Observational Health Data Sciences and Informatics (OHDSI): A Rapidly Growing International Network for Open Science and Data Analytics in Healthcare

Patrick Ryan, Vojtech Huser, Nigam Shah, George Hripcsak, Jon Duke

24 March 2016

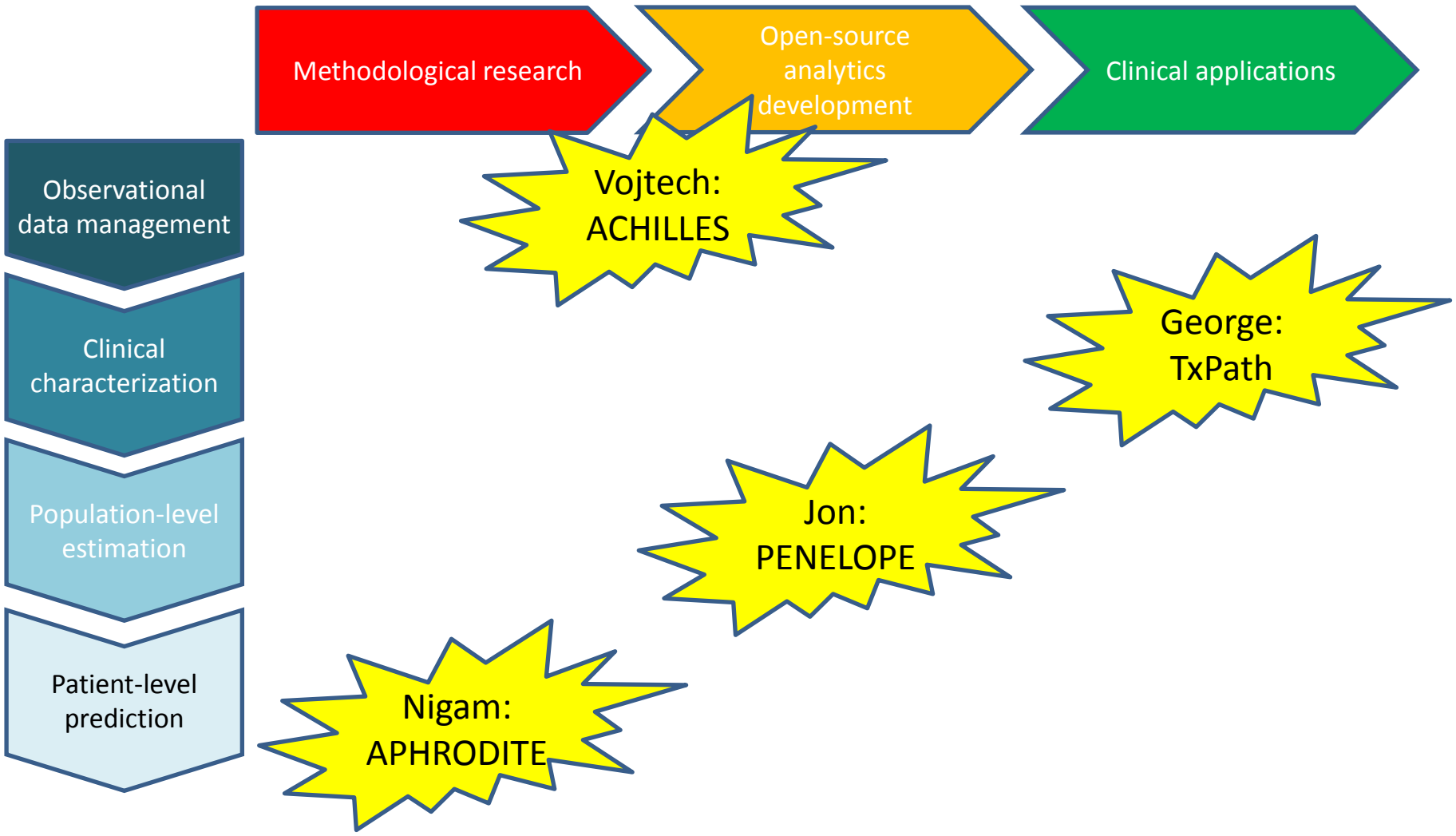
Introducing OHDSI

- The Observational Health Data Sciences and Informatics (OHDSI) program is a multi-stakeholder, interdisciplinary collaborative to create open-source solutions that bring out the value of observational health data through large-scale analytics
- OHDSI has established an international network of researchers and observational health databases with a central coordinating center housed at Columbia University

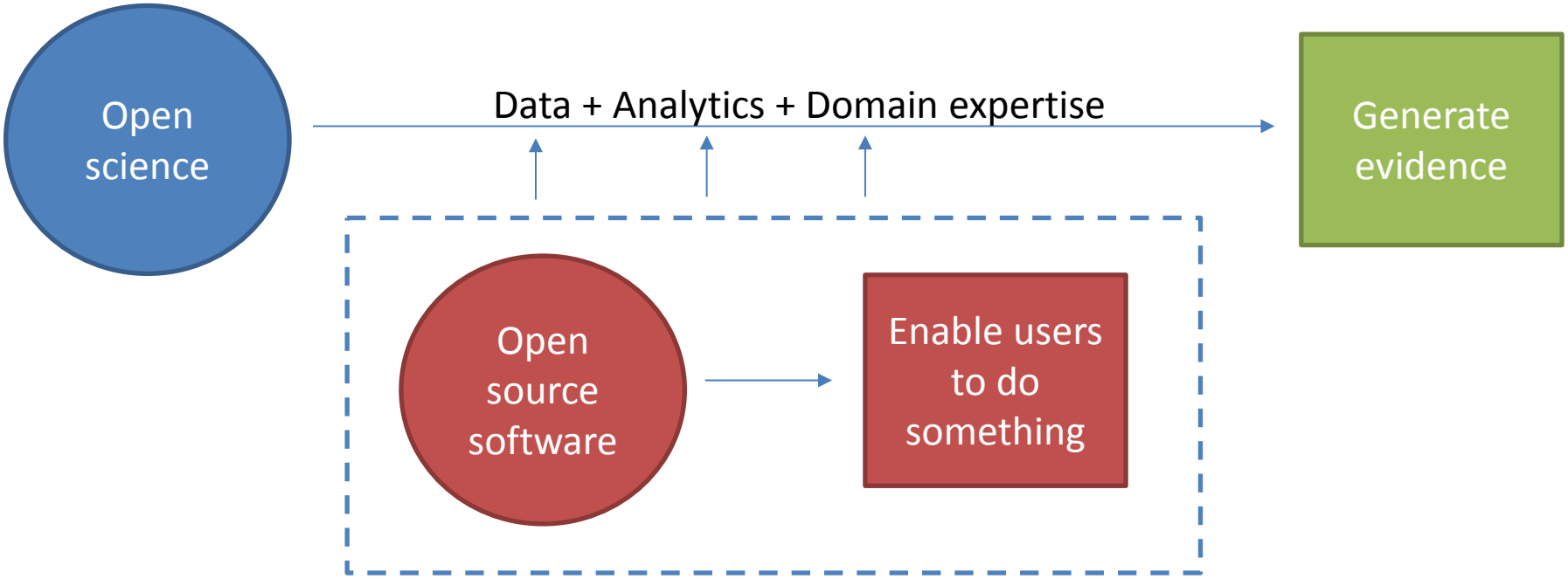
OHDSI's mission

To improve health, by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care.

OHDSI areas of focus



OHDSI's approach to open science



- Open science is about sharing the journey to evidence generation
- Open-source software can be part of the journey, but it's not a final destination
- Open processes can enhance the journey through improved reproducibility of research and expanded adoption of scientific best practices

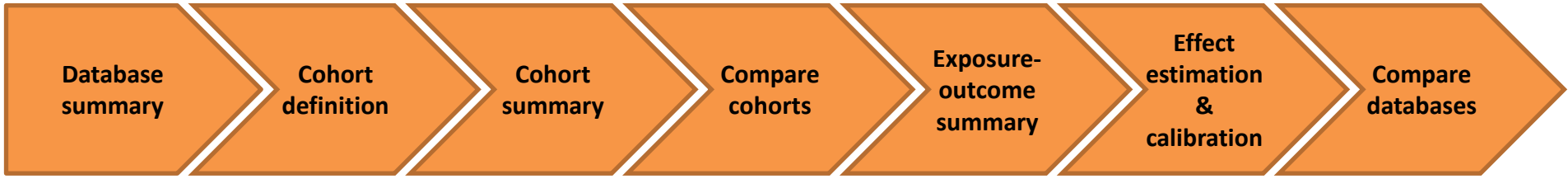
Standardizing workflows to enable reproducible research

Open science

Population-level estimation for comparative effectiveness research:

Is <intervention X> better than <intervention Y> in reducing the risk of <condition Z>?

Generate evidence



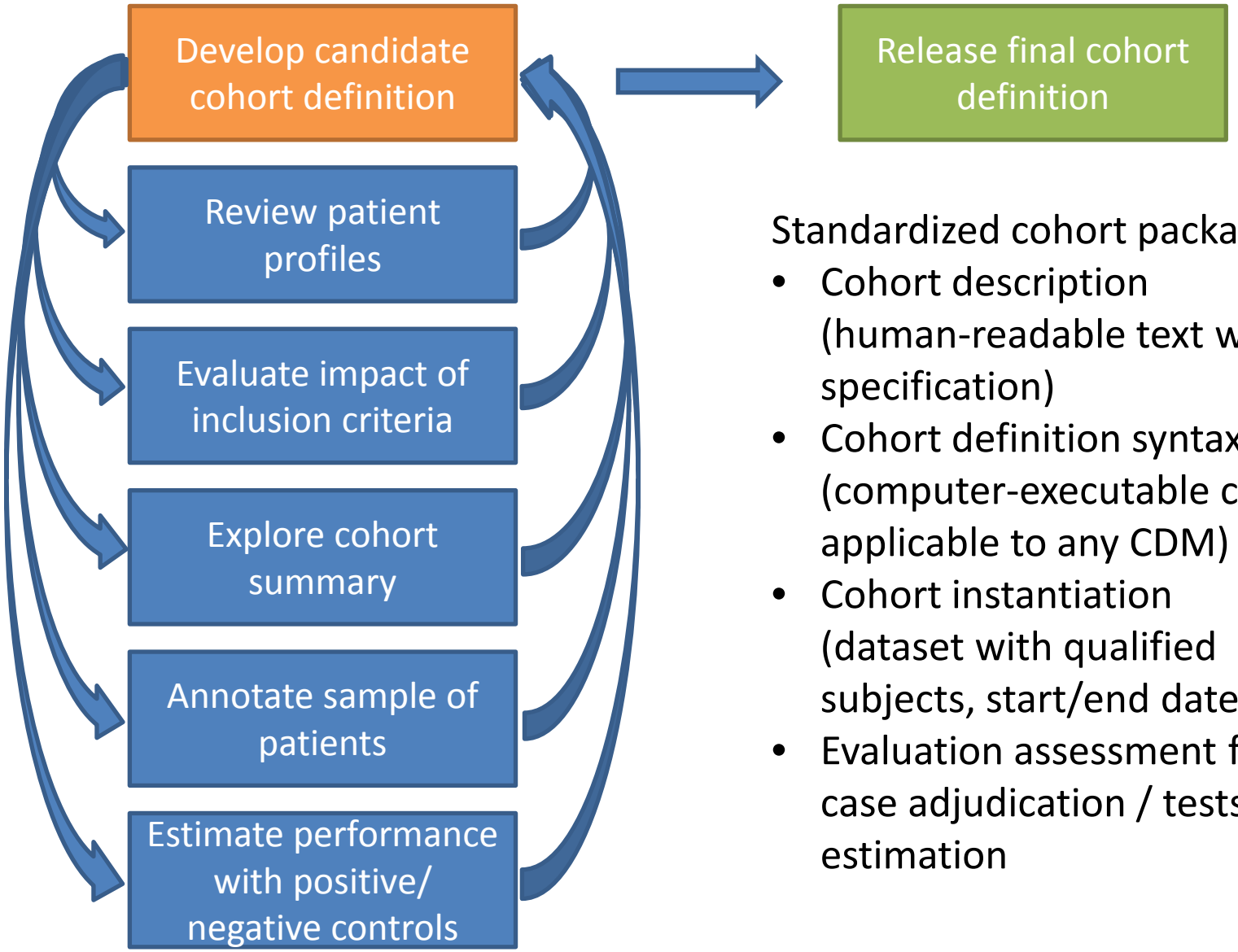
Defined inputs:

- Target exposure
- Comparator group
- Outcome
- Time-at-risk
- Model specification

Consistent outputs:

- analysis specifications for transparency and reproducibility (protocol + source code)
- only aggregate summary statistics (no patient-level data)
- model diagnostics to evaluate accuracy
- results as evidence to be disseminated
  - static for reporting (e.g. via publication)
  - interactive for exploration (e.g. via app)

Standardizing workflows for cohort definition



Standardized cohort package:

- Cohort description (human-readable text with full specification)
- Cohort definition syntax (computer-executable code applicable to any CDM)
- Cohort instantiation (dataset with qualified subjects, start/end dates)
- Evaluation assessment from case adjudication / testset estimation

OHDSI community in action

OHDSI Collaborators:

- >140 researchers in academia, industry, government, health systems
- >20 countries
- Multi-disciplinary expertise: epidemiology, statistics, medical informatics, computer science, machine learning, clinical sciences

Standardized process for network analyses:

Community:

Ask clinical question → Design protocol → Develop standardized analytics → Generate and disseminate evidence

Examples from the community across the evidence generation continuum

- Data characterization and data quality assessment: ACHILLES – Vojtech Huser
- Network studies in action: treatment pathways – George Hripcsak
- Automated phenotyping: APHRODITE – Nigam Shah
- Disseminating evidence into practice: PENELOPE – Jon Duke

Data characterization and data quality assessment: ACHILLES

Vojtech Huser MD PhD
National Institutes of Health

Content

- Why data quality
- Achilles and Achilles Heel
- What is new? (version 1.2; March 2016)
- Comparison study

Why Data Quality?

