Title

Trends in Prescriptions for Non-opioid Pain Medications Among U.S. Adults With Moderate or Severe Pain, 2014-2018

Journal

Journal of Pain, 23(7)

ISSN

1082-3174

Authors

Gorfinkel, Lauren R
Hasin, Deborah
Saxon, Andrew J
et al.

Publication Date

2022-07-01

DOI

10.1016/j.jpain.2022.01.006

Peer reviewed

HHS Public Access

Author manuscript

J Pain. Author manuscript; available in PMC 2023 July 01.

Published in final edited form as:

J Pain. 2022 July ; 23(7): 1187–1195. doi:10.1016/j.jpain.2022.01.006.

Trends in Prescriptions for Non-opioid Pain Medications Among U.S. Adults With Moderate or Severe Pain, 2014–2018

Lauren R. Gorfinkel[*,†], **Deborah Hasin**[*,‡,§], **Andrew J. Saxon**[¶,‖], **Melanie Wall**[**], **Silvia S. Martins**[‡], **Magdalena Cerdá**[††], **Katherine Keyes**[‡], **David S. Fink**[*], **Salomeh Keyhani**[‡‡,§§], **Charles C. Maynard**[¶¶], **Mark Olfson**[§]

[*]The New York State Psychiatric Institute, New York, New York,

[†]Department of Medicine, University of British Columbia, Vancouver, Canada,

[‡]Department of Epidemiology, Columbia University, New York, New York,

[§]Department of Psychiatry, Columbia University, New York, New York,

[¶]Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington,

[‖] Veteran Affairs Puget Sound Health System, United States of America,

[**]Department of Biostatistics, Columbia University, New York, New York,

[††]Department of Population Health, New York University School of Medicine, New York, New York,

[‡‡]San Francisco VA Medical Center, San Francisco, California,

[§§]Department of Medicine, University of California, San Francisco, California,

[¶¶]Department of Health Services, University of Washington, Seattle, Washington

Abstract

As opioid prescribing has declined, it is unclear how the landscape of prescription pain treatment across the U.S. has changed. We used nationally-representative data from the Medical Expenditure Health Survey, 2014 to 2018 to examine trends in prescriptions for opioid and non-opioid pain medications, including acetaminophen, non-steroidal anti-inflammatory drugs, gabapentinoids, and antidepressants among U.S. adults with self-reported pain. Overall, from 2014 to 2018, the percentage of participants receiving a prescription for opioids declined, (38.8% vs 32.8%), remained stable for non-steroidal anti-inflammatory drugs (26.8% vs 27.7%), and increased for acetaminophen (1.6% vs 2.3%), antidepressants (9.6% vs 12.0%) and gabapentinoids (13.2% vs 19.0%). In this period, the adjusted odds of receiving an opioid prescription decreased (aOR = .93, 95% CI = .90–.96), while the adjusted odds of receiving antidepressant, gabapentinoid and acetaminophen prescriptions increased (antidepressants: aOR = 1.08, 95% CI = 1.03–1.13

Address reprint requests to Lauren Gorfinkel, MPH, New York State Psychiatric Institute, University of British Columbia, 722 W. 168th Street, Room 228E, New York New York 10032, 2350 Health Sciences Mall, Vancouver, BC V6T 1Z3, Canada. lrgorfinkel@gmail.com.

Conflicts of Interest: The authors have no conflicts of interest to disclose.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2022.01.006.

gabapentinoids: aOR = 1.11, 95% CI = 1.06–1.17; acetaminophen: aOR = 1.10, 95% CI: 1.02–1.20). Secondary analyses stratifiying within the 2014 to 2016 and 2016 to 2018 periods revealed particular increases in prescriptions for gabapentinoids (aOR = 1.13, 95% CI = 1.05–1.21) and antidepressants (aOR = 1.23, 95% CI = 1.12–1.35) since 2016.

Perspective: These data demonstrate that physicians are increasingly turning to CDC-recommended non-opioid medications for pain management, particularly antidepressants and gabapentinoids. However, evidence for these medications' efficacy in treating numerous common pain conditions, including low back pain, remains limited.

Keywords

Pain; opioids; gabapentin; pregabalin; antidepressants; NSAIDs; acetaminophen; epidemiology

Introduction

Prescription opioids have been repeatedly implicated in the North American opioid crisis.[16,21,30,40] Although rates of opioid dispensing peaked in 2012, the prevalence of medical opioid use remains extremely high, with over 153 million opioid prescriptions dispensed in 2019.[14] During this year, prescription opioids were detected in over 14,000 overdose deaths, or the equivalent of approximately 40 deaths per day.[54] These deaths, in addition to those caused by unregulated synthetic opiates, have prompted several policy changes, including the introduction of prescription drug monitoring programs,[38,69] pain management clinic laws,[15] and harm reduction services.[1,48] One major policy response has been to discourage physicians from risky opioid prescribing practices.[56] In 2016, the U.S. Centers for Disease Control and Prevention (CDC) released new medical guidelines for the management of chronic pain, raising cautions around opioids and emphasizing alternative prescription pain treatments.[23,45] The effort to reduce opioid prescriptions was further aided by increased cultural awareness of the addictive potential of opioids,[37,43] and increasing evidence that long-term opioid treatment is not effective for some pain conditions.[9]

By many metrics, efforts to reduce opioid prescribing have been successful.[11,13,18,31,36,56,72] In 2016, an estimated 5.96 million fewer adults were prescribed opioids for pain than in 2014,[56] a decrease that extended across demographic subgroups and adults with varying pain levels.[56] Given these decreases, concerns have recently been raised over poorly controlled pain.[12,58,62] It has been speculated that some patients lose faith in physicians if their pain is not adequately controlled[12] and may seek more dangerous unregulated opioids.[51] However, opioids are not the only available medications for pain. Current CDC pain management guidelines highlight multiple non-opioid drug classes, including non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen for nociceptive pain, and antidepressants (ie, SNRIs and tricyclics) and gabapentinoids (ie, pregabalin and gabapentin) for neuropathic pain.[23,55]

At present, little is known about whether decreases in opioid prescriptions have been accompanied by increases in prescriptions for non-opioid analgesics. Such information is urgently needed to understand secular changes in pain prescriptions and inform discussions on adequate pain management. A recent study showed a small increase in non-opioid pain

prescriptions after release of the 2016 CDC guidelines, but grouped all classes of non-opioid drugs together.[24] Specific information is lacking on how the landscape of pharmacological pain management and the use of non-opioid pain medications may be evolving with the decline of prescription opioids.

