Chronic Pain Fuels Boom in Opioids

By John Fauber, Reporter, Milwaukee Journal Sentinel/MedPage Today
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Prescriptions for narcotic painkillers soared so much over the last decade that by 2010 enough were being dispensed to medicate every adult in the U.S. around-the-clock for a month.

Fueling that surge was a network of pain organizations, doctors and researchers that pushed for expanded use of the drugs while taking in millions of dollars from the very companies that made them, a Journal Sentinel/MedPage Today investigation found.

Last year, the Journal Sentinel/MedPage Today found that a University of Wisconsin-Madison based organization had been a national force in helping liberalize the way opioids are prescribed and viewed. During a decade-long campaign that promoted expanded use of opioids -- an agenda that critics say was not supported by rigorous science -- the UW Pain & Policy Studies Group received $2.5 million from makers of opioid analgesics.

After that article was published last April, the UW Pain group said it had decided to stop taking money from the drug industry.

But the UW Pain group is just one link in a network of national organizations and researchers with financial connections to the makers of narcotic painkillers.

Beginning 15 years ago, that network helped create a body of "information" that today is found in prescribing guidelines, patient literature, position statements, books and doctor education courses, all which favored drugs known as opioid analgesics.

Without rigorous scientific evidence to prove that their benefits out weigh potential harm, drugs like
OxyContin and Vicodin increasingly have been used to treat a wide array of chronic pain syndromes including low back pain and fibromyalgia.

Current practices reflect a gradual shift from the use of these drugs to treat short-term acute pain such as post-surgical pain, as well as severe pain associated with metastatic cancer or end-of-life pain -- uses that were based on solid evidence that such use was safe and effective.

But the benefit seen for those conditions was extended to treatment of chronic pain syndromes, an extrapolation that had no evidence to back it up.

Caught in the middle are millions of Americans with real pain that can last for years and thousands of doctors who want to help them.

It's a situation that was ripe for the influence of the pharmaceutical industry, said Mark Sullivan, MD, a professor of psychiatry and behavioral sciences at the University of Washington.

By 2010, those firms were selling four times as many prescription painkillers to pharmacies, doctors' offices and hospitals as in 1999.

Led by OxyContin, sales of prescriptions of opioid drugs totaled $8.4 billion in 2011, up from $5.8 billion in 2006, according to data supplied by IMS Health, a drug market research firm.

"We've never really exposed so many people to so much drug for so long," Sullivan said. "We don't really know what the long-term results are."
The Pendulum Swings Back

Several of the pain industry’s core beliefs about chronic pain and opioids are not supported by good science and contributed to the growing use of the drugs, a Journal Sentinel/MedPage Today review of records and interviews found.

Among the misconceptions:

The risk of addiction is low in patients who obtain their narcotic painkillers legitimately.

There is no maximum dose of the drugs that can’t be safely prescribed.

People who seek more frequent prescriptions or higher doses of the drugs aren’t addicts, they are “pseudoaddicts” who just need more pain relief and more opioids.

Underlying those fallacies, critics say, is an even larger one: That the use of narcotic painkillers to treat non-cancer pain lasting many months or years is supported by rigorous science.

Even doctors who have financial relationships with companies that make narcotic painkillers concede that the practice of pain medicine got ahead of the science.

Lynn Webster, MD, a Utah pain specialist who has worked as a consultant and adviser to most of the companies in the opioid analgesic market, said the pain community got some of it wrong.

"We overshot our mark, all well-intended, I believe," Webster, an officer of the American Academy of Pain Medicine, said in an interview. "We certainly have a lot of reverse education that needs to occur."

Some chronic pain sufferers do benefit from the drugs, Webster said.

"The problem is pain is complex," he said. "There is a whole family of opioids and we have not figured out how to best identify the individuals who can benefit long-term.

"I don’t think industry was trying to harm anyone. I think industry was trying to fill a need that we as physicians saw."

Others say that Webster is too forgiving in his analysis: they claim that the pharmaceutical industry chose profits over patient safety.
Over the past decade as many as 100,000 Americans have died from opioid overdoses and millions have become addicted to the drugs, said Andrew Kolodny, MD, a New York psychiatrist and opioid addiction specialist who co-founded Physicians for Responsible Opioid Prescribing.

"This is an out of control epidemic, not caused by a virus or a bacteria," said Kolodny, chairman of psychiatry at Maimonides Medical Center in New York. "This epidemic has been caused by a brilliant marketing campaign that dramatically changed the way physicians treat pain."

The pharmaceutical industry's alliance with pain groups is part of familiar playbook.

It has occurred with other organizations, though those financial relationships aren't always fully disclosed, said David Rothman, PhD, president of the Institute on Medicine as a Profession, part of Columbia University College of Physicians & Surgeons.

"They (drug companies) expect a certain return for their money and the sad thing is, they often get it," he said.

**Maximum dose**

Consider the American Pain Foundation, which has substantial financial ties to companies that make narcotic painkillers: a patient guide available on its website it claims there is no maximum dose for opioids as long as they are not combined with other drugs such as acetaminophen. The dose of any painkiller, the Foundation claims, can be gradually increased over time.

