Biyonka Liang
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Using Data to Investigate Drug-to-Drug Interactions

More and more Americans are taking prescription drugs. About 60% of Americans are on at least one prescription drug and about 15% are on five or more. Now more than ever, there is a need for research on drug-to-drug interactions. Though investigating genetic variations in enzymes that are a major metabolic pathway for prescription drugs such as CYP450 has proven somewhat helpful in identifying possibly harmful drug interactions, most interactions are still only detected from patient side effects.

In 2011, two Stanford data scientists, Russ Altman and Nicholas Tatonetti led one of the first drug to drug interactions experiments outside of a medical laboratory. They first used the FDA's public database on adverse event reports from doctors, pharmacists and other medical professionals from around America, and looked specifically at people who were taking both paroxetine, or Paxil, an antidepressant; and pravastatin, or Pravachol, a cholesterol medication. They found, that people who took both Paxil and Pravachol experienced spikes in their glucose measurements, but people who took one medication or the other did not. To put this discovery in context, depression and high cholesterol are two of the most commonly treated diseases in America. More than 15 million Americans are being treated for depression, another 15 million being treated for high cholesterol, and an estimated 1 million are being treated for both. Understanding the interactions between drugs meant to treat these two disease is crucial.

Altman and Tatonetti then borrowed data from Stanford's, Harvards and Vanderbilt's electronic medical records, and looked specifically at patients who were on one drug first and had a glucose measurement, and then on the other drug, and then had another glucose measurement. They found that among the 150 non-diabetic patients from three diverse medical centers, almost all had a 20 mg/dl rise in glucose on average. This rise is significant. The glucose levels of a non diabetic person is around 90 mg/dl. Glucose levels at 120-125 mg/dl put people at risk for diabetes. Their investigation also discovered that patients who already had diabetes were affected more heavily, as their levels rose 60 mg/dl on average.

From this, they suspected that non-diabetic patients taking both drugs might be experiencing the symptoms of hyperglycemia. They defined 50 words that someone may type in when they're experiencing symptoms of hyperglycemia, such as "loss of appetite" and "fatigue". They used Microsoft's data from Yahoo, Google and Bing searches to investigate how people were searching these "diabetes words". Out of all search data, about 0.5-1 percent of searches involve one of those words. Given that "pravastatin" was included in the search query, then the proportion of searches that include these "diabetes words" goes up about 3% of searches, and about 2% given that "Paxil" was in the query. However, when both Paxil and pravastatin are included together in the search query, the percentage of times that they were searched with one or more of the "diabetes words" was 10%, a 3 or 4 fold increase from the proportion of searches with just one of the drugs.

Tatonetti and Altman went on to investigate hundreds of drug pairs, something that may have taken decades to complete with only laboratory work. Their methodology defined a new way to conduct bioinformatics research by using big data.

Detecting Drug Interactions From Adverse-Event Reports: Interaction Between Paroxetine and Pravastatin Increases Blood Glucose Levels
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Prescription Overkill: Are Americans Taking Too Many Pills?
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