Provenance-Centered Dataset of Drug-Drug Interactions

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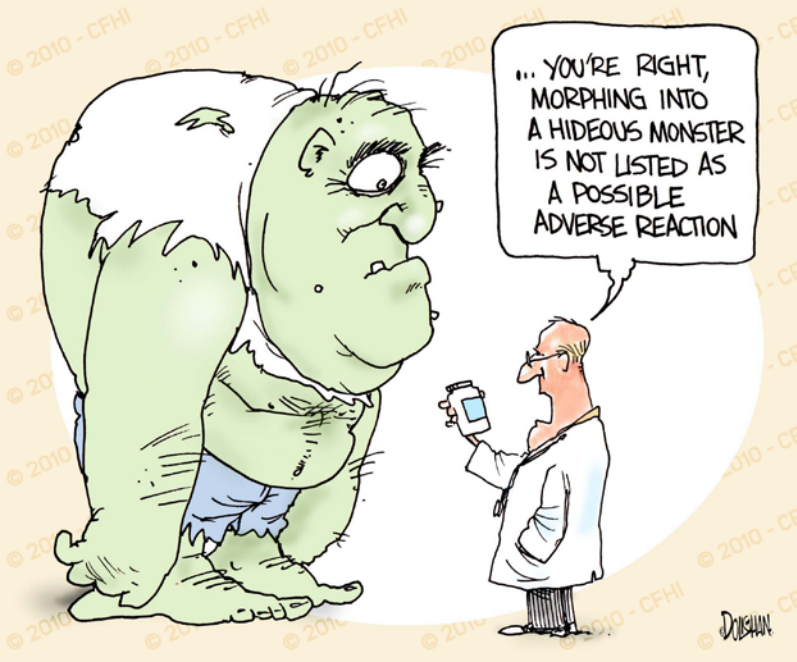
International Semantic Web Conference 2015

Datasets and Ontologies Track

Motivation

STUDIES ANALYZING COSTS OVER TIME HAVE SHOWN THAT ADVERSE DRUG REACTIONS (ADRS) COST OVER $136 BILLION A YEAR

ONE SIGNIFICANT CAUSE OF ADRS ARE DRUG-DRUG INTERACTIONS (DDIS) WHICH GREATLY AFFECT OLDER ADULTS DUE TO THE MULTIPLE DRUGS THEY ARE TAKING



Challenges

Oxford Journals › Science & Mathematics › Bioinformatics › Volume 26, Issue 18 › Pp. i547-i553.

Discovering drug–drug interactions: a text-mining and reasoning approach based on properties of drug metabolism

Luis Tari[1,*], Saadat Anwar[2], Shanshan Liang[2], James Cai[1] and Chitta Baral[2]

[1]Disease and Translational Informatics, Hoffmann-La Roche, Nutley, NJ 07110 and
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Discovering drug–drug interactions: a
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Luis

Statistics in Medicine

Statist. Med. 2008; **27**:3057–3070
Published online 14 March 2008 in Wiley InterScience
(www.interscience.wiley.com) DOI: 10.1002/sim.3247

A statistical methodology for drug–drug interaction surveillance

G. Niklas Norén[1, 2, *, †], Rolf Sundberg[2], Andrew Bate[1, 3] and I. Ralph Edwards[1]

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[2]*Mathematical Statistics, Stockholm University, Stockholm, Sweden*
[3]*School of Information Systems, Computing & Mathematics, Brunel University, London, U.K.*

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http://www.biomedcentral.com/1471-2105/11/S9/S7

PROCEEDINGS **Open Access**

Mining multi-item drug adverse effect associations in spontaneous reporting systems

Rave Harpaz*, Herbert S Chase, Carol Friedman

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Literature Based Drug Interaction Prediction with Clinical Assessment Using Electronic Medical Records: Novel Myopathy Associated Drug Interactions

Jon D. Duke[1☯], Xu Han[2,3☯], Zhiping Wang[4,5☯], Abhinita Subhadarshini[4], Shreyas D. Karnik[4], Xiaochun Li[6], Stephen D. Hall[7], Yan Jin[7], J. Thomas Callaghan[3], Marcus J. Overhage[8], David A. Flockhart[2,3,4,5,9], R. Matthew Strother[3,10], Sara K. Quinney[3,9,11], Lang Li[3,4,5,6,9]*

