

# Available genetic data could help doctors prescribe more effective cardiovascular drugs

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There is a wealth of published information describing interactions between drugs used to treat cardiovascular disease and the genetic variations that can affect how patients respond to them. But few heart specialists make routine use of this potentially life-saving data.

To help physicians make better-informed clinical decisions, researchers from the University of Chicago and Stanford University combed through scientific literature on the pharmacogenomics of 71 leading cardiovascular drugs and compiled summaries, published in the June issue of the *Mayo Clinic Proceedings*.

"Tens of thousands of patients have been studied and the connections between common medications and the genetic variants that can lead to adverse drug reactions or treatment non-response have been described, but few physicians track this information or even know where to find it," said study author Peter H. O'Donnell, MD, assistant professor of medicine at the University of Chicago.

"One dose does not fit all," he said. "So we set out to boost awareness and simplify access. We assessed the quantity and quality of the literature, ranked the most relevant studies for clinicians and condensed the data into a series of prescribing decision aids."

Cardiovascular drugs are a common cause of the estimated two million

adverse drug reactions that occur each year in the United States. More than 50,000 patients are treated in emergency rooms annually for bad reactions to cardiovascular drugs. Patients over age 65 are particularly at risk, especially those taking warfarin and anti-platelet agents.

Although adverse drug outcomes occur in specific patients, medications are studied and approved based on large, carefully selected populations, the authors note. Performance in that setting "is less informative when treating individual patients, who show remarkable variability in their response to medications."

So the researchers probed every paper published in English between January 2011 and May 2013, searching for articles that described a link between genetic variations and an unanticipated pharmacological or clinical outcome caused by a cardiovascular drug.

They found 597 unique publications, involving 611 genetic markers or "variants" and 884 drug-variant pairs. Fifty-one of the 71 cardiovascular drugs they focused on (71.8 percent) had detectable pharmacogenomic effects.

Of the 884 drug-variant pairs, 92 interactions involving 23 different drugs warranted summarization for consideration during clinical decision making. Four high-scoring drug-variant pairs—involving the drugs clopidogrel (Plavix®), metoprolol (Lopressor®), simvastatin (Zocor®) and warfarin (Coumadin® and others)—deserved particular attention.

The researchers also devoted extra attention to the nine most common cardiovascular drugs—such as simvastatin, which is prescribed 96.8 million times a year. They found that seven of these frequently prescribed medications warranted pharmacogenomic guidelines for clinical consideration. For the simvastatin example, roughly one to two percent of patients who take the ubiquitous drug develop myopathy, a

painful muscle injury that can lead to kidney complications and death in its most severe forms.

"Our findings are already making a difference in patient care," said co-author, cardiologist Matthew Sorrentino, MD, professor of medicine at the University of Chicago. "I have long been familiar with the common variations in response to drugs, but, like most physicians in my specialty, I had limited knowledge of the pharmacogenomics behind it, or the ability of this information to predict a problem."

"As we worked on this project, one of my patients developed chest pain caused by acid reflux. The standard drug for that situation didn't help," he said. "From his genetics we learned that he would probably respond better to another agent, so we changed his medication. His reflux—and his chest pain—promptly went away. Easy access to this information helped us make the change quickly, in days instead of weeks."

The problem, he added, is that "there is no one place where all this information is available, no fast, easy way to find it."

One recent survey, published in July 2014, confirmed that among physicians "familiarity with pharmacogenomics continues to be low and that knowledge gaps persist." The study reported just 12.6 percent of physicians were extremely or very familiar with pharmacogenomics. The authors cite other surveys. In one, only 10 percent of respondents felt they were adequately informed about the applicability of genetic testing to drug therapy. Another found that only 13 percent of respondents felt well informed about the role of pharmacogenomics in therapeutic decision making.

"There is substantial pharmacogenetic information on [cardiovascular drugs](#) that could potentially be applied to patient care," O'Donnell and colleagues conclude. "Considering the hundreds of millions of annual

cardiovascular drug prescriptions, the frequency of [adverse drug reactions](#), and the variable levels of drug response, the impact of this knowledge is potentially prodigious."

Provided by University of Chicago Medical Center

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