To fill this knowledge gap, we used a nationally representative sample of U.S. adults with self-reported pain to examine trends in prescriptions for opioids and major classes of non-opioid pain medications. Specifically, we examined trends from 2014 to 2018 in prescriptions for opioids, antidepressants, gabapentinoids, NSAIDs and acetaminophen among adults with self-reported moderate-to-severe pain.

Methods

Data Sources

Data for the current analysis come from the Medical Expenditure Panel Survey–Household Component (MEPS-HC), conducted by the Agency for Health Care Research and Quality (AHRQ). The MEPS-HC is a nationally representative survey of the U.S. civilian noninstitutionalized population. Each year, a new sample is drawn from the previous year's National Health Interview Survey. Participants undergo a series of 3 interviews prior to the end of the survey year in which they answer questions related to health care status, service utilization and related topics. Participants are instructed to record medical events in a calendar or journal, which is then reviewed in person during the interview. Participants are further asked for written consent to contact their doctors, pharmacies, hospitals and health insurance companies to verify and supplement health care service information. This information, known as the Medical Provider Component of MEPS, is asked of all participants completing the MEPS-HC, and includes a pharmacy authorization form for each pharmacy from which a participant obtained prescription medicines. From 2014 to 2018, 70 to 80% of respondents gave authorization for MEPS to contact their pharmacies.[2] African Americans, Hispanics, Asians and people with predicted low incomes are over-sampled to provide more accurate study estimates. A more detailed description of MEPS sampling, adjustments, and response is available elsewhere.[3] Because prior research with MEPS-HC data demonstrated national decreases in opioid prescriptions beginning in 2014,[56] we examined changes in prescriptions from 2014 onwards.

Participants

The analysis was limited to adults surveyed in MEPS 2014 to 2018 aged 18 and over with self-reported pain interference. Pain interference was identified using an item from the Short-From Health Survey 36 (SF-36), a validated measure frequently used in population surveys.[10,41,65,68] This item asked participants "During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?", with options "not at all", "a little bit", "moderately", "quite a bit", and "extremely". Consistent with prior literature,[10,26,41] a threshold of "moderately" or more was used to identify participants with moderate-to-severe pain. The use of self-reported pain captured individuals who may not have received a formal diagnosis of chronic pain conditions. For brevity, self-reported pain interference is hereafter referred to as self-reported pain.[37–39]

Prescription Pain Medications

Information on prescription medications was collected during each of the 3 interviews in a given survey year. Participants were asked to bring all their medication bottles, which were referenced when answering questions concerning prescribed medicines obtained during that year. Participants were additionally asked for consent to contact their pharmacies to confirm information about these prescriptions, and medical event diaries and calendars aided in recall. Data were only collected on medications obtained in outpatient settings (eg, hospital outpatient visits, office-based visits, and dental office visits). The current study examined prescriptions for opioids, gabapentinoids, antidepressants, non-steroidal anti-inflammatories (NSAIDs) and acetaminophen. Opioids included all Schedule II and III opioids listed by the Drug Enforcement Administration, including opioid/acetaminophen combinations and the Schedule IV opioid tramadol. Gabapentinoids included gabapentin and pregabalin. Antidepressants included serotonin and norepinephrine reuptake inhibitors (SNRIs, including duloxetine and venlafaxine) and tricyclic antidepressants. All medications were chosen to be consistent with a review of current guidelines[23] and literature on guidelines for pain management.[5,6,52,55] A full list of specific medications included in each class is presented in eTable 1.

Control Variables

Adjusted analyses controlled for age group (ages 18–29, 30–64, and 65 and over), sex (male, female), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, or non-Hispanic other), highest level of education (less than high school, high school or GED, or at least some college), and family income as a percentage of the Federal Poverty Level (less than 100 percent, 100–400 percent, and more than 400 percent). Analyses of antidepressant prescriptions additionally adjusted for depressive symptoms, measured with the Patient Health Questionnaire 2 (PHQ-2).[47]

Sensitivity Analyses

Because updated 2016 pain guidelines focused on chronic non-cancer pain, a sensitivity analysis removed all individuals who reported having cancer from the analytic sample. To avoid potential confounding by increases in the prevalence of depression and other psychiatric disorders, an additional sensitivity analyses removed all individuals reporting a diagnosis of mood or anxiety disorders from the analysis of antidepressant prescriptions. Cancer and psychiatric diagnoses were obtained from the MEPS Medical Conditions files,[3] and were identified by prompting respondents for the causes of medical events, disability episodes or from medical care records. Prior to 2016, conditions were coded by AHRQ staff using the International Classification of Diseases, ninth revision (ICD-9) system, then grouped into Clinical Classification Categories for the publicly-available dataset. From 2016 onwards, conditions were coded using the ICD-10 system. Therefore, the current study identified cancer and mood/anxiety disorders using Clinical Classification Categories codes from 2014 to 2015, and using ICD-10 codes from 2016 to 2018. A full list of condition codes included in this analysis are presented in eTables 2 and 3.

Statistical Analysis

The current analysis examined changes in prescription pain medications among U.S. adults with self-reported pain from 2014 to 2018. In all models, survey year was the primary independent variable and pain medication prescription was the outcome. Logistic regression was used to examine annual changes in prescriptions for each class of pain medication (opioids, antidepressants, gabapentinoids, NSAIDs and acetaminophen). Separate models were fit for each medication class. Crude and adjusted odds ratios described annual changes in the odds of being prescribed each medication class among adults with self-reported moderate or severe pain.

