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Nonmedical Prescription Opioid Use and *DSM-5* Nonmedical Prescription Opioid Use Disorder in the United States

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ABSTRACT

Objective: The authors present 12-month and lifetime prevalence, correlates, psychiatric comorbidity, and treatment of nonmedical prescription opioid use (NMPOU) and *DSM-5* NMPOU disorder (NMPOUD).

Methods: Data were derived from the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III) (N = 36,309).

Results: Prevalences of 12-month and lifetime NMPOU were 4.1% and 11.3%, exceeding rates in the 2001–2002 NESARC (1.8%, 4.7%). Twelve-month and lifetime rates of *DSM-5* NMPOUD were 0.9% and 2.1%. NESARC-III *DSM-IV* NMPOUD rates (0.8%, 2.9%) were greater than those observed in the 2001–2002 NESARC (0.4% and 1.4%). Rates of NMPOU were greater among men, but no sex differential was observed for NMPOUD. Prevalences of NMPOU and NMPOUD were generally greater among 18- to 64-year-old individuals, whites, and Native Americans, and individuals with lower socioeconomic status. Associations were observed between 12-month and lifetime NMPOU and NMPOUD and other drug use disorders, posttraumatic stress disorder, and borderline, schizotypal, and antisocial personality disorders; persistent depression and major depressive disorder (for NMPOU); and bipolar I disorder (for NMPOUD). Only 5.5% and 17.7% of individuals with 12-month NMPOU and NMPOUD were ever treated.

Conclusions: NMPOU and NMPOUD have considerably increased over the past decade, are associated with a broad array of risk factors and comorbidities, and largely go untreated in the United States. More information on the determinants, characteristics, and outcomes of NMPOU and NMPOUD is needed to support evidence-based interventions and prevention.

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Although opioid analgesics are important components of treatment for chronic pain, which is highly prevalent among American adults,[1] prescriptions for opioid analgesics and harms from nonmedical prescription opioid use (NMPOU) have increased dramatically during the last decade. Between 2002 and 2012, the number of opioid analgesics dispensed by US pharmacies has skyrocketed from 142 million to 248

million.[2,3] Drug-poisoning death rates more than tripled between 1999 and 2012,[4] the quarterly intentional abuse rates associated with opioids reported by US poison centers increased from 0.20/100,000 population to 0.56/100,000 population in 2012,[2] and emergency department visits increased by 153% from 2004 to 2011.[5] Drug treatment admission rates for nonheroin opiates increased by 236% from 2002 to 2012.[6] Additional adverse health consequences of NMPOU include transitions to injection drug or heroin use with resultant infection (eg, hepatitis C, human immunodeficiency virus)[6–9]; risk, falls, and fractures among older adults[10,11]; neonatal opioid withdrawal syndrome[12]; cognitive impairment[13]; and drug interactions.[13] Societal costs of NMPOU are estimated at $53 billion to $72 billion annually.[14–16]

Considerable concern stems from the dependence potential of NMPOU and the severity and disability of NMPOU disorder (NMPOUD) attributable to its comorbidity with other substance use and psychiatric disorders.[17,18] Although research has begun to identify correlates of NMPOU,[19–21] very few surveys[22,23] collect clinically relevant diagnostic information on NMPOUD and its comorbidities. In the 2001–2002 National Institute on Alcohol Abuse and Alcoholism (NIAAA) National Epidemiologic Survey on Alcohol and Related Conditions (NESARC),[24] 12-month and lifetime rates of *DSM-IV*[25] NMPOUD (abuse and/or dependence) were 0.34% and 1.4%,[22] with substantial comorbidity between NMPOUD and major mood, anxiety, personality, and other substance use disorders.[22,26–30] In the 2013 National Survey on Drug Use and Health (NSDUH), the 12-month prevalence of NMPOUD was 0.6%.[23] The NSDUH assesses only 12-month NMPOUD and does not address lifetime diagnoses or the full range of psychiatric disorders.

Previous national estimates of NMPOUD were all based on *DSM-IV* criteria. However, *DSM-5*[31] made major changes to the NMPOUD diagnosis, including combining most abuse and dependence criteria into a single diagnosis, adding a craving criterion, and setting a diagnostic threshold of ≥ 2 criteria.[32] Because of the seriousness of NMPOU and NMPOUD, the lack of current epidemiologic data on NMPOU and *DSM-5* NMPOUD in the United States from a single reliable and uniform source represents a critical knowledge gap for prevention and intervention. We therefore present national data on the prevalence, correlates, comorbidity, and treatment of NMPOU and *DSM-5* NMPOUD from the 2012–2013 NIAAA NESARC-III.[33] *DSM-IV* NMPOUD criteria were also assessed to examine trends.

