Doctors with links to drug companies influence treatment guidelines

By John Fauber and Ellen Gabler of the Journal Sentinel

Dec. 18, 2012 | (27) Comments

Doctors with financial ties to drug companies have heavily influenced treatment guidelines recommending the most lucrative drugs in American medicine, an analysis by the Milwaukee Journal Sentinel and MedPage Today has found.

The guidelines affect how doctors across the country treat patients for everything from diabetes to asthma, chronic pain, depression and high cholesterol.

Issued by leading medical associations and government institutions, treatment guidelines are supposed to be based on rigorous science. But the committees that write them have been dominated by doctors who have worked as paid speakers, consultants or advisers for companies selling the recommended drugs.

Critics say the financial relationships have corrupted medicine, resulting in cases where guidelines make dangerous or ineffective recommendations. Drug companies and some doctors counter that those with conflicts are often top experts in their field.

The Journal Sentinel examined 20 clinical practice guidelines for conditions treated by the 25 top-selling drugs in the United States.

The drugs sit in the medicine cabinets of millions of Americans - Nexium for acid reflux, Lipitor for high cholesterol, Cymbalta for depression and OxyContin for pain. Their collective sales topped $94 billion in 2011, accounting for 30% of drug revenue in the United States.

An analysis of the guideline panels, which involved 293 doctors, found:

- Nine guidelines were written by panels where more than 80% of doctors had financial ties to drug companies.
- Four panels did not require members to disclose any conflicts of interest. Of the 16 that did, 66% of doctors on the panels had ties to drug companies.
- Some guidelines written by conflicted panels recommend drugs that have not been scientifically proven to safely treat conditions, leading to inappropriate or over prescribing. Medical experts have raised such questions about guidelines for anemia, chronic pain and asthma.

Research funded by drug companies was not counted as a conflict in the Journal Sentinel analysis because experts disagree whether research poses as much of a conflict as speaking, consulting and advising.

The findings offer the latest glimpse into how pharmaceutical companies, with billions in sales at

stake, exert a powerful but often unrecognized influence over the practice of American medicine.

Past Journal Sentinel reports have revealed articles in medical journals that were ghostwritten by drug company marketers; instructional videos for doctors that made misleading claims about drugs; payments to medical organizations that advocated for more use of drugs; and drug companies paying for continuing medical education courses that, in essence, market their products.

"At the end of the day, the drug companies own medicine," said Eric Campbell, an associate professor at Harvard Medical School who has researched conflicts of interest in treatment guidelines. "We've created a system that allows this."

While it is impossible to measure how drug company payments influence doctors' judgment, the cozy relationships have raised concern among doctors and researchers who contend that conflicts of interest taint the highly influential treatment guidelines.

In March 2011, the Institute of Medicine issued a report that said fewer than 50% of members of a guideline-writing committee should have financial relationships with drug companies. No committee chairman should have a financial conflict of interest, the institute said.

At most, two panels met those requirements in guidelines analyzed by the Journal Sentinel.

Of the 16 panels that disclosed conflicts of interest, at least 10 had chairmen with financial ties to drug companies **.** Payment amounts were not disclosed in the guidelines, which were issued between 2001 and 2012.

Some medical societies have agreed to adopt the Institute of Medicine's recommendation, but many others complain it is too difficult, costly and contentious among members, said Sheldon Greenfield, chairman of the group that issued the report titled, "Clinical Practice Guidelines We Can Trust."

"By and large, most of the societies have ignored it," said Greenfield, a professor of medicine and executive co-director of the Health Policy Research Institute at University of California, Irvine.

Extensive time, research and expertise are poured into developing most guidelines, a process that can take years. The documents are complicated, dense and extremely technical. At their best, rigorously developed, unbiased guidelines can help synthesize new research and improve the quality of treatment that patients receive.

Even critics who want to minimize or eliminate conflicts acknowledge that guidelines written by doctors with financial ties to drug companies can offer solid, scientifically backed recommendations.

But protecting the integrity of clinical guidelines is essential to the practice of medicine, said Steven Nissen, chairman of cardiovascular medicine at the Cleveland Clinic.

"If those guidelines are produced in a way that is not completely free of bias, then we are guiding physicians and patients toward therapies based on opinions that may have been influenced by people's financial relationships," Nissen said. "That is a huge problem."

Some doctors and pharmaceutical industry representatives say physicians who consult for drug companies are among the most well-informed experts in their field and should help write guidelines.

Experienced doctors are trained to evaluate and base their decisions on complicated medical and scientific information, without being influenced by their ties with drug companies, said Marjorie Powell, senior assistant general counsel for PhRMA, a trade group that represents drug and

biotechnology companies doing research to develop new medicine.

Other doctors and researchers say there are countless experts to call upon who do not have relationships with drug companies.

In fact, doctors are often willing to cut ties with drug companies in order to sit on guideline writing panels, said Daniel Ouellette, vice chairman of the guidelines oversight committee for the American College of Chest Physicians and a senior staff physician at Henry Ford Hospital in Detroit.

Ouellette said he looks at excluding potential bias as part of the scientific process.