In a secondary analysis, we fit separate lines for the years 2014 to 2016 and 2016 to 2018. This was done in light of the 2016 release of CDC guidelines for pain management,[23] prior research demonstrating decreases in opioid prescriptions in MEPS-HC from 2014 to 2016[56] but not 2016 onwards,[39] and preliminary analyses of the relationship between survey year and log odds of pain prescriptions demonstrating best fit with 2 lines.

All statistical analyses were conducted using SAS version 9.4 and accounted for the complex sampling design of MEPS-HC, including variables for cluster, strata and adjusted sample weights. Taylor series estimation methods were used to obtain standard error estimates. Two-tailed differences of $P < .05$ were considered significant. As this study used publicly-available deidentified data, it was exempted from human subjects review by the Institutional Review Board of the New York State Psychiatric Institute.

Results

The final sample included 20,238 U.S. adults with moderate-to-severe pain, accounting for 18.3% of all U. S. adults from 2014 to 2018. Overall, a majority of adults with self-reported pain were female (57.4%), aged 30 to 64 (55.5%), non-Hispanic white (67.7%), and had family incomes that were 100 to 400 percent of the federal poverty level (50.6%). Sample characteristics by survey year are presented in Table 1.

Trends in Prescriptions Among U.S. Adults With Pain From 2014 to 2018

From 2014 to 2018, the prevalence of prescription opioids among adults with self-reported pain decreased from 38.8 to 32.1%, and the adjusted odds of receiving an opioid fell by an average of 7% per year (aOR = .93, 95% CI = .90–.96). In contrast, the prevalence and adjusted odds of receiving a prescription increased for antidepressants (9.6–12.0%, aOR = 1.08, 95% CI = 1.03–1.13), gabapentinoids (13.2–19.0%, aOR = 1.11, 95% CI = 1.06–1.17), and acetaminophen (1.6–2.3%, aOR = 1.10, 95% CI: 1.02–1.20), while the prevalence and adjusted odds of receiving prescription NSAIDs remained stable (26.8–27.7%, aOR = .99, 95% CI = .96–1.03). All prevalences and odds ratios by medication class are presented in Tables 2 and 3.

Differences in Trends Within the 2014 to 2016 and 2016 to 2018 Periods

From 2014 to 2016, prescriptions decreased for opioids (aOR = .86, 95% CI = .82–.91), increased for gabapentinoids (aOR = 1.10, 95% CI = 1.01–1.20) and acetaminophen (aOR

= 1.40, 95% CI: 1.19–1.65), and remained stable for antidepressants (aOR = .93, 95% CI = .84–1.03) and NSAIDs (aOR = .95, 95% CI = .90–1.01). From 2016 to 2018, prescriptions remained stable for opioids (OR = 1.02, 95% CI = .95–1.08) and acetaminophen (aOR = .87, 95% CI: .73–1.03), and increased for antidepressants (aOR = 1.23, 95% CI = 1.12–1.35) and gabapentinoids (aOR = 1.13, 95% CI = 1.05–1.21). Prescriptions also increased for NSAIDs (aOR = 1.08, 95% CI: 1.01–1.15), however, the absolute prevalence of prescriptions was similar to pre-2016 levels (Table 2). Odds ratios for the 2014 to 2016 and 2016 to 2018 periods are presented in Table 4.

Sensitivity Analyses

After excluding 2,636 respondents who reported cancer diagnoses, none of the results significantly changed (eTable 4). After excluding 7,606 respondents who reported diagnoses of mood or anxiety disorders, the adjusted odds of receiving an antidepressant prescription from 2014 to 2018 increased (aOR = 1.14, 95% CI = 1.04–1.25) – a rise that was driven by change in the 2016 to 2018 period (aOR = 1.38, 95% CI = 1.15–1.65) (eTable 5).

Discussion

This study examined national trends between 2014 and 2018 in prescriptions for opioid and non-opioid pain medications filled by U.S. adults with self-reported pain. Overall, we examined 5 classes of medications used to manage chronic pain: opioids, gabapentinoids, antidepressants, NSAIDs and acetaminophen. With this information, we aimed to characterize how the landscape of prescription pain treatment changed as opioid prescribing declined nationally. We highlight 3 main findings: 1) Although opioid prescribing decreased from 2014 to 2016, it was stable from 2016 to 2018. Consistent with prior studies, opioids remained the most commonly-prescribed pain medication[36,56]; 2) Throughout the full study period from 2014 to 2018, prescriptions for acetaminophen, gabapentinoids and antidepressants increased; and 3) In recent years from 2016 to 2018, there were particular increases in prescriptions for gabapentinoids and antidepressants. Gabapentinoid prescriptions showed the largest rise, with nearly 1 in 5 U.S. adults with pain obtaining gabapentin or pregabalin in 2018. NSAID prescriptions also increased during this period, however, there was not a substantial change in their absolute prevalence compared to 2014.

Our finding that opioid prescriptions were stable from 2016 to 2018 is consistent with another study of survey data from a nationally-representative U.S. sample,[39] however, our finding differs from other studies using administrative data, which report declines in opioid prescriptions during this period.[14] Factors that account for the differences in findings between survey and administrative data may include 1) the nationally-representative nature of our data, which is less subject to selection bias and confounding than administrative datasets; 2) our examination of individuals prescribed opioids rather than numbers of opioids dispensed, which may be biased by individuals with large numbers of opioid prescriptions; and 3) the substantial representation of older adults in our sample, who are more likely to have chronic pain interfere with their daily activities, and therefore be identified as adults with pain by the current study. For example, a recent study of commercial insurance claims

by adults aged 65 and older similarly found no decline in opioid prescriptions from 2016 to 2018.[46] In an additional study of a large national insurance database, the percent of patients filling an opioid prescription was stable among Medicare Advantage beneficiaries from 2016 to 2018.[32] As older adults remain 1 of the prime demographics for whom opioids are prescribed for chronic pain,[70] further research aimed at assessing recent trends in opioid prescriptions in this population is needed.

