American Journal of
Preventive Medicine

RESEARCH BRIEF

Changing Trends in Opioid Overdose Deaths and Prescription Opioid Receipt Among Veterans

Lewei (Allison) Lin, MD, MS,[1,2] Talya Peltzman, MPH,[3] John F. McCarthy, PhD, MPH,[1,2,3] Elizabeth M. Oliva, PhD,[4,5] Jodie A. Trafton, PhD,[4,5] Amy S.B. Bohnert, PhD, MHS[1,2]

Introduction: To inform overdose prevention, this study assessed both recent trends in opioid overdose mortality across opioid categories and receipt of prescription opioid analgesics among Veterans who died from overdose in the Veterans Health Administration.

Methods: Using Veterans Health Administration records linked to National Death Index data, annual cohorts (2010–2016) of Veterans who received Veterans Health Administration care were obtained and were examined by opioid overdose categories (natural/semisynthetic opioids, heroin, methadone, and other synthetic opioids) on (1) overdose rates and changes in rates adjusted for age, sex, and race/ethnicity; and (2) Veterans Health Administration prescription opioid receipt. Analyses were conducted in 2018.

Results: The overall rate of opioid overdose among Veterans increased from 14.47 per 100,000 person-years in 2010 to 21.08 per 100,000 person-years in 2016 (adjusted rate ratio=1.65, 95% CI=1.51, 1.81). There was a decline in methadone overdose (adjusted rate ratio=0.66, 95% CI=0.51, 0.84) and no significant change in natural/semisynthetic opioid overdose (adjusted rate ratio=1.08, 95% CI=0.94, 1.24). However, the synthetic opioid overdose rate (adjusted rate ratio=5.46, 95% CI=4.41, 6.75) and heroin overdose rate (adjusted rate ratio=4.91, 95% CI=3.92, 6.15) increased substantially. Among all opioid overdose decedents, prescription opioid receipt within 3 months before death declined from 54% in 2010 to 26% in 2016.

Conclusions: Opioid overdose rates among Veterans Health Administration Veterans increased because of increases in heroin and synthetic opioid overdose rates. Prescriptions of opioids declined among patients who died from all categories of opioid overdose; by 2016, only a minority received an opioid analgesic from Veterans Health Administration within 3 months of overdose. Future prevention efforts should extend beyond patients actively receiving opioid prescriptions.

Am J Prev Med 2019;57(1):106–110. Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine.

INTRODUCTION

Since the 1990s, mortality from opioid overdose in the U.S. increased substantially, initially because of natural/semisynthetic opioids (i.e., commonly prescribed opioids).[1] Receipt of prescription opioids has been found to be a key risk factor for opioid overdose.[2,3] This observation has informed initiatives that have contributed to substantial reductions in opioid prescribing.[4,5] However, there have not yet been decreases in opioid overdose mortality.[6] A key question is whether there has been a reduction in opioid prescriptions among individuals who have died from overdose. It is also critical to examine

From the [1]Department of Psychiatry, University of Michigan, Ann Arbor, Michigan; [2]Center for Clinical Management Research, Veterans Affairs (VA) Ann Arbor Healthcare System, Ann Arbor, Michigan; [3]Serious Mental Illness Treatment Resource and Evaluation Center, VA Office of Mental Health and Suicide Prevention, Ann Arbor, Michigan; [4]Program Evaluation and Resource Center, VA Office of Mental Health and Suicide Prevention, Menlo Park, California; and [5]Center for Innovation to Implementation, VA Palo Alto Health Care System, Palo Alto, California

Address correspondence to: Lewei (Allison) Lin, MD, MS, University of Michigan and VA Ann Arbor Healthcare System, Building 16, 2nd Floor, 2800 Plymouth Road, Ann Arbor MI 48109. E-mail: leweil@med.umich.edu.