"We would rather have our panel be completely non-conflicted," he said.

People with industry ties may be allowed to give insight if their expertise is so unique no one else can provide it, Ouellette said. But they can only add comments and participate in discussions, not vote on or draft guidelines.

First, do no harm?

In some cases, guideline panels have recommended treatments that have not been proven to make a meaningful difference - or that could even harm patients.

Guidelines written by conflicted panels have encouraged prescribing highly addictive narcotic painkillers to treat long-term chronic pain, an area where the safety and effectiveness of the drugs remain unproven.

OxyContin, a popular and addictive opioid, was the 19th best selling drug in the United States last year, with $2.9 billion in sales. In 2009, the American Pain Society and the American Academy of Pain Medicine issued a guideline endorsing opioids to treat chronic pain. The guideline was written by a panel where 14 of 21 members had ties to drug companies.

Also in 2009, the American Geriatrics Society advocated for greater opioid use to treat chronic pain in seniors. That guideline recommended that over-the-counter pain relievers, such as ibuprofen and naproxen, be used rarely and that doctors instead consider opioids for all patients with moderate to severe pain.

Panel members said they relied on research and their own experience in revising the guidelines, acknowledging "existing weak scientific evidence." Half the experts on the panel had financial ties to opioid companies.

Health and regulatory officials have declared misuse of opioids a national epidemic, citing skyrocketing addiction to painkillers and a tripling of fatal overdoses in the past decade. Emergency room departments across the country are adopting policies to discourage doctors from prescribing narcotics to patients with chronic pain and advocates are asking the U.S. Food and Drug Administration to restrict companies' marketing of the drugs.

The asthma drug Advair was the nation's fifth best selling drug in 2011, with $4.6 billion in sales. It is part of a class of drugs recommended in a 2007 guideline from the National Heart, Lung and Blood Institute.

Twelve of the 18 members of the guideline's panel had financial ties to GlaxoSmithKline, which makes Advair. Three other panel members had ties to other companies that market that same of

class of drugs, known as beta-agonists. In all, 83% of the panel had conflicts. Beta-agonists have been linked to higher rates of death and severe asthma attacks.

In recent years, medical studies, independent doctors and court records have declared that Advair has been massively overused and inappropriately prescribed.

Expensive anemia treatment

An anemia drug, once Medicare's most expensive, was recommended in guidelines issued in 2006 by the National Kidney Foundation.

The guidelines provided recommendations for treating anemia in chronic kidney disease patients and endorsed a class of drugs including Epogen. The drug helps raise levels of hemoglobin, a protein in red blood cells that carries oxygen. Epogen is marketed by Amgen and had 2011 sales of $2.8 billion.

On almost every level, the drug company was financially linked to the guideline process.

Fifteen of 18 panel members who wrote the guideline for the Kidney Foundation had financial ties to drug companies. Ten of those members, including both co-chairs, had financial relationships directly with Amgen.

Amgen paid $1.7 million in 2004 and 2005 to fund the guidelines for the Kidney Foundation. All told, foundation records show the group received $8.7 million from Amgen in those years.

Ashleigh Koss, a spokeswoman for Amgen, declined to comment.

Concerns about the safety of Epogen and drugs in its class have grown steadily over the past 10 years. Such drugs can increase blood clots and the risk of heart attack, stroke, heart failure and death.

The Kidney Foundation's guideline recommended higher hemoglobin targets than those approved by the FDA, said Daniel Coyne, a kidney disease specialist and professor of medicine at Washington University in St. Louis. Higher targets could require higher doses of Epogen and similar drugs, which could be harmful to patients, he said.

In 2007, Coyne wrote a paper in a kidney disease journal that was highly critical of the guideline and conflicts of interest. At the time, he was an adviser, speaker and consultant for Amgen and other drug companies. He said he no longer does that kind of consulting work.

In 2011, the FDA warned doctors to be more conservative in dosing drugs such as Epogen because data showed higher risk of cardiovascular problems and death in kidney disease patients.

The Kidney Foundation said Coyne's claim that the guideline raised the hemoglobin target is "a fundamental misinterpretation of the guideline." Foundation spokesman Sean Roach said there were subtleties to interpreting the guideline and FDA recommendations.

The foundation said drug companies that provide funding for the guidelines do not influence them and that a separate team of physicians without conflicts gathers evidence for the group writing guidelines.

Managing blood sugar vs. aiding health

In 2006, the American Diabetes Association and the European Association for the Study of Diabetes issued recommendations for managing high blood sugar in people with type 2 diabetes.

The recommendation included use of drugs known as glitazones. At the time, the two most popular glitazones were Avandia and Actos.

Both drugs were approved by the FDA in 1999 on the basis that they improved short-term blood sugar control - not because they reduced heart attacks and strokes.

Six of seven panel members had worked as speakers or advisers to drug companies, including three who worked for GlaxoSmithKline, maker of Avandia, and one who worked for Takeda, maker of Actos.

Less than a year after the guideline came out, Avandia was linked to substantially increased risk of heart attacks. In 2010 the drug was banned in Europe and severely restricted in the United States.