Critics of the use of opioids for chronic pain say that is a dangerous misinterpretation of information gleaned from the experience of treating cancer pain in hospitalized patients.

It should not be applied to chronic, non-cancer pain sufferers who are not getting their drugs in a hospital setting, said Sullivan, the University of Washington professor.

A philosophy of "no maximum dose" can lead to more people on high doses of the drugs, which, in turn, can result in serious problems, including more falls and fractures in older people, respiratory depression, overdoses and fatalities, he said.

Even when the dose is increased gradually, high doses add more risk, especially in people who take other prescription drugs, use alcohol, have a medical condition such as sleep apnea, or who take an opioid in a manner other than how it is prescribed, Sullivan said.
"Risk goes up with dose, even if it is well done," he said.

An April 2011 paper in the *Archives of Internal Medicine* found that as dose escalated the risk of opioid-related death increased. For high-dose patients the risk of death was three times greater than in lower-dose patients.

The "no ceiling" dose statement appears in the Pain Foundation's "guide for people living in pain," a publication that received funding from three drug companies.

Two of the companies, Purdue Pharma and Cephalon, were the subject of U.S. Justice Department investigations involving their opioid products.

In 2007, Purdue was accused of misleading doctors by claiming, with no proof, that its narcotic painkiller OxyContin was less addictive, less likely to cause withdrawal and less subject to abuse than other pain medications.

At the time, scores of deaths and an even greater number of addictions were attributed to OxyContin. The company and three of its executives pleaded guilty to various charges. A court imposed fines and restitution payments totaling $635 million.

In 2008, Cephalon settled an investigation of off-label marketing of three of its drugs, including Actiq, a powerful painkilling product manufactured as a lollipop with the drug fentanyl. The drug was approved for use only by cancer patients who no longer were getting pain relief from morphine based drugs. Cephalon allegedly promoted the drug for non-cancer patients with conditions ranging from migraines to injuries. It also promoted Actiq for use in patients who were not opioid-tolerant and for whom it could have been life-threatening.

Cephalon agreed to pay a $425 million penalty.

In recent years the American Pain Foundation has received millions of dollars from industry, including companies that market opioids. They include Purdue, Cephalon and several other opioid companies.

Foundation officials declined to be interviewed for this story.

In an email statement Micke Brown, a registered nurse and spokesperson for the foundation, said it stands by the statements in its pain guide, which was developed by leading pain experts.

"APF along with many from the pain community is concerned (about) the misuse and abuse of these
valued medications. Unfortunately, the weight of this complex problem has been placed on the backs of people living with pain."

**Addiction Risk**

In 1996, the American Academy of Pain Medicine and the American Pain Society, organizations that get substantial funding from drug companies, issued a joint statement endorsing the use of opioids to treat chronic pain and claiming the risk of addiction was low.

The chairman of the group that issued the statement was J. David Haddox, DDS, MD, a physician and paid speaker for Purdue Pharma, maker of the highly-prescribed opioid, OxyContin.

Three years after the chronic pain statement, Haddox became an executive at Purdue.

Doctors on both sides of the debate agree most people who are put on opioids long-term will become physically dependent. The risk of addiction, which is more severe than physical dependence, is significant, they say.

One of the problems in assessing addiction risk is that many of the clinical trials that involved opioids excluded people with mental illness or who had a family history of substance abuse, groups that are more likely to develop addiction.

But many of those people are put on opioid therapy for chronic pain.

Some people are able to come off opioids without much trouble while others will be addicted, said Jane Ballantyne, MD, a professor of anesthesiology and pain medicine at the University of Washington.

"The vast majority of people are somewhere in between," she said.

Part of the problem is that addiction has become more of a lay term defined by differently by different groups. Addiction rates have varied widely in studies.

The National Institute on Drug Abuse says addiction rates among chronic pain patients have ranged from 3% to 40%.

A 2011 study looking at different data also found a substantial problem.

The research involved 705 people on long-term opioid therapy for non cancer pain. It used a new
definition known as opioid-use disorder. This disorder is similar to addiction, said Joseph Boscarino, PhD, the study's lead author and senior investigator at the Geisinger Clinic in Danville, Pa.

Nearly 35% of those in the study had either moderate or severe opioid-use disorder at some point during their lives.

"It (addiction) is not low," said Boscarino, a professor of psychiatry at Temple University. "It's pretty high."

The 1996 consensus statement was taken down from the website of the American Academy of Pain Medicine last fall after a doctor complained about it. It should have been reviewed years earlier, said Philip Saigh, executive director of the academy.

Last year, the academy received $1.3 million from the pharmaceutical industry, including unrestricted grants, according to information supplied to the Journal Sentinel/MedPage Today.

In addition, the AAPM's "corporate relations council" allows companies that pay up to $25,000 each to gain access to physician leaders associated with the academy. Last year, that program took in $170,000.