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Molecular Systems Biology 8; Article number 592; doi:10.1038/msb.2012.26
Citation: ***Molecular Systems Biology*** **8:592**

www.molecularsystemsbiology.com

molecular systems biology

INDI: a computational framework for inferring drug interactions and their associated recommendations

Assaf Gottlieb[1,*], Gideon Y Stein[2,3], Yoram Oron[2], Eytan Ruppin[1,2] and Roded Sharan[1,*]

[1] The Blavatnik School of Computer Science, Tel-Aviv University, Tel-Aviv, Israel, [2] Department of Physiology & Pharmacology, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel and [3] Department of Internal Medicine 'B', Beilinson Hospital, Rabin Medical Center, Petah-Tikva, Israel
* Corresponding author. A Gottlieb or R Sharan, The Blavatnik School of Computer Science, Tel-Aviv University, Tel-Aviv, Israel 69978. Tel.: +972 3 6407139; Fax: +972 3 6407139; E-mail: assafgot@tau.ac.il or roded@tau.ac.il

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Molecular Systems Biology 8; Article number 592; doi:10.1038/msb.2012.26

molecular

Research and applications

EDITOR'S CHOICE

A novel signal detection algorithm for identifying hidden drug-drug interactions in adverse event reports

Nicholas P Tatonetti,[1,2] Guy Haskin Fernald,[1,2] Russ B Altman[2]

* Corresponding author. A Gottlieb or R Sharan, The Blavatnik School of Computer Science, Tel-Aviv University, Tel-Aviv, Israel 69978. Tel.: +972 3 6407139; Fax: +972 3 6407139; E-mail: assafgot@tau.ac.il or roded@tau.ac.il

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Pharmacointeraction Network Models Predict Unknown Drug-Drug Interactions

Aurel Cami[1,3]*, Shannon Manzi[2], Alana Arnold[2], Ben Y. Reis[1,3]

1 Division of Emergency Medicine, Boston Children's Hospital, Boston, Massachusetts, United States of America, **2** Department of Pharmacy, Boston Children's Hospital, Boston, Massachusetts, United States of America, **3** Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, United States of America

* Corresponding author. A Gottlieb or R Sharan, The Blavatnik School of Computer Science, Tel-Aviv University, Tel-Aviv, Israel 69978. Tel.: +972 3 6407139; Fax: +972 3 6407139; E-mail: assafgot@tau.ac.il or roded@tau.ac.il

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BMC Bioinformatics

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PROTOCOL

Similarity-based modeling in large-scale prediction of drug-drug interactions

Santiago Vilar[1,2], Eugenio Uriarte[2], Lourdes Santana[2], Tal Lorberbaum[1,3,4], George Hripcsak[1], Carol Friedman[1] & Nicholas P Tatonetti[1,4,5]

[1]Department of Biomedical Informatics, Columbia University Medical Center, New York, New York, USA. [2]Department of Organic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, Santiago de Compostela, Spain. [3]Department of Physiology and Cellular Biophysics, Columbia University Medical Center, New York, New York, USA. [4]Department of Systems Biology, Columbia University Medical Center, New York, New York, USA. [5]Department of Medicine, Columbia University Medical Center, New York, New York, USA. Correspondence should be addressed to S.V. (qosanti@yahoo.es) or N.P.T. (nick.tatonetti@columbia.edu).

Boston, Massachusetts, United States of America, [3]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, United States of America

Tel-Aviv University, Tel-Aviv, Israel and [2]Department of Internal Medicine 'D', Beilinson Hospital, Rabin Medical Center, Petah-Tikva, Israel.

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http://www.biomedcentral.com/1471-2105/11/S9/S7

Research and applications

Mining clinical text for signals of adverse drug-drug interactions

Srinivasan V Iyer, Rave Harpaz, Paea LePendu, Anna Bauer-Mehren, Nigam H Shah

[1]Department of Biomedical Informatics, Columbia University Medical Center, New York, New York, USA. [2]Department of Organic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, Santiago de Compostela, Spain. [3]Department of Physiology and Cellular Biophysics, Columbia University Medical Center, New York, New York, USA. [4]Department of Systems Biology, Columbia University Medical Center, New York, New York, USA. [5]Department of Medicine, Columbia University Medical Center, New York, New York, USA. Correspondence should be addressed to S.V. (qosanti@yahoo.es) or N.P.T. (nick.tatonetti@columbia.edu).

