Torture Data for Long Enough, You Can Make It Say Anything

By Red Lawhern — February 21, 2021

Richard Lawhern of the ACSH Board of Scientific Advisers points out that US national policy for regulating prescription opioids doesn't lack for data. It instead drowns in persistently biased anti-opioid misrepresentation of the data we already have.

I am a technically trained non-physician who advocates on behalf of patients who are now being widely denied safe and effective opioid therapy for their pain. I've been active in this field for 25 years, communicating with tens of thousands of patients, caregivers, and medical professionals. As you might imagine, I read a lot of medical literature. Some of it is sent to me by non-professionals trying to figure out what it means.

One of these recent inquiries involved a paper titled “Predictors of long-term use of prescription opioids in the community-dwelling population of adults without a cancer diagnosis: a retrospective cohort study [1],” published by an open access journal that is a subsidiary of the Canadian Medical Association. By “open access” we mean that the journal charges authors for the publication of their work, after what they advertise as a “rigorous” peer review process.
In this case, in my opinion, the authors of the paper shouldn’t have spent the money, and the journal’s peer reviewers shouldn’t have approved the paper. To see why let’s deconstruct the abstract of the paper.

**Methods:** Using Quebec administrative claims databases, we conducted a retrospective cohort study in a random sample of adult members (? 18 yr) of the public drug plan who did not have a cancer diagnosis and who initiated a prescription opioid in the outpatient setting between Jan. 1, 2012, and Dec. 31, 2016. The outcome of interest was long-term opioid use (? 90 consecutive days or ? 120 cumulative days over 12 mo). Potential predictors included sociodemographic factors, medical history, characteristics of the initial opioid prescription, and prescriber’s specialty. We used multivariable logistic regression to assess the association between each characteristic and long-term use. We used the area under the receiver operating characteristic curve to determine the predictive performance of full and parsimonious models.

**Results:** Of 124 664 eligible patients who initiated opioid therapy, 4172 (3.3%) progressed to long-term use of prescription opioids. The most important associated factors in the adjusted analysis were long-term prescription of acetaminophen–codeine (odds ratio [OR] 6.30, 95% confidence interval [CI] 4.99 to 7.96), prescription of a long-acting opioid at initiation (OR 6.02, 95% CI 5.31 to 6.84), initial supply of 30 days or more (OR 4.22, 95% CI 3.81 to 4.69), chronic pain (OR 2.41, 95% CI 2.16 to 2.69) and initial dose of at least 90 morphine milligram equivalents (MME) per day (OR 1.24, 95% CI 1.04 to 1.47). Our predictive model, including only the initial days’ supply and chronic pain diagnosis, had area under the curve of 0.7618.

**Interpretation:** This study identified factors associated with long-term prescription opioid use. Limiting the initial supply to no more than 7 days and limiting doses to 90 MME/day or less are actions that could be undertaken at the point of care.

Several aspects of this paper are troubling. The authors’ stated results can be read very differently than they chose to:

1. About 3.3% of a group of 124,664 patients who were started on opioids progressed to one or more conditions that generated chronic intractable pain, prompting extended use of prescription opioids to manage their pain.

2. Among patients under-treated with a weak opioid (codeine) combined with acetaminophen, patients transitioned into chronic pain and ongoing opioid prescriptions about six times more often than the general population of all patients treated. We should note that codeine has recently fallen out of favor in general pain practice for precisely this reason.

3. Higher incidence of long-term prescribing in patients immediately prescribed long-acting opioids for 30 days might reflect a combination of several factors. Among these are timely recognition by some physicians, of conditions likely to become chronic, which may require aggressive pain management. Also meaningful is more severe pain in some patients, that disturbs sleep and warrants use of long-acting opioids to reduce patient vulnerability to depression.
However, there is no indication in the paper that its authors had access to either pain scale metrics or the medical notes of prescribing physicians. “Long-acting” opioids are not demonstrated to be a "cause" of long-term use as such.

4. Long-term opioid prescription in patients who were initially diagnosed with a chronic pain condition occurred about 240% more often than in the treated population overall. This is an expected outcome and is not remarkable. Ask any patient: chronic pain generates more chronic pain.

5. Patients initially prescribed over 90 MME were 25% more likely to need long-term opioid maintenance than the general population of patients seen for pain. However, definitive cause and effect have not been established in this multi-factorial (but still quite small) outcome. Higher doses may reflect more severe pain.

As most operations research analysts (and apparently fewer physicians) are trained to understand, association or correlation between two sets of data does not establish "cause." In the data reported by these authors, we may be observing an artifact of observer (and journal peer reviewer) bias. There is no real "cause and effect" here. It seems plausible that some patients were prescribed higher initial doses because their pain is more severe or their doctors were better trained.

The interpretation section of this paper is highly problematic:

"Interpretation: This study identified factors associated with long-term prescription opioid use. Limiting the initial supply to no more than 7 days and limiting doses to 90 MME/day or less are actions that could be undertaken at the point of care."

To this interpretation, I must simply respond: “It does not follow.”

Given the number and variety of uncertainties in this retrospective cohort analysis, the data simply cannot be extrapolated to this conclusion. Likewise, retrospective studies are scientifically unable to generate “prediction models” that generalize to other populations. The authors’ section on Patient Characteristics largely confirms these insights:

“Patient characteristics
“Patients who progressed to long-term use were older, more likely to be female, and more likely to have a lower income than those with short-term use... They also had a higher frequency of risk factors for opioid use disorder, including previous diagnosis of psychiatric disorders and dementia, and had received more psychotropic medications in the year before the index date. **There was, however, no statistically significant difference in history of substance use disorder. The frequency of previous long-term use of pain medications was also higher among those with long-term use of prescription opioids.** The most frequent claims preceding the initiation of a prescribed opioid among patients who progressed to long-term use were related to chronic pain (47.4%), whereas among those with short-term use the most frequent claims were related to accident, fracture or surgery (31.2%). Overall, 24.1% and 15.0% of those with long-term and short-term use, respectively, had no claims or claims that were not associated with acute or chronic pain. [emphasis by the author]

First, we know from multiple sources that patients seen for chronic pain are more frequently females with lower incomes than in the general population of all patients seen by doctors. This should not seem remarkable.

Second, it is revealed without elaboration that patients with higher perceived “risk” factors show no significant difference in diagnosed history of substance abuse. This might suggest that a history of substance abuse is not particularly related to doctor-shopping for continuance of medical prescriptions -- an observation supported by published work of the US National Institute on Drug Abuse.

Likewise, **it is to be expected** that patients who have previously been prescribed opioids over the long term are likely to continue as chronic pain patients and therefore as candidates for long-term prescription of opioids. This is, after all, the meaning of “chronic.”

**A Concluding Observation**

The importance of this paper is not in its misdirected interpretation by these specific authors. It is rather, in the huge number of other published papers that make the same mistakes. These authors saw what they expected to see in the data they examined. They forgot a principle that many other medical professionals have also forgotten, despite being widely known to data analysts like me. This is attributed variously to H.L. Menkin, Peter Drucker, Mark Twain, and others:

“For every problem, there is at least one solution that is simple, neat – and wrong.”

The authors’ “interpretation” of the data they examined and reported is simply wrong. If acted upon, their interpretation seems more likely to increase than to improve the number of deaths attributed to opioid-involved overdose. Denying effective pain relief to millions of patients is a sure recipe for driving some of them to seek out much more dangerous and unregulated street drugs.

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