frequency, dosage, and amount—physicians, often family or emergency room doctors, actively harm thousands, if not millions, of patients, causing dependence, addiction, and myriad other social and physical harms. It not only wastes countless physician hours and drug dollars, but also costs many patients and their families (including a substantial number of teenagers) their emotional and physical well-being and, increasingly, their lives.

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Competing interests
None declared

Reference

1. Dhalla IA, Mamdani MM, Gomes T, Juurlink DN. Clustering of opioid prescribing and opioid-related mortality among family physicians in Ontario. *Can Fam Physician* 2011;57:e92-6. Available from: **www.cfp.ca/content/57/3/e92.full.pdf+html**. Accessed 2011 Apr 1.

Editor's response

The editors thank Dr Pakes for his letter and comments. Electronic publication of an article in *Canadian Family Physician (CFP)* does not reflect any lesser status of the published work. All Web Exclusive publications in *CFP* are fully indexed and searchable in PubMed and PubMed Central.

There is limited print space in medical journals owing to declines in pharmaceutical advertising, which has been a large source of revenue for medical journals. Our response to this has been to publish more research in the online version of *CFP* as Web Exclusive articles. In so doing we have been able to publish more research per issue.

—Nicholas Pimlott MD CCFP
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Treating patients versus numbers

As a group of Canadian physicians interested in the management of patients with chronic pain and addiction, we feel compelled to respond to the recent paper by Dhalla et al regarding opioid-related deaths in Ontario.[1]

Similar to a previous paper by some of the same authors,[2] Dhalla and colleagues once again confuse association with causation. They overinterpret statistics from administrative databases to make pronouncements on clinical pain management practice—an area in which none of the authors profess to have any expertise.

They have failed to discuss relevant confounders. It is like saying that cardiac surgeons in leading institutions have worse results than those in provincial hospitals, without taking into account the severity of the conditions treated. They have failed to consider alternative explanations for their results or discuss other important limitations of their study.

In 2006, there were approximately 12 million people in the province of Ontario. This would mean approximately 2.3 million people with moderate to severe chronic pain.[3] If we assumed that somewhere from 30% to 50% might be taking regular opioid therapy (likely higher than this), 406 deaths would result in a crude death rate of 50 to 60 per 100 000 people with pain who were taking opioids (or about 3 per 100 000 total population). With such small numbers, any flaws in the methodology of this study that change the numbers would have a very big effect on the reported percentages.

The reported suicide rate in the Canadian population is about 15 per 100 000 people.[4] In patients with persistent pain that number is at least doubled, to about 30 per 100 000 people.[5] Higher doses of opioids often are consistent with a longer time in treatment, poorer efficacy of other treatments, and more opportunity for patients to realize that their pain will not go away. There is little organized support and a lack of other, nonpharmacologic treatment options compared with other chronic diseases. All of us can recount hearing patients with chronic severe pain say they feel like they have nothing to live for. If we subtract the number of people who might have committed suicide from Dhalla's numbers, then the number of deaths "caused" by opioids shrinks substantially.

The authors used data from coroners to assign deaths "related to opioids." With all due respect to our hard-working coroners, assigning a cause of death in the case of a patient taking therapeutic opioids can be an extremely difficult challenge.[6-8] There can be a very large overlap between the blood levels of someone stable on long-term opioid therapy and those of someone found dead with opioids in their blood, and there is a poor correlation between opioid blood levels and death.[9] The definition of opioid-related death among coroners can be variable and can have a large influence (up to a 2-fold difference) on reported death rates.[10]

How did the authors account for the effects of other substances also found in the blood of decedents? Which substance actually caused the patients' deaths? Were the deaths most likely due to substance abuse or addiction (more than 90% in a study by Hall et al[11]) or was it therapeutic misadventure? The authors stated that they adjudicated questionable cases among themselves to come to a decision on cause of death, yet they did not report any expertise to allow them to do so.

The authors have suggested that there is an association between the number of deaths and the number of prescriptions written, particularly in the antemortem period. No information is provided regarding the drug or quantity prescribed. Therefore, the authors provide no evidence that the deaths among the patients of high prescribers are due to the drug they prescribed or the dose prescribed. What was the length of time between death and last prescription? If a physician writes a prescription for an opioid 12 months before the patient dies, is that doctor somehow responsible?