* Corresponding author. A Gottlieb or R Sharan, The Blavatnik School of Computer Science, Tel-Aviv University, Tel-Aviv, Israel 69978. Tel.: +972 3 6407139; Fax: +972 3 6407139; E-mail: assafgot@tau.ac.il or roded@tau.ac.il

Our solution

We present LIDDI – a LInked Drug-Drug Interactions nanopublication-based RDF dataset with trusty URIs

LIDDI combines data from various disparate sources, always aware of their provenance due to differences in individual quality and overall confidence

Bonus features

LIDDI provides the linking components to branch from DDIs into individual properties of each drug via Drugbank and UMLS, as well as mappings between all selected sources

Why nanopublications and trusty URIs?

Consisting of an assertion graph with triples expressing an atomic statement, a provenance graph reporting how this assertion came about, and a publication information graph that provides meta-data for the nanopublication

We want URIs that are verifiable, immutable, and permanent. Trusty URIs come with the possibility to verify with 100% confidence that a retrieved file represents the correct and original state of the resource

Sample DDIs

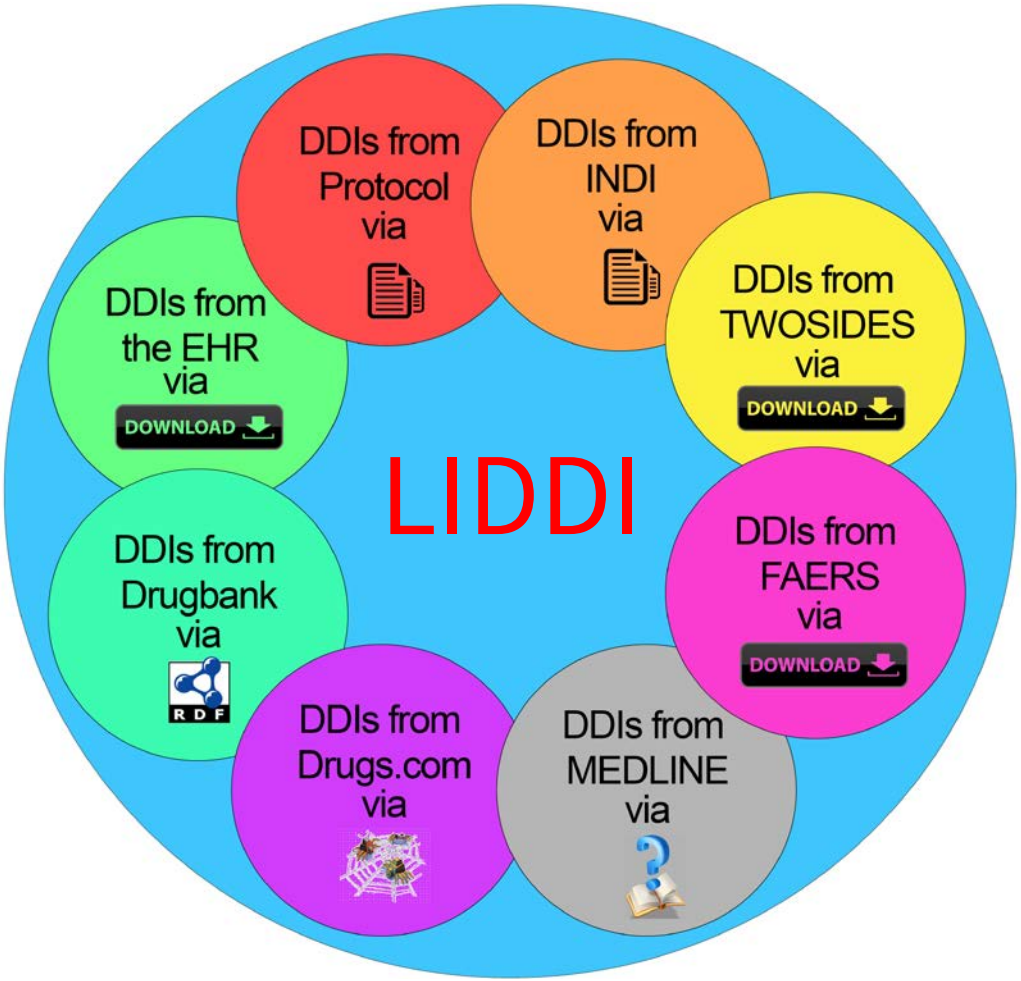
Sample DDI w event

Drug 1: rosuvastatin
Drug 2: caspofungin
Event: rhabdomyolysis

Sample DDI no event

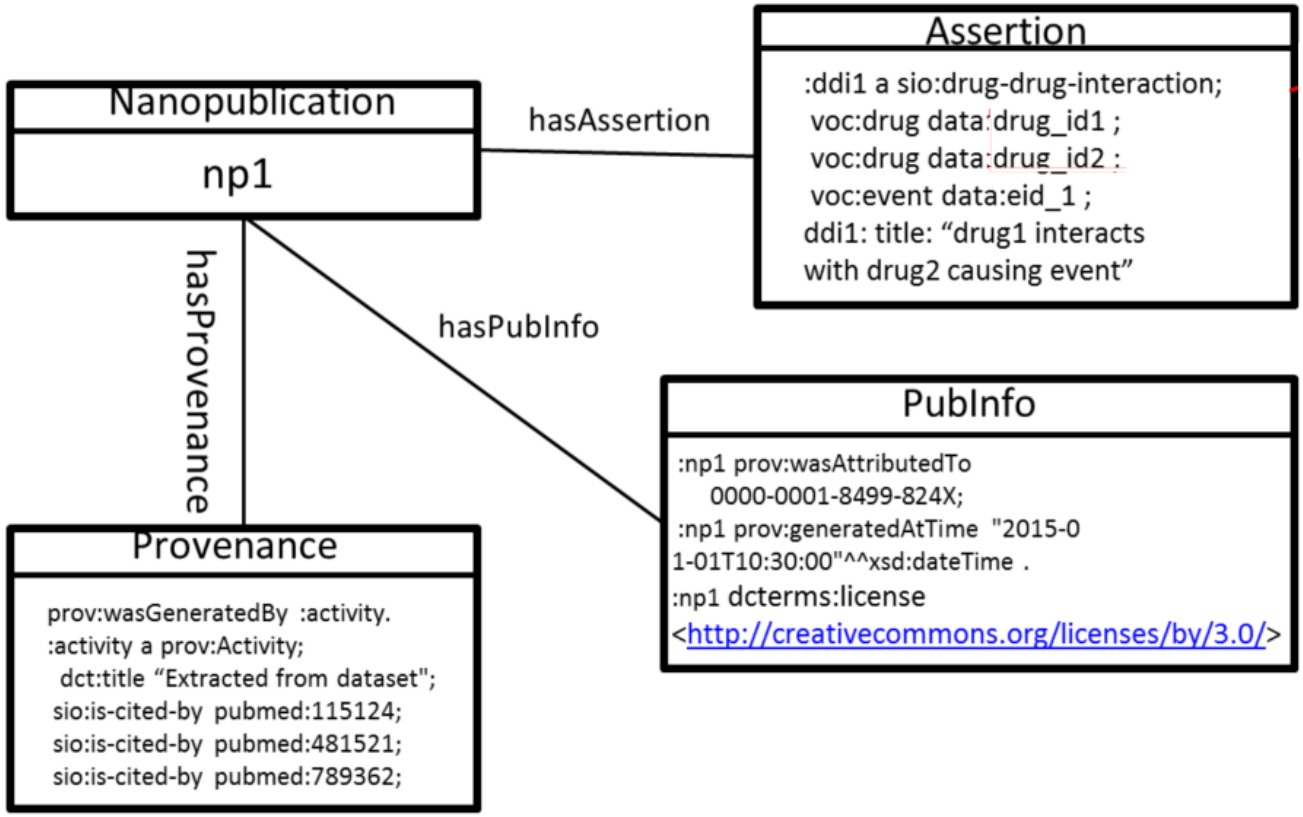
Drug 1: rosuvastatin
Drug 2: caspofungin