- Fitness for analysis, trust in outputs, completeness of data
- Data transformation: Source -> Target
- Errors in data:
  - Source error (typo in birth year; no pattern)
  - ETL error (has pattern)
    - Mapping error
- Common Data Models allows sharing of data quality rules and creating of data quality tools
- Existence of data quality tools allows sites to quickly implement a starter set of rules

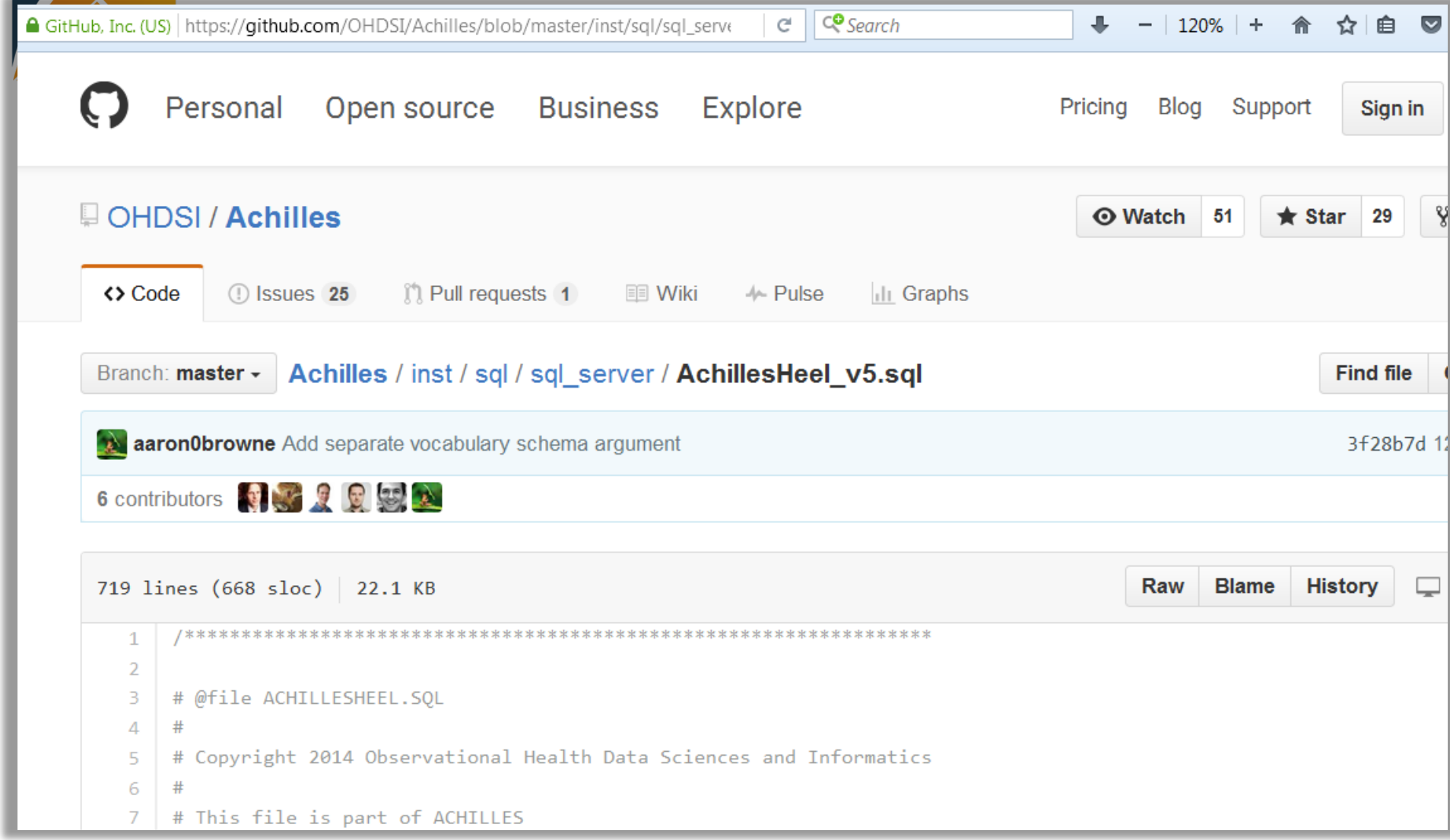
Achilles Heel (your free data quality tool)

- Achilles (step 1 of 2)
  - Pre-computed measures (Achilles.sql)
- Achilles Heel (step 2 of 2)
  - Data quality rules (AchillesHeel.sql)
- Achilles Web
  - Web-based “data viewer”

- Paradigm:

  Patient level data -> “something smaller”

  (10B rows) (2M rows)


GitHub, Inc. (US) https://github.com/OHDSI/Achilles/blob/master/inst/sql/sql_serve
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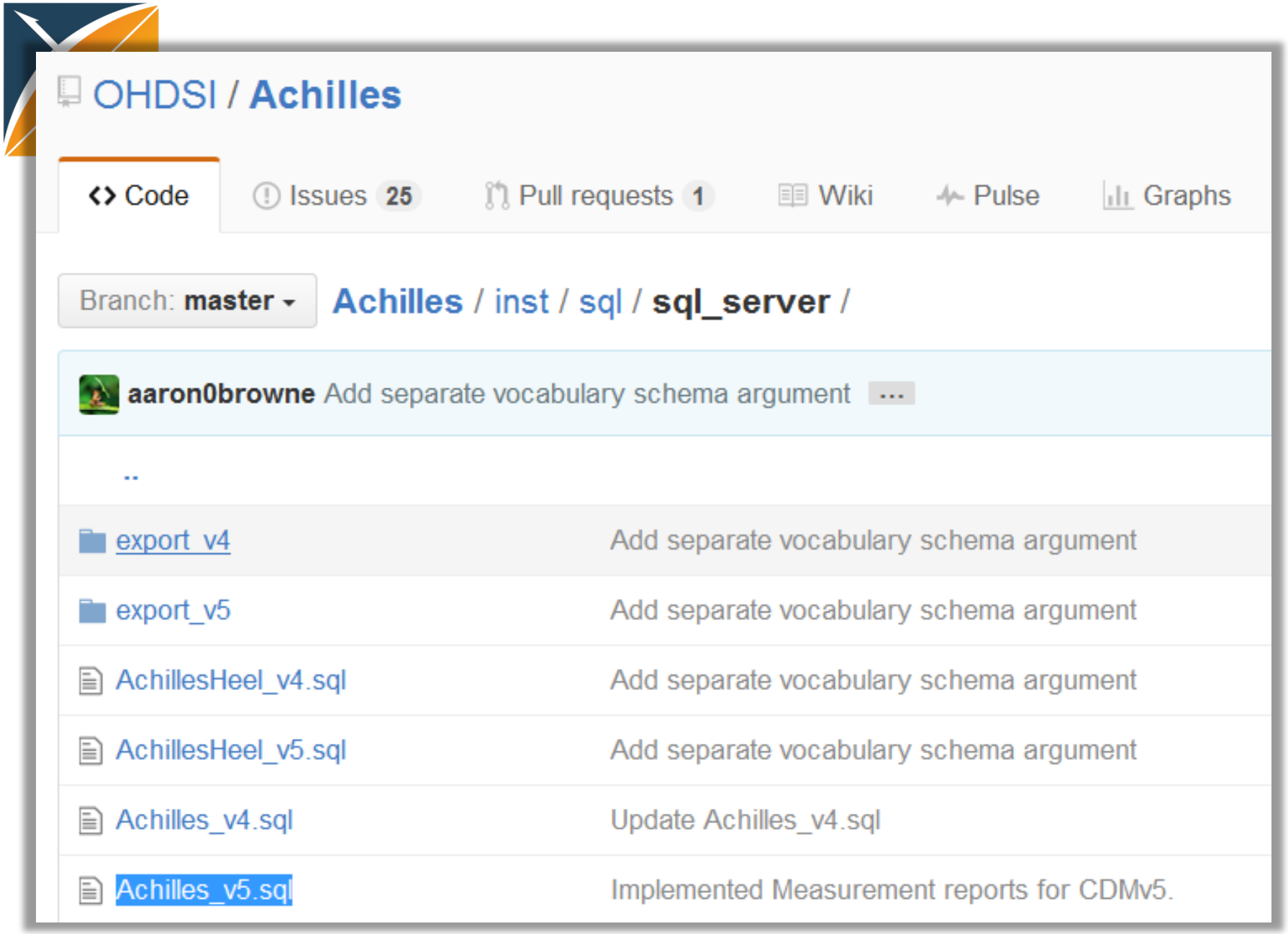
OHDSI / Achilles
Watch 51
Star 29
Code
Issues 25
Pull requests 1
Wiki
Pulse
Graphs
Branch: master
Achilles / inst / sql / sql_server / AchillesHeel_v5.sql
Find file
aaron0browne Add separate vocabulary schema argument
3f28b7d 12
6 contributors
719 lines (668 sloc)
22.1 KB
Raw
Blame
History
1 /***
2
3 # @file ACHILLESHEEL.SQL
4 #
5 # Copyright 2014 Observational Health Data Sciences and Informatics
6 #
7 # This file is part of ACHILLES

GitHub, Inc. (US) | https://github.com/OHDSI/Achilles/blob/master/inst/sql/sql_serv

Search

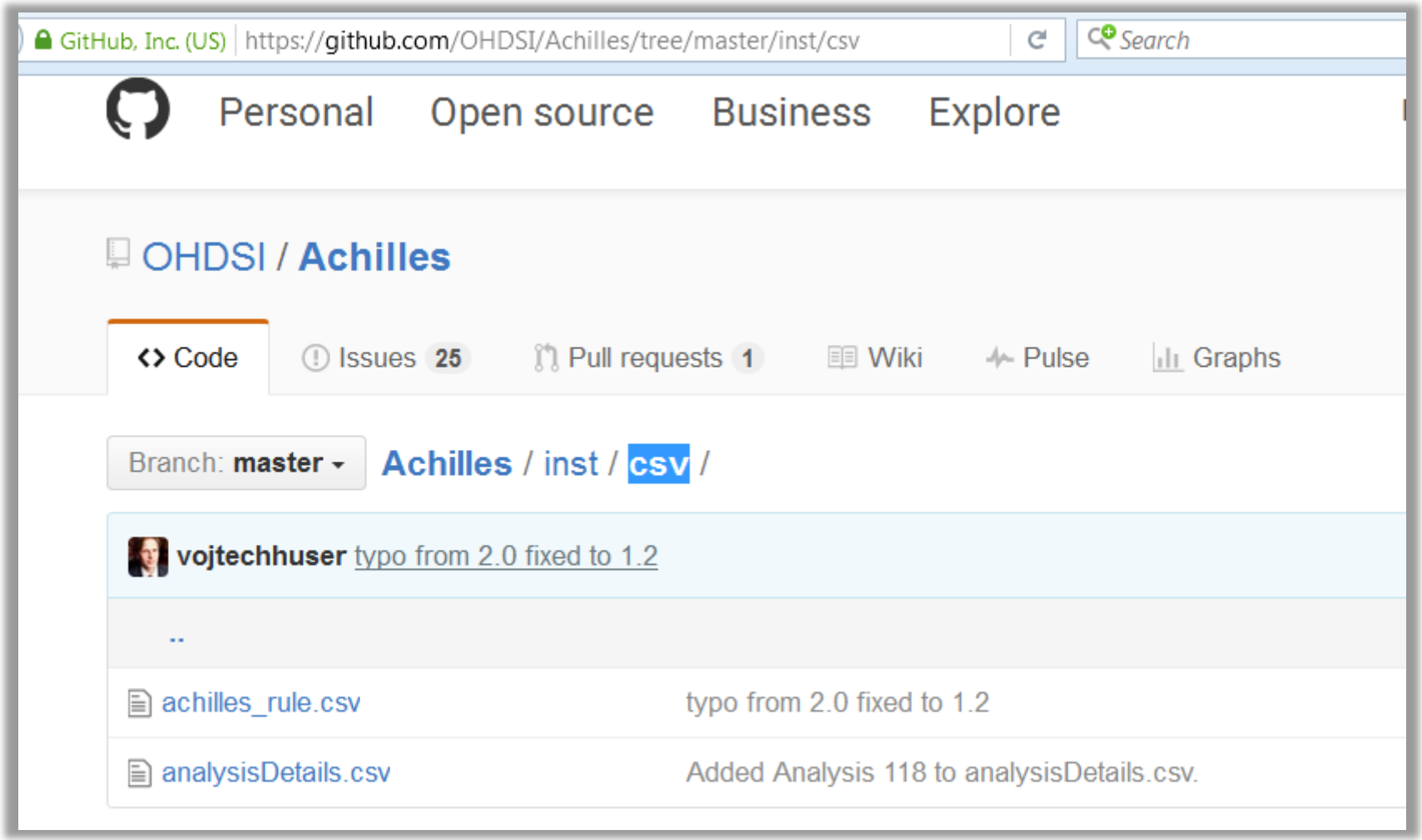
```
699 GROUP BY ord1.analysis_id, oa1.analysis_name;
700
701 --ruleid 26 WARNING: quantity > 600
702 INSERT INTO @results_database_schema.ACHILLES_HEEL_results (
703         analysis_id,
704         ACHILLES_HEEL_warning,
705         rule_id,
706         record_count
707         )
708 SELECT DISTINCT ord1.analysis_id,
709   'WARNING: ' + cast(ord1.analysis_id as VARCHAR) + '-' + oa1.analysis_name + ' (count
710   26 as rule_id,
711   count(ord1.max_value) as record_count
712 FROM @results_database_schema.ACHILLES_results_dist ord1
713 INNER JOIN @results_database_schema.ACHILLES_analysis oa1
714         ON ord1.analysis_id = oa1.analysis_id
715 WHERE ord1.analysis_id IN (717)
716         AND ord1.max_value > 600
717 GROUP BY ord1.analysis_id, oa1.analysis_name;
718
```


OHDSI / Achilles
Code
Issues 25
Pull requests 1
Wiki
Pulse
Graphs
Branch: master
Achilles / inst / sql / sql_server /
aaron0browne Add separate vocabulary schema argument
..
export_v4 Add separate vocabulary schema argument
export_v5 Add separate vocabulary schema argument
AchillesHeel_v4.sql Add separate vocabulary schema argument
AchillesHeel_v5.sql Add separate vocabulary schema argument
Achilles_v4.sql Update Achilles_v4.sql
Achilles_v5.sql Implemented Measurement reports for CDMv5.