Notably, we found increases in the prevalence of prescriptions for a number of non-opioid pain medications, including acetaminophen, gabapentinoids and antidepressants. Changes in gabapentinoids and antidepressants were particularly prominent after 2016, suggesting that the release of the 2016 CDC pain guidelines may have successfully encouraged their use for pain management. Indeed, the benefit of gabapentinoids and antidepressants for pain has been demonstrated in several studies.[19,28,60,63,71] These medications are recommended first-line agents for neuropathic pain, and often used off-label for nociceptive pain, particularly when NSAIDs and acetaminophen are ineffective or contraindicated.[35] This off-label use may be clinically warranted, as a growing body of literature has found some traditionally nociceptive pain conditions, such as osteoarthritis, to have neuropathic components.[7,22] In general, increasing use of acetaminophen, gabapentinoids and antidepressants among adults with pain may represent a positive step away from overuse of prescription opioids.

However, gabapentinoids and antidepressants are imperfect opioid replacements. With the exception of tricyclic antidepressants, all of these drugs have high Numbers Needed to Treat (NNT, a measure of the number of patients requiring treatment in order for 1 patient to achieve a 50% reduction in pain) compared to opioids (NNTs for chronic neuropathic pain: 7.2 for gabapentin, 7.7 for pregabalin, 6.4 for SNRIs, 3.6 for tricyclic antidepressants, 4.3 for strong opioids).[29] While several antidepressants, including amitriptyline, duloxetine, and venlafaxine, have demonstrated efficacy for controlling chronic neuropathic pain,[4,49,66] others such as nortriptyline and imipramine lack evidence.[20,42] Clinical trials demonstrating the efficacy of gabapentin are limited to post herpetic neuralgia and peripheral diabetic neuropathy.[59] Gabapentinoids have been shown to be ineffective in other common pain conditions, including low back pain and chronic pelvic pain.[25,44,50,64] Increasing use of gabapentinoids and antidepressants may therefore be cause for concern, as the urgent effort to reduce opioid use may have pushed clinical prescribing practices in directions not supported by current evidence.

This concern is amplified by 2 recent studies suggesting that gabapentinoids may increase the risk for overdose death involving opioids.[33,34,61] In December, 2019, the U.S. Food and Drug Administration began requiring a boxed warning on gabapentinoids concerning the risk of serious breathing difficulties.[67] Gabapentinoids can themselves can be misused,[27] although this risk may be limited to adults with preexisting opioid use disorder.[8,57] Though more research on the interaction between gabapentinoids with opioids is needed, physicians who prescribe these medications should be aware of potential interaction effects in promoting respiratory depression.[33,34]

Finally, we found that acetaminophen prescriptions increased from 2014 to 2016. While it is not entirely clear why these prescriptions remained stable following 2016, it is possible

that use of this medication was already optimized prior to the guideline release. Similarly, this finding could be due to our lack of information on over-the-counter acetaminophen use, which may have continued to increase despite stable prescriptions.

The current study has several limitations. First, our pain measure accounted for only intensity of work-related pain interference, and not pain type, duration, or condition, thereby complicating inferences concerning the effectiveness of treatments. Although the SF-36 is validated and widely used, future studies should include a more comprehensive pain measure.[53] Second, since MEPS relies on participant recall, calendars and diaries, participants could have underestimated their prescriptions, particularly those with greater temporal distance from the interview. However, follow-up surveys with prescribers and pharmacies helped confirm participant information. Third, we were only able to measure prescription medications. Over-the-counter NSAIDs and acetaminophen were not included, and their prevalence is significantly higher than reported in this study.[17] However, trends in prescriptions for NSAIDs and acetaminophen may serve as a proxy trend in overall use and characterize physician prescribing. Fourth, the current study lacked information regarding repeated use or dose. Fifth, we lack information on the conditions for which each medication was prescribed and whether they were used specifically for the purposes of pain management. However, by limiting the analysis to individuals who report pain, we increase the likelihood that prescriptions were used for pain management, and there is currently no evidence of differential trends in the rates of various pain conditions over time. Sixth, the MEPS is based on a household sample so the results may not generalize to adults who are homeless, incarcerated, or receiving residential care. Seventh, the current study examined prescriptions over the past 12 months among adults reporting pain over the past 4 weeks. We were therefore unable to account for individuals who may have had well-controlled pain, or comment on the clinical effectiveness of different pain management strategies. Finally, the current study examined only pharmacologic options for chronic pain management, and did not address non-pharmacologic interventions, such as physiotherapy and massage, which are often first-line and highly effective treatments for chronic pain. Future research should aim to investigate trends in the use of these interventions.

Conclusions

Overall, our findings suggest that U.S. physicians are increasingly prescribing CDC-recommended non-opioid medications for pain management, particularly antidepressants and gabapentinoids. While these changes are consistent with recent pain management guidelines, individual considerations concerning specific risks and evidence for these alternative medications are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

DH, AJS, MW, SSM, MC, KK, DSF, SK, CCM and MO would like to acknowledge funding from the National Institute on Drug Abuse (R01DA048860). SSM would like to acknowledge additional funding from the National

Institute on Drug Abuse (R01DA045872). AJS would like to acknowledge funding from the Center of Excellence in Substance Addiction Treatment and Education, VA Puget Sound Health Care System.