Dataset overview



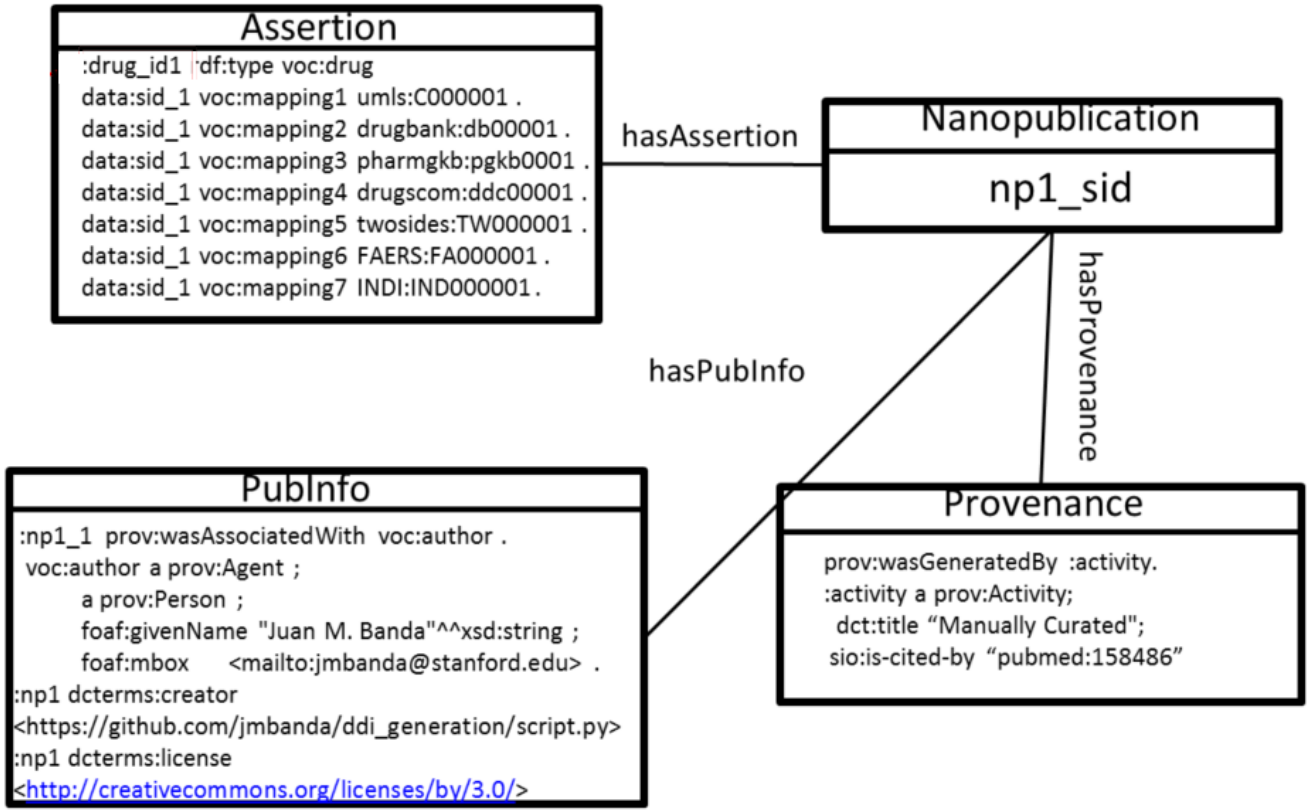
8 data sources covering 345 drugs and 10 adverse events

Data Schema: DDI



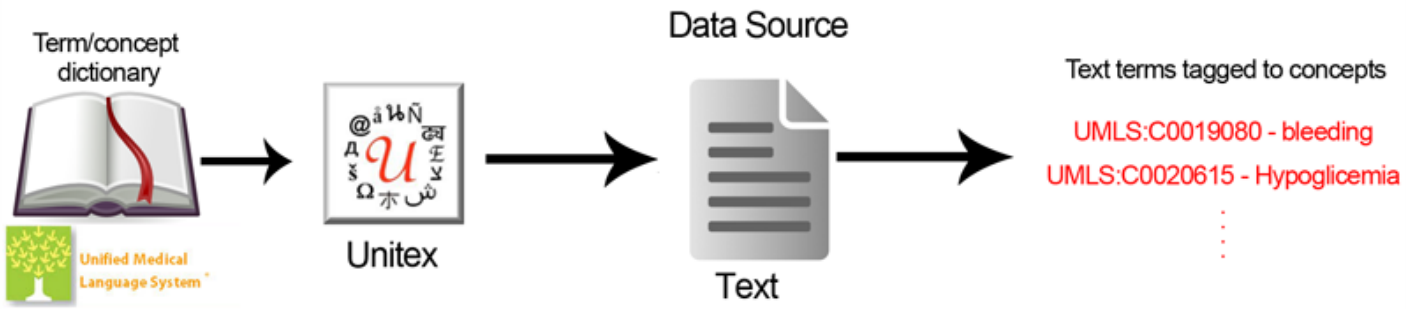
We use drug-drug-interaction from SIO and PROV for provenance