Clinical Points

- Lack of current epidemiologic data on nonmedical prescription opioid use (NMPOU) and *DSM-5* NMPOU disorder (NMPOUD) from a single reliable source represents a knowledge gap for prevention and treatment.
- Given the dramatic increases in NMPOU and NMPOUD over the last decade, it is important for clinicians to systematically screen for these conditions and educate patients about their risks.

METHODS

Sample

The target population for NESARC-III was the US noninstitutionalized adult civilian population, including residents of selected group quarters. As detailed elsewhere,[33] probability sampling was used to select respondents. Primary sampling units were counties or groups of contiguous counties, secondary sampling units comprised groups of Census-defined blocks, and tertiary sampling units were households within secondary sampling units. Eligible adults within sampled households were randomly selected. Hispanics, blacks, and Asians were oversampled; in households with ≥ 4 eligible minority persons, 2 respondents were selected (n = 1,661). The total sample size was 36,309. The screener- and person-level response rates were 72.0% and 84.0%, yielding a total response rate of 60.1%, comparable to most current US national surveys.[23,34]

Data were adjusted for oversampling and nonresponse, then weighted to represent the US civilian population based on the 2012 American Community Survey.[35] Weighting adjustments compensated adequately for nonresponse. Respondents did not differ from the total eligible sample, including nonrespondents, in percentage of Hispanics, blacks, or Asians; population density; vacancy rate; proportion of population in group quarters; or proportion of renters at the segment level. There were no differences between respondents and the total eligible sample on Hispanic ethnicity. Respondents in comparison to the eligible sample included slightly higher percentages of men (48.1% vs 46.2%) and individuals aged 60–69 years (13.7% vs 12.6%) and smaller percentages of individuals aged 40–49 (18.1% vs 18.3%) and 30–39 (16.7% vs 17.4%) years.

Respondents gave informed consent and received $90.00 for survey participation. Protocols were approved by National Institutes of Health and Westat institutional review boards.

Assessments

The diagnostic interview was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5),[36] designed to measure *DSM-5* alcohol use disorder, nicotine use disorder, other specific drug use disorders, and selected mood, anxiety, trauma-related, eating, and personality disorders.

Nonmedical Prescription Opioid Use and Nonmedical Prescription Opioid Use Disorder

Twelve-month and prior-to-past 12-months NMPOU information was aggregated into a lifetime measure. *Nonmedical prescription opioid use* was defined as use "without a prescription" or "in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them." The definition differs

in the NSDUH: "use without a prescription or only for the experience or feeling it caused."[23]

Lifetime *DSM-5* NMPOUD diagnoses required ≥2 of 11 criteria in the 12 months before interview or previously. Diagnoses prior to the past 12 months required clustering of ≥2 criteria within a single year. *DSM-IV* lifetime NMPOUD diagnoses required ≥1 of 4 abuse criteria or ≥3 of 7 dependence criteria clustered within a single year.

Symptom items (32) assessing *DSM-IV* 12-month NMPOUD in the 2001–2002 NESARC and NESARC-III were virtually identical. However, 3 items were slightly reworded, and an additional abuse item appeared in the NESARC and NESARC-III. Comparisons between *DSM-IV* diagnoses with and without the additional questions yielded identical prevalences (NESARC, 0.35% vs 0.35%; NESARC-III, 0.78% vs 0.78%), with near perfect concordance (κ = 1.00 and 0.99), suggesting that trivial differences between *DSM-IV* NMPOUD operationalizations did not yield the large differences reported below.

Test-retest reliability of NMPOU and frequency of NMPOU were substantial (κ = 0.66, 0.66) in a large general population sample.[37] Reliability of *DSM-5* NMPOUD categorical diagnoses (κ = 0.40, 0.47) and dimensional criteria scales (intraclass correlation coefficient [ICC] = 0.71, 0.73) were moderate to substantial in a large general population sample.[38] Procedural validity of *DSM-5* NMPOUD was assessed through blind clinical reappraisal using the clinician-administered, semistructured Psychiatric Research Interview for Substance Use and Mental Disorders, *DSM-5* version (PRISM-5).[39] Moderate concordances between AUDADIS-5 and PRISM-5 NMPOUD diagnoses (κ = 0.40, 0.49) and substantial concordances for their dimensional counterparts (ICC = 0.68, 0.79) were observed in a large general population sample.[40]

Test-retest reliability of *DSM-IV* NMPOUD diagnoses was moderate in clinical and general population samples.[37,41,42] Convergent, discriminant, and construct validities of AUDADIS-IV NMPOUD were moderate to substantial,[43–46] including in the World Health Organization/National Institutes of Health Study on Reliability and Validity (κ = 0.62).[47]

Table 1. Prevalence and Odds Ratios (ORs) of 12-Month and Lifetime Nonmedical Prescription Opioid Use by Sociodemographic Characteristics[a]