References

1. Abouk R, Pacula RL, Powell D: Association between state laws facilitating pharmacy distribution of naloxone and risk of fatal overdose. JAMA Intern Med 179:805–811, 2019 [PubMed: 31058922]
2. Agency for Healthcare Research and Quality: MEPS Household Component. Annual contractor methodology report. 2017. Available at: https://meps.ahrq.gov/data_files/publications/annual_contractor_report/hc_ann_cntrct_methrpt.shtml Accessed December 23, 2021
3. Agency for Healthcare Research and Quality: Household Components: Survey Basics. 2022. Available at: https://www.meps.ahrq.gov/mepsweb/survey_comp/household.jsp
4. Aiyer R, Barkin RL, Bhatia A: Treatment of neuropathic pain with venlafaxine: A systematic review. Pain Med 18:1999–2012, 2017 [PubMed: 27837032]
5. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older P: Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 57:1331–1346, 2009 [PubMed: 19573219]
6. Attal N, Cruccu G, Baron R, Haanpaa M, Hansson P, Jensen TS, Nurmikko T: EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. Eur J Neurol 17:1113–e1188, 2010 [PubMed: 20402746]
7. Baron R, Binder A, Attal N, Casale R, Dickenson AH, Treede RD: Neuropathic low back pain in clinical practice. Eur J Pain 20:861–873, 2016 [PubMed: 26935254]
8. Bastiaens L, Galus J, Mazur C: Abuse of Gabapentin is associated with opioid addiction. Psychiatr Q 87:763–767, 2016 [PubMed: 26887855]
9. Berthelot JM, Darrieutort-Lafitte C, Le Goff B, Maugars Y: Strong opioids for noncancer pain due to musculoskeletal diseases: Not more effective than acetaminophen or NSAIDs. Joint Bone Spine 82:397–401, 2015 [PubMed: 26453108]
10. Blanco C, Wall MM, Okuda M, Wang S, Iza M, Olfson M: Pain as a predictor of opioid use disorder in a nationally representative sample. Am J Psychiatry 173:1189–1195, 2016 [PubMed: 27444794]
11. Bohnert ASB, Guy GP Jr., Losby JL: Opioid prescribing in the United States before and after the centers for disease control and prevention's 2016 opioid guideline. Ann Intern Med 169:367–375, 2018 [PubMed: 30167651]
12. Busse JW, Juurlink D, Guyatt GH: Addressing the limitations of the CDC guideline for prescribing opioids for chronic noncancer pain. CMAJ 188:1210–1211, 2016 [PubMed: 27873754]
13. Centers for Disease Control and Prevention: 2018 Annual Surveillance Report of Drug-Related Risks and Outcomes — United States. Surveillance special report., 2018.
14. Centers for Disease Control and Prevention: U.S. Opioid Dispensing Rate Map Available at: https://www.cdc.gov/drugoverdose/rxrate-maps/index.html Accessed Aug 03, 2021
15. Cerda M, Wheeler-Martin K, Bruzelius E, Ponicki W, Gruenewald P, Mauro C, Crystal S, Davis CS, Keyes K, Hasin D, Rudolph KE, Martins SS: Spatiotemporal analysis of the association between pain management clinic laws and opioid prescribing and overdose deaths. Am J Epidemiol, 2021
16. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S: Cohort study of the impact of high-dose opioid analgesics on overdose mortality. Pain Med 17:85–98, 2016 [PubMed: 26333030]
17. Davis JS, Lee HY, Kim J, Advani SM, Peng HL, Banfield E, Hawk ET, Chang S, Frazier-Wood AC: Use of non-steroidal anti-inflammatory drugs in US adults: Changes over time and by demographic. Open Heart 4:e000550, 2017 [PubMed: 28674622]
18. Dayer LE, Breckling MN, Kling BS, Lakkad M, McDade ER, Painter JT: Association of the "CDC guideline for prescribing opioids for chronic pain" with emergency department opioid prescribing. J Emerg Med 57:597–602, 2019 [PubMed: 31594747]
19. Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA: Pregabalin for neuropathic pain in adults. Cochrane Database Syst Rev 1:CD007076, 2019 [PubMed: 30673120]

20. Derry S, Wiffen PJ, Aldington D, Moore RA: Nortriptyline for neuropathic pain in adults. Cochrane Database Syst Rev 1:CD011209, 2015 [PubMed: 25569864]
21. DeWeerdt S: Tracing the US opioid crisis to its roots. Nature 573:S10–S12, 2019 [PubMed: 31511672]
22. Dimitroulas T, Duarte RV, Behura A, Kitas GD, Raphael JH: Neuropathic pain in osteoarthritis: A review of patho-physiological mechanisms and implications for treatment. Semin Arthritis Rheum 44:145–154, 2014
23. Dowell D, Haegerich TM, Chou R: CDC Guideline for prescribing opioids for chronic pain–United States, 2016. JAMA 315:1624–1645, 2016 [PubMed: 26977696]
24. Encinosa W, Bernard D, Selden TM: Opioid and non-opioid analgesic prescribing before and after the CDC's 2016 opioid guideline. Int J Health Econ Manag 22:1–52, 2022 [PubMed: 33963977]
25. Enke O, New HA, New CH, Mathieson S, McLachlan AJ, Latimer J, Maher CG, Lin CC: Anticonvulsants in the treatment of low back pain and lumbar radicular pain: A systematic review and meta-analysis. CMAJ 190:E786–E793, 2018 [PubMed: 29970367]
26. Enkema MC, Hasin DS, Browne KC, Stohl M, Shmulewitz D, Fink DS, Olfson M, Martins SS, Bohnert KM, Sherman SE, Cerda M, Wall M, Aharonovich E, Keyhani S, Saxon AJ: Pain, cannabis use, and physical and mental health indicators among veterans and non-veterans: Results from national epidemiologic survey on alcohol and related conditions-III. Pain 163:267–273, 2022 [PubMed: 34108436]
27. Evoy KE, Sadrameli S, Contreras J, Covvey JR, Peckham AM, Morrison MD: Abuse and misuse of pregabalin and gabapentin: A systematic review update. Drugs 81:125–156, 2021 [PubMed: 33215352]
28. Ferreira GE, McLachlan AJ, Lin CC, Zadro JR, Abdel-Shaheed C, O'Keeffe M, Maher CG: Efficacy and safety of antidepressants for the treatment of back pain and osteoarthritis: Systematic review and meta-analysis. BMJ 372: m4825, 2021 [PubMed: 33472813]
29. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpaa M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice AS, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M: Pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis. Lancet Neurol 14:162–173, 2015 [PubMed: 25575710]
30. Fischer B, Pang M, Tyndall M: The opioid death crisis in Canada: Crucial lessons for public health. Lancet Public Health 4:e81–e82, 2019 [PubMed: 30579840]
31. Gleber R, Vilke GM, Castillo EM, Brennan J, Oyama L, Coyne CJ: Trends in emergency physician opioid prescribing practices during the United States opioid crisis. Am J Emerg Med 38:735–740, 2020 [PubMed: 31227419]
32. Goldstick JE, Guy GP, Losby JL, Baldwin G, Myers M, Bohnert ASB: Changes in initial opioid prescribing practices after the 2016 release of the CDC guideline for prescribing opioids for chronic pain. JAMA Netw Open 4:e2116860, 2021 [PubMed: 34255047]
33. Gomes T, Greaves S, van den Brink W, Antoniou T, Mamdani MM, Paterson JM, Martins D, Juurlink DN: Pregabalin and the risk for opioid-related death: A nested case-control study. Ann Intern Med 169:732–734, 2018 [PubMed: 30140853]
34. Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, van den Brink W: Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case-control study. PLoS Med 14:e1002396, 2017 [PubMed: 28972983]
35. Goodman CW, Brett AS: Gabapentin and pregabalin for pain - is increased prescribing a cause for concern? N Engl J Med 377:411–414, 2017 [PubMed: 28767350]
36. Guy GP Jr., Zhang K, Bohm MK, Losby J, Lewis B, Young R, Murphy LB, Dowell D: Vital signs: Changes in opioid prescribing in the United States, 2006–2015. MMWR Morb Mortal Wkly Rep 66:697–704, 2017 [PubMed: 28683056]
37. Hadlandsmyth K, Stewart KR, Paez MB, Steffen M, Meth M, Reisinger HS, Mosher HJ: Patient perspectives on opioids: Views of inpatient veterans with chronic pain. Pain Med 20:1141–1147, 2019 [PubMed: 30020506]
38. Haffajee RL, Mello MM, Zhang F, Zaslavsky AM, Larochelle MR, Wharam JF: Four states with robust prescription drug monitoring programs reduced opioid dosages. Health Aff (Millwood) 37:964–974, 2018 [PubMed: 29863921]