Data Schema: Drug and mappings



Contains all mappings between sources

How do we derive the event part of a DDI



Used to annotate clinical text at Stanford [1] and for the DDI descriptions

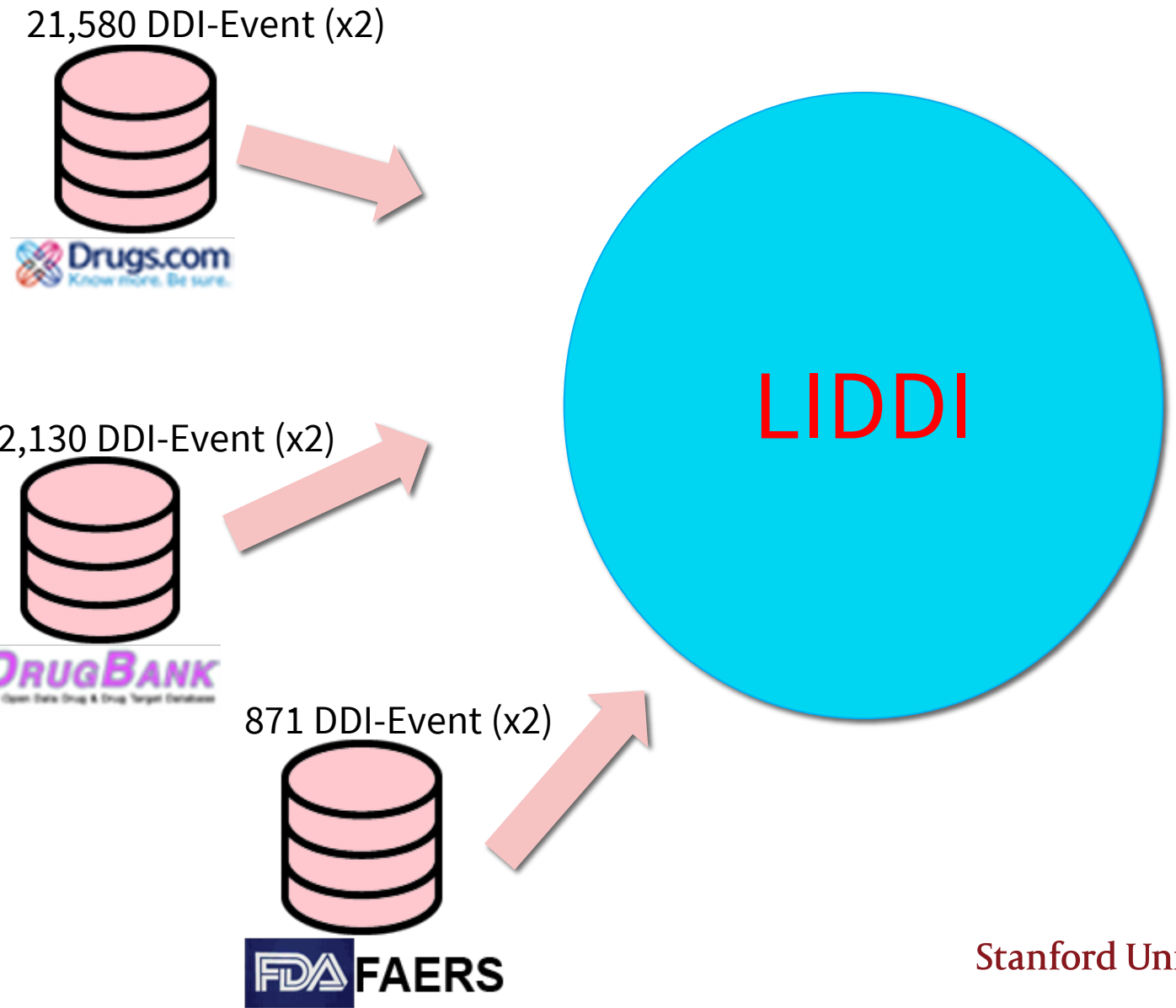
[1] Iyer SV, Harpaz R, LePendu P, Bauer-Mehren A, Shah NH. Mining clinical text for signals of adverse drug-drug interactions. *J Am Med Inform Assoc.* 2014;21(2):353-362.

