



nSides: An interactive drug—side effect gateway

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COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK

Introduction

- Adverse drug events a leading cause of morbidity and mortality
 - Many effects not detected during clinical trials
- FDA maintains large public collections of adverse event reports
- Developed method to detect drug effects from FDA Adverse Event Reporting System (FAERS) in 2012
 - OFFSIDES (drug effects) and TWOSIDES (drug interactions)
 - Databases available for download

Data-Driven Prediction of Drug Effects and Interactions

Nicholas P. Tatonetti, Patrick P. Ye, Roxana Daneshjou, and Russ B. Altman

Sci Transl Med 14 March 2012 4:125ra31. [DOI:10.1126/scitranslmed.3003377]

nSides

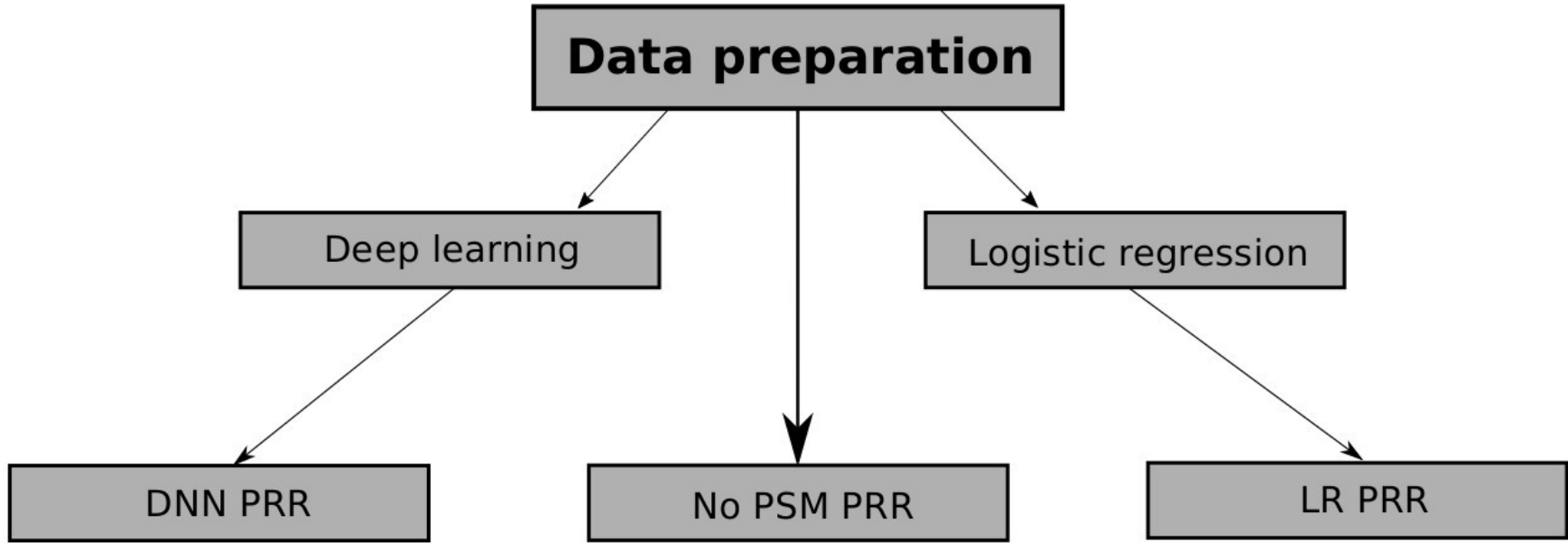
- Public gateway based on algorithm used to form OFFSIDES and TWOSIDES extended to arbitrary drug combinations
- Cases and controls from FAERS for a given drug are **propensity score matched** via logistic regression and multi-layer perceptron
- Involves forming one machine learning model per drug/drug combination
- Result disproportionality statistic
 - Proportional Reporting Ratio = Frequency of Effect on Cases/Controls

Open Science Grid

- Two machine learning models are generated per drug/drug combination
- Initially generate single drug models
 - ~4,000 models and ~7,000 effects per model
- Machine learning models generated on Open Science Grid
 - FAERS is a public data source
- Directed Acyclic Graph setup