39. Hales CM, Martin CB, Gu Q: Prevalence of prescription pain medication use among adults: United States, 2015–2018. NCHS Data Brief 369:1–8, 2020
40. Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ: Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 300:2613–2620, 2008 [PubMed: 19066381]
41. Hasin DS, Shmulewitz D, Cerda M, Keyes KM, Olfson M, Sarvet AL, Wall MM: U.S. adults with pain, a group increasingly vulnerable to nonmedical cannabis use and cannabis use disorder: 2001–2002 and 2012–2013. Am J Psychiatry 177:611–618, 2020 [PubMed: 31964162]
42. Hearn L, Derry S, Phillips T, Moore RA, Wiffen PJ: Imipramine for neuropathic pain in adults. Cochrane Database Syst Rev 5:CD010769, 2014
43. Hensley S: Americans Weigh Addiction Risk When Taking Painkillers. National Public Radio (NPR), 2014 https://www.npr.org/sections/health-shots/2014/06/20/323957823/americans-weigh-addiction-risk-when-taking-painkillers
44. Horne AW, Vincent K, Cregg R, Daniels J: Is gabapentin effective for women with unexplained chronic pelvic pain? BMJ 358:j3520, 2017 [PubMed: 28935652]
45. Houry D, Baldwin G: Announcing the CDC guideline for prescribing opioids for chronic pain. J Safety Res 57:83–84, 2016 [PubMed: 27178083]
46. Kern DM, Cepeda MS, Sena AG: Oral opioid prescribing trends in the United States, 2002–2018. Pain Med 21:3215–3223, 2020 [PubMed: 33106880]
47. Kroenke K, Spitzer RL, Williams JB: The patient health questionnaire-2: Validity of a two-item depression screener. Med Care 41:1284–1292, 2003 [PubMed: 14583691]
48. Lambdin BH, Davis CS, Wheeler E, Tueller S, Kral AH: Naloxone laws facilitate the establishment of overdose education and naloxone distribution programs in the United States. Drug Alcohol Depend 188:370–376, 2018 [PubMed: 29776688]
49. Lunn MP, Hughes RA, Wiffen PJ: Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev 1:CD007115, 2014
50. Mathieson S, Maher CG, McLachlan AJ, Latimer J, Koes BW, Hancock MJ, Harris I, Day RO, Billot L, Pik J, Jan S, Lin CC: Trial of pregabalin for acute and chronic sciatica. N Engl J Med 376:1111–1120, 2017 [PubMed: 28328324]
51. Meadowcroft D, Whitacre B: Do prescription drug monitoring programs encourage prescription - or illicit - opioid abuse? Subst Abus 42:65–75, 2021 [PubMed: 31821128]
52. Moulin DE, Clark AJ, Gilron I, Ware MA, Watson CP, Sessle BJ, Coderre T, Morley-Forster PK, Stinson J, Boulanger A, Peng P, Finley GA, Taenzer P, Squire P, Dion D, Cholkan A, Gilani A, Gordon A, Henry J, Jovey R, Lynch M, Mailis-Gagnon A, Panju A, Rollman GB, Velly A: Canadian pain S. Pharmacological management of chronic neuropathic pain - consensus statement and guidelines from the Canadian pain society. Pain Res Manag 12:13–21, 2007 [PubMed: 17372630]
53. Nahin RL, Sayer B, Stussman BJ, Feinberg TM: Eighteen-year trends in the prevalence of, and health care use for, noncancer pain in the United States: Data from the medical expenditure panel survey. J Pain 20:796–809, 2019 [PubMed: 30658177]
54. National Institute on Drug Abuse: Trends and Statistics: Overdose Death Rates. Available at: https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates Accessed Jun. 17, 2021
55. O'Connor AB, Dworkin RH: Treatment of neuropathic pain: An overview of recent guidelines. Am J Med 122:S22–S32, 2009
56. Olfson M, Wang S, Wall MM, Blanco C: Trends in opioid prescribing and self-reported pain among US adults. Health Aff (Millwood) 39:146–154, 2020 [PubMed: 31905067]
57. Peckham AM, Evoy KE, Covvey JR, Ochs L, Fairman KA, Sclar DA: Predictors of gabapentin overuse with or without concomitant opioids in a commercially insured U.S. population. Pharmacotherapy 38:436–443, 2018 [PubMed: 29484686]
58. Pergolizzi JV Jr., Rosenblatt M, LeQuang JA: Three years down the road: The aftermath of the CDC guideline for prescribing opioids for chronic pain. Adv Ther 36:1235–1240, 2019 [PubMed: 31016474]