LIDDI: DDIs from HER [1]

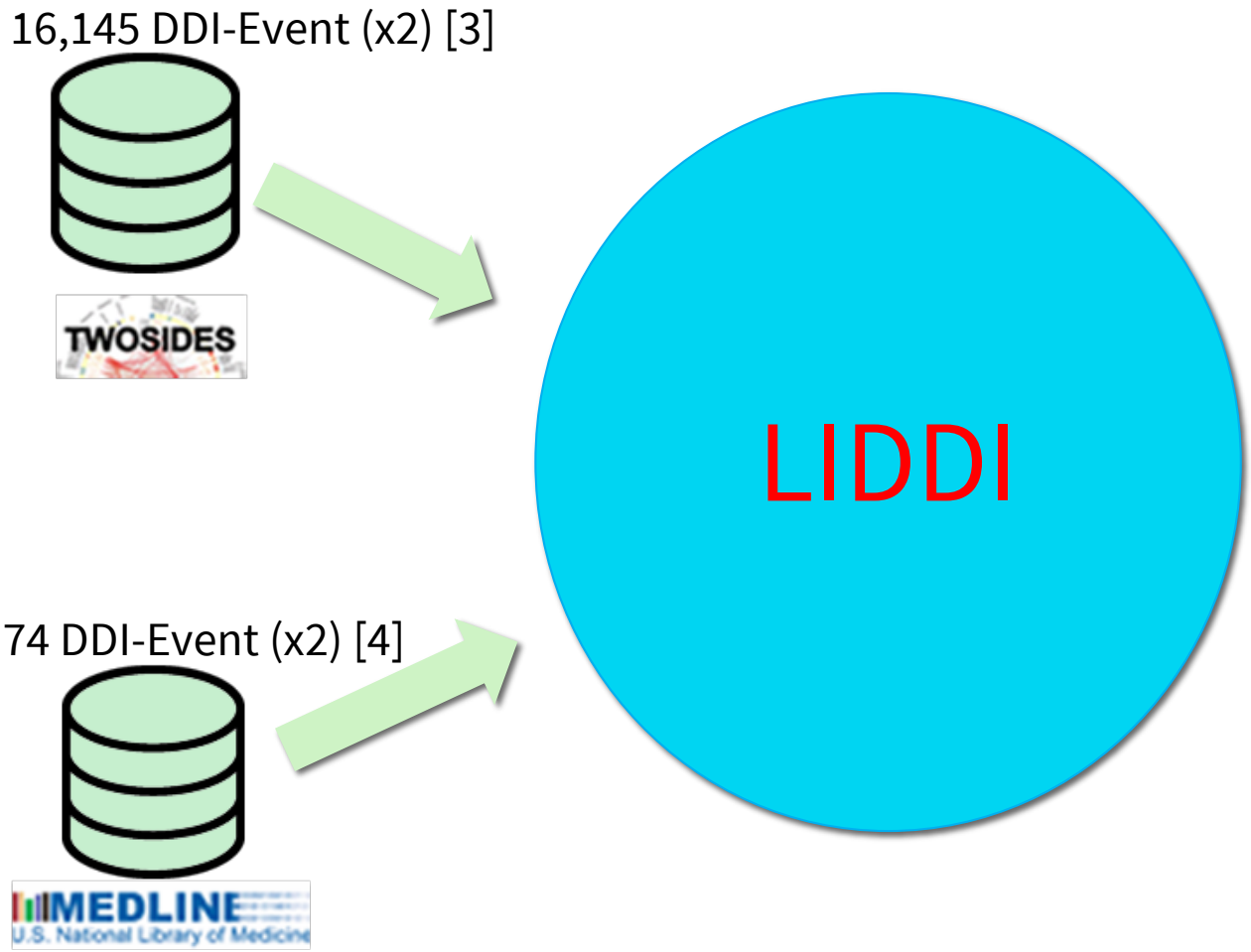
5,983 DDI-Event (x2)

[1] Iyer SV, Harpaz R, LePendu P, Bauer-Mehren A, Shah NH. Mining clinical text for signals of adverse drug-drug interactions. *J Am Med Inform Assoc.* 2014;21(2):353-362.