Sociodemographic Characteristic	12-Month (n = 1,579)		Lifetime (n = 4,090)	
	Prevalence, % (SE)	OR (95% CI)[b]	Prevalence, % (SE)	OR (95% CI)[b]
Total	4.10 (0.16)	…	11.29 (0.36)	…
Sex				
Male	4.38 (0.19)	**1.17** (1.04–1.32)	12.96 (0.40)	**1.42** (1.30–1.55)
Female	3.85 (0.20)	1.00 (reference)	9.75 (0.43)	1.00 (reference)
Race-ethnicity				
White	4.27 (0.19)	1.00 (reference)	12.79 (0.45)	1.00 (reference)
Black	5.18 (0.50)	0.93 (0.74–1.18)	9.85 (0.82)	0.59 (0.49–0.71)
Native American	5.88 (1.21)[c]	1.09 (0.70–1.71)	14.07 (2.00)[c]	0.91 (0.65–1.26)
Asian/Pacific Islander	1.55 (0.30)	**0.31** (0.21–0.47)	4.52 (0.56)	**0.27** (0.21–0.35)
Hispanic	3.32 (0.26)	**0.55** (0.44–0.68)	8.09 (0.47)	**0.44** (0.38–0.51)
Age, y				
18–29	5.67 (0.33)	**2.87** (2.21–3.72)	14.78 (0.58)	**3.89** (3.20–4.73)
30–44	4.41 (0.28)	**2.64** (2.01–3.46)	12.56 (0.53)	**3.56** (2.90–4.36)
45–64	3.87 (0.24)	**2.11** (1.63–2.74)	11.36 (0.46)	**2.87** (2.37–3.48)
≥65	2.18 (0.25)	1.00 (reference)	5.01 (0.45)	1.00 (reference)
Marital status				
Married/cohabiting	3.28 (0.20)	1.00 (reference)	9.73 (0.44)	1.00 (reference)
Widowed/separated/divorced	4.73 (0.27)	**1.33** (1.12–1.58)	12.54 (0.49)	**1.40** (1.24–1.59)
Never married	5.66 (0.33)	1.15 (0.96–1.38)	14.23 (0.51)	1.09 (0.97–1.23)
Education				
Less than high school	4.76 (0.39)	**1.24** (1.03–1.49)	10.58 (0.68)	1.00 (0.87–1.15)
High school	5.04 (0.26)	**1.30** (1.13–1.49)	12.19 (0.45)	1.07 (0.97–1.17)
Some college or higher	3.57 (0.18)	1.00 (reference)	11.07 (0.41)	1.00 (reference)
Family income				
0–$19,999	6.55 (0.32)	**2.15** (1.76–2.63)	14.51 (0.56)	**1.81** (1.56–2.09)
$20,000–$34,999	4.10 (0.30)	**1.40** (1.11–1.77)	11.76 (0.52)	**1.46** (1.25–1.69)
$35,000–$69,999	3.58 (0.26)	**1.23** (1.01–1.50)	10.75 (0.52)	**1.24** (1.10–1.39)
≥$70,000	2.77 (0.21)	1.00 (reference)	9.12 (0.51)	1.00 (reference)
Urbanicity				
Urban	4.15 (0.19)	1.10 (0.85–1.43)	11.40 (0.42)	1.14 (0.96–1.35)
Rural	3.94 (0.44)	1.00 (reference)	10.91 (0.74)	1.00 (reference)
Region				
Northeast	3.26 (0.31)	**0.68** (0.53–0.88)	10.40 (0.73)	**0.78** (0.64–0.96)
Midwest	4.50 (0.45)	0.87 (0.67–1.14)	11.91 (1.25)	0.82 (0.63–1.08)
South	4.09 (0.23)	**0.78** (0.63–0.97)	10.85 (0.43)	**0.79** (0.68–0.92)
West	4.42 (0.34)	1.00 (reference)	12.14 (0.51)	1.00 (reference)

[a]Controlling for all other sociodemographic characteristics.
[b]Significant ($P < .05$) ORs appear in bold font.
[c]Low precision.
Abbreviation: SE = standard error.

Other Psychopathology

DSM-5 alcohol use disorder, nicotine use disorder, and other drug use disorder diagnoses (sedative/tranquilizer, cannabis, stimulant, cocaine, club drug, opioid, heroin, hallucinogen, and solvent/inhalant) were derived similarly to NMPOUD. Sedative/tranquilizer and stimulant use disorders were aggregated to yield other nonmedical prescription drug use disorder diagnoses, with the remaining drug use disorders aggregated to yield diagnoses of any other drug use disorder. Test-retest reliabilities were moderate to substantial for alcohol use disorder (κ = 0.60, 0.62), nicotine use disorder (κ = 0.50, 0.87), and all other drug use disorders (κ = 0.41–0.54) and were higher for their dimensional counterparts (ICCs = 0.45–0.85).[38] AUDADIS-5 and PRISM-5 concordance on alcohol use disorder, nicotine use disorder, and other drug use disorder diagnoses and dimensional scales was moderate to substantial (κ = 0.35–0.72; ICCs = 0.38–0.92).[40]