GitHub, Inc. (US) | https://github.com/OHDSI/Achilles/blob/master/inst/sql/sql_serve | Search

```
3791
3792  --{717 IN (@list_of_analysis_ids)}?{
3793  -- 717  Distribution of quantity by drug_concept_id
3794  with rawData(stratum_id, count_value) as
3795  (
3796    select drug_concept_id,
3797      quantity as count_value
3798    from @cdm_database_schema.drug_exposure
3799          where quantity is not null
3800  ),
3801  overallStats (stratum_id, avg_value, stdev_value, min_value, max_value, total) as
3802  (
3803    select stratum_id,
3804      avg(1.0 * count_value) as avg_value,
3805      stdev(count_value) as stdev_value,
3806      min(count_value) as min_value,
3807      max(count_value) as max_value,
3808      count_big(*) as total
3809    FROM rawData
3810          group by stratum_id
3811  ),
```

Non-SQL view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https://github.com/OHDSI/Achilles/tree/master/inst/csv
Search
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Branch: master
Achilles / inst / csv /
vojtechhuser typo from 2.0 fixed to 1.2
..
achilles_rule.csv
typo from 2.0 fixed to 1.2
analysisDetails.csv
Added Analysis 118 to analysisDetails.csv.

Branch: **master** ▾ **Achilles** / inst / csv / achilles_rule.csv

vojtechhuser typo from 2.0 fixed to 1.2

1 contributor

29 lines (28 sloc) | 1.85 KB **Raw** **Blame**

Search this file...

	rule_id	rule_name	severity	rule_description
2	0	Achilles Heel version 1.2		this rule is not used for data analysis. It communicates th
3	1	multiple checks	error	multiple error checks
4	2	multiple checks	error	distributions where min should not be negative
5	3	multiple checks	warning	death distributions where max should not be positive
6	4	invalid concept_id	error	invalid concept_id
7	5	invalid type concept_id	error	invalid type concept_id
8	6	concept from the wrong vocabulary	error	concepts from wrong vocabulary 12 HL7
9	7	concept from the wrong vocabulary	error	concept from the wrong vocabulary
10	8	concept from the wrong vocabulary; race	error	concept from the wrong vocabulary; race
11	9	concept from the wrong vocabulary; ethnicity	error	concept from the wrong vocabulary; ethnicity
12	10	concept from the wrong vocabulary; place of service	error	concept from the wrong vocabulary; place of service

Branch: **master** ▾ **Achilles** / inst / csv / achilles_rule.csv

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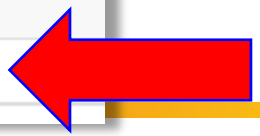
11	9	concept from the wrong vocabulary; ethnicity	error	concept from the wrong vocabulary; ethnicity
12	10	concept from the wrong vocabulary; place of service	error	concept from the wrong vocabulary; place of service

20	18	year of birth is in the future	error	year of birth should not be in the future
21	19	year of birth is prior 1800	warning	year of birth < 1800
22	20	age below 0	error	age < 0
23	21	age too high	error	age > 150
24	22	monthly trend	warning	monthly change > 100%
25	23	monthly trend	warning	monthly change > 100% at concept level
26	24	too high days_supply	warning	days_supply > 180
27	25	too high number of refils	warning	refills > 10
28	26	implausible quantity for drug	warning	quantity > 600



Step 1 Pre-computed analyses

ANALYSIS_ID	ANALYSIS_NAME	STRATUM_1_NAME	STRATUM_2_NAME	STRATUM_3_NA	STRATUM_4_I	STRATUM_5_NA
0	Source name	NA	NA	NA	NA	NA
1	Number of persons	NA	NA	NA	NA	NA
2	Number of persons by gender	gender_concept_id	NA	NA	NA	NA
3	Number of persons by year of birth	year_of_birth	NA	NA	NA	NA
4	Number of persons by race	race_concept_id	NA	NA	NA	NA
5	Number of persons by ethnicity	ethnicity_concept_id	NA	NA	NA	NA
7	Number of persons with invalid provider_id	NA	NA	NA	NA	NA
8	Number of persons with invalid location_id	NA	NA	NA	NA	NA
9	Number of persons with invalid care_site_id	NA	NA	NA	NA	NA
101	Number of persons by age, with age at first observation period	age	NA	NA	NA	NA
102	Number of persons by gender by age, with age at first observatio	gender_concept_id	age	NA	NA	NA
103	Distribution of age at first observation period	NA	NA	NA	NA	NA
104	Distribution of age at first observation period by gender	gender_concept_id	NA	NA	NA	NA
105	Length of observation (days) of first observation period	NA	NA	NA	NA	NA
106	Length of observation (days) of first observation period by gende	gender_concept_id	NA	NA	NA	NA
107	Length of observation (days) of first observation period by age de	age decile	NA	NA	NA	NA
108	Number of persons by length of observation period, in 30d incren	Observation period le	NA	NA	NA	NA
109	Number of persons with continuous observation in each year	calendar year	NA	NA	NA	NA
110	Number of persons with continuous observation in each month	calendar month	NA	NA	NA	NA
111	Number of persons by observation period start month	calendar month	NA	NA	NA	NA
112	Number of persons by observation period end month	calendar month	NA	NA	NA	NA
113	Number of persons by number of observation periods	number of observatio	NA	NA	NA	NA
114	Number of persons with observation period before year-of-birth	NA	NA	NA	NA	NA
115	Number of persons with observation period end < observation pe	NA	NA	NA	NA	NA
116	Number of persons with at least one day of observation in each y	calendar year	gender_concept_id	age decile	NA	NA
117	Number of persons with at least one day of observation in each n	calendar month	NA	NA	NA	NA

Drug quantity by drug ID

ANALYSIS_ID	ANALYSIS_NAME	STRATUM_1_NAME	STRATUM_2_NAME	STRATUM_3_NA	STRATUM_4_N	STRATUM_5_NAI
701	Number of drug exposure records, by drug_concept_id	drug_concept_id	NA	NA	NA	NA
702	Number of persons by drug exposure start month, by drug_conce	drug_concept_id	calendar month	NA	NA	NA
703	Number of distinct drug exposure concepts per person	NA	NA	NA	NA	NA
704	Number of persons with at least one drug exposure, by drug_con	drug_concept_id	calendar year	gender_concep	age decile	NA
705	Number of drug exposure records, by drug_concept_id by drug_t	drug_concept_id	drug_type_concept_id	NA	NA	NA
706	Distribution of age by drug_concept_id	drug_concept_id	gender_concept_id	NA	NA	NA
709	Number of drug exposure records with invalid person_id	NA	NA	NA	NA	NA
710	Number of drug exposure records outside valid observation perio	NA	NA	NA	NA	NA
711	Number of drug exposure records with end date < start date	NA	NA	NA	NA	NA
712	Number of drug exposure records with invalid provider_id	NA	NA	NA	NA	NA
713	Number of drug exposure records with invalid visit_id	NA	NA	NA	NA	NA
715	Distribution of days_supply by drug_concept_id	drug_concept_id	NA	NA	NA	NA
716	Distribution of refills by drug_concept_id	drug_concept_id	NA	NA	NA	NA
717	Distribution of quantity by drug_concept_id	drug_concept_id	NA	NA	NA	NA
720	Number of drug exposure records by drug exposure start month	calendar month	NA	NA	NA	NA
800	Number of persons with at least one observation occurrence, by	observation_concept_	NA	NA	NA	NA
801	Number of observation occurrence records, by observation_conc	observation_concept_	NA	NA	NA	NA
802	Number of persons by observation occurrence start month, by ob	observation_concept_	calendar month	NA	NA	NA
803	Number of distinct observation occurrence concepts per person	NA	NA	NA	NA	NA
804	Number of persons with at least one observation occurrence, by	observation_concept_	calendar year	gender_concep	age decile	NA
805	Number of observation occurrence records, by observation_conc	observation_concept_	observation_type_con	NA	NA	NA
806	Distribution of age by observation_concept_id	observation_concept_	gender_concept_id	NA	NA	NA
807	Number of observation occurrence records, by observation_conc	observation_concept_	unit_concept_id	NA	NA	NA
809	Number of observation records with invalid person_id	NA	NA	NA	NA	NA
810	Number of observation records outside valid observation period	NA	NA	NA	NA	NA
812	Number of observation records with invalid provider_id	NA	NA	NA	NA	NA

What is new? (Achilles Heel v1.2; March 2016)

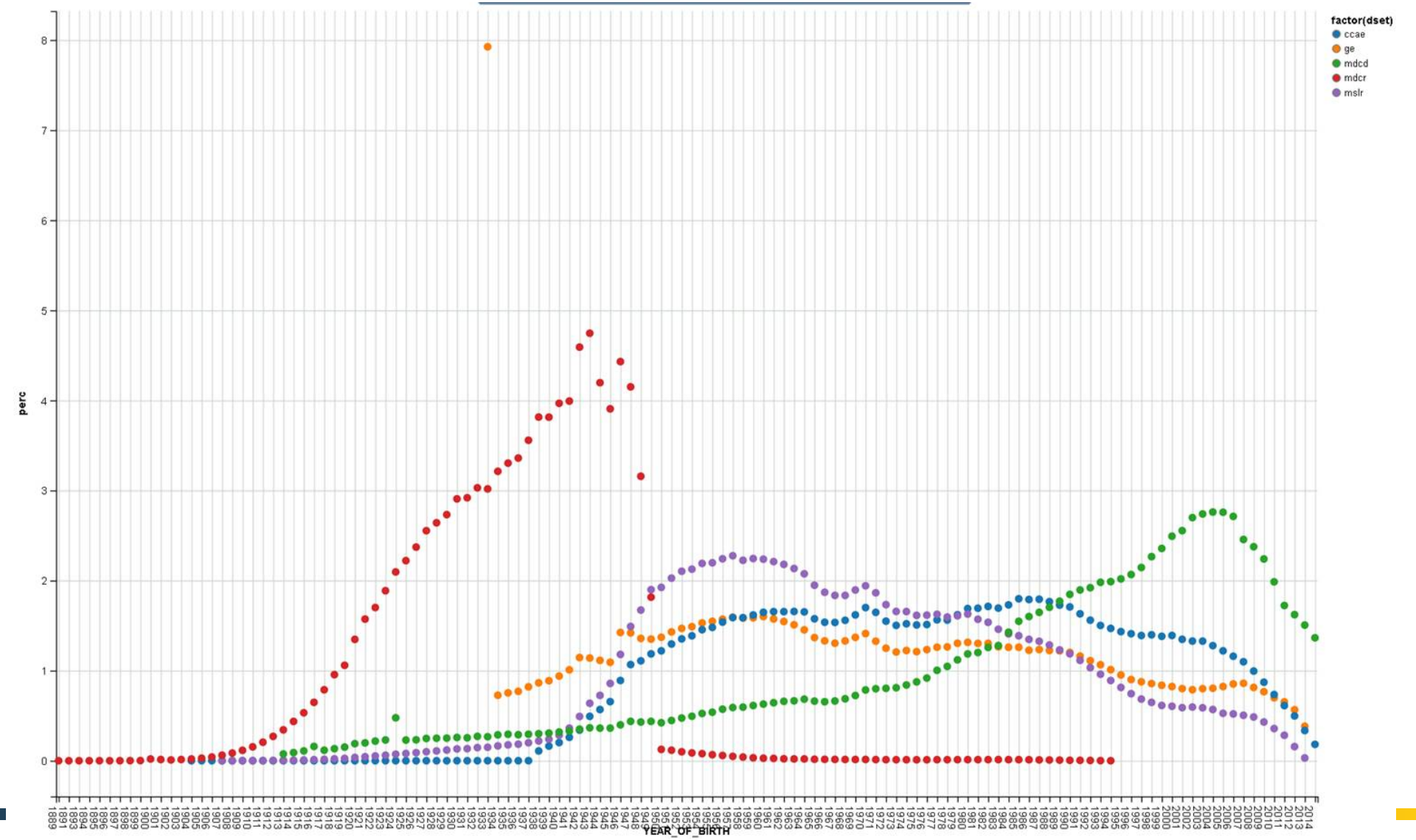
- Introduction of RULE_ID and rule overview CSV file
- Better reporting of “depth of the error” (number of rows with a given error)
- Support for CDM v5
- Generalizability to other CDMs
  - Separation of model-conformance rules from rules examining “source” data (zombie events)
  - Data measure vs. data quality measure; target model terminology (RxNorm)
- More rules (contribute your favorite DQ rule); non-Achilles efforts (IRIS)

Comparison Study

- 7 sites; 24 datasets
- Achilles Heel output

Site	# of datasets	Type of data included
Site A	5	claims data
Site B	1	drug dispensing + administrative data
Site C	1	EHR data
Site D	7	claims + EHR data
Site E	1	claims + EHR data
Site F	1	EHR data
Site G	8	EHR data

Visualization example



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NewYork-Presbyterian

OHDSI in action: network studies

George Hripcsak, MD, MS
Biomedical Informatics,
Columbia University

OHDSI

- Driven by research, not infrastructure
- Vertically integrated initiative
  - Research
  - Policy development
  - Data science methods
  - Software engineering
  - Data modeling
  - Data holders
  - Infrastructure

OHDSI Assets

- Geographic, national, and practice variation
- Sample size
- Community (interdisciplinary)
- Critical mass (terminology mappings)

OHDSI Network

- 140 investigators from 14 countries
- 60 databases and 600M records in total
  - 12 databases and 250M records on first study
- Community
  - Weekly community meeting
  - Workgroup meetings
  - Web site
- Code base on Github
- Common data model and terminology

Research Goal

- Generate evidence
  - Randomized trial is the gold standard
  - Observational research seen as supporting

Observational Data & Clinical Trials

- Sample size calculations
  - Do we have enough patients to carry out a trial?
- Recruitment
  - Find patients or their clinicians from EHRs
- Pragmatic trials: recruitment and data collection
  - ADAPTABLE aspirin trial

…

- Complementary causal evidence (future)
  - New methods to handle confounding and ascertain causes from retrospective observational databases

Characterization

- Today we carry out RCTs without clear knowledge of actual practice
- There will be no RCTs without an observational precursor
  - It will be required to characterize a population using large-scale observational data before designing an RCT
  - Disease burden
  - Actual treatment practice
  - Time on therapy
  - Course and complication rate
  - Done now somewhat through literature and pilot studies

