The opioid replacement problem

How the role of opioids for chronic pain management has evolved amid the current crisis BY TRISTAN BRONCA

To understand the medical profession's role in the opioid epidemic, it's essential to consider how prescribing habits have evolved. In the 1980s, opioids were used almost solely for cancer or other life-ending pain because the risk of addiction was believed to be too high to prescribe them for anything else. That began to change in the late 1980s, when studies showed benefits for other kinds of pain.

"Prior to 1980, the fear of addiction was actually overblown," said Dr. Dwight Moulin, a neurologist and pain specialist in London, Ont. He was one of the first clinicians to study the utility of opioids for chronic non-cancer pain in the 1990s. But the body of research that evolved into the 1990s and early 2000s had a serious limitation. Trials would exclude patients with mood or anxiety disorders. After all, it would have been unethical to enlist those who might be at risk of suicide. A selection bias started to take shape. The most-studied populations became those who were the most likely to see benefit and the least likely to abuse them—in short, they were the "best" patients for the drugs.

"A clinical trial is a very artificial environment," Dr. Moulin explained. "They're being followed very carefully and only being administered so much drug, etc." Not only that, but all of these studies were short term, never exceeding three months.[1] Nevertheless, drug companies built massive marketing campaigns around these kinds of studies, and the clinical paradigm around the treatment of chronic pain underwent a titanic shift. Between 1996 and 2012, OxyContin sales soared from $48 million to more than $2.4 billion, and between 1991 and 2007, the number of prescriptions written for oxycodone shot up 850%.

The studies were well-intentioned. But the real-life patients who seemed to need these drugs the most were also those who were most likely to be harmed by them. "The bottom line is that the group benefitting was actually a lot smaller than we thought," Dr. Moulin said. "We were using opioids when the risks outweighed the benefits, and we didn't realize we were doing that."

[1] Most chronic pain patients are on opioids for much longer, but such use hasn't been studied in a rigorous clinical trial setting—it's never been proven or disproven, even today.

THE SYNDEMIC

Today, the scale of the opioid crisis in North America is so baffling that many of us have become numb to the

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horrifying statistics. History can be a useful framing device. Consider in the 1980s, during the crack epidemic, overdose deaths in the U.S. averaged about two per 100,000 per year, leading to the now infamous war on drugs. As of 2015, in both the U.S. and Canada, opioids kill more than 10 people per 100,000.

All kinds of comparisons are used to convey the gravity of that figure. In 2015, the epidemic killed more people than at the height of the AIDS epidemic, and then, the very next year in the U.S., the death rate rose 20%. Today, opioids are the leading cause of death for people under 50. For the first time in modern history, this epidemic has single handedly dragged down the average life expectancy for Americans. Canada—which has now surpassed our neighbours to the south as the highest per capita consumer of opioids in the world—is expected to experience a similar effect.

Earlier this year, Austin Frakt, a prominent U.S. health economist, wrote in the New York *Times* that the epidemic is actually a "syndemic," a phenomenon comprised of multiple concurrent epidemics, including the proliferation of illicit heroin and fentanyl, prescription opioids, and the rise of chronic pain.

Doctors are frustrated that many of these trends get conflated.

For example, while overdose deaths from illicit opioids, particularly more powerful ones such as fentanyl, have continued to rise, prescribing across Canada has actually declined since 2012. B.C., which has been the hardest hit by the crisis in Canada, didn't declare a public emergency until 2016. Today the province has one of the lowest opioid prescribing rates in the country and still some of the highest rates of death from overdose. Frakt, writing for the *Times*, pointed to a recent study in *JAMA* that suggested further clamping down on prescribing could help, but not as much as many would like to think. The study's model predicted no more than a 5% decline in overdose deaths in the next five years.