Mood disorders assessed in the NESARC-III included 12-month and lifetime persistent depression, major depressive disorder, and bipolar I and II disorders. Anxiety disorders included panic, agoraphobia, generalized anxiety, and social and specific phobias. Posttraumatic stress disorder (PTSD) was also assessed. All diagnoses excluded substance- and medical illness–induced cases. Lifetime personality disorders included antisocial, borderline, and

schizotypal. Psychometric properties of these psychiatric disorders are described in detail elsewhere.[48]

Statistical Analysis

Weighted means, frequencies, and cross-tabulations were computed for 12-month and lifetime NMPOU and *DSM-5* NMPOUD. Adjusted odds ratios (ORs) derived from multiple logistic regression indicated associations between NMPOU and NMPOUD and each sociodemographic characteristic controlling for all others. Logistic regressions of psychiatric comorbidity of NMPOU and NMPOUD controlled for sociodemographic characteristics and other substance use and psychiatric disorders. Anorexia nervosa, bulimia nervosa, and binge-eating disorder were too rare to assess comorbid associations with NMPOU and NMPOUD but were used as covariates in comorbidity analyses. Opioid-specific treatment seeking among individuals with NMPOU and NMPOUD was assessed across treatment modality. All analyses utilized SUDAAN[49] software that accounts for the NESARC-III's complex design.

RESULTS

Nonmedical Prescription Opioid Use

Prevalences of 12-month and lifetime NMPOU were 4.1% and 11.3% (Table 1), considerably higher than those in the 2001–2002 NESARC[22] (1.8% and 4.7%). Twelve-month rates were greater among men, the 3 youngest age groups, and those with annual incomes < $70,000, ≤ high school education, and those previously married. Prevalences were lower among Asian/Pacific Islanders and Hispanics and among those residing in the Northeast and South. Lifetime prevalence showed similar distributions.

Nonmedical Prescription Opioid Use Disorder

Twelve-month and lifetime rates of *DSM-5* NMPOUD were 0.9% and 2.1% (Table 2), with similar rates for *DSM-IV* (0.8% and 2.9%). Asians/Pacific Islanders and Hispanics had lower rates of 12-month and lifetime NMPOUD, and blacks had lower rates of lifetime NMPOUD than whites. Although rates were greatest among Native Americans (1.4% and 3.7%), low precision precluded reliable statistical comparisons. For both time frames, NMPOUD prevalences were greater among respondents < 65 years old and among those with ≤ high school education, those with lower incomes, and the previously married (for lifetime NMPOUD).

Table 2. Prevalence and Odds Ratios (ORs) of 12-Month and Lifetime *DSM-5* Nonmedical Prescription Opioid Use Disorder by Sociodemographic Characteristics[a]

Sociodemographic Characteristic	12-Month (n = 330)		Lifetime (n = 688)	
	Prevalence, % (SE)	OR (95% CI)[b]	Prevalence, % (SE)	OR (95% CI)[b]
Total	0.89 (0.05)	…	2.05 (0.09)	…
Sex				
Male	0.92 (0.08)	1.12 (0.85–1.48)	2.19 (0.13)	1.17 (0.98–1.40)
Female	0.86 (0.08)	1.00 (reference)	1.93 (0.12)	1.00 (reference)
Race-ethnicity				
White	0.96 (0.07)	1.00 (reference)	2.42 (0.13)	1.00 (reference)
Black	1.04 (0.14)	0.73 (0.52–1.02)	1.55 (0.20)	**0.44** (0.32–0.59)
Native American	1.42 (0.58)[c]	1.01 (0.43–2.39)	3.67 (0.93)[c]	1.08 (0.64–1.81)
Asian/Pacific Islander	0.16 (0.09)	**0.15** (0.05–0.52)	0.42 (0.16)	**0.15** (0.07–0.33)
Hispanic	0.70 (0.11)	**0.43** (0.29–0.64)	1.26 (0.17)	**0.30** (0.22–0.42)
Age, y				
18–29	1.16 (0.14)	**4.17** (2.23–7.80)	2.92 (0.22)	**8.30** (5.14–13.43)
30–44	0.94 (0.13)	**3.93** (2.04–7.56)	2.47 (0.19)	**7.75** (5.01–11.99)
45–64	0.94 (0.10)	**3.32** (1.92–5.73)	1.98 (0.17)	**5.21** (3.39–8.03)
≥ 65	0.39 (0.10)	1.00 (reference)	0.53 (0.11)	1.00 (reference)
Marital status				
Married/cohabiting	0.71 (0.07)	1.00 (reference)	1.67 (0.10)	1.00 (reference)
Widowed/separated/divorced	1.23 (0.13)	1.32 (0.95–1.83)	2.59 (0.25)	**1.42** (1.12–1.81)
Never married	1.05 (0.13)	0.81 (0.59–1.11)	2.55 (0.21)	0.89 (0.67–1.17)
Education				
Less than high school	1.49 (0.20)	**1.96** (1.33–2.90)	2.70 (0.29)	**1.62** (1.21–2.18)
High school	1.21 (0.13)	**1.62** (1.23–2.14)	2.60 (0.20)	**1.42** (1.13–1.79)
Some college or higher	0.63 (0.05)	1.00 (reference)	1.68 (0.10)	1.00 (reference)
Family income				
0–$19,999	1.84 (0.18)	**4.26** (2.35–7.70)	3.43 (0.24)	**3.24** (2.23–4.71)
$20,000–$34,999	0.90 (0.13)	**2.22** (1.21–4.08)	2.25 (0.26)	**2.21** (1.52–3.22)
$35,000–$69,999	0.65 (0.11)	1.59 (0.92–2.73)	1.86 (0.15)	**1.73** (1.24–2.42)
≥ $70,000	0.39 (0.08)	1.00 (reference)	1.08 (0.13)	1.00 (reference)
Urbanicity				
Urban	0.89 (0.06)	1.21 (0.85–1.71)	2.02 (0.10)	1.12 (0.85–1.47)
Rural	0.88 (0.13)	1.00 (reference)	2.17 (0.27)	1.00 (reference)
Region				
Northeast	0.85 (0.11)	0.95 (0.62–1.45)	2.11 (0.20)	0.98 (0.75–1.29)
Midwest	0.93 (0.10)	0.89 (0.60–1.32)	1.98 (0.17)	0.77 (0.59–1.00)
South	0.90 (0.08)	0.82 (0.56–1.20)	2.05 (0.18)	0.83 (0.63–1.08)
West	0.87 (0.13)	1.00 (reference)	2.07 (0.19)	1.00 (reference)

