Nonmedical Use and Substance Use Disorder Symptoms Among US Adults Coprescribed Opioids and Benzodiazepines

Emily Pasman, PhD; Phil Veliz, PhD; Elizabeth Hoffman, MD; Rebecca Evans-Polce, PhD; Ty S. Schepis, PhD; Megan E. Patrick, PhD; Joshua Truchan, BSN; Timothy E. Wilens, MD; John Jardine, MS; Vita V. McCabe, MD; and Sean Esteban McCabe, PhD

Prescription opioids[1] and benzodiazepines[2] are each associated with health risks, which are heightened when the 2 are used concurrently.[3] The Centers for Disease Control and Prevention recommends caution when coprescribing these medications.[4] Still, little is known about the early warning signs, such as nonmedical use (NMU) and substance use disorder (SUD) symptoms, that often precede overdose and injuries. This study examined NMU and SUD symptoms among US adults prescribed opioids and benzodiazepines.

Methods

Longitudinal data were from 22 nationally representative cohorts of US 12th graders (N = 53,679; baseline years 1976–1997) followed prospectively through adulthood in the Monitoring the Future Panel study (retention rate = 51.0%).[5] Between ages 40–60 (follow-up years 1998–2019), participants were surveyed at 5-year intervals. The analytic sample for SUDs included respondents aged 40–55 for follow-up years 2007–2016. The analytic sample for NMU included respondents aged 40–60 for follow-up years 2007–2019.

Surveys assessed medical use of prescription opioids (ie, "narcotics other than heroin") and benzodiazepines (ie, "tranquilizers"), with examples of generic and brand name medications provided. A 4-category variable was constructed to indicate past-5-year medical use of (1) neither opioids nor benzodiazepines (ie, population controls), (2) opioids only, (3) benzodiazepines only, or (4) both opioids and benzodiazepines (ie, co-use).

Respondents reported past-5-year NMU of opioids or benzodiazepines (ie, "without a doctor telling you to take them"). Past-5-year SUD symptoms were measured using 8 *DSM-IV* and *DSM-5* criteria (failure to fulfill role obligations, use in physically hazardous situations, social/interpersonal problems, tolerance, withdrawal, desire to cut down, physical/psychological problems, cravings). For consistency with *DSM-5* SUD recommendations, ≥2 alcohol, ≥2 cannabis, or ≥2 other drug use criteria were independently coded; ≥2 symptoms for at least 1 substance indicated multiple SUD symptoms.

Analyses were weighted for sampling and attrition. Missing data were handled using listwise deletion. Logistic regression models with clustering at the individual level to account for repeated measures were fitted to assess within-wave associations of medical use with NMU and SUD symptoms, controlling for relevant covariates.

Results

Participants were 50.7% female and 76.8% White, 10.8% Black, 6.1% Hispanic, and 6.2% another race-ethnicity. One-third (38.6%; 95% CI, 38.0%–39.2%) reported past-5-year medical use of prescription opioids or benzodiazepines, and 10.4% (95% CI, 10.0%–10.7%) reported co-use (Supplementary Table 1). Adults who used opioids and benzodiazepines had greater adjusted odds of NMU and SUD symptoms relative to population controls (Table 1). Adults with co-use had greater adjusted odds of NMU relative to those who used opioids only (adjusted odds ratio [aOR = 1.62, 95% CI, 1.42-1.84]) and benzodiazepines only (aOR = 1.42, 95% CI, 1.20–1.67). Similarly, adults with co-use had greater adjusted odds of SUD symptoms relative to those who used opioids only (aOR = 1.52, 95% CI, 1.31-1.75) and benzodiazepines only (aOR = 1.42, 95% CI, 1.18–1.71). A sensitivity analysis assessed

Table 1.

Associations Between Medical Use of Prescription Opioids and/or Benzodiazepines and Nonmedical Use (NMU) and Substance Use Disorder (SUD) Symptoms in Adulthood (Ages 40–60)[a]