0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2019.01.016

prescription opioid receipt across specific categories of opioid overdose, as overdose patterns in recent years have shifted from natural/semisynthetic opioids to heroin and synthetic opioids, primarily from illicit sources.[6,7]

Reducing Veteran overdose mortality is a key priority of the Veterans Health Administration (VHA),[8] the largest integrated health system in the U.S. In 2013, the VHA began the Opioid Safety Initiative, a multifaceted intervention that has been associated with significant reductions in opioid prescribing.[8,9] Decreases in opioid prescribing were largely due to decreased initiation of long-term prescribing rather than discontinuation of long-term prescribing.[10] To inform VHA overdose prevention efforts, this study compared VHA opioid overdose rates and receipt of prescription opioids among Veterans receiving VHA care who died from opioid overdose in 2010 and 2016 across opioid overdose categories: natural/semisynthetic opioids, methadone, other synthetic opioids, and heroin.

METHODS

Study Sample

Annual cohorts from 2010 through 2016 were generated for recent Veteran VHA users, defined as Veterans aged ≥18 years with at least one VHA inpatient or outpatient encounter in the year or the prior year who were alive at the start of the year.[11] Vital status, date of death, and cause of death through 2016 were drawn from National Death Index search results from the Veterans Affairs/Department of Defense Suicide Data Repository. This project was conducted as part of national VHA evaluation for quality improvement and was exempt from IRB review.

Measures

Overdose deaths were identified using established definitions used in the Centers for Disease Control and Prevention surveillance using the following cause of death codes: X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and further specified opioid overdose deaths (T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6).[7] Categories of opioid overdoses were identified using the following ICD-10 multiple cause-of-death codes: natural/semisynthetic opioids (T40.2); methadone (T40.3); synthetic opioids other than methadone (T40.4); and heroin (T40.1). Categories were not mutually exclusive; if a death was related to more than one opioid type, then it was counted in each category. People who died from overdose involving multiple opioids were included in an additional category.

Prescription fill data for overdose decedents were obtained from VHA's Corporate Data Warehouse. Receipt of an opioid analgesic in the prior 3 months and 1 year was determined by any VHA opioid analgesic fill with days' supply of medications that covered the time period (Appendix lists opioids included).

Statistical Analysis

For each annual cohort between 2010 and 2016, overdose mortality rates were calculated by dividing the number of overdose deaths by the total risk time. Risk time was calculated starting January 1 of the year for Veterans who had VHA encounters the previous year or at the first encounter of the year for individuals with no encounters in the prior year. Risk time continued until death or end of the year, whichever came first.[11] Rates were calculated per 100,000 person-years of risk time.

Age, sex, and race/ethnicity were extracted from VHA records for all overdose decedents. Poisson regressions with log person-years as an offset were used to compare changes in unadjusted overdose rates and in rates adjusted for demographic differences between the 2010 and 2016 overall VHA patient populations. Given increasing prevalence of mental health and substance use disorder diagnoses in VHA patients,[12] sensitivity analyses were conducted adjusting for prevalence of these conditions.

The proportion of overdose decedents with an active opioid prescription within 3 months and 1 year prior to death was calculated among decedents in each overdose category. Percentages of decedents with active prescriptions in 2010 to 2016 were compared using Poisson regression models that adjusted for changes in sex, age, and race/ethnicity. Analyses were conducted in 2018.

RESULTS

From 2010 to 2016, there were 6,485 VHA Veterans who died from any opioid overdose, with increasing trend over time (Figure 1). Appendix Table 1 (available online) provides demographic characteristics. Opioid overdose rates in the VHA population increased from 14.47 in 2010 to 21.08 in 2016 (adjusted rate ratio=1.65, 95% CI=1.51, 1.81), mostly from increases in overdoses from heroin and non-methadone synthetic opioids (Table 1). In sensitivity analysis, adjustment for the prevalence of mental health or substance use disorder diagnoses did not substantially alter the magnitude or significance.

Among opioid overdose decedents, past-year VHA opioid analgesic receipt declined from 66% in 2010 to 41% in 2016 (Table 2), and past 3-month receipt declined from 54% to 26%. In 2016, Veterans who died from semisynthetic opioids had the highest prevalence of past 3-month opioid receipt (38%) followed by Veterans who died from synthetic opioid overdose (22%) and from heroin overdose (18%).