[a]Controlling for all other sociodemographic characteristics.
[b]Significant ($P < .05$) odds ratios appear in bold font.
[c]Low precision.
Abbreviation: SE = standard error.

Comorbidity

Nonmedical prescription opioid use and *DSM-5* NMPOUD were strongly related to other nonmedical prescription drug use disorders, other drug use disorders, alcohol use disorder, nicotine use disorder, PTSD, and schizotypal, borderline, and antisocial personality disorders, regardless of time frame (Table 3). Twelve-month and lifetime NMPOU were associated with persistent depression and major depressive disorder (12-month only), whereas NMPOUD was associated with bipolar I disorder for each time period.

Treatment/Help Seeking

Overall, only 5.5% and 7.9% of individuals with 12-month and lifetime NMPOU were treated; corresponding rates for NMPOUD were 17.7% and 28.9% (Table 4). Among those with 12-month NMPOU, 3.2% received treatment from physicians/health care practitioners, 2.1% from 12-step programs, and 0.9%–1.3% from outpatient clinics, emergency departments, detoxification programs, and

Table 3. Odds Ratios (ORs) of 12-Month and Lifetime Nonmedical Prescription Opioid Use/*DSM-5* Nonmedical Prescription Opioid Use Disorder and Psychiatric Disorders[a]

