New Algorithms Identify Side Effects of Prescription Drugs

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Madigan in the classroom

(PhysOrg.com) -- We're all used to hearing disclaimers about prescription drug side effects. They drone on in television commercials and take up pages of tiny print accompanying the prescriptions themselves. But with an estimated 10,000 prescription drugs available in the U.S. market alone, surprisingly little research has been done about the adverse effects each drug can cause.

Enter professor David Madigan, chair of Columbia's statistics department. He was recently tapped by the Food and Drug Administration and the Foundation for the National Institutes of Health to create algorithms that can help medical experts determine which drugs

cause which side effects.

Madigan is midway through a two-year project to test those algorithms, relying on up to a dozen massive databases jam-packed with millions of medical-claims records dating to 1995. Madigan leads a team of researchers, including two Columbia post-doctoral scholars and one Ph.D. student, as it pores over data regarding the 10,000 side effects listed in the Medical Dictionary for Regulatory Activities.

The initiative, called the Observational Medical Outcomes Partnership (OMOP), is a novel public-private partnership chaired by the FDA and administered by the NIH foundation, a nonprofit that raises funds for NIH-supported programs. It is funded by a consortium of 17 pharmaceutical companies. “Nobody has ever done anything on the scale that we’re doing it on,” says Madigan.

A member of the Columbia faculty for three years, Madigan—who specializes in the application of statistical methods to largescale data problems—began working on drug safety when he was at AT&T Labs, where he worked for more than a decade. Other applications he works on include text mining and analysis of large trauma-care databases.

“Dr. Madigan’s research is at the core of OMOP’s research agenda,” said Thomas P. Scarnecchia, executive director of the project. “He has successfully established a community of scholars who are working toward the development of novel analysis methods for identifying drug safety issues.”

Indeed, the project marks one of the first attempts to systematically study methods that monitor the safety of drugs after they are released, says Madigan. Until now, the FDA has monitored the safety of licensed drugs through a passive surveillance system that relies on voluntarily submitted safety reports. The change was prompted by the 2007 FDA

Amendments Act, which Congress passed after the drug Vioxx was linked to more than 27,000 heart attacks and sudden cardiac deaths. The FDA had approved Vioxx in 1999, but its manufacturer, Merck, pulled it from the market in 2004 after studies showed the drug significantly increased the risk of heart attack or stroke. Merck paid billions in legal settlements in more than 50,000 lawsuits.

“There were severe problems with the system,” says Madigan, adding that if an active surveillance system had been in place a decade ago, a potentially disastrous drug such as Vioxx might have been pulled from the market soon after its release.

By using reams of medical claims data, Madigan and his colleagues can determine which side effects are statistically significant and which ones are due solely to chance. Imagine, for example, that a medical report suggests that a certain drug causes skin rashes. Madigan’s algorithms first determine the percentage of users who have made similar complaints. Next, they factor in other medications that those individuals might be taking (some might take aspirin, which is known to cause skin rashes). Finally, they consider the number of drug users who don’t take that particular drug but develop skin rashes and start calculating.

As if that wasn’t complicated enough, Madigan’s team is also charged with finding links across multiple databases that were developed using different computer systems. “The databases speak different languages, which presents huge challenges,” says Madigan. The largest database he works with includes 70 million people and is based on primary care records, hospital records, lab results and drug reports.

Madigan hopes his research will keep the FDA informed as it establishes the Sentinel System, a national surveillance drug safety network that Madigan also works on. “Without a system in place like Sentinel, there will be more Vioxxes,” he says. “It’s going to happen again unless we put

into place a method of detecting these things early."

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