"If you were to ask how many people became addicted after being prescribed an opioid for chronic pain, that figure is probably between 5% and 12%," said Dr. Owen Williamson, a pain specialist based out of the Surrey Memorial Hospital in B.C. There is a subtle difference, he said, between "prescription drugs" (legally manufactured drugs) and "prescribed drugs" (legally manufactured drugs used for the purpose intended by the prescribing physician)—one that often gets overlooked when doctors are demonized as the cause of this crisis. U.S. data indicate that fewer than 20% of those who misuse or abuse opioids had their initial exposure to the drug as a result of a physician prescription.[2]

[2] Canadian data was unavailable.

Dr. Williamson argued that now that doctors have been labelled a cause of the crisis, many are wary of working with opioids at all. Which is a problem, because without doctors overseeing appropriate therapies, some patients will turn to more dangerous avenues. The consensus is that opioids still have a role to play for treating chronic non-cancer pain in certain patients. Regardless of any fault the medical profession may bear for the several epidemics at play here, none of them will be solved without doctors' help.

THE CHILL ON PRESCRIBING

Though we've made some progress tearing down the stigma surrounding mental illness and addiction, new stigmas have developed around the medical use of opioids. Dr. Chris Giorshev is the section chair for chronic pain at the Ontario Medical Association. He pointed out that after the U.S. Centers for Disease Control and Prevention issued new guidelines advising stricter limitations on opioid prescribing for chronic pain, Canada followed suit with similar guidelines. This was accompanied, at least in Ontario, with a concerted effort from the regulator to ensure doctors were prescribing appropriately.

Dr. Giorshev was clear that he did not think the guidelines, issued first in 2010 and then in 2017, were inappropriate. However, he did say that the recommendations put a chill on what had been—in the vast majority of cases—appropriate prescribing, and this has had a series of negative effects on chronic pain management. Dr. Williamson said he was seeing the same in B.C.

"They're good guidelines, but the biggest problem I have is that doctors don't read them and the regulators become overzealous in enforcing them," he said. The 2017 Canadian Guideline for Opioids for Chronic Con-Cancer Pain was authored by an expert panel based out of McMaster University in Hamilton, Ont. There are 10 recommendations—four "strong" recommendations, meaning they apply to all or almost all patients and could be adopted as policy by medical institutions; and six "weak" ones, which apply to the majority of patients but not necessarily all of them. The most noteworthy change was a strong recommendation to drop the daily dose of opioids for patients starting on long-term therapy from 200 mg of morphine equivalent to 90 mg.

However doctors felt about the 105-page guideline, the advice was inarguably nuanced. The guiding rationale is simple: Try not to resort to opioids first, and when that's what's best for the patient, start low and go slow.

THE VULNERABLE PATIENTS

While chronic pain and addiction are two entirely separate patient populations the risk factors for opioid abuse and the drivers of chronic pain are related. Sadly, this overlap manifests in some unfortunate ways.

Mood disorders, for instance, place people at greater risk of abusing opioids. Cruelly, these disorders also enhance chronic pain. "They take a pain that's a four out of 10 and make it a 10 out of 10," explained Dr. Dwight Moulin. Or consider substance abuse. One of the strong and absolutely non-controversial recommendations from the McMaster guidelines advises against prescribing opioids for patients with an active substance use disorder—whether that's narcotics or alcohol. These patients are driven to these substances by some combination of extreme pain and a lack of alternatives. Which makes it a sort

of cruel irony that for these chemical copers, doctors are mostly limited to non-chemical ways of helping them cope.

Then there are the social factors correlated to substance abuse—income, family supports, level of education, food security, housing, traumatic formative experiences—which are also correlated with chronic pain.

It might seem like a banal insight: that people of lower socioeconomic status are more likely to suffer and, when they do, to suffer *more*. Still, it's worth highlighting just how significant this difference can be. Researchers from the University of Buffalo looked at 12 years of data from 19,000 chronic (non-cancer) pain patients over the age of 51. They found that people who didn't finish high school were 80% more likely to experience chronic pain than those with graduate degrees. Not only that, but less-educated patients were also 370% more likely to experience severe pain than the ones who were more educated. Another 2011 study, published in the *European Journal of Pain*, found that patients of lower socioeconomic status also suffer from greater functional impairment when they experience the same self-reported level of pain as those with higher status. This is important, considering that restoring a patient's ability to live and act as they did before the pain is often more important than alleviating the pain itself.