Causation

Similar leaps:

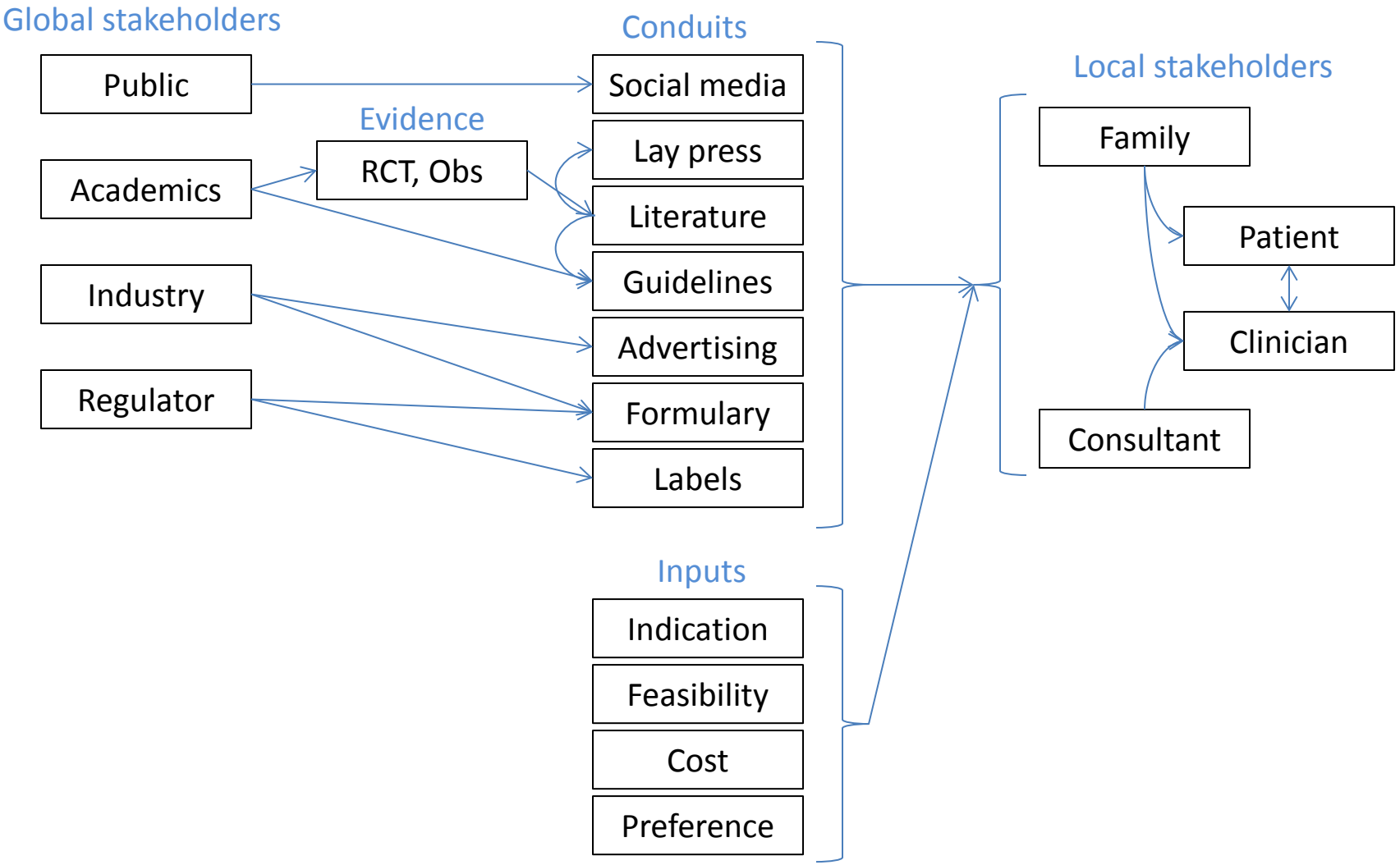
- Observational associations -> Causes
- RCT-based causes -> Individual treatment
  1. Study population -> Local population
     - Characterization
  2. Local population -> Individual
     - Precision medicine
  - Are the same causes operative, confounders, etc.
  - That is, if deriving causes from observational data is futuristic, then so is using RCT results

(Fuller 2015)

Treatment Pathways

- In literature
  - Recommended sequence of treatments
- How are patients actually treated?
  - Sequence of medications each patient took

Treatment Pathways



Treatment Pathways

- Defining a pathway
  - What the clinician orders
  - What prescriptions the patient fills
  - What the patient takes

Network process

1. Join the collaborative
2. Propose a study to the open collaborative
3. Write protocol
   - http://www.ohdsi.org/web/wiki/doku.php?id=research:studies
4. Code it, run it locally, debug it (minimize others' work)
5. Publish it: https://github.com/ohdsi
6. Each node voluntarily executes on their CDM
7. Centrally share results
8. Collaboratively explore results and jointly publish findings

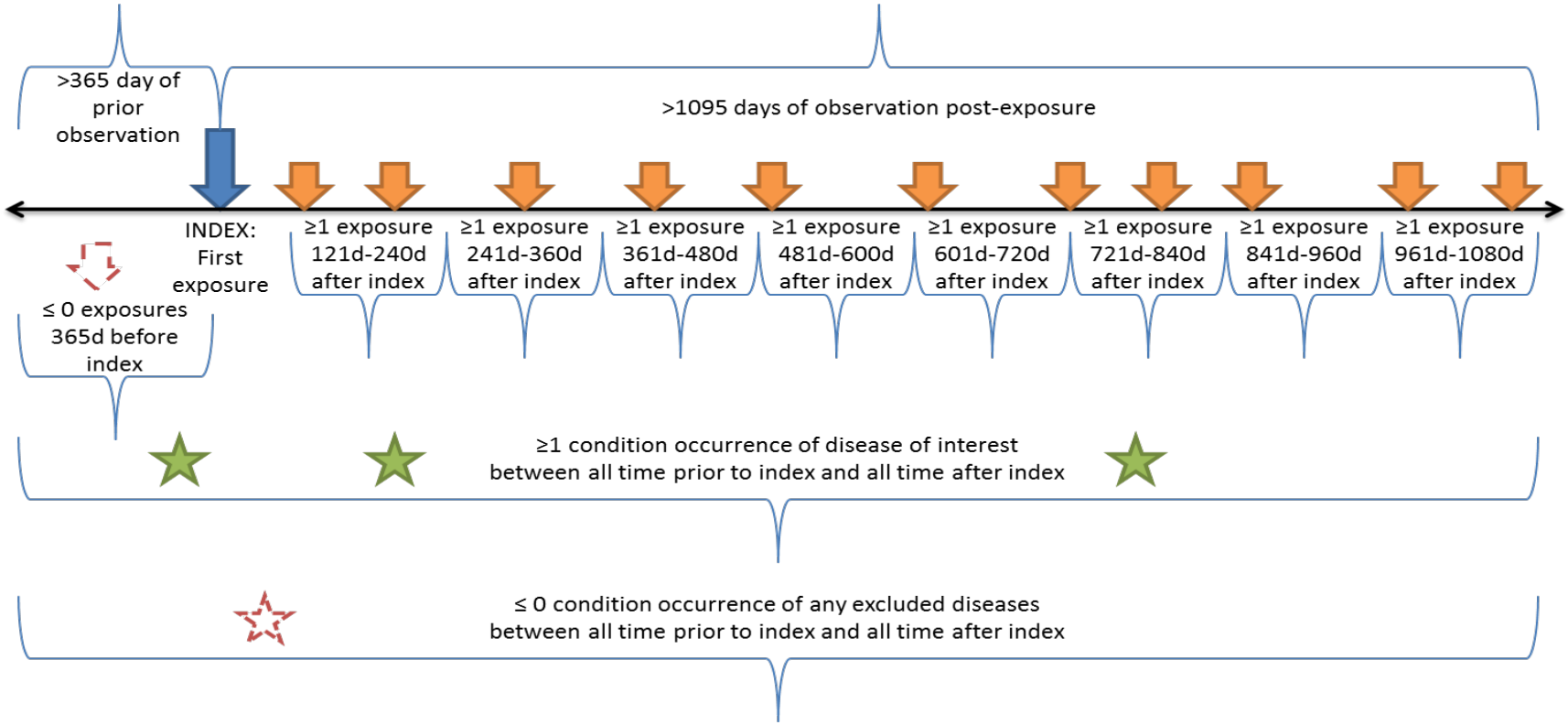
OHDSI in action:
Chronic disease treatment pathways

- Conceived at AMIA 15Nov2014
- Protocol written, code written and tested at 2 sites 30Nov2014
- Analysis submitted to OHDSI network 2Dec2014
- Results submitted for 7 databases 5Dec2014

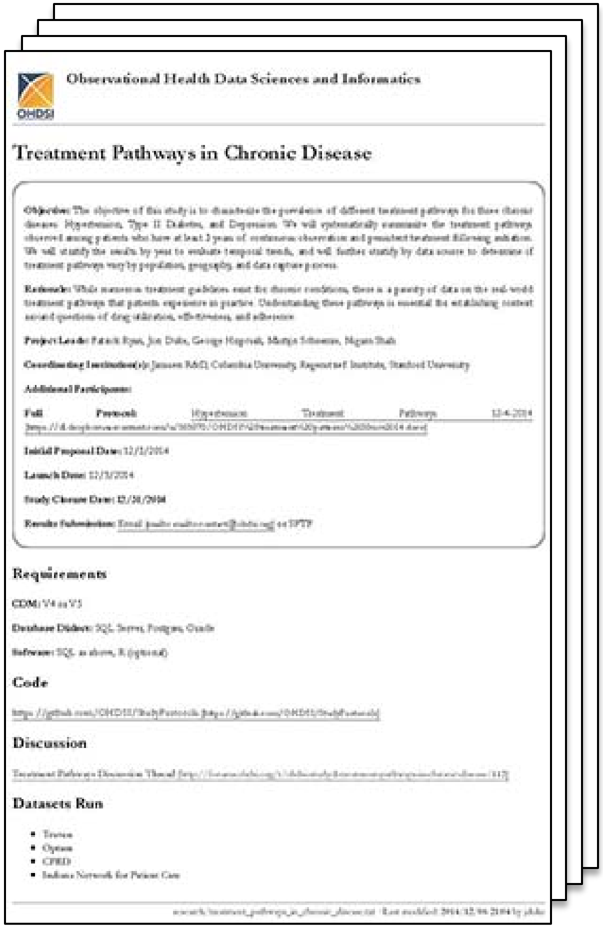
Condition definitions

Disease	Medication classes	Diagnosis	Exclusions
Hypertension (“HTN”)	antihypertensives, diuretics, peripheral vasodilators, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system (all ATC)	hyperpiesis (SNOMED)	pregnancy observations (SNOMED)
Diabetes mellitus, Type 2 (“Diabetes”)	drugs used in diabetes (ATC), diabetic therapy (FDB)	diabetes mellitus (SNOMED)	pregnancy observations (SNOMED), type 1 diabetes mellitus (MedDRA)
Depression	antidepressants (ATC), antidepressants (FDB)	depressive disorder (SNOMED)	pregnancy observations (SNOMED), bipolar I disorder (SNOMED), schizophrenia (SNOMED)

Treatment pathway event flow



Protocol



Observational Health Data Sciences and Informatics
Treatment Pathways in Chronic Disease
Requirements
Code
Discussion
Datasets Run

# R script for creating SQL files (and sending the SQL
# commands to the server) for the treatment pattern
# studies for these diseases:
# - Hypertension (HTN)
# - Type 2 Diabetes (T2DM)
# - Depression
# Requires: R and Java 1.6 or higher
# Install necessary packages if needed
install.packages("devtools")
library(devtools)
install_github("ohdsi/SqlRender")
install_github("ohdsi/DatabaseConnector")
# Load libraries
library(SqlRender)
library(DatabaseConnector)
# Parameters: Please change these to the correct values: #
cdmSchema = "cdm_schema"
resultsSchema = "results_schema"
sourceName = "source_name"
user <- NULL
pw <- NULL
server <- "server_name"
port <- NULL
# End of parameters. Make no changes after this #
setwd(folder)
source("HelperFunctions.R")
# Create the parameterized SQL files:
# Execute the SQL:
connectionDetails <- createConnectionDetails(dbms=dbms,
conn <- connect(connectionDetails)
# Extract tables to CSV files:
dbDisconnect(conn)

OHDSI participating data partners

Code	Name	Description	Size (M)
AUSOM	Ajou University School of Medicine	South Korea; inpatient hospital EHR	2
CCAE	MarketScan Commercial Claims and Encounters	US private-payer claims	119
CPRD	UK Clinical Practice Research Datalink	UK; EHR from general practice	11
CUMC	Columbia University Medical Center	US; inpatient EHR	4
GE	GE Centricity	US; outpatient EHR	33
INPC	Regenstrief Institute, Indiana Network for Patient Care	US; integrated health exchange	15
JMDC	Japan Medical Data Center	Japan; private-payer claims	3
MDCD	MarketScan Medicaid Multi-State	US; public-payer claims	17
MDCR	MarketScan Medicare Supplemental and Coordination of Benefits	US; private and public-payer claims	9
OPTUM	Optum ClinFormatics	US; private-payer claims	40
STRIDE	Stanford Translational Research Integrated Database Environment	US; inpatient EHR	2
HKU	Hong Kong University	Hong Kong; EHR	1

Strict criteria

- 250,000,000+ patient records to start
- 4 years continuous observation
- (first treatment for disease)
- 3 years continuous treatment
- 327,110 type 2 diabetes mellitus
- 1,182,792 hypertension
- 264,841 depression