**Propensity
Scores**

**Effect
PRRs**



Drug

Effect

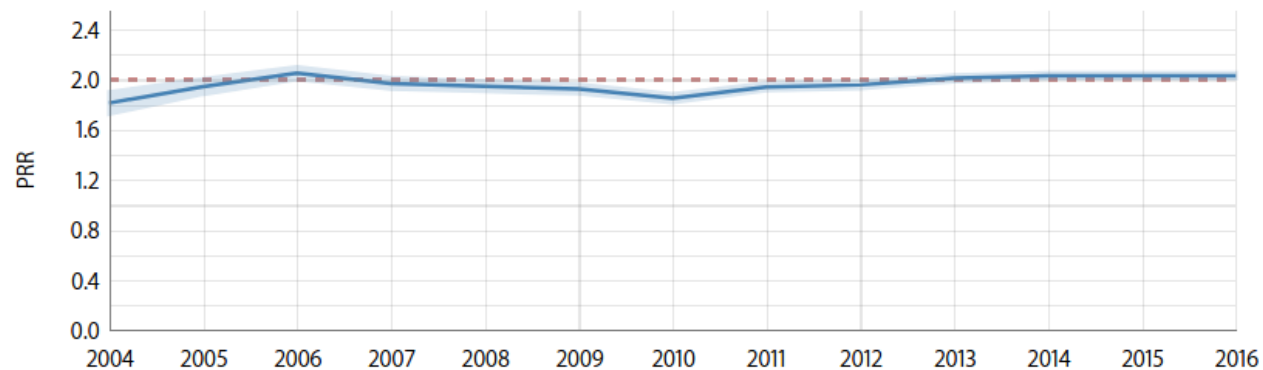
× Amiodarone

× ▾

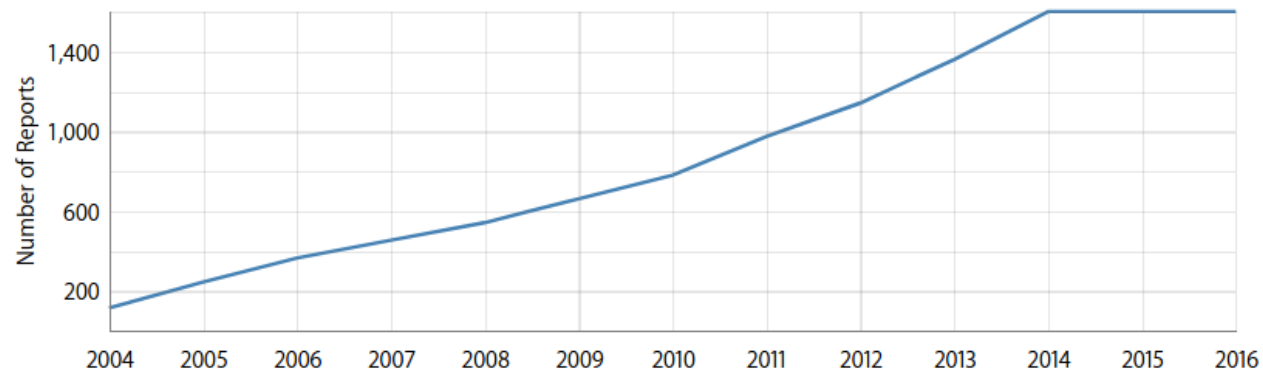
|| - Drug interaction

× ▾

Proportional Reporting Ratio over time

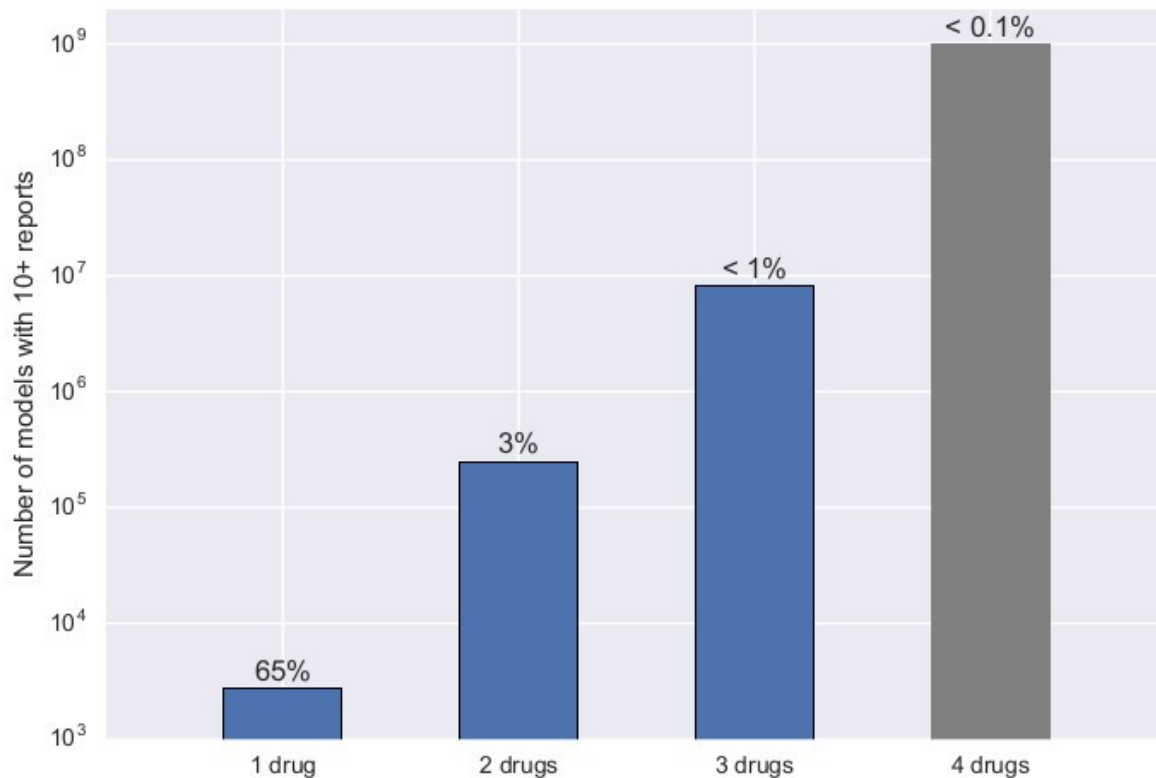


Number of reports by year



Drug Interactions

- Computationally intractable and not useful to calculate all possible drug combinations a priori



Drug Interactions

- On-demand model request system
- Science Gateways Community Institute Extended Developer Support
 - Choonhan Youn
- Implemented via Agave Platform hosted by TACC
 - Takes care of the management of authentication/authorization, jobs, permission, etc
 - Uses RESTful APIs to access services



A comprehensive database of drug-drug(s)-effect relationships

[log out](#)

Current user: [rvanguri](#)

[View submitted jobs](#)

Drug

×

 Simvastatin

×

 Amiodarone

|

×

 ▼

Effect

Select effect...

▼

We have not yet generated a model for this drug / drug combination.

If you would like to submit this drug for computation, click on the following button:

[Submit model](#)

Note: this will redirect you to an external page for authentication if you are not already logged in.