LIDDI: DDIs from public sources



LIDDI: DDIs generated by prediction methods (1)

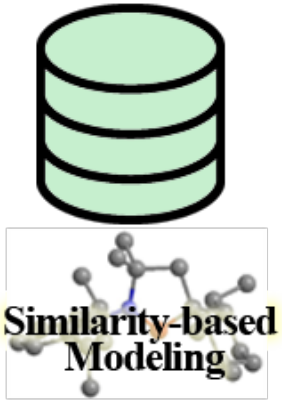


[3] Tatonetti NP, Fernald GH, Altman RB. A novel signal detection algorithm for identifying hidden drug-drug interactions in adverse event reports. J Am Med Inform Assoc 2012;19:79–85.
[4] Avillach P, Dufour JC, Diallo G, Salvo F, Joubert M, Thiessard F, Mougin F, Trifiro G, Fourrier-Reglat A, Pariente A, Fieschi M. Design and validation of an automated method to detect known adverse drug reactions in MEDLINE: a contribution from the EU-ADR project. J Am Med Inform Assoc. 2013;20(3):446–452.

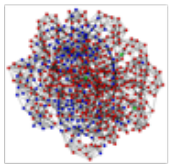
LIDDI: DDIs generated by prediction methods (2)

4,185 DDI no event (x2) [5]

112 DDI no event (x2) [6]



684 DDI no event [7]



Pharmacointeraction Networks

LIDDI

[5] Gottlieb A, Stein GY, Oron Y, et al. INDI: a computational framework for inferring drug interactions and their associated recommendations. *Mol Syst Biol* 2012;8:592.
[6] Vilar S, Uriarte E, Santana L, et al. Similarity-based modeling in large-scale prediction of drug-drug interactions. Nat Protocols. 2014 09//print;9(9):2147-63.
[7] Cami A, Manzi S, Arnold A, Reis BY. Pharmacointeraction Network Models Predict Unknown Drug-Drug Interactions. PLoS ONE. 2013;8(4):e61468.

Dataset Statistics

Event Name	EHR	MEDLINE	Drugbank	Drugs.com	FAERS	TWOSIDES	INDI*	Protocol*
Arrhythmia	700	68	286	3,148	100	4,632	NA*	NA*
Bradycardia	254	88	408	4,896	194	4,824	NA*	NA*
Hyperkalaemia	1,888	42	422	4,248	146	3,840	NA*	NA*
Hypoglycaemia	1,460	386	796	6,214	104	5,150	NA*	NA*
Long QT syndrome	14	270	334	3,510	2	0	NA*	NA*
Neutropenia	4,608	192	402	4,218	616	3,702	NA*	NA*
Pancytopenia	1,880	4	270	3,146	148	5,440	NA*	NA*
Parkinsonism	144	0	566	5,978	70	884	NA*	NA*
Rhabdomyolysis	122	198	392	3,842	214	3,264	NA*	NA*
Serotonin syndrome	896	0	384	3,960	122	1,094	NA*	NA*
Total:	11,966	1,248	4,260	43,160	1,716	32,830	8,370	224

98,085 nanopublications, 392,340 total graphs, 2,051,959 triples totaling 723MB in n-quad representation

Usages of LIDDI

Prioritization of Drug-Drug Interactions found in the EHR

Original Research Article
Drug Safety
pp 1-13

First online: 08 October 2015
Open Access

Feasibility of Prioritizing Drug–Drug-Event Associations Found in Electronic Health Records

Juan M. Banda ✉ , Alison Callahan, Rainer Winnenburg, Howard R. Strasberg, Aurel Cami, Ben Y. Reis, Santiago Vilar, George Hripcsak, Michel Dumontier, Nigam Haresh Shah Show less

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Future Work

Add more drugs to LIDDI

Over 1,200 drugs are being mapped to add to this resource

Add more data sources

We have identified and started mapping 3 new data sources

Add additional information to the DDIs

Some sources provide statistical confidence values for their DDIs

Acknowledgements to our data providers

Stanford

- Assaf Gottlieb

Harvard University

- Aurel Cami
- Ben Reis

Columbia University

- Santiago Vilar
- George Hripcsak

QUESTIONS?

THANK YOU

SPARQL endpoint:
http://liddi.stanford.edu:8890/sparql

Faceted Browser:
http://liddi.stanford.edu:8890/fct

Get:
http://np.inn.ac/RA7SuQ0e661LJdKpt5EOS2DKykf1ht9LFmNaZtFSDMrXg

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