Commentary by Roger Chou, MD

Biography

Roger Chou is a Professor in the Departments of Medicine, and Medical Informatics & Clinical Epidemiology at Oregon Health & Science University (OHSU) School of Medicine, and Staff Physician in the Internal Medicine Clinic at OHSU. He has served as Director of the Pacific Northwest Evidence-based Practice Center since 2012. Dr. Chou's research interests are systematic review methodology, meta-analysis, screening and preventive services, guideline development, and drug effectiveness. He has conducted systematic reviews in a number of areas, including chronic pain and musculoskeletal conditions, screening and prevention, diagnostic testing, and prognosis. He has served as Director of the American Pain Society clinical guidelines program, is the GRADE methodologist for several World Health Organization guidelines, and is a Coordinating Editor for the Cochrane Back and Neck Group. Dr. Chou is on several journal editorial boards and is an author on numerous scientific articles published in peer-reviewed journals.

Commentary on Patterns of Chronic Higher-dose and Lower-dose Opioid Use in Federal Workers' Compensation Claimants

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Dr. Roger Chou, MD is under contract to the Office of Workers’ Compensation Programs to provide consultation on policy development and case review for opioid related issues.

Long-term opioid therapy is associated with dose-dependent risks of serious harms, including overdose and death. Such harms could be exacerbated by presence of other additional factors that further increase opioid-associated risk, such as presence of co-morbid psychiatric or medical conditions, use of concomitant medications, use of immediate- versus extended-release opioids, and obtaining opioid prescriptions from multiple prescribers or pharmacies. Therefore, understanding prescribing patterns among persons prescribed higher doses of opioids is important to inform strategies for reducing opioid-related risks. The study by Cook evaluates factors associated with lower or higher doses of opioids among a large sample of federal workers with compensation claims receiving long-term opioid therapy. Long-term opioid use was based on receipt of ≥120 days or ≥10 refills and >90 total days’ supply over a two-year period and classified as higher dose (≥90 morphine equivalent dose per day [MEDD]) or lower dose (<90 MEDD), using established MED calculation methods.

In the analysis, a number of factors associated with increased risk in persons prescribed opioids were more common in persons prescribed high doses. Studies in other settings have also shown that persons who are at increased risk of adverse opioid-related outcomes are also more likely to be prescribed opioids and to receive higher doses—a phenomenon referred to as “adverse selection.” Patients on higher doses of opioids were more likely to have mental health diagnoses associated with increased risk of opioid misuse or opioid use disorder such as depression or bipolar disease, and slightly more likely to have anxiety. However, the proportion of patients with these conditions was relatively low in both the high and lower dose groups, with small absolute differences (1.1% for anxiety to 3.4% for depression). Patients on high doses of opioids were also more likely to be co-prescribed benzodiazepines, a combination associated with increased risk of overdose. Use of benzodiazepines was relatively common (21.6%), with an absolute difference of about 10% compared with the low opioid dose group. A difference was also noted in the rate of co-prescribing of the “z-hypnotics” zolpidem, zopiclone, and zaleplon (18.4% vs. 11.1%), sedatives with similar respiratory depressant effects as benzodiazepines.
which may be associated with similar overdose risk, though data are limited. High dose patients had a tendency to receive opioids from multiple pharmacies and providers, factors also associated with increased risk of overdose, though average differences were relatively small (mean difference in number of pharmacies or providers ~0.25). Statistically significant but small differences were noted for a number of other risk factors; the large sample had statistical power to detect small effects.

An important limitation of the analysis is that important factors that could account for the differences in prescribing patterns (e.g., severity of pain, response to therapy, and presence of other comorbidities) were not available and could not be evaluated. In addition, the analysis relied on univariate analyses; therefore, findings don’t account for potential interactions between different factors. The analysis wasn’t designed to assess effects of prescribing patterns on clinical outcomes such as pain or function, or how reducing the proportion of patients in the high dose group with risk factors impacts risk of overdose, mortality, or other opioid-related harms. The definition for chronic opioid users could have included some persons who received opioids episodically rather than on a consistent (i.e., daily or near-daily) basis. However, the average days of opioid use over the two year period was nearly 600 days in the high-dose group, indicating a predominantly chronic use population. More data are needed to confirm the association between some factors that were more frequent in the high dose group, such as gabapentin prescribing, and risk of opioid-related adverse events.

Nonetheless, this study shows that use of higher doses of chronic opioid therapy in federal workers with compensation claims is associated with a number of potential risk factors that could exacerbate opioid-related risks. These data are useful for targeting risk mitigation strategies in persons on higher doses of opioids who are at particularly higher risk, by addressing modifiable risk factors (e.g., co-prescribing of medications that increase overdose risk, obtaining opioids from multiple prescribers or pharmacies) and identifying candidates who could benefit from opioid tapering. However, the limitations of the analysis indicate that strict implementation of risk mitigation policies (e.g., mandatory dose reductions or discontinuation of benzodiazepines in all patients prescribed opioids) is not warranted. Rather, risk mitigation efforts require individualized assessments based on the potential benefits and harms of current doses of opioids and prescribing practices, including impacts on pain, function, opioid-related side effects, and comorbid conditions, as well as risks related to the abuse and overdose potential of opioids. Implementation of risk mitigation strategies should be accompanied by analyses on effects of risk factors as well as on clinical outcomes, in order to further inform efforts in this area in an iterative process.

References