	Opioid Use		Opioid Use Disorder	
Comorbid Disorder	12-Month, OR (95% CI)	Lifetime, OR (95% CI)	12-Month, OR (95% CI)	Lifetime, OR (95% CI)
Any substance use disorder	**2.95**[b] (2.54–3.44)	**3.07** (2.67–3.53)	**4.28** (3.05–6.00)	**7.65** (5.48–10.67)
Alcohol use disorder	**1.77** (1.49–2.10)	**1.73** (1.55–1.93)	**1.50** (1.08–2.10)	**1.93** (1.56–2.40)
Any drug use disorder	**3.68** (2.97–4.57)	**3.49** (3.10–3.93)	**6.92** (5.11–9.37)	**5.12** (3.89–6.74)
Any other nonmedical prescription drug use disorder	**10.69** (7.33–15.58)	**6.80** (5.61–8.25)	**17.67** (10.69–29.21)	**11.73** (8.83–15.58)
Any drug use disorder except nonmedical prescription drug use disorders	**2.79** (2.21–3.52)	**2.99** (2.63–3.40)	**4.27** (2.95–6.17)	**3.94** (3.11–5.00)
Nicotine use disorder	**1.84** (1.58–2.13)	**1.80** (1.63–1.97)	**2.25** (1.67–3.05)	**1.89** (1.47–2.42)
Any mood disorder	**1.59** (1.36–1.87)	**1.20** (1.07–1.36)	**2.47** (1.81–3.36)	**1.66** (1.29–2.12)
Major depressive disorder	**1.26** (1.05–1.52)	1.09 (0.96–1.23)	1.24 (0.78–1.98)	1.01 (0.78–1.32)
Persistent depression	**1.43** (1.06–1.92)	**1.28** (1.10–1.49)	1.74 (1.00–3.03)	1.21 (0.88–1.64)
Bipolar I disorder	1.27 (0.92–1.76)	1.09 (0.89–1.34)	**1.73** (1.09–2.74)	**1.50** (1.07–2.12)
Bipolar II disorder	1.19 (0.57–2.49)	1.19 (0.70–2.04)	1.65 (0.51–5.32)	1.12 (0.44–2.88)
Any anxiety disorder	1.14 (0.94–1.39)	1.05 (0.93–1.20)	1.48 (0.98–2.24)	**1.32** (1.04–1.66)
Panic disorder	1.08 (0.80–1.46)	1.12 (0.94–1.34)	1.41 (0.83–2.39)	1.32 (0.97–1.80)
Agoraphobia	0.91 (0.64–1.31)	1.20 (0.92–1.56)	1.09 (0.61–1.95)	1.26 (0.79–2.00)
Social phobia	0.95 (0.70–1.28)	1.14 (0.93–1.39)	1.01 (0.63–1.61)	1.02 (0.74–1.41)
Specific phobia	0.91 (0.68–1.21)	0.91 (0.76–1.09)	1.07 (0.67–1.71)	1.00 (0.73–1.38)
Generalized anxiety disorder	1.10 (0.86–1.40)	0.95 (0.79–1.13)	0.92 (0.56–1.51)	0.99 (0.74–1.32)
Posttraumatic stress disorder	**1.41** (1.13–1.75)	**1.30** (1.11–1.51)	**1.57** (1.06–2.33)	**1.65** (1.29–2.12)
Any personality disorder	**1.70** (1.45–1.99)	**1.97** (1.75–2.22)	**2.04** (1.42–2.94)	**2.54** (2.06–3.12)
Schizotypal	**1.42** (1.14–1.77)	**1.36** (1.13–1.64)	1.44 (0.94–2.22)	**1.35** (1.01–1.80)
Borderline	**1.39** (1.12–1.72)	**1.47** (1.25–1.72)	**1.78** (1.16–2.75)	**1.68** (1.21–2.32)
Antisocial	**1.59** (1.30–1.96)	**2.13** (1.81–2.51)	**1.60** (1.16–2.22)	**2.39** (1.84–3.10)

[a]Controlling for sociodemographic characteristics and other psychiatric disorders.
[b]Significant ($P < .05$) ORs appear in bold font.

Table 4. Treatment/Help-Seeking Settings Among Individuals With 12-Month and Lifetime Nonmedical Prescription Opioid Use and Nonmedical Prescription Opioid Use Disorder

	Opioid Use		Opioid Use Disorder	
Treatment/Help-Seeking Setting	12-Month, % (SE)	Lifetime, % (SE)	12-Month, % (SE)	Lifetime, % (SE)
12-Step program (eg, AA)	2.13 (0.50)	4.66 (0.48)	8.46 (2.03)	18.31 (2.01)
Family/social services	0.36 (0.17)	1.29 (0.25)	1.66 (0.76)	5.08 (0.95)
Detoxification	1.16 (0.32)	2.68 (0.33)	4.91 (1.33)	10.30 (1.35)
Other inpatient facility	0.71 (0.25)	1.67 (0.28)	3.29 (1.13)	6.15 (1.14)
Outpatient clinic	0.91 (0.26)	2.38 (0.27)	3.39 (1.07)	10.93 (1.21)
Rehabilitation program	1.30 (0.40)	3.30 (0.41)	4.03 (1.43)	12.4 (1.74)
Methadone maintenance	0.51 (0.20)	1.05 (0.17)	1.99 (0.80)	5.05 (0.82)
Emergency department	1.04 (0.32)	1.70 (0.24)	4.80 (1.46)	7.68 (1.03)
Halfway house	0.04 (0.04)	0.68 (0.17)	0.18 (0.18)	2.10 (0.59)
Crisis center	0.32 (0.16)	0.36 (0.09)	1.03 (0.60)	1.34 (0.39)
Employee assistance program	…	0.21 (0.09)	…	0.63 (0.37)
Clergy	0.65 (0.39)	0.72 (0.18)	0.81 (0.52)	2.81 (0.82)
Physician/other health care professional	3.24 (0.66)	3.50 (0.34)	10.31 (2.28)	13.87 (1.76)
Other	0.47 (0.21)	0.58 (0.15)	2.07 (0.94)	2.33 (0.67)
Any treatment or help-seeking settings	5.46 (0.80)	7.86 (0.50)	17.69 (2.80)	28.92 (2.07)

Abbreviations: AA = Alcoholics Anonymous, SE = standard error.
Symbol: … = no observation.

rehabilitation programs; other modalities were utilized less frequently. Treatment among individuals with lifetime NMPOU followed a similar distribution except that 12-step participation (4.7%) was utilized more frequently than health care practitioners (3.5%).

