Networking fuels painkiller boom

February 20 2012, By John Fauber

Prescriptions for narcotic painkillers soared so much over the last decade that by 2010 enough were being dispensed to medicate every adult in the United States around the clock for a month.

Behind 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 companies that made them, a Milwaukee Journal Sentinel/MedPage Today investigation found.

Last year, the newspaper found that a University of Wisconsin- based organization in Madison had been a national force in helping liberalize how opioids are prescribed and viewed. While pushing a pharmaceutical industry agenda that critics say was not supported by rigorous science, the UW Pain & Policy Studies Group took in $2.5 million over a decade from opioid companies.

After the story ran in April, the UW Pain group said it had decided to stop taking money from the drug industry.

But the UW group is just one link in a network of national organizations and researchers with financial connections to the makers of narcotic painkillers that paved the way for the boom in prescribing drugs such as OxyContin and Vicodin.

Beginning 15 years ago, the network helped create a body of dubious information that can be found in prescribing guidelines, patient literature, position statements, books and doctor education courses, all

which favored drugs known as opioid analgesics.

Doctors say the increased use sprang from research that showed the drugs were safe and effective for short-term pain, such as after surgery, as well as cancer and end-of-life pain. Without rigorous research, they say, those beliefs then were applied to a much larger population of people with long-term pain, such as low back pain and fibromyalgia.

With millions of Americans suffering real pain that can last for years and thousands of doctors wanting to help them, it was a situation ripe for the influence of the pharmaceutical industry, said Mark Sullivan, a professor of psychiatry and behavioral sciences at the University of Washington.

By 2010, those companies were selling four times as many prescription painkillers to pharmacies, doctors' offices and hospitals than in 1999, according to the most recent data from the U.S. Centers for Disease Control and Prevention.

Led by OxyContin, sales on 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 company.

"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."

A band of doctors who get little or no money from opioid makers has begun to challenge the hype behind the drugs. They say pharmaceutical industry clout has caused doctors to go overboard in prescribing the drugs, leading to addiction, thousands of overdose deaths each year and other serious complications.

Several of the pain industry's core beliefs about chronic pain and opioids are not supported by sound research, the Journal Sentinel/MedPage Today investigation found. Among them:

-The risk of addiction is low in patients with prescriptions.

-There is no unsafe maximum dose of the drugs.

-The concept of "pseudoaddiction."

That concept holds those who display addictive behavior, such as seeking more drugs or higher doses, may not be actual addicts - they are people who need even more opioids to treat their pain.

Even some 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, a Utah pain specialist who has worked as a consultant and adviser to most of the companies that make opioids, said: "We overshot our mark, all well-intended, I believe. We certainly have a lot of reverse education that needs to occur."

Some chronic pain sufferers do benefit from the drugs, said Webster, an officer of the American Academy of Pain Medicine.

"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."

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, 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 atÂ 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 a familiar playbook.

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

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

Consider the American Pain Foundation, which has substantial financial ties to companies that make narcotic painkillers. In a patient guide available on its website, it says there is no ceiling dose for opioids as long as they are not combined with other drugs such as acetaminophen. It says the dose can gradually be increased over time if pain worsens.

Independent doctors say that practice developed to treat the pain of cancer patients in the hospital or at the end of life.

It should not be applied to chronic 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.

"Risk goes up with dose, even if it is well done," Sullivan said.

An April 2011 paper in the *Archives of Internal Medicine* found that the risk of death for high-dose patients 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 fraudulently 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. 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. But Cephalon allegedly promoted the drug for non-cancer patients with conditions ranging from migraines to

injuries. 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 would not 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."

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

The chairman of the group issuing the statement was J. David Haddox, a physician and paid speaker for Purdue Pharma, maker of OxyContin. Haddox would become a Purdue executive three years later.

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 were skewed because, as a

precaution, they excluded people with mental illness or with a family history of substance abuse, groups that are more likely to develop addiction.

But many of those people develop serious chronic pain and are put on opioid therapy.

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

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 uses a newer term known as "opioid-use disorder." The disorder is similar to addiction, said Joseph Boscarino, the study's lead author and senior investigator at the Geisinger Clinic in Danville, Pa.

They both involve compulsive drug use with serious consequences.

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

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 information supplied to the Journal Sentinel.

In addition, its "corporate relations council" allows companies that pay up to $25,000 each to gain access to physician leaders associated with

the academy. Last year, the program took in $170,000.

If they pay another $60,000 they can have their educational programs included as independent dinner symposia in conjunction at the academy's annual meeting in Palm Springs. An academy brochure describes it is 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, got more than $1.6 million in financial support from opioid companies in the last two years, or 23 percent of its revenue, according to figures it provided for this story.

Its president, Seddon Savage, 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 effect the statement had on opioid prescribing. The statement is not an official society document "at this time," she said.

She said it is 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 is low-quality or insufficient.

Even that document is tainted by allegations of pharmaceutical industry influence.

In 2008, Joel Saper, 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 adviser to numerous drug companies, including those that make headache medications and opioids, provided a copy of his resignation letter to the Journal Sentinel.

"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, Roger Chou, who headed up the guidelines project, said Saper never brought up any concerns about financial ties to drug companies before his letter.

Chou, an associate professor of medicine at Oregon Health & Science

University, has no financial relationships with drug companies.

Saper, a former board member of the American Academy of Pain Medicine, uses the term "narcopharma" to explain how opioid companies have affected the practice of pain medicine.

"Even some of the most reasonable and cautious physicians were influenced by the strong and pervasive advocacy by many of this nation's expert physicians and the programming at major pain meetings, promoted and underwritten by the narcopharma money," he told the Journal Sentinel after last year's story on the UW Pain group.

Closely tied to the addiction definition is a term - "pseudoaddiction" - that has been widely used in the field of pain medicine.

The term was coined by Haddox, the doctor who would later become a Purdue Pharma executive, and David Weissman, a Medical College of Wisconsin physician, 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 it spread to the chronic pain literature, ranging from American Pain Foundation documents to the Federation of State Medical Boards, another national group that has received funding from opioid companies. The federation included pseudoaddiction in its model policy for the use of controlled substances in treating pain.

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.

"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."

How did such an unproven concept become widely believed?

Even pain specialists such as Russell Portenoy, who has had extensive financial ties to opioid companies, 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."