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Short communication

Trends in and correlates of tranquilizer misuse among adults who misuse opioids in the United States, 2002–2014

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ABSTRACT

Purpose: Almost a third of opioid overdose deaths also involve benzodiazepines, but few representative studies have examined misuse of benzodiazepines and other tranquilizers by adults who misuse opioids. This study estimated the prevalence and frequency of tranquilizer misuse among adults who misuse opioids and examined characteristics associated with tranquilizer misuse.
Methods: A sample of adults who misused opioids in the past year (n = 36,043) were identified in the National Surveys on Drug Use and Health 2002–2014. Tranquilizer misuse prevalence was estimated for each year from 2002 to 2014. Data were then pooled for all years. Multiple logistic and Poisson regression was used to identify characteristics independently associated with the prevalence and frequency tranquilizer misuse respectively.
Results: Twenty-eight percent of adults who misused illicit opioids in the past year also reported tranquilizer misuse. This prevalence did not change notably over the 13-year period examined. Among those who misused opioids, meeting criteria for opioid abuse or dependence was associated with a 134% increase in the odds of misusing tranquilizers during the same year. Other characteristics associated with increased odds of tranquilizer misuse included being aged 18–25 years, non-Hispanic white, uninsured, unemployed, and having used heroin.
Conclusions: Tranquilizer misuse is common among adults who misuse opioids and has not changed substantially over the past decade. Meeting criteria for abuse or dependence of opioids is associated with more than double the odds of tranquilizer misuse among adults who misuse opioids.

1. Introduction

Opioid misuse has reached epidemic proportions in the United States. The concomitant use of opioids and tranquilizers may potentiate respiratory depression, increasing risk for fatal overdose (Jones et al., 2012), and in the United States, an estimated 30% of fatal opioid overdoses also involve tranquilizers such as benzodiazepines (Saunders et al., 2012; Morasco et al., 2010). From 1996 to 2013, opioid overdose deaths involving benzodiazepines rose at a faster rate than the number of people filling benzodiazepine prescriptions and the amount filled (Bachhuber et al., 2016). A large retrospective study of privately insured patients found concurrent benzodiazepine and opioid prescribing increased by almost 80% from 2001 to 2013 (Sun et al., 2017). In 2008, among persons entering treatment for opioid misuse, about 54% also reported benzodiazepine misuse (Substance Abuse and Mental Health Services Administration and Center for Behavioral Health Statistics and Quality, 2011). Despite the growing need to better understand co-occurring opioid and tranquilizer misuse, no previous work has examined 1) trends in self-reported tranquilizer misuse among adults who misused opioids; 2) demographic or health-related characteristics associated with tranquilizer misuse among adults who have reported opioid misuse; or 3) how the association of these characteristics with tranquilizer misuse has changed over time.

2. Methods

2.1. Data

The National Survey on Drug Use and Health (NSDUH) collects annual information about the misuse of drugs, alcohol, tobacco, and other related behavioral health indicators among the non-institutionalized U.S. civilian population aged ≥12 years via household face-to-face interviews using a computer-assisted personal interviewing system. We used data from the 2002–2014 surveys. Analysis was restricted to adults 18 years and older as certain important covariates of interest (i.e. employment and education level) did not have a valid

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interpretation for respondents aged 12–17 years. Analysis of prevalence trends (see "2.3.1 Analysis – Trends") included this full sample of adults (n = 482,369). Analyses of characteristics associated with tranquilizer misuse among adults who misused opioids (see "2.3.2 Analysis – Correlates" and "2.3.3 Analysis – Change in Correlates Over Time") were further restricted to the subsample of respondents who misused opioids (n = 36,043).