DISCUSSION

Overall opioid overdose rates in the VHA increased from 2010 to 2016. Similar to the general U.S. population, trends varied substantially across opioid categories.[7] Overdose from semisynthetic/natural opioids, which includes commonly prescribed opioids, did not change significantly. However, overdose rates from heroin and synthetic opioids rose sharply. These changes were concurrent with substantial reductions in receipt of opioid analgesics across all opioid overdose categories.

This study presents recent trends in both overdose mortality and opioid prescribing, which have implications

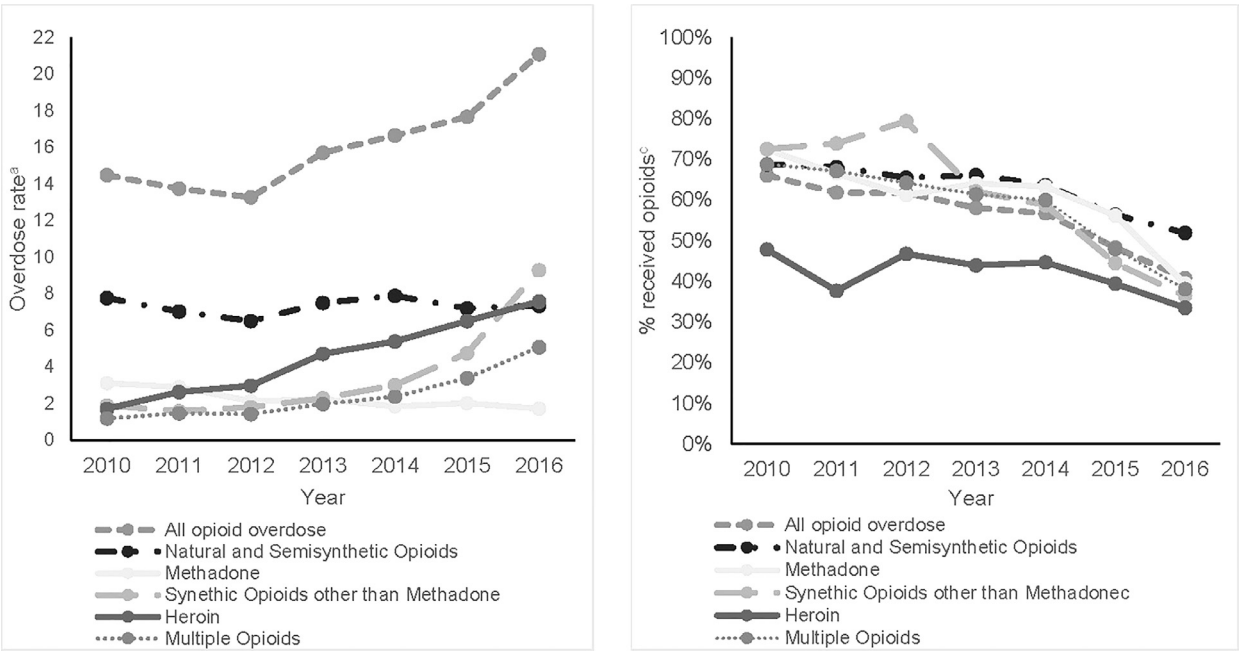

Figure 1. Opioid overdose rates and opioid prescribing trends among Veterans Health Administration (VHA) patients (2010–2016). [a]Overdose rate is measured as deaths per 100,000 person-years. [b]Natural/semisynthetic opioids include the commonly prescribed opioids such as hydrocodone and oxycodone and also morphine. Synthetic opioids include high potency opioids such as fentanyl, typically from illicit sources in recent years.[7] Multiple opioids include individuals who died from overdoses involving more than one opioid. [c]Measured as the proportion of Veterans who died from overdose who received a VHA opioid prescription fill in the year prior to death.

for overdose prevention. First, risk for semisynthetic/natural opioid overdose may need to be considered separately from heroin and synthetic opioid overdose, as receipt of prescription opioids may account for less risk for the latter groups. Second, given that only a third of patients filled opioids within 3 months prior to death, overdose prevention efforts must broaden beyond patients actively receiving opioids. Finally, although the VHA has implemented

Table 1. Changes in Opioid Overdose Rates Among Veterans Receiving VHA Care (2010–2016)