Most opioids prescribed for palliative care are prescribed by FPs who are often not identified as palliative care physicians, as they have had no extra training that would justify a formal label even though it might be the focus of their work. How was this population of physicians identified or accounted for in the high-prescribers group? What about those who do both palliative care and chronic pain management?

The authors have provided no denominators. Although more deaths occurred among the patients of the high prescribers, the death rate per prescription written, drug used, or dose taken is not calculated. If high prescribers were "responsible" for 63% of the deaths, but wrote more than 63% of the prescriptions, then it might be that they are actually safer prescribers compared with those who prescribe less frequently.

Dhalla et al conclude from their data that a small number of FPs are irresponsibly prescribing high-dose opioids, causing deaths among patients. They suggest targeting these doctors for further education or regulatory attention. What we know from our communities is that a large proportion of FPs are already reluctant to take on the care of patients with complex pain and will not prescribe any opioids even when appropriate. This leaves a small number of compassionate family doctors who have a special interest in pain to take on a disproportionate number of patients, which likely accounts for the small number of high-dose opioid prescribers.

The high prescribers were noted to be older and more experienced. Does this mean that, on average, they also have an older practice with a higher prevalence of chronic pain? The authors have provided no evidence to support any assertion that older, experienced practitioners are less likely to follow safe prescribing guidelines and hence are more in need of, or amenable to, "academic detailing" or regulatory scrutiny. On the contrary, those who write more opioid prescriptions might be more likely to seek further training, particularly given the regulatory environment for opioids that already exists in Canada. Family physicians are expected to manage complex patients experiencing pain, despite very little formal education and very few funded nonpharmacologic treatment resources available. Subjects used in this study were drawn from the Ontario Drug Benefit Program database. This group comprises a vulnerable population that has less access to the determinants of health and that is more at risk than the general population of Ontario. This group might also have even less access to appropriate nonpharmacologic care than most Ontarians. Dhalla et al

offer a blanket criticism of, and a call for a reduction in, the use of opioids for chronic pain, yet do not suggest alternative solutions. Although the published scientific evidence for the use of opioids to treat chronic pain is still evolving, the balance of current evidence suggests that opioids can be an effective treatment in some people, with a low overall risk of adverse effects, including addiction.[12] All physicians recognize that no treatment is risk-free and the potential benefits must always be balanced with the potential harms. Even those clinicians with expertise in pain management know that there are no risk-free treatment options for severe pain. Acetaminophen, available for decades over the counter, has risks of organ toxicity when used chronically.[13] The recent Scottish Health Survey found an increased risk of cardiovascular events and death in people taking tricyclics.[14] The chronic use of nonsteroidal anti-inflammatory drugs is associated with an increased risk of stroke and cardiovascular deaths as well as the known risks of death due to upper gastrointestinal bleeds and perforations.[15,16] The best type of care for chronic pain is an interdisciplinary biopsychosocial-spiritual approach. Opioids can be an important pharmacologic component of such multimodal care. Unfortunately, prescribing medication is often the only type of treatment funded by our health care system. When prescribed carefully and monitored appropriately, opioid therapy can result in reduced pain and suffering and improved quality of life. The key is to educate all physicians on appropriate assessment, efficacious treatment, and careful prescribing rather than targeting a small number for "overprescribing" opioids. Studies, such as that of Dhalla et al, that report on numbers without considering the clinical context do nothing to advance solutions for the epidemic of poorly treated chronic pain in Canada. They only make family doctors even more reluctant to treat patients with pain. We would have appreciated a more thorough peer review of this paper before publication. We are doing our utmost to promote more dialogue and understanding to optimize patient care, and we hope for the same from all our colleagues.

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Lydia Hatcher, Lori Montgomery, Murray Opdahl, Nadia Plach, Mark Ware, and **Erica L. Weinberg.**

Competing interests

Dr Jovey has consulted for or been a member of speakers' bureaus for AstraZeneca, Bayer, Biovail, Boehringer Ingelheim, Eli Lilly, Janssen-Ortho, GlaxoSmithKline, King Pharmaceuticals, Merck Frosst, Mundipharma Australia, Nycomed, Pfizer, Paladin, Purdue Pharma, Sanofi-Aventis, Valeant, and Wyeth. **Dr Squire** has received grants and research support from Pfizer; speakers honoraria from Janssen-Ortho, Eli Lilly, Boehringer Ingelheim, Paladin, Merck Frosst, and AstraZeneca; and consulting fees from Valeant, Janssen-Ortho, Pfizer, Purdue, Eli Lilly, Boehringer Ingelheim, Paladin, Merck Frosst, and AstraZeneca. **Dr Williamson** has received speakers honoraria from Pfizer, Purdue Pharma, Eli Lilly, and Boehringer Ingelheim.