Among individuals with 12-month NMPOUD, 10.3% received treatment from physicians/health care practitioners, 8.5% from self-help programs, and 3.4%–4.9% from outpatient clinics, rehabilitation programs, emergency departments, and detoxification programs, with utilization of other modalities less frequent. Similar patterns were observed for lifetime NMPOUD except that a greater percentage of respondents sought treatment from 12-step programs (18.3%) than from physicians/health care practitioners (13.9%).

DISCUSSION

In 2012–2013, prevalences of 12-month and lifetime NMPOU were 4.1% and 11.3%, representing about 9.7 million and 26.6 million US adults. Consistent with substantial increases in opioid prescriptions[2,3] and NMPOU-associated morbidity and mortality during the past decade,[1–6] these rates were considerably greater than those reported in the 2001–2002 NESARC (1.8%, 4.7%).[22] The NSDUH rates of 12-month and lifetime NMPOU in 2013 were similar (4.2%, 14.2%).[23]

Twelve-month and lifetime rates of *DSM-5* NMPOUD were 0.9% and 2.1%, representing about 2.1 million and 4.8 million US adults. In NESARC-III, corresponding prevalences of *DSM-IV* NMPOUD were similar, 0.8% and 2.9%, but greater than corresponding rates reported in the 2001–2002 NESARC (0.4%, 1.4%).[22] The 12-month prevalence of *DSM-IV* NMPOUD in the 2013 NSDUH was 0.6%.[23]

Dramatic increases in NMPOU (161%) and NMPOUD (125%) observed in this study over the last decade may reflect, in part, increases in opioid prescribing and dosage; increased

advocacy for opioid treatment of chronic noncancer pain; availability of long-acting formulations; lessened perceived risk or greater social acceptability of substances that can be obtained by legitimate prescription; drug diversion; aggressive marketing by pharmaceutical companies; disregard for the lack of long-term effectiveness; and lack of understanding of opioids' addiction potential.[50–54]

Consistent with most prior studies,[10–22,26,55–57] men had greater rates of NMPOU. Although reasons for this sex differential are unclear, women more frequently report pain as motivation for first opioid use, while euphoria is the major motivation for men.[55] Women also more often use opioids via legitimate prescriptions and intended route of administration, whereas men more often report obtaining opioids from illicit markets and using unintended routes of administration.[58,59]

The absence of sex differences in NMPOUD is inconsistent with higher prevalences among men in earlier studies,[19,21,22] including the NSDUH,[23] and across many other substance use disorders.[60–64] This finding may reflect that women are increasingly more likely to be prescribed opioids,[10] a shift related in part to the greater prevalence of comorbid pain and affective disorders among women.[65,66] Nonetheless, the narrowing gender gap in NMPOUD is important for screening, prevention, and treatment. Of note, most risk stratification and screening tools identify male sex as a NMPOUD risk factor.[54]

Much debate surrounding the opioid epidemic has focused on the dependence liability of opioids. Recent studies on dependence risk among pain patients have yielded estimates of 0.00%–45.0%.[67–72] These studies generally failed to define dependence, and most excluded patients with histories of substance use disorders or psychiatric disorders. In this study, 18.2% of individuals with NMPOU were classified with NMPOUD. Considering the key role of dependence liability in the opioid debate, uniform definitions and validated assessments based on current scientific and clinical understanding are essential to establish liability parameters. Within this context, the *DSM-5* definition of opioid use disorder explicitly excludes tolerance and withdrawal as criteria if the individual is "taking opioids solely under appropriate medical supervision."[31] This exclusion does not apply to individuals with NMPOUD.

Nonmedical prescription opioid use and NMPOUD prevalences decreased with age. Whether the declining rates observed here and previously[22,23,73–75] reflect cohort, age, or period effects[76]; differential mortality; or recall bias merits further investigation. Although rates of NMPOU and NMPOUD were substantially lower among individuals ≥ 65 years old, rates among these individuals may rise with increasing life expectancy and as the proportion of the US population aged 65 to 74 years achieves its projected growth rate of 74% by 2020.[77] Even if rates among the elderly remain steady, the projected increase in population size portends substantial increases in the number at risk in this cohort, in which illicit drug use was also common.[74,78]

Consistent with most research,[19–23,79–81] rates of NMPOU and NMPOUD were generally greater among whites and individuals with lower incomes, lower education, and widowed/separated/divorced marital status. Prevalences of NMPOUD were lower among blacks, and Native Americans had the greatest rates of NMPOU and NMPOUD, but low precision precluded reliable significance testing. In contrast to the results of a recent state-level study[82] in which opioid prescription rates were greatest in the South and Northeast followed by the West, this study showed that rates of NMPOU were significantly lower in the South and Northeast relative to West. Further, no regional differences were found for NMPOUD. These regional discrepancies suggest that opioid prescription rates may be imperfectly related to the rates of NMPOU and NMPOUD. Understanding the mechanism of underlying sociodemographic risk and protective factors will be important to elucidate causes of NMPOU and NMPOUD. These findings highlight the need for more targeted prevention efforts and research on optimal treatment for subgroups of the population at risk of NMPOU and NMPOUD, as well as potential barriers to their treatment.