59. Puljak L: Can gabapentin alleviate chronic neuropathic pain in adults?: A cochrane review summary with commentary. Am J Phys Med Rehabil 99:558–559, 2020 [PubMed: 32251104]
60. Quilici S, Chancellor J, Lothgren M, Simon D, Said G, Le TK, Garcia-Cebrian A, Monz B: Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. BMC Neurol 9:6, 2009 [PubMed: 19208243]
61. Rhee TG, Maust DT, Fiellin DA, Olfson M: Trends in Coprescribing of opioids and opioid potentiators among U.S. adults, 2007–2018. Am J Prev Med 60:434–437, 2021 [PubMed: 33199162]
62. Rich RLC Jr: Prescribing opioids for chronic pain: Unintended consequences of the 2016 CDC guideline. Am Fam Physician 101:458–459, 2020 [PubMed: 32293841]
63. Riediger C, Schuster T, Barlinn K, Maier S, Weitz J, Siepmann T: Adverse effects of antidepressants for chronic pain: A systematic review and meta-analysis. Front Neurol 8:307, 2017 [PubMed: 28769859]
64. Robertson K, Marshman LAG, Plummer D, Downs E: Effect of gabapentin vs pregabalin on pain intensity in adults with chronic sciatica: A randomized clinical trial. JAMA Neurol 76:28–34, 2019 [PubMed: 30326006]
65. Rubio JM, Olfson M, Villegas L, Perez-Fuentes G, Wang S, Blanco C: Quality of life following remission of mental disorders: Findings from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry 74:e445–e450, 2013 [PubMed: 23759465]
66. Saarto T, Wiffen PJ: Antidepressants for neuropathic pain. Cochrane Database Syst Rev 4:CD005454, 2007
67. U.S. Food and Drug Administration: FDA in Brief: FDA Requires New Warnings for Gabapentinoids About Risk of Respiratory Depression. Silver Spring, MD, U.S. Food and Drug Administration, 2019
68. Ware JEJ, Snow KK, Kosinski M, Gandek B: SF-36 Health Survey: Manual and Interpretation Guide. Boston, MA, New England Medical Center, Health Institute, 1993
69. Wen H, Hockenberry JM, Jeng PJ, Bao Y: Prescription drug monitoring program mandates: Impact on opioid prescribing and related hospital use. Health Aff (Millwood) 38:1550–1556, 2019 [PubMed: 31479368]
70. West NA, Severtson SG, Green JL, Dart RC: Trends in abuse and misuse of prescription opioids among older adults. Drug Alcohol Depend 149:117–121, 2015 [PubMed: 25678441]
71. Wiffen PJ, Derry S, Bell RF, Rice AS, Tolle TR, Phillips T, Moore RA: Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev 6:CD007938, 2017 [PubMed: 28597471]
72. Woods C, Chai G, Meyer T, Staffa J, Dal Pan G: Patterns of opioid analgesic use in the U.S., 2009 to 2018. Pain 162:1060–1067, 2021 [PubMed: 33021566]

Table 1.

Sample Characteristics Among U.S. Adults with Moderate-to-Severe Pain, Medical Expenditure Panel Survey – Household Component, 2014–2018

N (WEIGHTED %)	SURVEY YEAR					TOTAL
	2014	2015	2016	2017	2018	
Sex						
Male	1,728 (43.1)	1,779 (42.6)	1,754 (41.8)	1,376 (42.4)	1,391 (43.3)	**8,028 (42.6)**
Female	2,648 (56.9)	2,726 (57.4)	2,679 (58.2)	2,168 (57.6)	1,989 (56.7)	**12,210 (57.4)**
Age						
18–29	409 (8.6)	369 (8.2)	339 (7.4)	175 (6.0)	141 (5.8)	**1,433 (7.3)**
30–64	2,633 (56.7)	2,724 (57.1)	2,621 (55.2)	2,004 (54.9)	1,791 (52.7)	**11,773 (55.5)**
65+	1,334 (34.7)	1,412 (34.7)	1,473 (37.4)	1,364 (39.1)	1,448 (42.0)	**7,031 (37.2)**
Race/Ethnicity						
Non-Hispanic White	1,930 (68.2)	2,083 (67.8)	2,107 (67.6)	1,847 (66.2)	2,057 (68.7)	**10,024 (67.7)**
Non-Hispanic Black	1,118 (13.1)	1,036 (12.5)	952 (12.8)	765 (14.5)	585 (13.0)	**4,456 (13.2)**
Hispanic	934 (11.4)	998 (12.3)	1,002 (12.1)	662 (11.6)	492 (10.8)	**4,088 (11.7)**
Other or multiracial *	394 (7.3)	388 (7.4)	372 (7.5)	270 (7.5)	246 (7.5)	**1,670 (7.5)**
Level of education						
Less than high school	1,260 (20.8)	1,087 (18.3)	1,139 (19.5)	854 (18.6)	698 (16.7)	**4,617 (18.9)**
High school or GED	1,207 (29.5)	1,567 (34.7)	1,506 (34.7)	1,224 (32.4)	1,221 (33.7)	**7,160 (33.0)**
At least some college	1,869 (49.7)	1,811 (47.0)	1,742 (45.8)	1,436 (49.0)	1,441 (49.6)	**8,289 (48.1)**
Family income (percentage of federal poverty level)						
<100 percent	1,241 (20.0)	1,146 (17.7)	1,176 (18.3)	896 (19.2)	853 (20.0)	**5,312 (19.0)**
100–400 percent	2,288 (50.5)	2,401 (51.3)	2,272 (49.2)	1,918 (53.3)	1,675 (49.1)	**10,554 (50.6)**
>400 percent	847 (29.4)	958 (30.9)	985 (32.5)	730 (27.5)	852 (30.9)	**4,372 (30.3)**
Total †	**4,376**	**4,505**	**4,433**	**3,544**	**3,380**	**20,238**

NOTE: Bold type denotes that these are total value.