References

1. Dhalla IA, Mamdani MM, Gomes T, Juurlink DN. Clustering of opioid prescribing and opioid-related mortality among family physicians in Ontario. *Can Fam Physician* 2011;57:e92-6. Available from: **www.cfp.ca/content/57/3/e92.full.pdf+html**. Accessed 2011 Apr 1.
2. Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, Juurlink DN. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. *CMAJ* 2009;181(12):891-6. Epub 2009 Dec 7.
3. Jovey R. *Canadian pain survey 2007-2008.* Toronto, ON: Nanos Research Group; 2009.
4. Canadian Mental Health Association [website]. *Suicide statistics.* Toronto, ON: Canadian Mental Health Association; 2011. Available from: **www.ontario.cmha.ca/fact_sheets.asp?cID=3965.** Accessed 2011 Apr 7.
5. Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychol Med* 2006;36(5):575-86. Epub 2006 Jan 18.
6. Wallage HR, Palmentier JP. Hydromorphone-related fatalities in Ontario. *J Anal Toxicol* 2006;30(3):202-9.
7. Thompson JG, Vanderwerf S, Seningen J, Carr M, Kloss J, Apple FS. Free oxycodone concentrations in 67 postmortem cases from the Hennepin County medical examiner's office. *J Anal Toxicol* 2008;32(8):673-9.
8. Ferner RE. Post-mortem clinical pharmacology. *Br J Clin Pharmacol* 2008;66(4):430-43. Epub 2008 May 29.
9. Tennant F. Opioid serum concentrations in patients with chronic pain. *J Palliat Med* 2007;10(6):1253-5.
10. Jauncey ME, Taylor LK, Degenhardt LJ. The definition of opioid-related deaths in Australia: implications for surveillance and policy. *Drug Alcohol Rev* 2005;24(5):401-9.
11. Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA* 2008;300(22):2613-20.
12. Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, et al. Long-term opioid management for chronic noncancer pain. *Cochrane Database Syst Rev* 2010;(1):CD006605.
13. US Food and Drug Administration [website]. *Acetaminophen information.* Silver Spring, MD: US Food and Drug Administration; 2011. Available from: **www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm.** Accessed 2011 Apr 7.
14. Hamer M, David Batty G, Seldenrijk A, Kivimaki M. Antidepressant medication use and future risk of cardiovascular disease: the Scottish Health Survey. *Eur Heart J* 2011;32(4):437-42. Epub 2010 Nov 30.
15. Trelle S, Reichenbach S, Wandel S, Hildebrand P, Tschannen B, Villiger PM, et al. Cardiovascular safety of non-steroidal anti-inflammatory drugs: network meta-analysis. *BMJ* 2011;342:c7086. DOI: 10.1136/bmj.c7086.
16. Straube S, Tramèr MR, Moore RA, Derry S, McQuay HJ. Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. *BMC Gastroenterol* 2009;9:41.

Clustering of opioid prescribing—what is really going on?

In the recent study by Dhalla et al,[1] the statement that "the findings in this study suggest that family physicians might be able to reduce opioid related harm by writing fewer prescriptions" is unsupported by the data presented. Further, in the absence of information regarding the appropriateness of the prescriptions written, such action might harm patients.

The authors have failed to consider alternate explanations for the data. This study used data from the Ontario Public Drug Program; it is important to remember that this population has less access to determinants of health and will likely be a sicker population than the general Ontario population. In addition, those requiring opioids might have more severe illnesses. It is possible that the variation in prescribing is related to the fact that many family doctors prefer to avoid seeing patients with chronic pain. There are a number of potential reasons that might contribute to this. The cases are complex and time consuming. People with chronic pain have been found to have the worst quality of life and high levels of depression compared with patients suffering from other chronic diseases.[2] They have often suffered job loss or are on disability leave, so there are forms that must be completed. Many have been injured in motor vehicle accidents, so there might be lawsuits requiring the involvement of the health care professional.[3] There is also inadequate training and education in medical school for chronic pain management—in fact veterinarians get 5 times more education regarding pain management than physicians do.[4] In many cases, family physicians with an interest in pain management have had to seek specific training offered through continuing medical education programs, through the Canadian Pain Society Special Interest Group refresher courses, or through mentorship networks such as those offered