cited in Fulton's editorial provides convincing data on causation of mortality, but rather promote the questionable assumption that the opioids themselves are responsible for the increased mortality in the most severely affected patients.[8,9] A climate of fear is created and physicians might be dissuaded from making correct medical decisions when treating these unfortunate patients.

Given the above, it is all the more reassuring that Dr Fulton can "sit on the same side of the desk" as her patients to discuss their prescriptions.

—David L. Shulman MD CCFP FCFP
Thornhill, Ont

Competing interests

Dr Shulman has been on advisory boards and has facilitated small group educational sessions for family physicians on behalf of the following organizations: PARC (a chronic pain patient advocacy group), the Canadian Consortium for the Investigation of Cannabinoids, Purdue Pharma, Eli Lilly, Solvay, Janssen-Ortho, Valeant, and Paladin.

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Response

The contrasting responses to our study illustrate that physicians hold widely divergent opinions regarding the prescribing of opioids for chronic noncancer pain. Sometimes, however, the opinions are so strident that the facts are overshadowed.

Here are some facts about opioids and chronic noncancer pain:

1. The long-term use of opioids for chronic noncancer pain is supported by very little evidence; the evidence that does exist is of poor quality.[1]
2. Almost all trials span less than 4 months and include only very carefully selected patients.[1]
3. The few available observational studies suggest that the long-term risks of opioids in real-world clinical practice might exceed the benefits.[2,3]
4. Despite a lack of evidence, opioid prescribing for chronic noncancer pain has increased dramatically over the past 20 years, as have the number of deaths involving prescription opioids.[4,5]
5. Most opioid-related deaths are accidental and occur in relatively young people who have also consumed alcohol or other central nervous system depressants.[4-6]
6. Most opioid-related deaths occur in individuals who have been prescribed opioids.[4,7]

Having stated these facts—all of which are repeatedly downplayed by pharmaceutical companies and the physicians with financial ties to them—we turn to the comments on our article.

Longhurst[8] ascribes to us political motives, but does not specify what these might be. As clinicians and researchers with an interest in patient safety, our motivation is the promotion of safe prescribing, with the ultimate goal of better outcomes for patients. Regrettably, several of Longhurst's comments suggest that he did not read our paper carefully. For example, we clearly stated that we analyzed publicly funded prescription claims and we did not assert that physicians had "caused death" or that "opiates are bad."

As noted above, we agree with White[9] that opioid-related deaths are typically associated with the use of alcohol or other central nervous system depressants. We also agree that the risk of mortality increases with opioid dose.[7,10,11] But 3 important points remain. First, patients frequently receive opioids at doses far in excess of those recommended in clinical practice guidelines.[12-14] Second, the mortality risk is elevated even at seemingly moderate doses (ie, 50 to 100 mg of morphine per day, and possibly

even 20 to 50 mg of morphine per day).[7,10] Third, opioids are associated with increased mortality when compared with nonsteroidal anti-inflammatory drugs.[2]

We agree with Dubin[15] that education and licensure requirements ought to be improved and that pain management should be holistic. Although physicians are remunerated by provincial health insurance plans for counseling, they are paid more for short, frequent visits—encounters that, in the context of pain, often culminate in a prescription. This financial inequity should be addressed. Of course, we also agree with Dubin that correlation is not synonymous with causation, and we were careful not to assert causality in our article. Nevertheless, the totality of evidence does indeed suggest that increased opioid prescribing has resulted in an epidemic of opioid-related deaths in North America.

In their protracted defense of chronic opioid therapy, Jovey et al[16] falsely assert that we confuse association with causation. They also imply that a large proportion of opioid-related deaths are suicides. This is wrong. As we and others have noted, most opioid-related deaths are accidents.[4,5] Furthermore, accidental opioid-related deaths have increased dramatically, while the number of suicides involving opioids has remained static.[4] It is difficult to overstate the importance of this observation.

Jovey et al[16] suggest that other substances (eg, benzodiazepines and alcohol) might be responsible for death, rather than opioids themselves. These and other co-intoxicants are best characterized as contributing factors. Although they are commonly identified in the postmortem toxicology of patients with opioid-related deaths, their presence does little to exonerate the opioid. Most physicians will appreciate that deaths resulting solely from acute alcohol intoxication or acute benzodiazepine overdose are very rare, whereas deaths due solely to opioid intoxication are common by comparison. In a sample of 239 single-drug deaths in Virginia, 166 were due to opioids alone, compared with fewer than 5 from benzodiazepines alone.[6] Consequently, when death occurs in an individual who has consumed opioids along with 1 or more other central nervous system depressants, it is entirely appropriate to focus on the opioid.

Jovey et al[16] also assert that the inadvertent inclusion of palliative care physicians might explain our study's findings. This too is wrong. Because deaths occurring among patients receiving palliative care are generally not investigated by coroners, the inclusion of physicians who prescribe opioids for palliative care would actually diminish any observed association between opioid prescribing frequency and opioid-related deaths.

We disagree with Jovey et al[16] that the "death rate per prescription" is a useful metric. While both the number of opioid-related deaths and the number of opioid prescriptions have increased over time, the "death rate per prescription" has actually decreased. The explanation for this is simple—most patients receive more than 1 prescription yet each individual can obviously die only once. In any case, the absolute number of deaths is obviously far more important than the "death rate per prescription."

In support of her assertion that "opioids exhibit efficacy in some people with chronic pain," Lynch[17] cites a Cochrane review that did not include a single randomized controlled trial comparing opioids with other therapies. Why? Because, as the authors of the review note, the published trials were too short to merit inclusion in the review.

The lack of evidence for long-term opioid use is both lamentable and unjustifiable. Such a paucity of safety and effectiveness data would never be sufficient to inform the care of patients with coronary artery disease or cancer. Why has no high-quality evidence been produced to support the long-term use of opioids in patients with chronic noncancer pain? One reason might be that many pain specialists—particularly those who are vocal advocates for chronic opioid therapy—receive large amounts of money from pharmaceutical companies that manufacture opioids. These "thought leaders" have little incentive to press pharmaceutical companies to improve

the evidence base for chronic opioid therapy. Even the Canadian Pain Society, of which Lynch is the current president, has received considerable funding from opioid manufacturers over the past 20 years. As Ballantyne has recently noted, "It has been the drug companies that have for years picked the message and the messengers while sponsoring much of the postgraduate education and all the major pain meetings."[18]

We appreciate the letters of Pakes[19] and Kahan.[20] We would emphasize Pakes' point that opioid prescribing is an important ethical issue for physicians, and Kahan's point that most physicians who prescribe opioids frequently or at high doses are well intentioned, but have been unwittingly influenced or misled by the promotional tactics of the pharmaceutical industry.

We agree with Shulman[21] and Fulton[22] that physicians should "sit on the same side of the desk" as their patients when discussing opioids. But we also believe that physicians should consider the modified Hippocratic Oath, which states that physicians "will apply, for the benefit of the sick, all measures [that] are required, avoiding those twin traps of overtreatment and therapeutic nihilism."[23]

In the present-day treatment of chronic noncancer pain, the pendulum has swung too far toward overtreatment, placing huge numbers of patients at risk of addiction and death. Until there is better evidence that the benefits of long-term opioids justify these risks, we should all reevaluate our prescribing of opioids for patients with chronic noncancer pain.

—Irfan A. Dhalla MD MSc FRCPC
—Muhammad M. Mamdani PharmD MA MPH
—Tara Gomes MHSc
—David N. Juurlink MD PhD FRCPC
Toronto, Ont

Competing interests
None declared

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