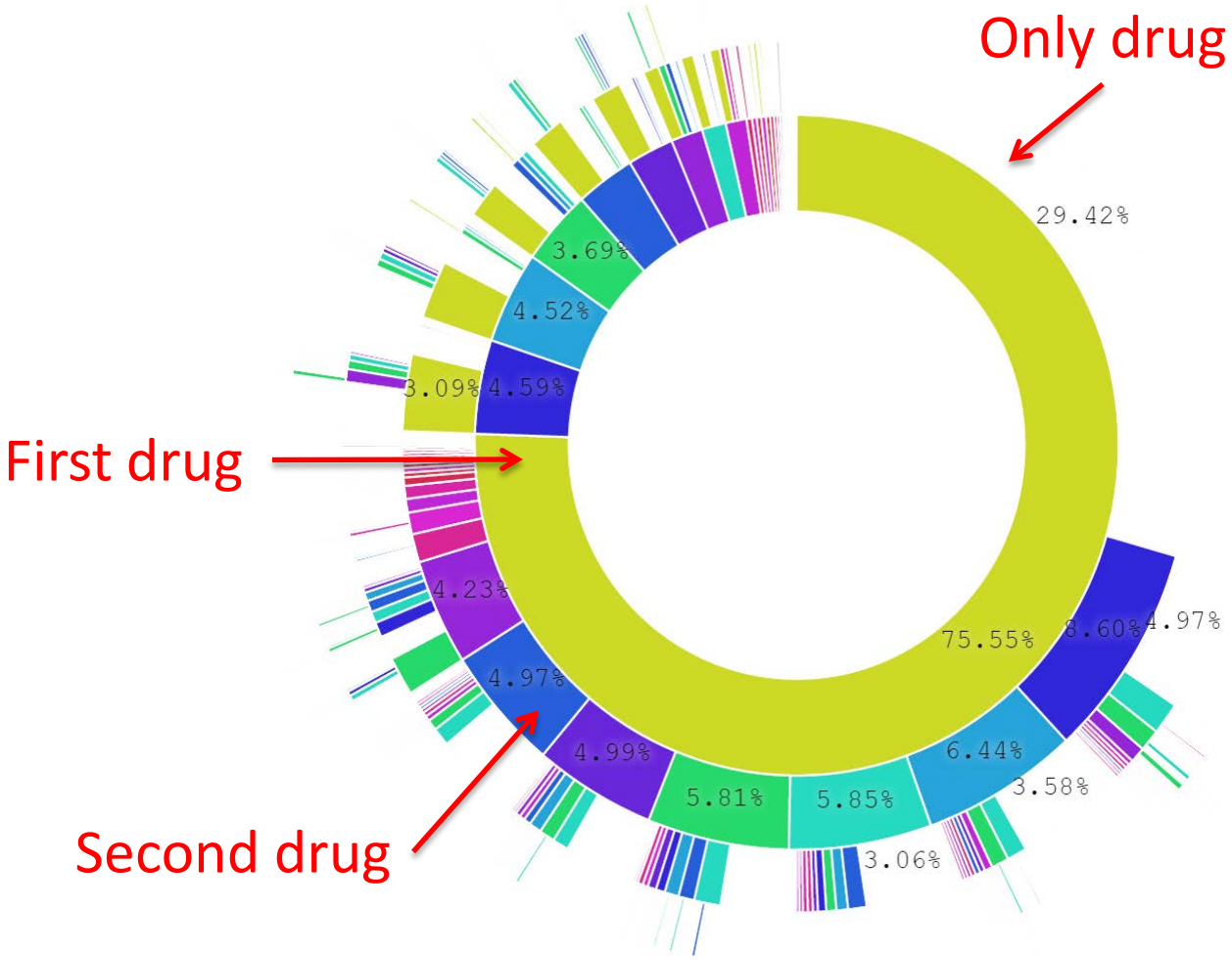
- Sequential and simultaneous are mixed

Publication in revision

- Submitted to PNAS
  - Policy of open sharing pre-publication
  - Will share more details on publication

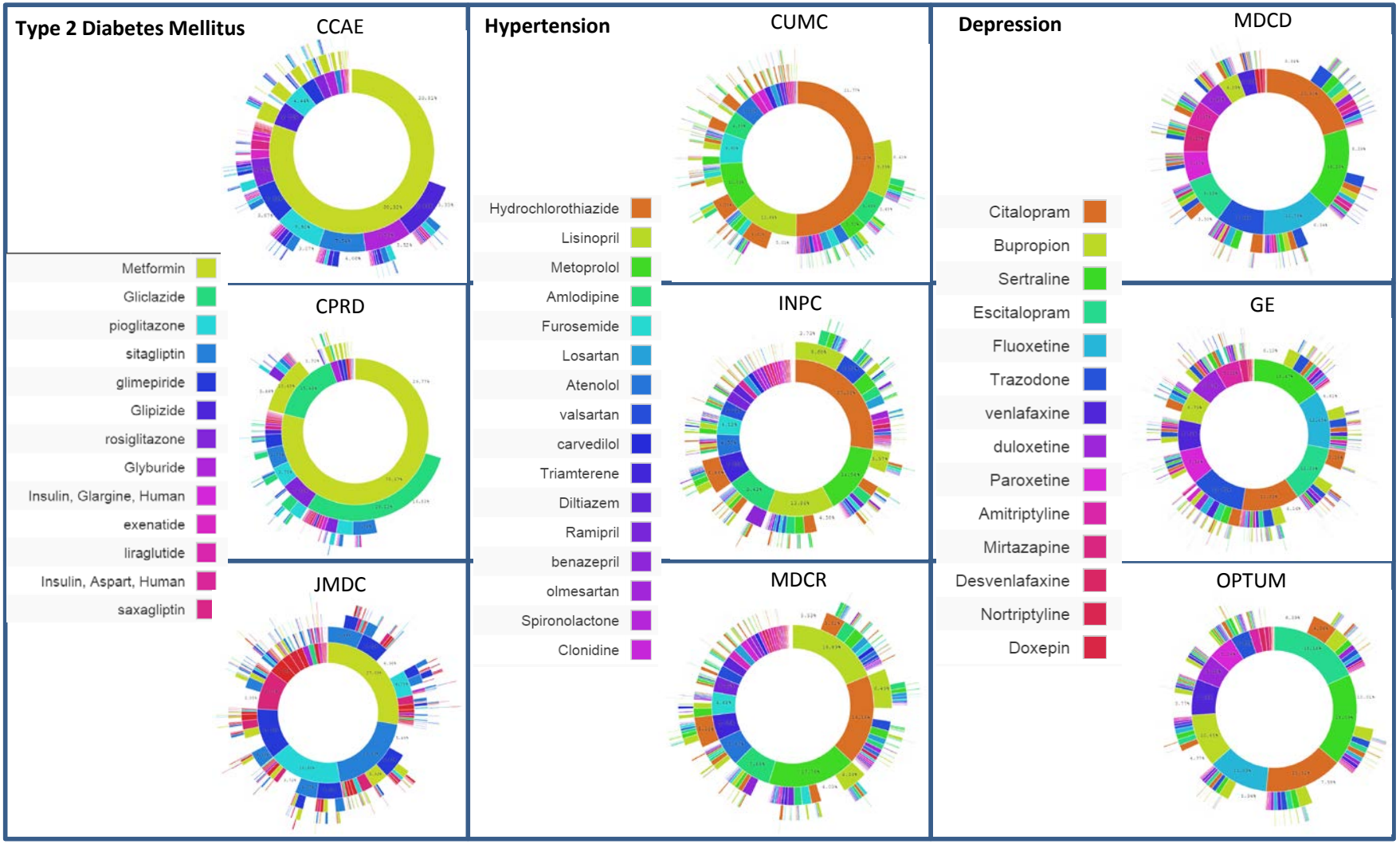
Treatment pathways for diabetes

T2DM : All databases



- Metformin
- pioglitazone
- sitagliptin
- Glipizide
- glimepiride
- Gliclazide
- Glyburide
- rosiglitazone
- Insulin, Glargine, Human
- exenatide
- Insulin, Aspart, Human
- liraglutide
- saxagliptin
- Insulin, Lispro, Human
- Glucose
- Insulin, Isophane, Human

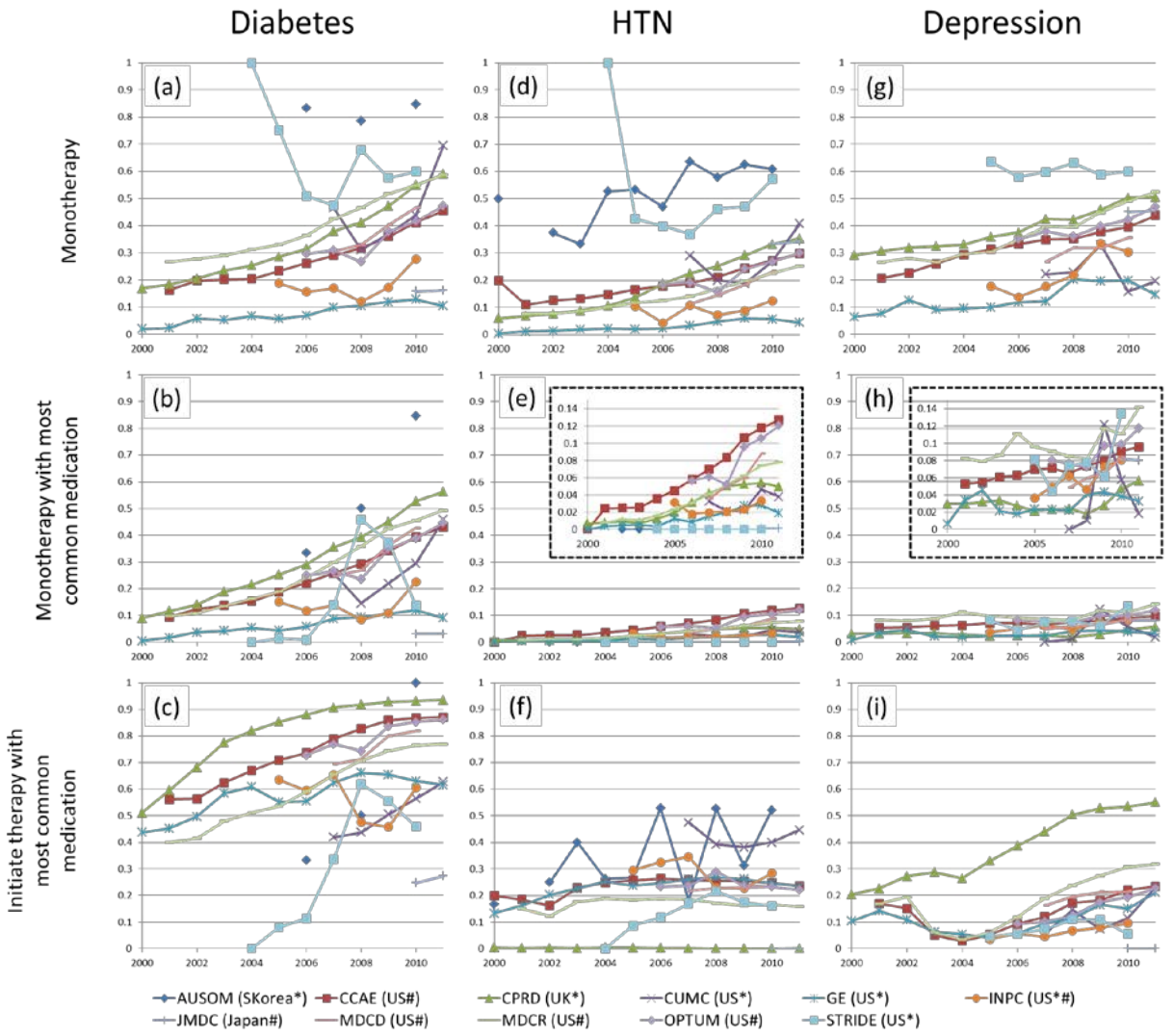
Population-level heterogeneity



Medication-use metrics

- Define generic metrics to be used on all diseases
  - Monotherapy: patients who used exactly one medication in the three-year window (one at a time and no changes)
  - Monotherapy with common medication: patients whose monotherapy was the most common mono-med for that condition
  - Start with common medication: patients who started with the most common starting med for that condition

Medication-use metrics by data source



Conclusions: Treatment pathways

- General progress toward more consistent therapy over time and across locations
- Differ by country
- Differ by practice type
- Not differ so much by data type (claims, EHR)
- Differ by disease
  - Even before guidelines published
  - Disease differences and literature
- Huge proportion of unique pathways

Conclusions: Network research

- It is feasible to encode the world population in a single data model
  - Over 500,000,000 records by voluntary effort (682,000,000)
- Generating evidence is feasible
- Stakeholders willing to share results
- Able to accommodate vast differences in privacy and research regulation