Actos has not been shown to increase heart attacks, though the drug has been linked to increased risk of heart failure. U.S. sales for Actos have remained over $3 billion a year in recent years.

David Nathan, chairman of the 2006 diabetes guideline panel, said members did not have data showing Avandia was dangerous and as soon as that information came to light, the panel changed its recommendation.

Nathan, a professor of medicine at Harvard Medical School, was the only panel member who did not work as a speaker or adviser to drug companies. (He has received research grants from drug companies, according to his disclosure in the guideline.)

Nathan said if people with conflicts of interest were eliminated from guideline panels, "we wouldn't be able to put together committees with enough expertise to make them worthwhile."

In an email, Nathan acknowledged that, at the time, there was no rigorous evidence showing that either Avandia or Actos reduced the risk of cardiovascular disease, blindness or kidney damage. He said there is no compelling data that any diabetes drug reduces cardiovascular risk.

Research has shown that improving blood sugar generally lowers the risk of microvascular events such as blindness and kidney damage. It was on that basis that the panel recommended the drugs, he said.

A statement provided by the diabetes association said its policies on guidelines have been evolving and "were radically revised" after the 2011 report by the Institute of Medicine.

"We currently are striving to meet all of the IOM requirements, but recognize that older efforts may not have lived up to that new more rigorous standard," the statement said.

In 2011, the association received $15 million in funding from drug and medical device companies, including $145,325 from GlaxoSmithKline and $638,250 from Takeda, according to its revenue statement. The association would not provide drug company funding amounts from the years before the 2006 guideline.

The guideline panel's recommendation is an example of an ongoing problem in medicine, especially in diabetes care, said John Yudkin, an emeritus professor of medicine at University College London.

Panelists may make recommendations to use certain drugs based on a "surrogate measure," such

as improving blood glucose levels, and then assume this also reduces the risk of heart disease, kidney damage or blindness.

But an improvement in a blood measure doesn't always mean a patient is facing less risk of serious health problems. Avandia and Actos never have been proven to reduce kidney damage, amputations, blindness, heart attacks or strokes, Yudkin noted.

Psychiatrists make changes

Increased political scrutiny of drug companies over the past few years has led to more transparency, including the Physician Payment Sunshine Act, which will require drug, device and medical supply companies to disclose any payments made to doctors or teaching hospitals. The first reports are due next spring.

But reformers say that merely disclosing a conflict does not eliminate it.

Four guidelines examined by the Journal Sentinel did not disclose members' conflicts with drug companies. Those guidelines were issued between 2001 and 2005. The American Psychiatric Association issued one of the guidelines in 2004 for treating schizophrenia.

A few years later, the group was embroiled in controversy when it decided to disclose conflicts of interest for a different guideline on depression. That panel included six of seven panel members who had worked as consultants, advisers or speakers for drug companies.

Before the guideline was released in 2010 the association had an independent panel with no drug company ties review the recommendations. No bias was found, said Joel Yager, chairman of the group's steering committee on practice guidelines and a professor of psychiatry at the University of Colorado.

Even so, the American Psychiatric Association no longer allows any doctors with conflicts of interest to sit on its guideline writing panels. It aims to achieve "no possibility of industry bias," Yager said.

"You have to play by the rules," he said.

This story was reported as a joint project of the Journal Sentinel and MedPage Today. MedPage Today provides a clinical perspective for physicians on breaking medical news at medpagetoday.com.

Next

Wauwatosa police confirm two people being questioned after tactical situation

27 Comments
Read and share your thoughts.

248

Tweet 150

More News

Wisconsin traffic fatalities increase in 2012
1:20 p.m. - Madison - The number of people killed in Wisconsin traffic crashes increased in 2012, after four consecutive years of decline.

Wauwatosa police confirm two people being questioned after tactical situation
1:14 p.m. - Wauwatosa police have reopened the neighborhood from 120th to 122nd streets and Watertown Plank and Elmhurst roads, which had been cordoned off this morning while they investigated a home in the 1300 block of 121st Street.

Muskego moves to ensure gun club safety after incident
12:33 p.m. - With a resident saying that he and his children hit the dirt in their backyard one afternoon due to gunfire believed to have come from a nearby gun club, the Muskego Common Council decided last week to try to set safety standards for gun ranges.

Psychiatric exam ordered for man charged with killing teenage neighbor
11:58 a.m. - The elderly north side man accused of shooting his 13-year-old neighbor in May will undergo a psychiatric examination to determine whether he is competent to stand trial, the judge in the case ruled Monday.

Morgridge Institute appoints UW professor as CEO
11:42 a.m. - The Morgridge Institute for Research, a private, nonprofit biomedical research institute affiliated with the University of Wisconsin-Madison, announced the appointment Monday of Brad Schwartz as chief executive officer.

JS Everywhere Subscription:
- Login
- Subscribe
- Manage Subscription

Public Profile:
- Sign in
- Create profile

Privacy Policy/Your California Privacy Rights | Terms of Use

© 2013, Journal Sentinel Inc.