2.2. Measures

Opioid misuse was defined as a past 12-month report of either using opioid analgesics (e.g., codeine, morphine, oxycodone) that were not prescribed or taken only for the experience or feeling they caused or using any heroin during the past 12 months. Opioid abuse or dependence was based on meeting diagnostic criteria contained in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* within the past 12 months (American Psychiatric Association, 2000). Tranquilizer misuse was defined as a past 12-month report of using tranquilizers ("nerve pills") such as benzodiazepines (e.g., clonazepam, alprazolam, diazepam), other anxiolytics (e.g., buspirone, meprobamate), or muscle relaxants (e.g., carisoprodol, cyclobenzaprine) that were not prescribed or were taken only for the experience or feeling they caused. Among adults who misused tranquilizers at least once, frequency of misuse was defined as the number of days of use in the past 12 months. Factors examined for an association with tranquilizer misuse among adults who misused opioids include sex, age, race/ethnicity, education status, employment status, poverty status, insurance coverage, use of heroin, and meeting criteria for opioid abuse or dependence.

2.3. Analysis

2.3.1. Trends

We weighted, clustered, and stratified data to provide nationally representative estimates. Tranquilizer misuse prevalence among adults who did and did not misuse opioids was estimated and plotted during each year from 2002 to 2014.

2.3.2. Correlates

Data were then pooled for all years and restricted to adults who misused opioids. The prevalence of tranquilizer misuse was estimated for each characteristic examined. We then used multiple logistic regression analysis to examine characteristics independently associated with tranquilizer misuse. Further, among adults who misused both opioids and tranquilizers, the median number of days of tranquilizer misuse was estimated for each characteristic examined. We used Poisson regression analysis to examine characteristics independently associated with number of days of tranquilizer misuse. We obtained adjusted odds ratios and adjusted rate ratios by taking the exponential of logistic and Poisson regression model coefficients respectively.

2.3.3. Change in correlates over time

To test if the observed association of each covariate with tranquilizer misuse grew stronger or weaker over time, we added an interaction term between each covariate and a linear time trend to both regression models. Models with and without interaction were compared with a Rao-Scott F-test; a significant F-test indicates allowing interaction would significantly improve model fit. For correlates identified as significant in the no-interaction model, individual statistically significant interaction coefficients and their direction were reported to indicate whether the association of each covariate with tranquilizer misuse grew stronger or weaker over time.

In all analyses, standard errors and 95% confidence intervals were estimated using Taylor series linearization to account for complex survey design elements.

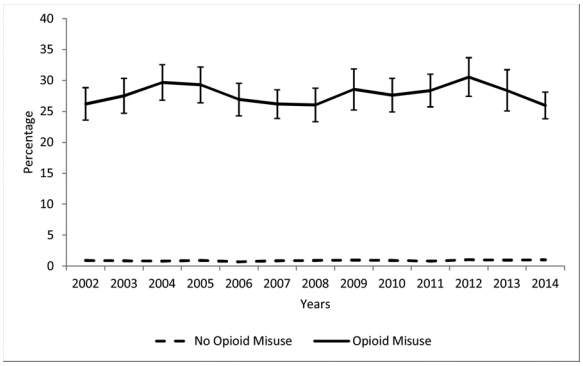

Fig. 1. Percentage of persons aged ≥18 years who reported tranquilizer misuse among those who did and did not report opioid misuse in the past year — National Survey on Drug Use and Health, United States, 2002–2014.

3. Results

3.1. Trends

In the United States, between 2002 and 2014, 28% of adults who misused opioids also misused tranquilizers, compared with < 1% of adults who did not misuse opioids (Fig. 1). During this period, there was no change in the prevalence of tranquilizer misuse among adults who misused opioids.

3.2. Correlates

During 2002–2014, among adults who misused opioids, the factor most strongly associated with tranquilizer misuse in the same year was having opioid abuse or dependence (aOR 2.34, 95% CI = 2.11–2.59). Among adults who misused opioids, those who were aged 18–25 years, non-Hispanic white, uninsured, unemployed, using heroin, or had at least some college education also had increased odds of tranquilizer misuse in the same year compared with each respective reference group (Table 1).

In this population, the factor most strongly associated with a higher number of days of tranquilizer misuse was also having opioid abuse or dependence (aRR 1.89, 95% CI = 1.71–2.09). Having a high school education or less, being aged ≥26 years, non-Hispanic black, unemployed, or not in the labor force were also associated with increased number of days of tranquilizer misuse in the same year (Table 1).