Collaborators

George Hripcsak	Columbia University Medical Center, New York, NY, USA
Patrick B Ryan	Janssen Research & Development, LLC, Titusville, NJ, USA
Jon D Duke	Regenstrief Institute, Indianapolis, IN, USA
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Martijn J Schuemie	University of Hong Kong, Hong Kong; Janssen Research & Development, LLC, Titusville, NJ, USA
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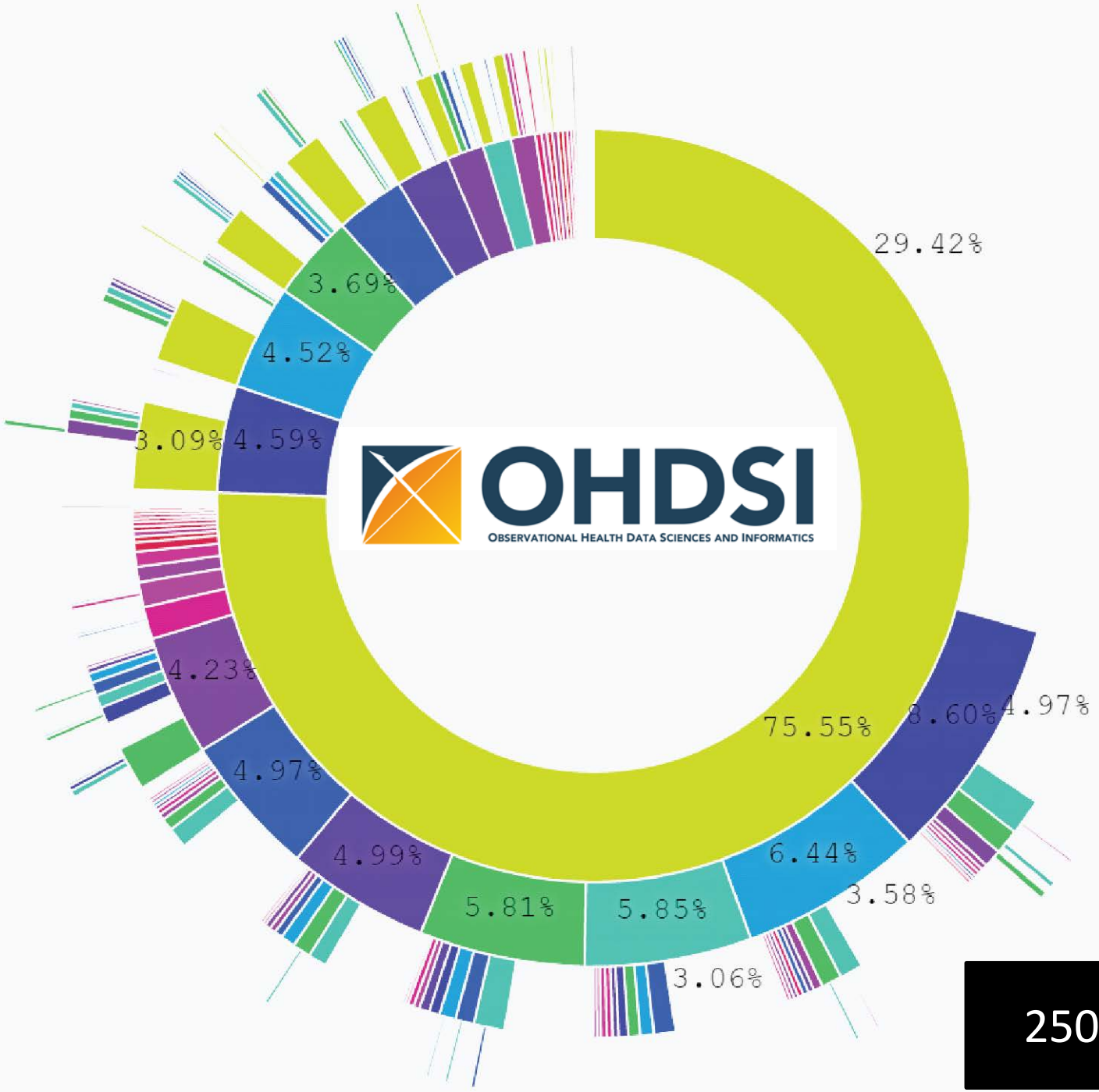
Daniella Meeker	University of Southern California, Los Angeles, CA
Nicole Pratt	University of South Australia, Australia
David Madigan	Columbia University, New York, NY, USA

Automated Learning of Phenotype Models

Nigam Shah, MBBS, PhD
nigam@stanford.edu

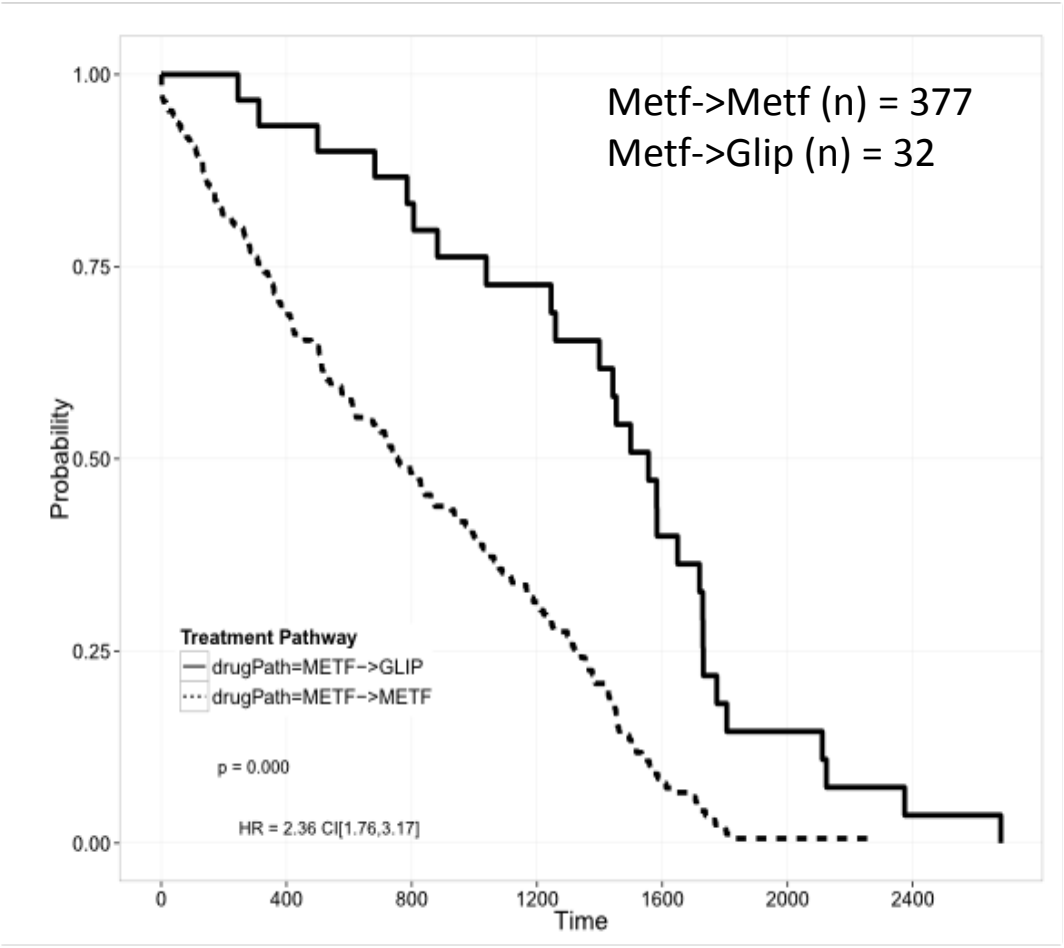
OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

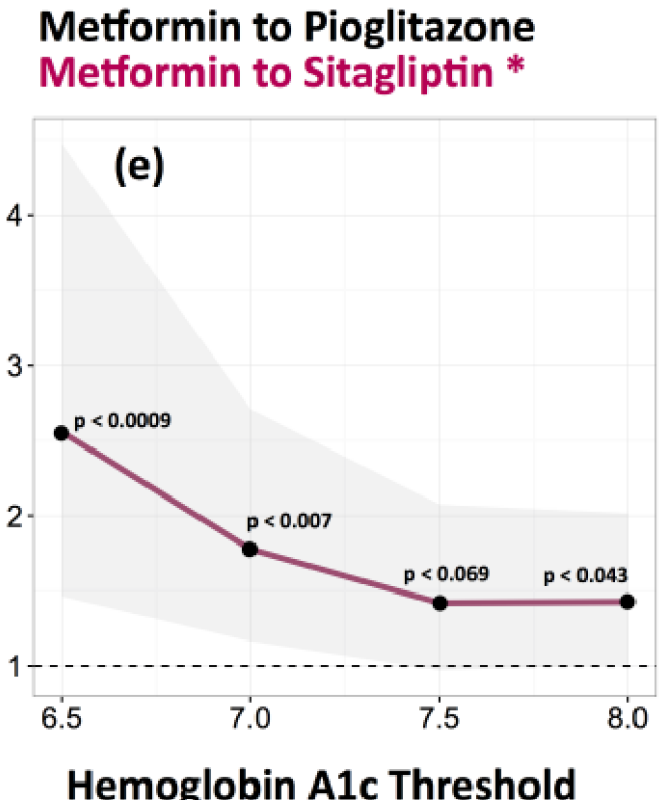
STANFORD
SCHOOL OF MEDICINE



250 million patients

Drug sequences and outcomes

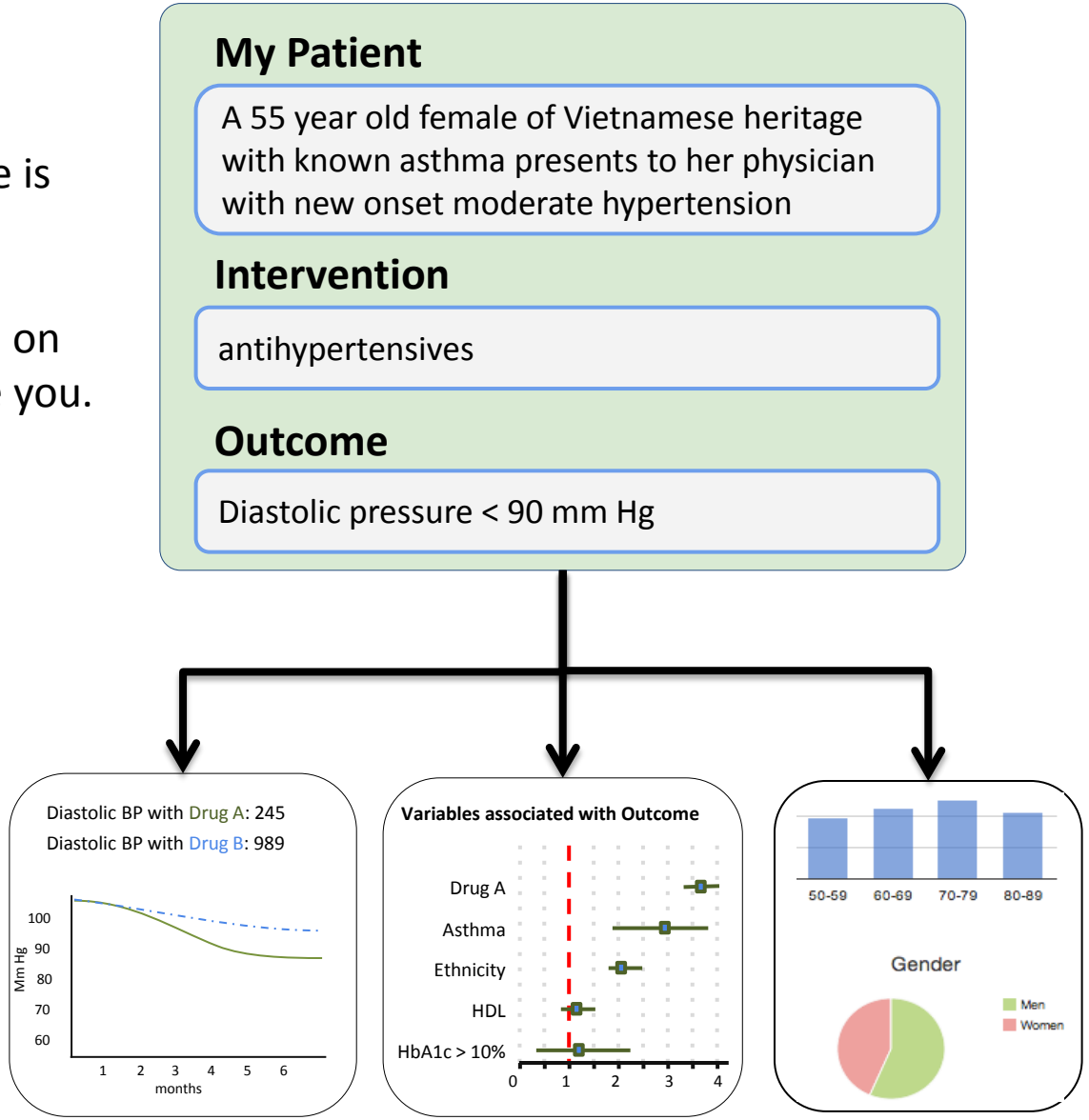




http://greenbutton.stanford.edu

Problem: A lot of medical care is educated guesses

Opportunity: Decisions based on what happened to people like you.



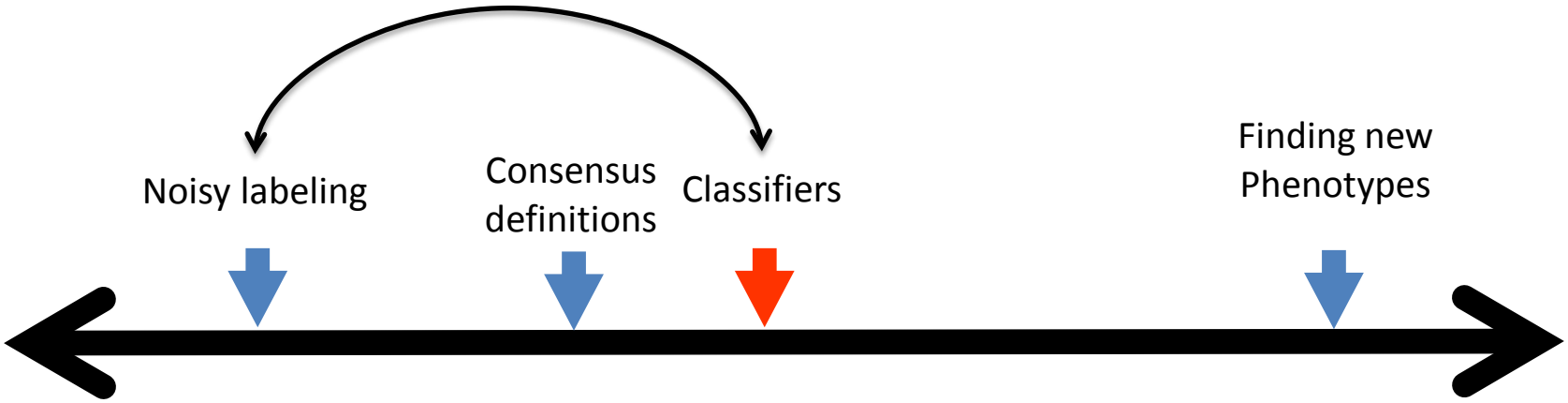
Goal

- Build phenotype models in 5 easy steps!
- Designed and Implemented using OHDSI CDMv5 and Vocabulary 5

```
          Reference
Prediction  F  T
         F 86 15
         T  1 72

               Accuracy : 0.908
                 95% CI : (0.855, 0.9465)
    No Information Rate : 0.5
    P-Value [Acc > NIR] : < 2.2e-16

                  Kappa : 0.8161
 Mcnemar's Test P-Value : 0.001154

            Sensitivity : 0.8276
            Specificity : 0.9885
         Pos Pred Value : 0.9863
         Neg Pred Value : 0.8515
             Prevalence : 0.5000
         Detection Rate : 0.4138
   Detection Prevalence : 0.4195
      Balanced Accuracy : 0.9080

       'Positive' Class : T


Model Details

glmnet

 526 samples
1932 predictors
   2 classes: 'F', 'T'
```

