford et al., 2018; Ford and Perna, 2015). Considering attendance at religious services, our study is consistent with prior studies (which did not focus on older adults) that failed to demonstrate an association with prescription drug misuse in adjusted analyses (Ford et al., 2018) or in longitudinal data (Burdette et al., 2018). Finally, regarding living alone, our study was consistent with a study by Chang et al., which showed that in a small population of older adults (n = 130) there was no association between living alone and general prescription drug misuse (Chang, 2018).

4.4. Strengths and limitations

There are several strengths to our study. To our knowledge, it is the first to use a large, nationally representative dataset to evaluate the association between social isolation proxy variables and prescription drug misuse in older adults. Previous studies were limited to small samples of older adults or large samples of adults of all ages, from which conclusions about older adults may differ. Next, given the extensive nature of the data collected in the NSDUH, we were able to control for multiple potential confounders in examining these relationships. Finally, by combining three years' worth of data, we increased our sample size substantially which may have helped detect relationships which might not be identifiable in smaller samples.

There are also a number of limitations to our study. First, although we chose to use proxy variables to assess social isolation based on prior research (Cornwell and Waite, 2009), we are unable to assess the correlation between these variables and a more direct measure of social isolation, such as using a specific scale, in this dataset. Given the differing findings for each proxy variable, it is possible they may have varying degrees of correlation with social isolation. Furthermore, it is also possible that our findings may have more to do with the proxy variable itself (e.g. marital status) than the actual phenomenon of social isolation. Second, given the cross-sectional nature of the study, we are unable to infer causality and our findings may also be biased by "reverse causality," or the negative impact prescription drug misuse or related factors may have on marital status. Third, there may be residual confounding since we were unable to control for illicit drug use other than marijuana. However, the effect size of our finding suggests that residual confounding is unlikely to completely explain these results. Fourth, because the NSDUH is self-reported, there may be inaccuracies in individuals' reporting of drug misuse and other behaviors. However, NSDUH data collection is highly private and utilizes methods such as pictures of medications to improve the accuracy of respondents' recall (Center for Behavioral Health Statistics and Quality, 2018a). Fifth, we studied past-year prescription drug misuse without regard to history of prescription drug misuse. Although past-year initiation of prescription drug misuse may provide more clarity to the direction of an association with social isolation proxy variables, we anticipated the sample sizes of this less common behavior would be too small to detect such a relationship. Sixth, for consistency with prior literature (Chang, 2018; Schepis and McCabe, 2016; Wu and Blazer, 2011), we chose to study 'older adults' using the age cutoff of 50 years old. However, adults in their 50 s are very likely to be different from adults in their 70 s or 80 s in many ways. Although we tested for interaction by age in our preliminary analysis and controlled for age in our final models, it is still possible that this approach did not fully capture age-related differences which might contribute to prescription drug misuse behaviors. Finally, the NSDUH excludes institutionalized individuals so our findings are not applicable to older adults in institutionalized settings (e.g. nursing homes, prisons, etc.).

4.5. Implications

This study has important implications from both a public health and research perspective. From a public health perspective, these findings support prior literature which suggests that being unmarried is

associated with increased odds of prescription drug misuse. Our study identifies unmarried older adults (in particular divorced/separated and never married individuals) as having increased odds of combined prescription opioid and benzodiazepine misuse. It also identifies never married older adults as a subgroup with increased odds of benzodiazepine misuse alone. These findings are concerning given the susceptibility of older adults to the harms of psychoactive medications and the attendant risks of these two medication classes, especially when combined (e.g. increased risk of fatal and non-fatal overdose) (Jones et al., 2012). This serves as a reminder of the importance of limiting older adults' exposure to psychoactive medications by avoiding unnecessary or inappropriate prescriptions of opioids and benzodiazepines. From a research perspective, it provides the impetus for further exploration of the drivers of the relationship between marital status and prescription drug misuse behaviors. Longitudinal studies and studies which utilize specific social isolation scales are likely to help elucidate this important association further.

5. Conclusions

In this cross-sectional analysis of pooled data from NSDUH (2015–2017), we examined the association between social isolation proxy variables (lives alone, unmarried, no religious services) and past-year opioid/benzodiazepine prescription drug misuse. We found that being unmarried was significantly associated with increased odds of combined opioid and benzodiazepine misuse (OR 2.98, 95% CI 1.75, 5.08) even after adjusting for multiple potential confounders. This research suggests unmarried older adults may be a subgroup at risk for opioid/benzodiazepine misuse, and serves as a reminder of the importance of limiting older adults' exposure to psychoactive prescription drugs.

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Contributors

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Declaration of Competing Interest

No conflict declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.06.020.

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