Dr. John Crosby, a family doctor in Cambridge, Ont., has been treating chronic pain patients for 45 years. "It's a war," he said. "I treat chronic pain with everything: that means exercise, physio, Advil, chiropractic, mindfulness, diet, heat, Voltaren rubs and massage." He treats depression and other mood disorders which might exacerbate the pain just as aggressively, with counselling and antidepressants. He tries to avoid narcotics which he views as often being a cheap fix—literally cheap, inasmuch as these are available at little cost or free to patients on social support programs. At one point, he said that in his practice of 1,400 he had only eight patients on long-term opioids and he's trying to wean them off slowly. That's not to say he hasn't had problems with others who press for the drugs, unable to find sufficient relief from non-opioid treatments.

Interestingly, there's one group of patients he's had the fewest problems treating for this kind of pain: farmers. He said it's because they must return to work as quickly as possible. "They have to, otherwise the cows will explode," he joked. But, for him, it also revealed a useful guiding principle: Treat acute pain vigorously and get them back to work, because for those who can't, problems have a tendency to become worse.

For most doctors, opioids are simply another tool in the toolkit to achieve this, one to be used judiciously, as Dr. Crosby does. This doesn't mean patients who are out of work or of lower socioeconomic status should be ineligible for these treatments. As Dr. Williamson pointed out, there are workarounds even for higher risk patients who may be in these situations, such as supervised medication pick-ups. But poorer outcomes are a reality that many, many more patients of lower socioeconomic status must contend with. And opioids can introduce more problems than they solve.

NOT ENOUGH SUPPORT

One of the more unusual paradoxes to develop in B.C.'s opioid crisis is the misconception that regular illicit drug users are at greatest risk of overdose death—"that most deaths are on the street," wrote Dr. Matthew Chow, a psychiatrist at B.C. Children's Hospital, in an email to the *Medical Post*. True, substance abuse patients living in the streets are at greatest risk of overdose, but those patients are actually more likely to survive than others, "because we are blanketing high-risk areas with healthcare resources, including naloxone kits, outreach workers, and first-responders." Dr. Chow explained that in actual fact, the people who are now most likely to succumb to an overdose are the people in the middle-class, using at home. "No one is there to call 911."

This demonstrates the value of intervention and dangers that emerge when it is absent. Family doctors, who have unique insight into the risk factors of their patients, can provide wraparound care.

Dr. Melissa Holowaty is a doctor in rural Ontario in the town of Marmora, north of Belleville. After witnessing the demand in her community, Dr. Holowaty trained to become an addiction specialist. Soon after arriving, she opened the town's only addiction clinic, drawing patients from neighbouring towns.

When she finished her residency in 2011, it was the beginning of the shift away from opioids, when the myth still persisted that opioids were the best way to turn off pain, which she emphasized, isn't true. NSAIDs are just as effective as opioids for many kinds of pain, including the passage of kidney stones, which is widely regarded as one of the most intense pains a human can experience. Patient expectations about their painkillers can also have a profound influence on the experience of pain itself. She pointed to a 2011 study that showed burn patients who were given a placebo and told it was fast-acting fentanyl reported greater pain relief than patients who were given real fast-acting fentanyl believing it was a placebo.

Dr. Holowaty uses this evidence in service to a more holistic approach. "If opioids are required, then I absolutely prescribe them," she said. "But it has to be indicated, and there has to be a functional improvement." It doesn't stop there, either. In her practice, 80% of her patients are in the bottom quintile of income for Ontario, and she's personally seen many of the afflictions that stem from such poverty. Making sure those who are food insecure know about food banks, helping those who need it sign up for social assistance programs, helping those whose disability applications have been inappropriately turned down—all of these are functions that she and her staff believe are important to the practice of good medicine.

She wants to do more, but there are limits to what family doctors can do. They need support. If there's one simple conclusion we can draw from the vast devastation we've witnessed during this crisis, it's that neither the doctors nor the people in pain have enough of that support. **MP**