			Nonmedical use of opioids or benzodiazepines					
			n = 25,238 obs. = 46,594	n = 22,307 obs. = 39,620	n = 25,238 obs. = 46,594	n = 22,307 obs. = 39,620	n = 25,238 obs. = 46,594	n = 22,307 obs. = 39,620
Medical use	obs.[b]	% (95% CI)	uOR (95% CI)	aOR (95% CI)	uOR (95% CI)	aOR (95% CI)	uOR (95% CI)	aOR (95% CI)
Neither	1,929/33,219	5.16 (4.88–5.46)	Ref.	Ref.	0.23 (0.21–0.25)	0.27 (0.24–0.29)	0.19 (0.17–0.21)	0.23 (0.20–0.27)
Opioids	1,588/7,743	19.41 (18.33–20.53)	4.40 (4.03–4.82)	3.76 (3.40–4.15)	Ref.	Ref.	0.83 (0.72–0.94)	0.87 (0.75–1.02)
Benzodiazepines	580/2,489	22.44 (20.56–24.44)	5.34 (4.71–6.05)	4.30 (3.71–4.98)	1.21 (1.06–1.38)	1.14 (0.98–1.33)	Ref.	Ref.
Co-use	975/3,143	29.84 (27.90–31.84)	7.85 (7.03–8.76)	6.08 (5.36–6.90)	1.78 (1.59–2.00)	1.62 (1.42–1.84)	1.47 (1.28–1.70)	1.42 (1.20–1.67)
			2+ Any SUD symptoms					
			n = 22,244 obs. = 34,541	n = 19,570 obs. = 29,437	n = 22,244 obs. = 34,541	n = 19,570 obs.= 29,437	n = 22,244 obs. = 34,541	n = 19,570 obs. = 29,437
Medical use	obs.[b]	% (95% CI)	uOR (95% CI)	aOR (95% CI)	uOR (95% CI)	aOR (95% CI)	uOR (95% CI)	aOR (95% CI)
Neither	5,203/24,367	19.66 (19.03–20.31)	Ref.	Ref.	0.62 (0.57–0.67)	0.71 (0.65–0.78)	0.61 (0.54–0.69)	0.67 (0.58–0.77)
Opioids	1,777/5,898	28.46 (27.09–29.88)	1.62 (1.50–1.75)	1.40 (1.29–1.53)	Ref.	Ref.	0.99 (0.86–1.13)	0.94 (0.80–1.10)
Benzodiazepines	569/1,841	28.47 (26.05–31.02)	1.64 (1.44–1.86)	1.50 (1.29–1.73)	1.01 (0.88–1.16)	1.07 (0.91–1.25)	Ref.	Ref.
Co-use	968/2,435	37.85 (35.44–40.32)	2.51 (2.25–2.80)	2.13 (1.86–2.44)	1.55 (1.37–1.75)	1.52 (1.31–1.75)	1.53 (1.31–1.79)	1.42 (1.18–1.71)

[a]All sample sizes (n) and observation counts (obs.) are unweighted. Medical use, NMU, and SUD symptoms are assessed over the past 5 years. Models for SUD symptoms include data from 2007 to 2016 due to changes in survey methodology in 2017. Models examining nonmedical use include data from 2007–2019. All prevalence rates (%), unadjusted odds ratios (uOR), adjusted odds ratios (aOR), and CIs incorporate panel analysis weights from the MTF. For adjusted models, control variables include cohort group, population density, region, sex, race-ethnicity, parental education, grade point average, cigarette use, binge drinking, marijuana use, other illicit drug use, and nonmedical prescription drug use at baseline. Other controls include completion of a bachelor's degree by age 35, and time-varying controls for marital status, employment status, and trouble sleeping in the past 30 days. Unadjusted and adjusted models also control for age (0 = 40, 1 = 45, 2 = 50, 3 = 55, 4 = 60). The SUD outcome variable represents ≥2 alcohol use disorder, ≥2 cannabis use disorder, or ≥2 other drug use disorder symptoms. All outcomes and the main independent variable are time varying.
[b]Observation counts show the total number of positive responses for the outcome (numerator) over the total number of observations in the given medical use group (denominator).

past-year medical and NMU, and results were substantively the same (Supplementary Table 2). SUD results held when examining other drug use disorder symptoms only (Supplementary Tables 3–4).

Discussion

Despite increased attention to the risks associated with concurrent use of opioids and benzodiazepines,[4] coprescribing remains a concern.[6] While most adults with co-use reported no NMU, they demonstrated increased odds of NMU and SUD symptoms relative to those prescribed opioids only, benzodiazepines only, and population controls. Early detection of NMU and SUD symptoms is critical for preventing overdose and related harms. Study limitations include self-report bias and measurement constraints. SUD symptoms were assessed using 8 of 11 SUD criteria, which likely underestimated the prevalence of SUD. Future research should employ more frequent data collection intervals to clarify temporality and examine how associations between co-use and NMU and SUD have shifted over time. Findings indicate a need to carefully counsel, screen, monitor, and treat adults prescribed opioids and benzodiazepines, particularly in combination, for comorbid SUD.

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Author Affiliations: Jane Addams College of Social Work, University of Illinois Chicago, Chicago, Illinois (Pasman); Center for the Study of Drugs, Alcohol, Smoking and Health, University of Michigan, Ann Arbor, Michigan (Pasman, Veliz, Hoffman, Evans-Polce, Schepis, Patrick, Truchan, Wilens, Jardine, V. McCabe, S. McCabe); Institute for Social Research, University of Michigan, Ann Arbor, Michigan (Veliz, Evans-Polce, Patrick, S. McCabe); Institute for Research on Women and Gender, University of Michigan, Ann Arbor, Michigan (Veliz, S. McCabe); Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, Michigan (Veliz, S. McCabe); Department of Psychiatry, University of Michigan, Ann Arbor, Michigan (Hoffman, V. McCabe); Department of Psychology, Texas State University, San Marcos, Texas (Schepis); Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts (Wilens); Harvard Medical School, Harvard University, Boston, Massachusetts (Wilens).

Corresponding Author: Emily Pasman, PhD, Jane Addams College of Social Work, University of Illinois Chicago, 1040 W. Harrison St, Chicago, Illinois 60607 (pasman@uic.edu).

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Supplementary Material: Available at Psychiatrist.com.