Corporate relations council members who pay another $60,000 also can have their educational programs included as satellite dinner symposia at the academy's annual meeting in Palm Springs -- a meeting slated for Feb. 23-26. An academy brochure describes the meeting as an "exclusive venue" for presenting continuing medical education material for doctors.

Saigh said payments by pharmaceutical companies do not give them the right to influence positions or statements made by the academy.

The American Pain Society, which funded the 1996 consensus statement on opioids and chronic pain, received more than $1.6 million in financial support from opioid companies in the last two years, more than 20% of its revenue, according to figures it provided for this story.

Its president, Seddon Savage, MD, an addiction and pain medicine specialist, declined to be interviewed for this story, but provided written responses.

In her statement, Savage, an associate adjunct professor at Dartmouth Medical School, said there is no evidence of the impact the statement had on opioid prescribing. The statement is not an official society document "at this time," she said.
She said it was unfair to say that the society's position on opioids has been influenced by pharmaceutical companies. The society did not advocate for or against the use of opioids, she said.

"For some individuals with pain, opioids relieve disabling suffering and allowed them to re-engage in a life worth living," she said. "For others, opioids can be associated with serious harm."

She said the group's position now is reflected in clinical guidelines issued in 2009. The guidelines were commissioned by the American Pain Society in conjunction with the American Academy of Pain Medicine.

The new guidelines say doctors can consider a trial of opioids for patients with chronic pain, but acknowledge that the evidence for such a "trial" is low-quality or insufficient.

And even that 2009 guideline document is tainted by allegations of pharmaceutical industry influence.

In 2008, Joel Saper, MD, a Michigan pain specialist, resigned from the guidelines committee, in part citing support of the project by the opioid industry.

Saper who has worked as an advisor to numerous drug companies, including those that make headache medications and opioids, provided a copy of his resignation letter to the Journal Sentinel/MedPage Today.

"The sponsoring organizations have received a large amount of funding from the opioid manufacturers over the past decade," wrote Saper, director of the Michigan Head Pain & Neurological Institute, in Ann Arbor. "Many members of the committee have personally received sizable funding from the opioid industry as well."

Disclosure statements accompanying the guidelines indicate 14 of the 21 people who served on the project had financial ties to companies that make opioids.

In a statement to the Journal Sentinel/MedPage Today, Roger Chou, MD, who chaired the guidelines project, said Saper never brought up any concerns about financial ties to drug companies prior to his letter.

Chou, an associate professor of medicine at Oregon Health & Science University, has no financial relationships with drug companies.

Pseudoaddiction: A Non-starter
Closely tied to the addiction issue is a term -- pseudoaddiction -- that has been widely used in the field of pain medicine.

When patients seek more frequent prescriptions or higher doses of opioids, it often is a sign of addictive behavior. But the pseudoaddiction approach -- essentially taking them at their word -- argues they aren’t addicts, they just need more pain relief.

Even doctors who have financial relationships with opioid makers concede that term is not backed up by good science.

"It obviously became too much of an excuse to give patients more medication," said Webster, the Utah pain specialist and officer of the American Academy of Pain Medicine. "It led us down a path that caused harm. It is already something we are debunking as a concept."

The term was coined by Haddox, the doctor who is now a Purdue Pharma executive, and David Weissman, MD, a Medical College of Wisconsin physician, who used it in a 1989 paper in a medical journal. Weissman, now retired, could not be reached for comment.

Haddox, vice president of health policy at Purdue, declined to comment.

In the paper, the two used the term to describe a teenage leukemia patient with pneumonia and chest-wall pain who was being treated at a hospital.

But without adequate evidence, over the years it became an established belief in the world of chronic, non cancer pain.

It can be found throughout the pain literature, ranging from American Pain Foundation documents to documents issued by the Federation of State Medical Boards, the national group representing state medical boards. The FSMB includes pseudoaddiction in its , model policy for the use of controlled substances in treating pain.

Steven Weisman, MD, a professor of anesthesiology and pediatrics at Medical College of Wisconsin, said there is one group of patients who might accurately be described as suffering pseudoaddiction -- sickle cell patients who develop chronic degenerative hip and back pain that responds to treatment with morphine.

But even pain specialists such as Russell Portenoy, MD, who has had extensive financial ties to opioid companies, now acknowledge that the concept of pseudoaddiction in chronic pain was not
supported by evidence.

"The term has taken on a bit of a life of its own," said Portenoy, chairman of pain medicine and palliative care at Beth Israel Medical Center in New York, "That's a mistake."

Portenoy conceded there has been a lack of evidence supporting the use of opioids in chronic non-cancer pain, but said much of medical care is not based on rigorous evidence.

"This is not a simple story," he said.

**Same Tune, Different Words**

It reminds Howard Bauchner, MD, editor-in-chief of the *Journal of the American Medical Association*, of the situation that existed a decade ago with antibiotics.

The drugs were being vastly over-prescribed. They were being given to people with viral-based respiratory infections, against which they were useless. Or they were given to children for undocumented throat infections.

It wasn't until the situation became the focus of public attention that the inappropriate use of the drugs declined, Bauchner said.

"I'm hoping we can write the same story about opioid use in a decade," he said.

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