Electronic Phenotyping

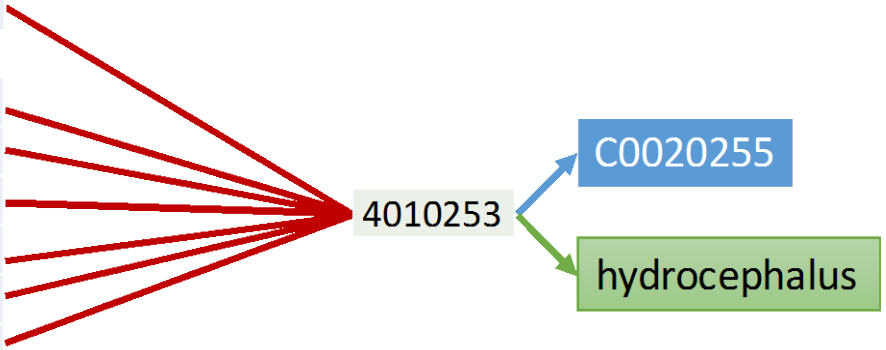
$$(1-2t)^2$$



Error rate in labeling	Sample size
10 %	1.56 x
20 %	2.77 x
30 %	6.25 x
40 %	25 x

“noisy labeling” to create training data

2933	hydrocephalus
90773	water on the brain
3107785	hydrocephalus [disease/finding]
42612	hydrocephaly
2889104	hydrocephalus (disorder)
1936514	hydrocephalus, unspecified
2001177	hydrocephalus nos

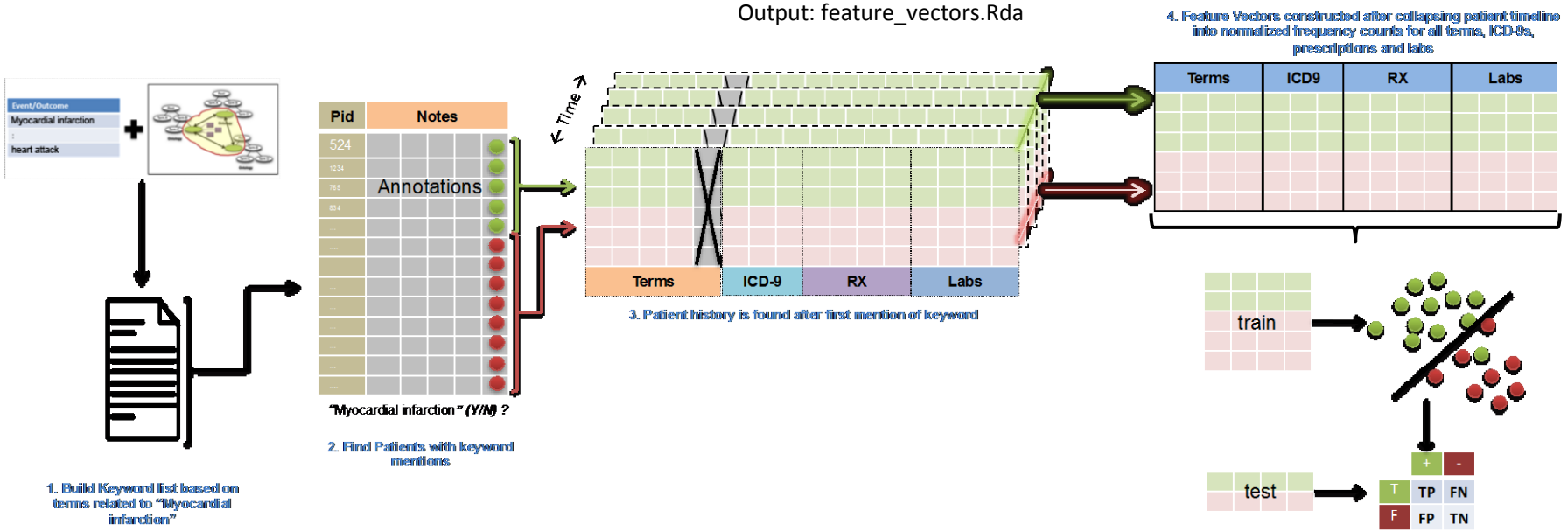


tid	cui	str	Note freq	syn	Medline freq	% noun
2933	C0020255	hydrocephalus	29,634	NNS	19,541	64.61
42612	C0020255	hydrocephaly	113	NN	275	49.81
90773	C0020255	water on the brain	8	ROOT	1	50

Assumption: “long mention” is a reliable indicator of presence

XPRESS- EXtraction of Phenotypes from clinical Records using Silver Standards

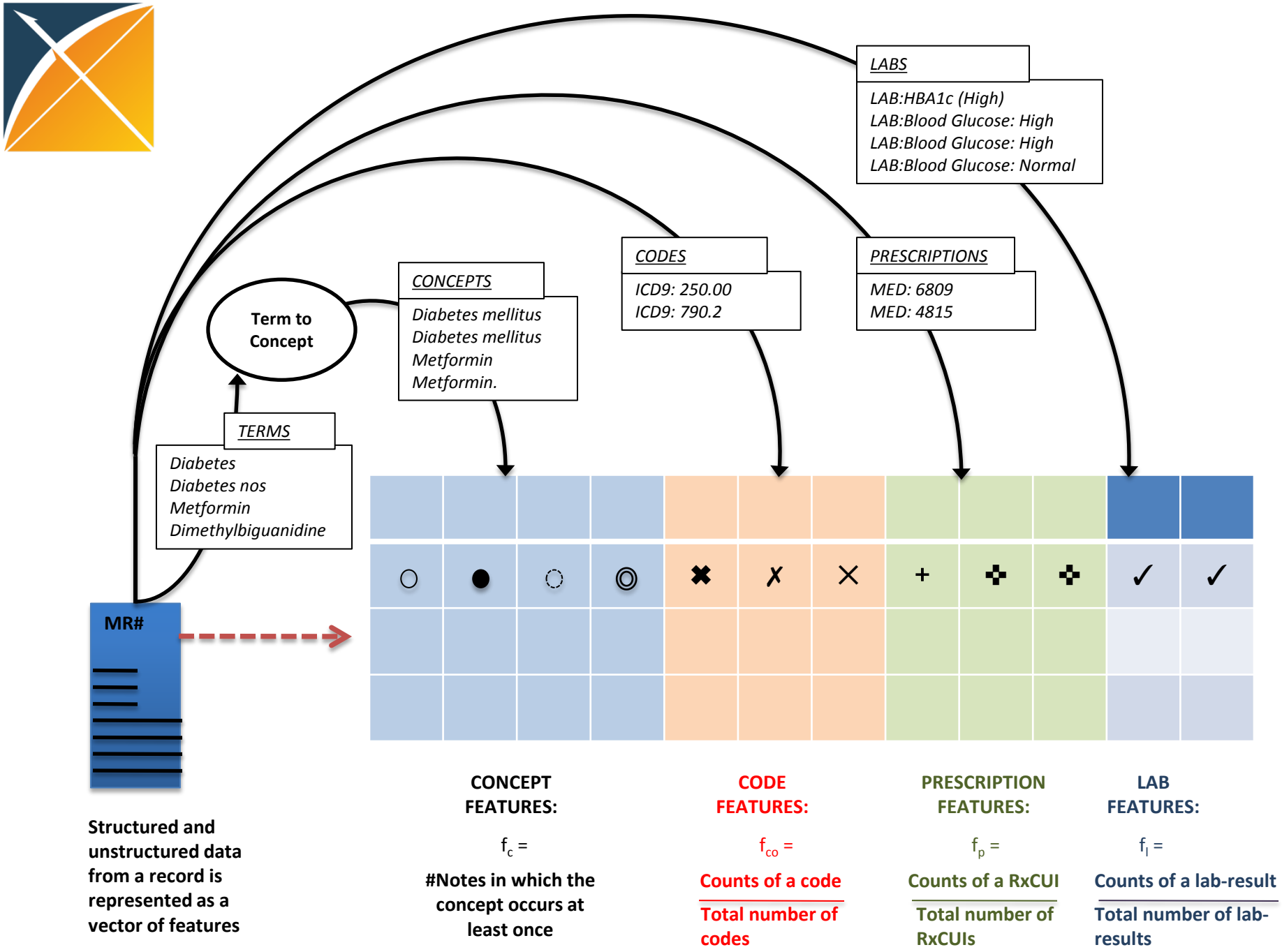
Input: getPatients.R -- config.R, keywords.tsv, ignore.tsv
Output: feature_vectors.Rda



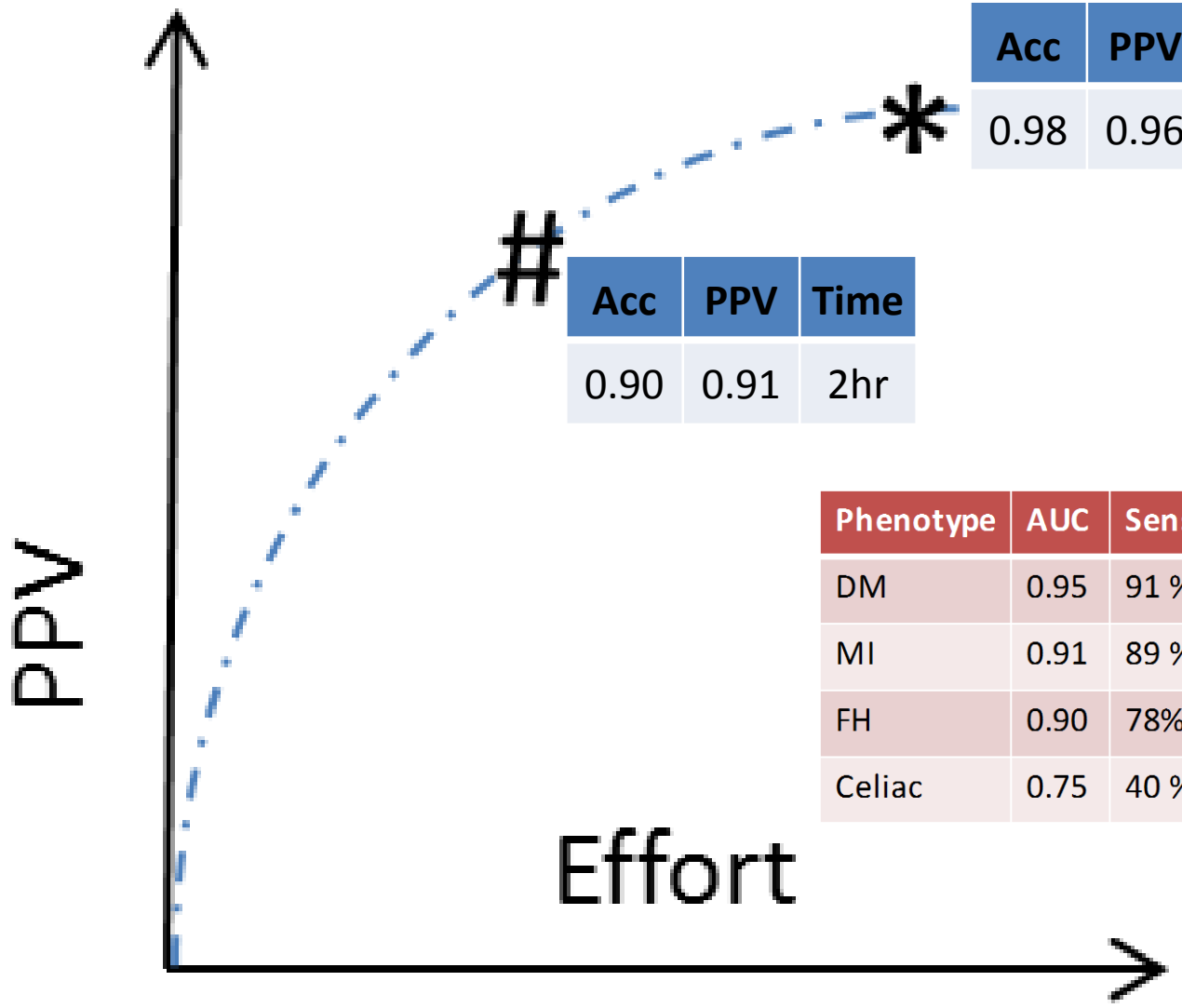
Input: config.R – with term search settings
Output: keywords.tsv and ignore.tsv

Phenotype	AUC	Sens.	Spec.	PPV
DM	0.95	91 %	83 %	83 %
MI	0.91	89 %	91 %	91 %
FH	0.90	76.5%	93.6%	~20%
Celiac	0.75	40 %	90 %	~4 %

Input: buildModel.R -- config.R, feature_vectors.Rda
Output: model.Rda


LABS
LAB:HBA1c (High)
LAB:Blood Glucose: High
LAB:Blood Glucose: High
LAB:Blood Glucose: Normal
CODES
ICD9: 250.00
ICD9: 790.2
PRESCRIPTIONS
MED: 6809
MED: 4815
CONCEPTS
Diabetes mellitus
Diabetes mellitus
Metformin
Metformin.
Term to Concept
TERMS
Diabetes
Diabetes nos
Metformin
Dimethylbiguanidine
MR#
Structured and unstructured data from a record is represented as a vector of features
CONCEPT FEATURES:
f_c =
#Notes in which the concept occurs at least once
CODE FEATURES:
f_{co} =
Counts of a code / Total number of codes
PRESCRIPTION FEATURES:
f_p =
Counts of a RxCUI / Total number of RxCUIs
LAB FEATURES:
f_l =
Counts of a lab-result / Total number of lab-results

Effort precision trade off



Acc	PPV	Time
0.98	0.96	1900

Acc	PPV	Time
0.90	0.91	2hr

Phenotype	AUC	Sens.	Spec.	PPV
DM	0.95	91 %	83 %	83 %
MI	0.91	89 %	91 %	91 %
FH	0.90	78%	92%	73%
Celiac	0.75	40 %	90 %	~4 %

Anchor and Learn

(with Yoni Halpern and David Sontag)

	Cases	Cont.	Acc.	Recall	PPV
Myocardial Infarction (MI)					
OMOP definition [2]	*94*	*94*	*0.87*	*0.91*	*0.84*
XPRESS [2]	94	94	0.89	0.93	0.86
APHRODITE	94	94	0.91	0.93	0.90
APHRODITE w Anchors (features mod.)	94	94	**0.93**	0.96	0.91
Type 2 Diabetes Mellitus (T2DM)					
PheKB definition [2]	*152*	*152*	*0.92*	*0.88*	*0.96*
XPRESS [2]	152	152	0.89	0.99	0.9
APHRODITE	152	152	0.91	0.98	0.88
APHRODITE w Anchors (features mod.)	152	152	**0.93**	0.95	0.91

Current state

- APHRODITE 1.2 released on November 30th, 2015.
- Anchors incorporate on version 1.2 - November 30th, 2015.
- Fully Oracle/Postgres/MSSQL server compliant as of version 1.1.
- 6 sites have attempted building a model
  - 2 sites failed because of data in CMD v4 version issues.
  - 3 sites successfully finished all tests.
  - 1 site has successfully executed the Anchors code.