Categories of opioid overdose	Opioid overdose rate per 100,000 person-years[a] (95% CI)		Rate ratio, unadjusted[b]	Rate ratio, adjusted[c]
	2010	2016		
All opioid overdose deaths	14.47 (13.45, 15.49)	21.08 (19.92, 22.24)	1.46 (1.33, 1.59)	1.65 (1.51, 1.81)
Natural and semisynthetic opioid overdose[d]	7.77 (7.02, 8.52)	7.35 (6.66, 8.03)	0.95 (0.83, 1.08)	1.08 (0.94, 1.24)
Methadone overdose	3.12 (2.65, 3.59)	1.73 (1.39, 2.06)	0.55 (0.43, 0.71)	0.66 (0.51, 0.84)
Other synthetic opioid overdose[e]	1.91 (1.54, 2.27)	9.29 (8.52, 10.06)	4.88 (3.95, 6.02)	5.46 (4.41, 6.75)
Heroin overdose	1.72 (1.39, 2.11)	7.58 (6.89, 8.28)	4.41 (3.53, 5.52)	4.91 (3.92, 6.15)
Multiple opioid overdose	1.19 (0.93, 1.53)	5.09 (4.55, 5.69)	4.26 (3.26, 5.58)	4.75 (3.62, 6.23)

[a]In 2010, there were a total of 5,843,852 VHA Veterans who contributed a total of 5,356,364 person-years. In 2016, there were a total of 6,465,403 Veterans who contributed a total of 6,029,567 person-years.
[b]Unadjusted rate ratio comparing 2016 with 2010 unadjusted overdose rates.
[c]Adjusted for changes in sex, age, race/ethnicity in the overall VHA Veteran population between 2016 and 2010.
[d]Natural/semisynthetic opioids include the commonly prescribed opioids such as hydrocodone and oxycodone and also morphine.
[e]Synthetic opioids include high-potency opioids such as fentanyl, typically from illicit sources in recent years.[7]

Table 2. Change in Prescription Opioid Receipt in Veterans Receiving VHA Care Who Died From Opioid Overdose (2010–2016)

Categories of opioid overdose	% of overdose decedents receiving prescription opioids (95% CI)		Unadjusted risk ratio[a]	Adjusted risk ratio[b]
	2010	2016		
All opioid overdose deaths				
In prior 12 months	66 (63, 69)	41 (38, 43)	0.62 (0.55, 0.70)	0.59 (0.52, 0.67)
In prior 3 months	54 (50, 57)	26 (24, 29)	0.48 (0.42, 0.55)	0.47 (0.41, 0.54)
Natural and semisynthetic opioid overdose[c]				
In prior 12 months	69 (64, 73)	52 (47, 57)	0.76 (0.63, 0.90)	0.72 (0.60, 0.86)
In prior 3 months	58 (53, 63)	38 (33, 42)	0.65 (0.53, 0.79)	0.61 (0.50, 0.75)
Methadone overdose				
In prior 12 months	73 (66, 79)	39 (30, 49)	0.54 (0.38, 0.78)	0.54 (0.38, 0.78)
In prior 3 months	62 (54, 69)	23 (15, 32)	0.37 (0.24, 0.58)	0.38 (0.24, 0.59)
Other synthetic opioid overdose[d]				
In prior 12 months	73 (64, 81)	36 (32, 40)	0.50 (0.38, 0.66)	0.51 (0.38, 0.67)
In prior 3 months	60 (50, 69)	22 (19, 26)	0.37 (0.27, 0.51)	0.40 (0.29, 0.54)
Heroin overdose				
In prior 12 months	48 (38, 58)	33 (29, 38)	0.70 (0.50, 0.98)	0.60 (0.43, 0.84)
In prior 3 months	30 (21, 40)	18 (15, 22)	0.60 (0.39, 0.92)	0.50 (0.32, 0.77)
Multiple opioid overdose				
In prior 12 months	69 (57, 80)	38 (32, 44)	0.55 (0.39, 0.78)	0.53 (0.37, 0.76)
In prior 3 months	55 (43, 67)	23 (19, 28)	0.43 (0.29, 0.64)	0.45 (0.30, 0.68)