nSides compute jobs

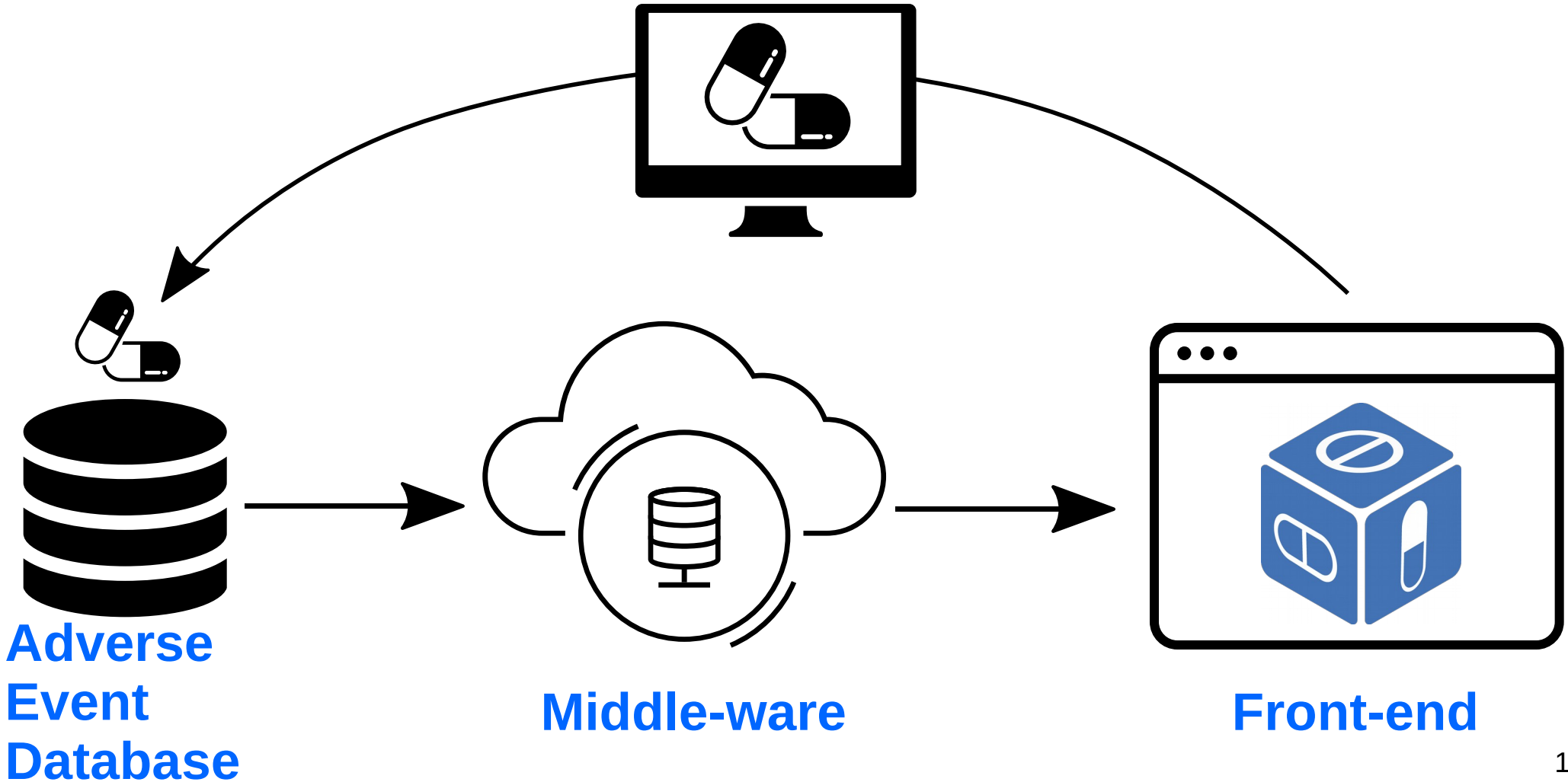
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nSides Stack

- Front-end
 - Displays plots, model request system
- Middle-ware
 - Agave Platform to handle model requests, authentication
 - Python Flask framework
- Back-end
 - Models computed via OSG
 - Populated on mongoDB hosted on AWS

On-demand Interface



Summary

- Data-driven analysis of drug effects using FAERS
- Accessible by researchers, clinicians, and patients
- Intended use to be hypothesis generator for further studies
 - See also: <http://deltaqt.org>
- Initial population done via Open Science Grid
- Novel on-demand job submission system which could be useful for others
- Full stack is open source
<https://github.com/tatonetti-lab/nsides>

Future Directions

- PRRs for drugs in same drug class
- Incorporate other data sources
 - Drug structure information
 - Other reporting systems: European Medicines Agency analog: EudraVigilance
- Dynamic analysis on FAERS data
 - Other signal detection algorithms for drug interactions

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