Identifying Drug–Drug Interactions by Data Mining - DTU Orbit (04/05/2019)

**Identifying Drug–Drug Interactions by Data Mining: A Pilot Study of Warfarin-Associated Drug Interactions**

**Background**—Knowledge about drug–drug interactions commonly arises from preclinical trials, from adverse drug reports, or based on knowledge of mechanisms of action. Our aim was to investigate whether drug–drug interactions were discoverable without prior hypotheses using data mining. We focused on warfarin–drug interactions as the prototype.

**Methods and Results**—We analyzed altered prothrombin time (measured as international normalized ratio [INR]) after initiation of a novel prescription in previously INR-stable warfarin-treated patients with nonvalvular atrial fibrillation. Data sets were retrieved from clinical work. Random forest (a machine-learning method) was set up to predict altered INR levels after novel prescriptions. The most important drug groups from the analysis were further investigated using logistic regression in a new data set. Two hundred and twenty drug groups were analyzed in 61,190 novel prescriptions. We rediscovered 2 drug groups having known interactions (β-lactamase-resistant penicillins [dicloxacillin] and carboxamide derivatives) and 3 antithrombotic/anticoagulant agents (platelet aggregation inhibitors excluding heparin, direct thrombin inhibitors [dabigatran etexilate], and heparins) causing decreasing INR. Six drug groups with known interactions were rediscovered causing increasing INR (antiarrhythmics class III [amiodarone], other opioids [tramadol], glucocorticoids, triazole derivatives, and combinations of penicillins, including β-lactamase inhibitors) and two had a known interaction in a closely related drug group (oripavine derivatives [buprenorphine] and natural opium alkaloids). Antipropulsives had an unknown signal of increasing INR.

**Conclusions**—We were able to identify known warfarin–drug interactions without a prior hypothesis using clinical registries. Additionally, we discovered a few potentially novel interactions. This opens up for the use of data mining to discover unknown drug–drug interactions in cardiovascular medicine.

**General information**
Publication status: Published
Organisations: Department of Applied Mathematics and Computer Science, Statistics and Data Analysis
Number of pages: 8
Pages: 621-628
Publication date: 2016
Peer-reviewed: Yes

**Publication information**
Journal: Circulation: Cardiovascular Quality and Outcomes
Volume: 9
Issue number: 6
ISSN (Print): 1941-7713
Ratings:
Scopus rating (2016): CiteScore 3.77 SJR 3.443 SNIP 1.563
Web of Science (2016): Impact factor 4.524
Original language: English
Keywords: big data, data mining, drug interactions, machine learning, registry, warfarin
Electronic versions:
Document_3912989_35003.pdf
DOIs:
10.1161/CIRCOUTCOMES.116.003055
Source: FindIt
Source-ID: 2348799186
Research output: Contribution to journal › Journal article – Annual report year: 2016 › Research › peer-review