[a]Receipt of opioid prescriptions among those who died from overdose were compared 2010 to 2016 using Poisson regression.
[b]Adjusted for changes in sex, age, race/ethnicity among Veterans who died from overdose between 2010 and 2016.
[c]Natural/semisynthetic opioids include the commonly prescribed opioids such as hydrocodone and oxycodone and also morphine.
[d]Synthetic opioids include high-potency opioids such as fentanyl, typically from illicit sources in recent years.[7]
VHA, Veterans Health Administration.

numerous efforts including Overdose Education and Naloxone Distribution and the Opioid Safety Initiative,[8,13,14] additional efforts are needed including increasing medication treatment for patients with opioid use disorders.[14]

Limitations

This study cannot specify the causal relationship between opioid prescriptions and overdose deaths, which would require detailed information about each patient's death. Also, heroin may be particularly undercounted in mortality data because it is metabolized to morphine, a natural opioid categorized along with semisynthetics, and more so recently with the surge in heroin contaminated with synthetic opioids.[7,15,16] The study focuses on Veterans, an important population at higher risk for overdose than the general population.[17] However, Veterans obtain opioids outside of the VHA[18] and Veterans not receiving VHA care are not included in these data, a population that may need additional interventions. Finally, the population studied is predominantly male, which means the findings may not be representative of the general U.S. population.

CONCLUSIONS

The impacts of efforts reducing opioid supply on overdose remain unclear,[19] and further studies are needed. However, increased exposure to opioids in recent decades nationally and the link between prescription opioid misuse and heroin use suggest the epidemic of overdoses will continue with illicit opioids.[20–22] Currently, it is critical to broaden the scope of prevention efforts beyond individuals actively prescribed opioids and

prioritize approaches associated with overdose reduction, such as medication-assisted treatment.[23]

ACKNOWLEDGMENTS

We thank H. Myra Kim of the Center for Clinical Management Research, Veterans Affairs Ann Arbor Healthcare System, and University of Michigan for statistical support.

This study was conducted as part of ongoing surveillance in the VA Office of Mental Health and Suicide Prevention.

The study was developed and conducted and the manuscript drafted independently by the study authors, who made the decision to submit the manuscript. The manuscript was shared with VA mental health leadership for review.

Author contributions were as follows: study concept and design: Lin, McCarthy, Peltzman, and Bohnert; acquisition, analysis, or interpretation of data: all authors; drafting of the manuscript: Lin; critical revision of the manuscript for important intellectual content: all authors; statistical analysis: Lin and Peltzman; administrative, technical, or material support: all authors; and study supervision: Lin and McCarthy.

No financial disclosures are reported by the authors of this paper.

SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2019.01.016.

