# Long-term Opioid Treatment of Nonmalignant Pain

*Braden JB, Russo J, Fan M, et al. Emergency department visits among chronic opioid therapy recipients. Arch Intern Med 2010;170:1425–32.*

## Study Overview

Objective. To determine the association between chronic opioid therapy and subsequent emergency department (ED) visits and alcohol- or drug-related encounters (ADEs) among individuals prescribed opioids for at least 90 continuous days.

Design. Secondary analysis of longitudinal administrative data from the Trends and Risks of Opioid Use for Pain (TROUP) study.

Setting and participants. The TROUP study was designed to assess trends in and risks of chronic opioid therapy for noncancer pain among insured individuals with arthritis and/or joint pain, back pain, neck pain, headaches, or HIV/AIDS. The TROUP study collected information on 2 distinct populations: a national commercially insured population (HealthCore) ($n$ = 38,491) and Arkansas Medicaid enrollees ($n$ = 10,159). Adult enrollees were ≥ 18 years of age and used opioids for at least 90 continuous days over a 6-month period between 1 Jan 2001 and 31 Dec 2004. The index date was defined as the first day of opioid use, and in order to be included in the study individuals needed to have 12 months of eligibility prior to and following the index date. The authors included as covariates in their multivariable regression models demographics, clinical characteristics including the overall medical comorbidity and diagnoses of pain conditions, number of mental health disorders, substance use disorders, and medication use (dosages of and days' supply of opioids and use of sedative/hypnotics). Sociodemographic and clinical data came from claims records in the 12-month period prior to the index date of opioid use. The Charlson comorbidity index was used to measure overall medical comorbidity. The tracer pain diagnoses were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). Information on nontracer pain diagnoses was obtained using the ICD-9-CM and summed to get the total number. Mental health and substance use disorders were classified using the ICD-9-CM into the following categories: adjustment disorders, anxiety disorders, mood disorders, personality disorders, and substance use disorders. Substance use disorders were further classified as alcohol use disorder, nonopioid-use disorder (abuse or dependence), or opioid-use disorder (abuse or dependence). Information on prescribed opioids was obtained using prescription claims. Opioids were categorized into short-acting schedule II opioids, long-acting schedule II opioids, and non-schedule II opioids. The authors calculated the opioid daily dose and categorized it as less than the median (32 mg morphine equivalent dose [MED]/day for the HealthCore sample and 35 mg MED/day for the Arkansas Medicaid sample), median to 120 mg MED/day, and > 120 mg MED/day. Opioid days' supply was categorized into 160 days or less, more than 160 but less than 185 days, and greater than 185 days. The authors also obtained information on use of sedative and/or hypnotic agents.

Main outcome measures. The main outcome measure was health services utilization, measured as ED visits and ADEs in the 12-month period following the index date of opioid use. For ADEs, the authors combined inpatient, outpatient and those occurring in the ED because the total number of ADE visits was small. ICD-9-CM codes were used to track diagnoses for admissions to the ED.

Main results. HealthCore and Arkansas Medicaid enrollees who were on chronic opioid therapy were middle-aged and mostly female. One-quarter to one-third of the enrollees in both insurance groups had an ED visit in the 12 months following the index date of chronic opioid therapy, and less than 3% had an AED. The most common diagnoses for ED visits among the HealthCore insurance cohort were headache (10.0%) and back problems (9.9%), whereas for the Arkansas Medicaid cohort, back problems (10.4%) and heart disease (7.7%) were the most prevalent. Both samples had similar opioid usage, with the majority being prescribed less than 120 mg MED/day and less than a 160-day supply. Three-fourths of the samples were prescribed non-schedule II opioids. Among chronic opioid therapy users, 43% of both samples used sedative/hypnotic agents for an average of about 2 months. For both samples, the lowest mean daily dose of opioids was among those receiving non-schedule II drugs, and the highest was among those receiving schedule II long- and short-acting drugs. Among

chronic opioid therapy users, younger age, female sex, more medical comorbidities, presence of back pain and headache, and more nontracer medical conditions were associated with ED visits after adjusting for other covariates. Alcohol use, nonopioid use, and opioid use disorders were strongly associated with ED visits in both insurance samples. Receiving an opioid dose above the median but less than 120 mg MED/day was associated with ED visits in the HealthCore sample but not in the Arkansas Medicaid sample. Receiving schedule II short-acting opioids and use of sedative/hypnotic agents were associated with increased ED visits in both samples. Among chronic opioid therapy users, younger age, back pain (HealthCore sample only), and headache (Arkansas Medicaid sample only) were associated with ADEs after adjusting for covariates. Having 2 or more mental health disorders increased the risk of having an ADE by twofold in both samples. Alcohol use and nonopioid use disorders were strongly associated with ADE in both samples, but opioid use disorders was only associated with ADEs in the HealthCore sample. Opioid dose of more than 120 mg MED/day was associated with ADE in the HealthCore sample, but not the Arkansas Medicaid sample. In both samples, using schedule II short-acting opioids was associated with ADE.