* This category includes respondents who identified their race as American Indian/Alaska Native, Asian, Native Hawaiian/Pacific Islander, or multiracial.

† Sample size decreases by year in accordance with decreases in overall MEPS-HC sample sizes.[68]

Table 2.

Prevalence of Prescription Pain Medications Among U.S. Adults with Moderate-to-Severe Pain (N = 20,238)

WEIGHTED PREVALENCE (SE)	SURVEY YEAR				
	2014	2015	2016	2017	2018
Opioids *	38.8 (1.1)	37.7 (1.0)	32.1 (1.0)	33.2 (1.0)	32.8 (1.0)
Antidepressants †					
With opioids ‡	5.2 (.4)	5.3 (.3)	4.4 (.3)	5.5 (.5)	6.1 (.4)
Without opioids §	4.5 (.4)	3.4 (.4)	4.1 (.3)	5.3 (.4)	5.9 (.5)
Total	9.6 (.5)	8.7 (.5)	8.5 (.5)	1.8 (.6)	12.0 (.7)
Gabapentinoids					
With opioids ‡	8.5 (.6)	9.0 (.6)	8.6 (.5)	9.2 (.6)	1.3 (.7)
Without opioids §	4.6 (.4)	5.6 (.5)	6.9 (.5)	8.7 (.6)	8.8 (.6)
Total	13.2 (.8)	14.6 (.8)	15.5 (.7)	17.9 (.8)	19.0 (.8)
NSAIDs					
With opioids ‡	14.6 (.7)	12.9 (.7)	1.7 (.7)	1.9 (.6)	12.1 (.7)
Without opioids §	12.1 (.6)	14.6 (.8)	14.1 (.7)	14.1 (.7)	15.6 (.8)
Total	26.8 (.9)	27.5 (.9)	24.8 (.9)	25.0 (.9)	27.7 (.9)
Acetaminophen					
With opioids ‡	.6 (.1)	.8 (.1)	1.0 (.2)	.8 (.2)	.9 (.2)
Without opioids §	1.0 (.2)	.8 (.2)	1.9 (.2)	1.4 (.2)	1.4 (.2)
Total	1.6 (.2)	1.7 (.2)	2.9 (.3)	2.2 (.3)	2.3 (.3)

Abbreviation: SE, standard error.

* Includes Schedule II and III opioids, and tramadol.

† Includes select pain-indicated Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) and tricyclic antidepressants.

‡ Respondents who reported receiving both an opioid and non-opioid prescription within the same calendar year.

§ Respondents who reported receiving only non-opioid prescriptions in a given calendar year.

Table 3.

Unadjusted and Adjusted Odds Ratios for Annual Changes in Pain Prescriptions Among U.S. Adults with Moderate-to-Severe Pain, 2014–2018

OR (95% CI)	SURVEY YEARS:2014–2018
Opioids	
Unadjusted	.93 (.90–.96)***
Adjusted†	.93 (.90–.96)***
Antidepressants	
Unadjusted	1.07 (1.03–1.12)***
Adjusted‡	1.08 (1.03–1.13)***
Gabapentinoids	
Unadjusted	1.12 (1.07–1.17)***
Adjusted†	1.11 (1.06–1.17)***
NSAIDs	
Unadjusted	.99 (.96–1.03)
Adjusted†	.99 (.96–1.03)
Acetaminophen	
Unadjusted	1.11 (1.02–1.21)*
Adjusted†	1.10 (1.02–1.20)*

Abbreviations: SE, standard error; OR, odds ratio; CI, confidence interval.

*$P < .05$.

**$P < .01$.

***$P < .001$.

†Adjusted for sex, age, race, level of education, and level of income.

‡Adjusted for sex, age, race, level of education, level of income and depression.

Table 4.

Unadjusted and Adjusted Odds Ratios for Annual Changes in Pain Prescriptions Among U.S. Adults with Moderate-to-Severe Pain, 2014–2018

OR (95% CI)	SURVEY YEARS	
	2014–2016	2016–2018
Opioids		
Unadjusted	.87 (.82–.91)***	1.02 (.95–1.09)
Adjusted†	.86 (.82–.91)***	1.02 (.95–1.08)
Antidepressants		
Unadjusted	.93 (.86–1.02)	1.21 (1.11–1.32)***
Adjusted‡	.93 (.84–1.03)	1.23 (1.12–1.35)***
Gabapentinoids		
Unadjusted	1.10 (1.01–1.19)*	1.14 (1.06–1.22)**
Adjusted†	1.10 (1.01–1.20)*	1.13 (1.05–1.21)**
NSAIDs		
Unadjusted	.95 (.90–1.01)	1.08 (1.01–1.15)*
Adjusted†	.95 (.90–1.01)	1.08 (1.01–1.15)*
Acetaminophen		
Unadjusted	1.40 (1.19–1.66)***	.88 (.74–1.04)
Adjusted†	1.40 (1.19–1.65)***	.87 (.73–1.03)

Abbreviations: SE, standard error; OR, odds ratio; CI, confidence interval.

*$P < .05$.

**$P < .01$.

***$P < .001$.

†Adjusted for sex, age, race, level of education, and level of income.

‡Adjusted for sex, age, race, level of education, level of income and depression.