REFERENCES

1. Okie S. A flood of opioids, a rising tide of deaths. *N Engl J Med.* 2010;363(21):1981–1985. https://doi.org/10.1056/NEJMp1011512.
2. Park TW, Lin LA, Hosanagar A, Kogowski A, Paige K, Bohnert ASB. Understanding risk factors for opioid overdose in clinical populations to inform treatment and policy. *J Addict Med.* 2016;10(6):369–381. https://doi.org/10.1097/ADM.0000000000000245.
3. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med.* 2015;162(4):276–286. https://doi.org/10.7326/M14-2559.
4. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA.* 2016;315(15):1624–1645. https://doi.org/10.1001/jama.2016.1464.
5. Guy GP, Zhang K, Bohm MK, et al. Vital signs: changes in opioid prescribing in the United States, 2006–2015. *MMWR Morb Mortal Wkly Rep.* 2017;66(26):697–704. https://doi.org/10.15585/mmwr.mm6626a4.
6. Hedegaard H, Warner M, Minino AM. *Drug Overdose Deaths in the United States, 1999–2016. National Center for Health Statistics. 2017/ CDC. Wide-Ranging Online Data for Epidemiologic Research (WONDER).* Atlanta, GA: CDC, National Center for Health Statistics; 2016. http://wonder.cdc.gov. Accessed February 5, 2019.
7. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. *MMWR Morb Mortal Wkly Rep.* 2016;65(50–51):1445–1452. https://doi.org/10.15585/mmwr.mm655051e1.
8. Gellad WF, Good CB, Shulkin DJ. Addressing the opioid epidemic in the United States: lessons from the Department of Veterans Affairs. *JAMA Intern Med.* 2017;177(5):611–612. https://doi.org/10.1001/jamainternmed.2017.0147.
9. Lin LA, Bohnert ASB, Kerns RD, Clay MA, Ganoczy D, Ilgen MA. Impact of the Opioid Safety Initiative on opioid-related prescribing in Veterans. *Pain.* 2017;158(5):833–839. https://doi.org/10.1097/j.pain.0000000000000837.
10. Hadlandsmyth K, Mosher H, Vander Weg MW, Lund BC. Decline in prescription opioids attributable to decreases in long-term use: a retrospective study in the Veterans Health Administration 2010–2016. *J Gen Intern Med.* 2018;33(6):818–824. https://doi.org/10.1007/s11606-017-4283-8.
11. McCarthy JF, Valenstein M, Kim HM, Ilgen M, Zivin K, Blow FC. Suicide mortality among patients receiving care in the Veterans Health Administration health system. *Am J Epidemiol.* 2009;169(8):1033–1038. https://doi.org/10.1093/aje/kwp010.
12. Office of Mental Health and Suicide Prevention. VA National Suicide Data Report 2005–2015. www.mentalhealth.va.gov/docs/data-sheets/2015/OMHSP_National_Suicide_Data_Report_2005-2015_06-14-18_508.pdf. Published 2018. Accessed August 7, 2018.
13. Oliva EM, Christopher MLD, Wells D, et al. Opioid overdose education and naloxone distribution: development of the Veterans Health Administration's national program. *J Am Pharm Assoc (2003).* 2017;57 (2 suppl):S168-S179.e4. https://doi.org/10.1016/j.japh.2017.01.022.
14. Wyse JJ, Gordon AJ, Dobscha SK, et al. Medications for opioid use disorder in the Department of Veterans Affairs (VA) health care system: historical perspective, lessons learned and next steps. *Subst Abus.* 2018;39(2):139–144. https://doi.org/10.1080/08897077.2018.1452327.
15. Horon IL, Singal P, Fowler DR, Sharfstein JM. Standard death certificates versus enhanced surveillance to identify heroin overdose-related deaths. *Am J Public Health.* 2018;108(6):777–781. https://doi.org/10.2105/AJPH.2018.304385.
16. O'Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by Census region—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep.* 2017;66(34):897–903. https://doi.org/10.15585/mmwr.mm6634a2.
17. Bohnert ASB, Ilgen MA, Galea S, McCarthy JF, Blow FC. Accidental poisoning mortality among patients in the Department of Veterans Affairs health system. *Med Care.* 2011;49(4):393–396. https://doi.org/10.1097/MLR.0b013e318202aa27.
18. Moyo P, Zhao X, Thorpe CT, et al. Patterns of opioid prescriptions received prior to unintentional prescription opioid overdose death among Veterans. *Res Social Adm Pharm.* In press. Online October 17, 2018. https://doi.org/10.1016/j.sapharm.2018.10.023.
19. Von Korff M, Saunders K, Dublin S, et al. Impact of chronic opioid therapy risk reduction initiatives on opioid overdose. *J Pain.* 2019;20 (1):108–117. https://doi.org/10.1016/j.jpain.2018.08.003.
20. Carlson RG, Nahhas RW, Martins SS, Daniulaityte R. Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: a natural history study. *Drug Alcohol Depend.* 2016;160:127–134. https://doi.org/10.1016/j.drugalcdep.2015.12.026.
21. Banerjee G, Edelman EJ, Barry DT, et al. Non-medical use of prescription opioids is associated with heroin initiation among U.S. Veterans: a prospective cohort study. *Addiction.* 2016;111(11):2021–2031. https://doi.org/10.1111/add.13491.
22. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med.* 2016;374(2):154–163. https://doi.org/10.1056/NEJMra1508490.
23. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. *Ann Intern Med.* 2018;169(3):137–145. https://doi.org/10.7326/M17-3107.