Conclusion. Among chronic opioid therapy users, previously diagnosed substance use disorders and use of schedule II opioid therapy were strongly associated with ED visits and ADEs in the subsequent year. Receipt of high-potency schedule II opioid therapy is an important determinant of future medical risk associated with chronic opioid therapy. Minimizing the use of schedule II opioid therapy in high-risk patients may be one strategy to decrease the risk associated with these medications.

## Commentary

Opioid analgesics are commonly used for the treatment of chronic noncancer pain, but with increasing use there has been a rise in misuse [1]. Chronic opioid therapy is not without harm, with recent data showing increased rates of death from prescription opioid overdose, especially among recipients of high doses of these medications [2]. Although there are data on overall rates of prescription opioid overdose, there are none on the demographic and clinical characteristics of chronic opioid therapy recipients who face adverse clinical outcomes from opioid use. This study by Braden et al aims to determine whether chronic opioid therapy prescribing practices are associated with subsequent ED visits and ADEs. This study adds to the literature by showing the demographic and clinical characteristics associated with ED visits and ADEs among adult enrollees of commercial insurance plans and a state Medicaid program who used prescription opioids continuously for at least 90 days.

Not surprisingly, the authors found that chronic opioid therapy was associated with increased likelihood of ED visits and ADEs in both insurance samples. Individuals with substance use disorder diagnoses in the previous year had 18% to 73% more ED use and were 3 to 5 times more likely to have an ADE. Prior studies have demonstrated that history of substance abuse is one of the strongest predictors of prescription opioid abuse [3,4]. This study goes further by demonstrating that prior history of substance abuse among recipients of chronic opioid therapy is strongly associated with subsequent ED visits and ADEs. As suggested by other studies and guidelines, these data point towards the importance of screening for substance use disorders among any recipient of opioid therapy, maintaining close follow-up, and evaluating and referring to substance abuse treatment when appropriate [5]. Concurrent use of sedative and/or hypnotics with prescription opioid analgesics was also associated with increased ED use and ADEs, suggesting that individuals who are likely to misuse opioids are also likely to abuse other substances like alcohol and other drugs [6].

Contrary to their hypothesis, the authors did not observe a consistent dose-response effect with health service outcomes. For instance, an opioid dose above the median but less than 120 mg MED/day was associated with ED use only in the HealthCore sample but not in the Medicaid sample. Doses higher than 120 mg MED/day were not associated with any adverse health encounters in either sample. Use of high-potency schedule II opioids was consistently associated with ED use and ADEs in both samples; the authors speculate that dose adjustments are harder to make with these medications and health care visits could be related to adverse effects from these dose adjustments.

As with other studies using data from administrative claims, this study has limitations. Because most diagnoses were based on ICD-9-CM codes, there is a likelihood that not all cases were identified and a few were misclassified. While there was a strong association between chronic opioid therapy and ED visits and ADEs, there is no definitive way to determine if these visits were caused by prescription opioid use. There is a potential for residual confounding by other factors that are associated with opioid use and ED visits and ADEs, including race, income, and other factors that could affect health care use. Despite these limitations, this study is important because it evaluates the risk-benefit equation of using chronic opioid therapy for noncancer pain among high-risk patients. By using 2 large samples representative of 2 insurers and multiple regions in the United States, the authors have enhanced the generalizability of these findings.

## Applications for Clinical Practice

Given that prior history of substance abuse and mental illness was strongly associated with health services use outcomes among recipients of chronic opioid therapy, clinicians should evaluate and refer these patients to substance abuse and psychiatric treatment when appropriate. Increasing safety of chronic opioid therapy by minimizing use of high-potency schedule II opioids among high-risk patients may be another strategy to decrease risk associated with these medications. Clinicians should use all available tools, although imperfect, including pain agreements and urine testing, to determine if chronic opioid therapy users are at risk for prescription opioid misuse and concurrent substance abuse.

*—Review by Maya Vijayaraghavan, MD*

## References


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