Consistent with earlier findings,[17,22,26–30,83–86] this study revealed strong associations between NMPOU and NMPOUD and other nonmedical prescription drug use disorders (sedative/tranquilizer, stimulant) and smaller, but significant, associations with other psychopathology. These findings underscore the need to diagnose and treat comorbidities among individuals with NMPOU and NMPOUD. This is especially critical because individuals presenting with substance use disorders and psychiatric disorders are more likely to receive prescription opioids and long-term opioid therapy, be prescribed concurrent sedative-hypnotics, and have more physical pain[72,87–96] than those without these disorders. Accurate diagnosis and care of NMPOU and NMPOUD complicated by psychiatric comorbidity and pain will be a substantial challenge in the future.

Similar to the results of prior research,[22] past-year and lifetime treatment rates of NMPOU and NMPOUD were low (5.5% and 17.7%). The reasons for these particularly low treatment rates are not known but may reflect the belief that prescription drugs are less dangerous than illegal drugs. Individuals may also be reluctant to discuss potential prescription drug problems with their physicians that may endanger future prescriptions.[97] Alternatively, individuals prescribed opioids may be ambivalent about giving up the rewarding effects of the substance despite negative consequences associated with their use.[98] Stigmatization, shown to be a critical barrier to substance abuse treatment,[99] may also contribute to the low treatment rates found in this study. Taken together, these results highlight the need for physicians to periodically and systematically screen for NMPOU and NMPOUD and to educate patients and their families about the risks associated with them,

The present results contrast with NSDUH findings of stable rates of 12-month NMPOU (4.2%–4.9%) and NMPOUD (0.6%–0.8%) between 2002 and 2013.[100] Differing

definitions of NMPOU could explain these discrepancies, since only respondents answering NMPOU questions affirmatively are asked NMPOUD items. The AUDADIS versions used in the NESARC-III and 2001–2002 NESARC include many more items than the NSDUH instruments, and their test-retest reliability and validity are extensively documented.[37,38,40–48] Better sensitivity through more extensive probing of NMPOUD criteria has been identified as another reason for discrepancies in rates between these surveys.[101]

Strengths of NESARC-III included its large sample; reliable and valid measures of NMPOU, NMPOUD, and other psychopathology; and rigorous methodology. The NESARC-III is also unique in providing current, comprehensive information on the epidemiology of NMPOU and *DSM-5* NMPOUD in the United States from a single uniform source. Limitations include that not all psychiatric disorders were assessed, similar to other large US surveys. Because some population segments (homeless individuals, prisoners) were not covered, the prevalence of NMPOU and NMPOUD may have been underestimated. The NESARC-III was also cross-sectional. Longitudinal surveys are needed to further investigate the stability of relationships found herein.

Nonmedical prescription opioid use and NMPOUD have increased considerably over the past decade, are associated with a broad array of risk factors and comorbidities, and largely go untreated in the United States. Valid assessment tools and algorithms are needed to stratify patients by risk based on current methodologically rigorous epidemiologic studies. This study demonstrated strong associations of NMPOU and NMPOUD with pain, other substance use disorders, and psychiatric disorders that may indicate the severe impact of pain on mental health or difficulties in translating comorbidity care into clinical practice. The critical treatment gap observed in this study highlights the need for research on evidence-based treatments for NMPOUD that may better match affected individuals' clinical characteristics.[102–104] As more information emerges on determinants, characteristics, and outcomes of NMPOU and NMPOUD, appropriate prevention and intervention must balance the complexity of these conditions with access to prescription opioids for all who need them.

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POSTTEST

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1. You treat patients among the following demographic groups. Which of your patients are at highest risk for nonmedical prescription opioid use (NMPOU) and *DSM-5* nonmedical prescription opioid use disorder (NMPOUD)?

a. Women older than 65 years and in higher income categories

b. Asian or Hispanic individuals who attended college and are married

c. Those younger than 65 years who are widowed/separated/divorced and in lower income categories

2. What are the main clinical correlates of both 12-month and lifetime NMPOU and NMPOUD?

a. NMPOU and NMPOUD are not associated with psychiatric comorbidity

b. NMPOU and NMPOUD are strongly related to other nonmedical prescription drug use disorders, alcohol use disorder, nicotine use disorder, mood disorders, posttraumatic stress disorder, and personality disorders

c. NMPOU and NMPOUD are strongly related to bipolar II disorder, panic disorder, and specific phobias