3.3. Change in correlates over time

Both models for prevalence (2logLR = 50.11, df = 133, p = 0.002) and frequency of misuse (2logLR = 38.50, df = 133, p = 0.025) were significantly improved by adding interaction terms. Examining individual interaction terms showed that the following associations with any tranquilizer misuse prevalence changed over time: 1) The protective effect of being 26–34 years old compared to being 18–25 years old grew weaker (B = 0.025, p = 0.02; 2). 2) The respective protective effects of being black and Hispanic as compared to being white grew weaker (B = 0.067, p = 0.002; B = 0.038, p = 0.032). 3) The protective effect of having health insurance grew weaker (B = 0.027, p = 0.014). 4) The associated risk of having met criteria for opioid abuse or dependence grew stronger (B = 0.027, p = 0.049). Further, examining individual interaction terms showed that one association with the frequency of tranquilizer misuse changed over time: 1) being 26–34 years old as compared to being 18–25 years old was associated with increased frequency of tranquilizer misuse over time (B = 0.028, p = 0.031).

Table 1
Reported tranquilizer misuse among persons aged ≥18 years who reported opioid misuse in the past year by selected characteristics — National Survey on Drug Use and Health, United States, 2002–2014.
Source: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2002–2014.

Characteristic	Opioid misuse %	Tranquilizer misuse		aOR (95% CI)[†]	aRR (95% CI)[§]
		%	Median no. of use days[*]		
Sex					
Male	55.90	27.67	15	1.00	1.00
Female	44.10	28.01	12	1.08 (0.99–1.17)	0.99 (0.91–1.07)
Age group (yrs)					
18–25	35.34	32.54	14	1.00	1.00
26–34	24.59	29.73	12	0.86 (0.78–0.95)[††]	1.15 (1.04–1.27)[**]
35–49	26.21	24.12	15	0.68 (0.61–0.74)[††]	1.17 (1.04–1.31)[¶]
≥50	13.86	19.41	20	0.52 (0.43–0.62)[††]	1.26 (1.00–1.58)[¶]
Race/Ethnicity					
Non-Hispanic white	72.12	31.66	12	1.00	1.00
Non-Hispanic black	9.33	16.37	48	0.41 (0.36–0.48)[††]	1.21 (1.03–1.42)[¶]
Hispanic	13.66	18.41	15	0.48 (0.41–0.55)[††]	0.85 (0.70–1.02)
Other	4.90	19.33	12	0.52 (0.44–0.63)[††]	0.84 (0.71–1.01)
Highest level of education					
Less than high school	19.55	26.60	25	1.00	1.00
High school graduate	32.05	28.30	24	1.09 (1.00–1.20)	0.84 (0.75–0.94)[**]
Some college	29.64	29.05	12	1.15 (1.05–1.26)[**]	0.75 (0.67–0.85)[††]
College graduate	18.77	26.33	7	1.17 (1.04–1.33)[¶]	0.51 (0.43–0.60)[††]
Employment					
Full time	54.97	26.03	12	1.00	1.00
Part time	16.47	29.33	12	1.07 (0.95–1.19)	1.00 (0.87–1.15)
Unemployed	9.45	36.08	24	1.39 (1.21–1.60)[††]	1.13 (1.01–1.26)[¶]
Not in labor force	19.11	27.60	24	1.11 (0.98–1.25)	1.19 (1.06–1.34)[**]
Poverty status					
Living in poverty	18.84	28.38	24	1.00	1.00
Income up to 2x federal poverty threshold	22.57	27.34	21	0.96 (0.84–1.10)	1.01 (0.88–1.17)
Income > 2x federal poverty threshold	58.58	27.83	12	1.03 (0.92–1.14)	0.94 (0.83–1.06)
Health insurance					
No	26.87	32.72	24	1.00	1.00
Yes	73.13	26.02	12	0.76 (0.70–0.82)[††]	0.88 (0.81–0.98)[¶]
Heroin use					
No	94.99	26.94	12	1.00	1.00
Yes	5.01	44.49	36	1.34 (1.14–1.59)[††]	1.06 (0.91–1.23)
Opioid abuse or dependence					
No	83.72	24.61	10	1.00	1.00
Yes	16.28	44.34	36	2.34 (2.11–2.59)[††]	1.89 (1.71–2.09)[††]

Abbreviation: aOR = adjusted odds ratio; aRR = adjusted rate ratio; CI = confidence interval.
[*] Among persons who reported tranquilizer misuse at least once in the past year.
[†] Relative odds of reporting tranquilizer use at least once in the past year.
[§] Relative increase in number of days of tranquilizer misuse among persons who reported tranquilizer misuse at least once in the past year.
[¶] *P*-value < 0.05.
[**] *P*-value ≤0.01.
[††] *P*-value < 0.001.

4. Discussion

During 2002–2014, nearly 3 in 10 adults who misused opioids also misused tranquilizers. Despite recent actions taken by federal and state health departments, legislators, and professional societies to mitigate the current opioid crisis (Cicero et al., 2015), the prevalence of tranquilizer misuse among adults who misuse opioids has not changed substantially over the past decade. Further, these findings suggest that the high rate of tranquilizer-involved opioid overdose seen in recent years in the United States is not due to an increase in tranquilizer misuse among adults who misuse opioids, but rather an overall increase in the prevalence of opioid misuse during which time the prevalence of tranquilizer use has remained stable.

To our knowledge, this is the first report to identify a number of characteristics significantly associated with increased odds and frequency of tranquilizer misuse among adults who misuse opioids. The strength of the risk factors we identified for the most part did not change from 2002 to 2014, and those changes in strength over the time period that did occur were relatively small. The strongest risk factor identified for both using tranquilizers and using tranquilizers more frequently was meeting criteria for opioid abuse or dependence. Among those meeting criteria for opioid abuse or dependence, 45% misused tranquilizers, and the median number of days per year of misuse among tranquilizer misusers was 36. As people with opioid use disorder are already at high risk for fatal overdose, it is especially concerning that this population may be heightening their risk even more by misusing tranquilizers. Future work is needed to discern whether the socio-demographic and health-related risk factors identified are also related to tranquilizer-involved opioid overdose rates. Additionally, the motivation for tranquilizer misuse among opioid users is poorly understood, and is an important topic for future research.

The findings in this report are subject to at least three limitations.

First, self-reported data might be subject to recall and social desirability bias. Second, NSDUH uses a cross-sectional design; we cannot be determine whether opioids and tranquilizers were misused simultaneously or at widely spaced intervals. Third, NSDUH excludes homeless persons who do not use shelters, active duty military personnel, and residents of institutional group quarters, all groups that likely have substance use behavior different from that of the surveyed population.

5. Conclusions

The findings presented here provide evidence that tranquilizer misuse is common among adults who misuse opioids and has not changed substantially over the past decade. Additionally, we found that meeting criteria for abuse or dependence of opioids more than doubles the odds of tranquilizer misuse among adults who misuse opioids. Methods to educate clinicians using the *CDC Guideline for Prescribing Opioids for Chronic Pain* should be established so that clinicians avoid concurrent tranquilizers and opioid prescription when possible (Ali et al., 2017). Clinician review of a Prescription Drug Monitoring Program (PDMP) has been shown to reduce the amount of opioids prescribed and associated deaths (Dowell et al., 2016), and PDMPs may likely also be an effective tool to monitor concurrent opioid and tranquilizer prescribing and reduce misuse. Finally, the findings of our risk factor analysis suggest substance use disorder treatment is likely essential to reduce co-occurring opioid and tranquilizer misuse. Medication-Assisted Treatment (MAT) is the highest standard of care for opioid use disorder, and the Food and Drug Administration has recently clarified that MAT should not be withheld from patients taking benzodiazepines (U.S. Food and Drug Administration, 2017). Clear and well-disseminated guidance for clinicians on how to treat patients with opioid use disorder and tranquilizer misuse using MAT could improve treatment outcomes and save lives.

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Contributors

Ms. Boggis and Mr. Feder developed the research question, planed and conducted the analysis and drafted the manuscript. Both authors have approved the final article.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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