Acknowledgements

Group Members:

- **Fellows:** Suzanne Tamang, Yen Low, Alison Callahan, Elsie Gyang, Juan Banda, Rainer Winnenburg, Rohit Vashisht
- **BMI Students:** Ken Jung, Sarah Poole, Alejandro Schuler, Albee Ling, Vibhu Agarwal, Tanya Podchiyska, David Stark
- **Med Students:** Greg Gaskin, Jassi Pannu

Alums: Anna Bauer-Mehren (Roche), Srini Iyer (Facebook), Amogh Vasekar (Citrix), Sandy Huang (Berkeley), Paea LePendu (PCCI), Rave Harpaz (Oracle), Sam Finlayson (Harvard), Will Chen (Yale)

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- Fellowships – Med Scholars, Siebel Scholars Foundation, Stanford Graduate Fellowship
- Industry – Apixio, CollabRx, Healogics, Janssen R&D, Oracle, Baidu USA, Amgen

BMIR-IT: Alex Skrenchuk

Disseminating Evidence in Practice: Enhancing Product Labeling through OHDSI

Jon D. Duke MD, MS

Regenstrief Institute

Real-World Impact

How to take evidence generated by the OHDSI community and deliver to end-users?

Drug Safety Information

Other Events Observed During the Premarketing Evaluation of ZOLOFT (sertraline hydrochloride)

Following is a list of treatment-emergent adverse events reported during premarketing assessment of ZOLOFT in clinical trials (over 4000 adult subjects) except those already listed in the previous tables or elsewhere in labeling.

In the tabulations that follow, a World Health Organization dictionary of terminology has been used to classify reported adverse events. The frequencies presented, therefore, represent the proportion of the over 4000 adult individuals exposed to multiple doses of ZOLOFT who experienced an event of the type cited on at least one occasion while receiving ZOLOFT. All events are included except those already listed in the previous tables or elsewhere in labeling and those reported in terms so general as to be uninformative and those for which a causal relationship to ZOLOFT treatment seemed remote. It is important to emphasize that although the events reported occurred during treatment with ZOLOFT, they were not necessarily caused by it.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients. Events of major clinical importance are also described in the PRECAUTIONS section.

Autonomic Nervous System Disorders–*Frequent* impotence; *Infrequent* flushing, increased saliva, cold clammy skin, mydriasis; *Rare* pallor, glaucoma, priapism, vasodilation.

Body as a Whole–General Disorders–*Rare* allergic reaction, allergy.

Cardiovascular–*Frequent* palpitations, chest pain; *Infrequent* hypertension, tachycardia, postural dizziness, postural hypotension, peripheral edema, peripheral ischemia, syncope, edema, dependent edema; *Rare* precordial chest pain, substernal chest pain, aggravated hypertension, myocardial infarction, cerebrovascular disorder.

Central and Peripheral Nervous System Disorders–*Frequent* hypertonia, hypoesthesia; *Infrequent* twitching, confusion, hyperkinesia, vertigo, ataxia, migraine, abnormal coordination, hyperesthesia, leg cramps, abnormal gait, nystagmus, hypokinesia; *Rare* dysphonia, coma, dyskinesia, hypotonia, ptosis, choreoathetosis, hyporeflexia.

Disorders of Skin and Appendages–*Infrequent* pruritus, acne, urticaria, alopecia, dry skin, erythematous rash, photosensitivity reaction, maculopapular rash; *Rare* follicular rash, eczema, dermatitis, contact dermatitis, bullous eruption, hyperhidrosis, skin discoloration, pustular rash.

Endocrine Disorders–*Rare*: exophthalmos, gynecomastia.

Gastrointestinal Disorders–*Frequent* appetite increased; *Infrequent* dysphagia, tooth caries aggravated, eructation, esophagitis, gastroenteritis; *Rare*: melena, glossitis, gum hyperplasia, hiccup, stomatitis, tenesmus, colitis, diverticulitis, fecal incontinence, gastritis, rectum hemorrhage, hemorrhagic peptic ulcer, proctitis, ulcerative stomatitis, tongue edema, tongue ulceration.

General–*Frequent* back pain, asthenia, malaise, weight increase; *Infrequent* fever, rigors, generalized edema; *Rare* face edema, aphthous stomatitis.

Hearing and Vestibular Disorders–*Rare* hyperacusis, labyrinthine disorder.

Hematopoietic and Lymphatic–*Rare* anemia, anterior chamber eye hemorrhage.

Liver and Biliary System Disorders–*Rare* abnormal hepatic function.

Metabolic and Nutritional Disorders–*Infrequent* thirst; *Rare* hypoglycemia, hypoglycemia reaction.

Musculoskeletal System Disorders–*Frequent* myalgia; *Infrequent* arthralgia, dystonia, arthrosis, muscle cramps, muscle weakness.

Psychiatric Disorders–*Frequent* yawning, other male sexual dysfunction; *Infrequent* depression, amnesia, paronitia, teeth-grinding, emotional lability, apathy, abnormal dreams, euphoria, paranoid reaction, hallucination, aggressive reaction, aggravated depression, delusions; *Rare* withdrawal syndrome, suicide ideation, libido increased, somnambulism, illusion.

Reproductive–*Infrequent* menstrual disorder, dysmenorrhea, intermenstrual bleeding, vaginal hemorrhage, amenorrhea, leukorrhea; *Rare* female breast pain, menorrhagia, balanoposthitis, breast enlargement, atrophic vaginitis, acute female mastitis.

Respiratory System Disorders–*Frequent* rhinitis; *Infrequent* coughing, dyspnea, upper respiratory tract infection, epistaxis, bronchospasm, sinusitis; *Rare* hyperventilation, bradypnea, stridor, apnea, bronchitis, hemoptysis, hypoventilation, laryngismus, laryngitis.

Special Senses–*Frequent* tinnitus; *Infrequent* conjunctivitis, earache, eye pain, abnormal accommodation; *Rare*: xerophthalmia, photophobia, diplopia, abnormal lacrimation, scotoma, visual field defect.

Urinary System Disorders–*Infrequent* micturition frequency, polyuria, urinary retention, dysuria, nocturia, urinary incontinence; *Rare*: cystitis, oliguria, pyelonephritis, hematuria, renal pain, strangury.

Incidence of Adverse Events in Short-Term, Placebo-Controlled and Combination Trials

The following findings are based on premarketing trials of (1) oral clonazapine for schizophrenia, bipolar mania, a subsequent trial of patients having various psychiatric symptoms in association with Alzheimer's disease, and premarketing combination trials, and (2) intramuscular clonazapine for injection in agitated patients with schizophrenia or bipolar mania.

Adverse Events Associated with Discontinuation of Treatment in Short-Term, Placebo-Controlled Trials

Schizophrenia — Overall, there was no difference in the incidence of discontinuation due to adverse events (5% for oral clonazapine vs 6% for placebo). However, discontinuations due to increases in SGPT were considered to be drug-related (2% for oral clonazapine vs 0% for placebo) (see PRECAUTIONS).

Bipolar Mania Monotherapy — Overall, there was no difference in the incidence of discontinuation due to adverse events (2% for oral clonazapine vs 2% for placebo).

Agitation — Overall, there was no difference in the incidence of discontinuation due to adverse events (0.4% for intramuscular clonazapine for injection vs 0% for placebo).

Adverse Events Associated with Discontinuation of Treatment in Short-Term Combination Trials

Bipolar Mania Combination Therapy — In a study of patients who were already tolerating either lithium or valproate as monotherapy, discontinuation rates due to adverse events were 11% for the combination of oral clonazapine with lithium or valproate compared to 2% for patients who remained on lithium or valproate monotherapy. Discontinuations with the combination of oral clonazapine and lithium or valproate that occurred in more than 1 patient were: somnolence (3%), weight gain (1%), and peripheral edema (1%).

Commonly Observed Adverse Events in Short-Term, Placebo-Controlled Trials

The most commonly observed adverse events associated with the use of oral clonazapine (incidence of 5% or greater) and not observed at an equivalent incidence among placebo-treated patients (clonazapine incidence at least twice that for placebo) were:

Common Treatment-Emergent Adverse Events Associated with the Use of Oral Clonazapine in 6-Week Trials — SCHIZOPHRENIA

Adverse Event	Percentage of Patients Reporting Event	
	Clonazapine (N=248)	Placebo (N=118)
Postural hypotension	5	2
Constipation	9	3
Weight gain	6	1
Dizziness	11	4
Personality disorder*	8	4
Akathisia	5	1

* Personality disorder is the COSTART term for designating non-aggressive objectionable behavior.

Common Treatment-Emergent Adverse Events Associated with the Use of Oral Clonazapine in 3-Week and 4-Week Trials — BIPOLAR MANIA

Adverse Event	Percentage of Patients Reporting Event	
	Clonazapine (N=126)	Placebo (N=129)
Asthenia	18	6
Dry mouth	22	7
Constipation	11	6
Dyspepsia	11	6
Increased appetite	6	3
Somnolence	55	13
Dizziness	18	6
Tremor	8	3

TABLE 3 TREATMENT-EMERGENT ADVERSE EVENTS: INCIDENCE IN PLACEBO-CONTROLLED CLINICAL TRIALS Percentage of Patients Reporting Event Major Depressive Disorder/Other†, OCD, Panic Disorder, PTSD, PMDD and Social Anxiety Disorder combined

Body System/Adverse Event‡	ZOLOFT (N=2799)	Placebo (N=2394)
Autonomic Nervous System Disorders		
Ejaculation Failure§	14	1
Mouth Dry	12	8
Sweating Increased	7	2
Centor. & Periph. Nerv. System Disorders		
Somnolence	13	7
Dizziness	12	7
Headache	26	23
Paresthesia	2	1
Tremor	8	2
Disorders of Skin and Appendages		
Rash	3	2
Gastrointestinal Disorders		
Anorexia	6	2
Constipation	6	4
Diarrhea/Loose Stools	20	10
Dyspepsia	8	4
Nausea	26	11
Vomiting	4	2
General		
Fatigue	12	7
Psychiatric Disorders		
Agitation	5	3
Anxiety	4	3
Insomnia	21	11
Libido Decreased	6	2
Nervousness	5	4
Special Senses		
Vision Abnormal	3	2

† Major depressive disorder and other premarketing controlled trials.

‡ Included are events reported by at least 2% of patients taking ZOLOFT except the following events, which had an incidence on placebo greater than or equal to ZOLOFT: abdominal pain, back pain, flatulence, malaise, pain, pharyngitis, respiratory disorder, upper respiratory tract infection.

§ Primarily ejaculatory delay. Denominator used was for male patients only (N=1118 ZOLOFT, N=926 placebo).

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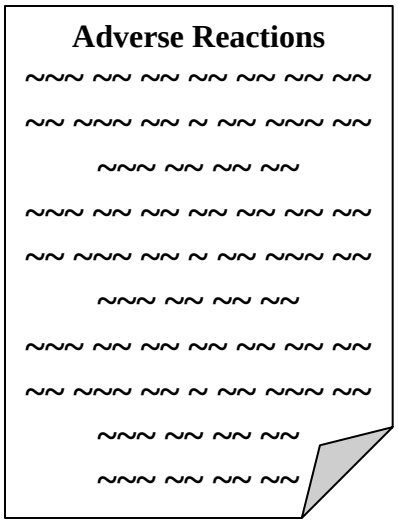
Urinary System Disorders–*Infrequent:* micturition frequency, polyuria, urinary retention, dysuria, nocturia, urinary incontinence; *Rare:* cystitis, oliguria, pyelonephritis, hematuria, renal pain, strangury.

Product Labels Have a Problem

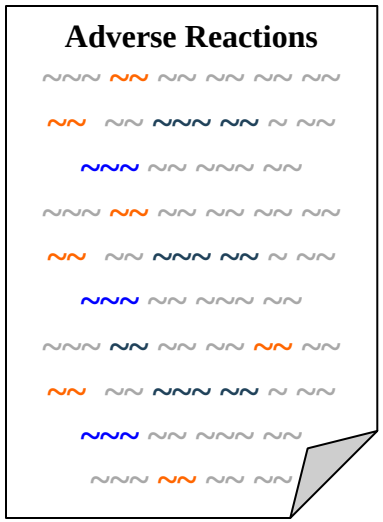
While considered the official source of drug safety information

- Labels are infrequently read by patient or providers
- The evidence for a given ADR is often scant
- They are one-size-fits-all and do not support personalized decision-making

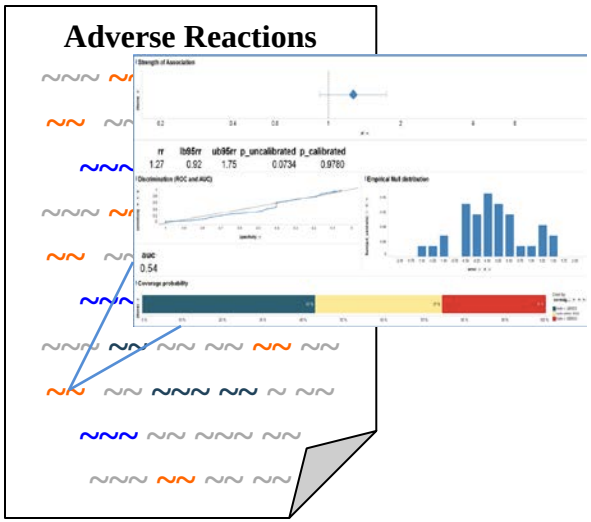
What if we could take real product labels and inject them with OHDSI evidence?



Structured Product Label

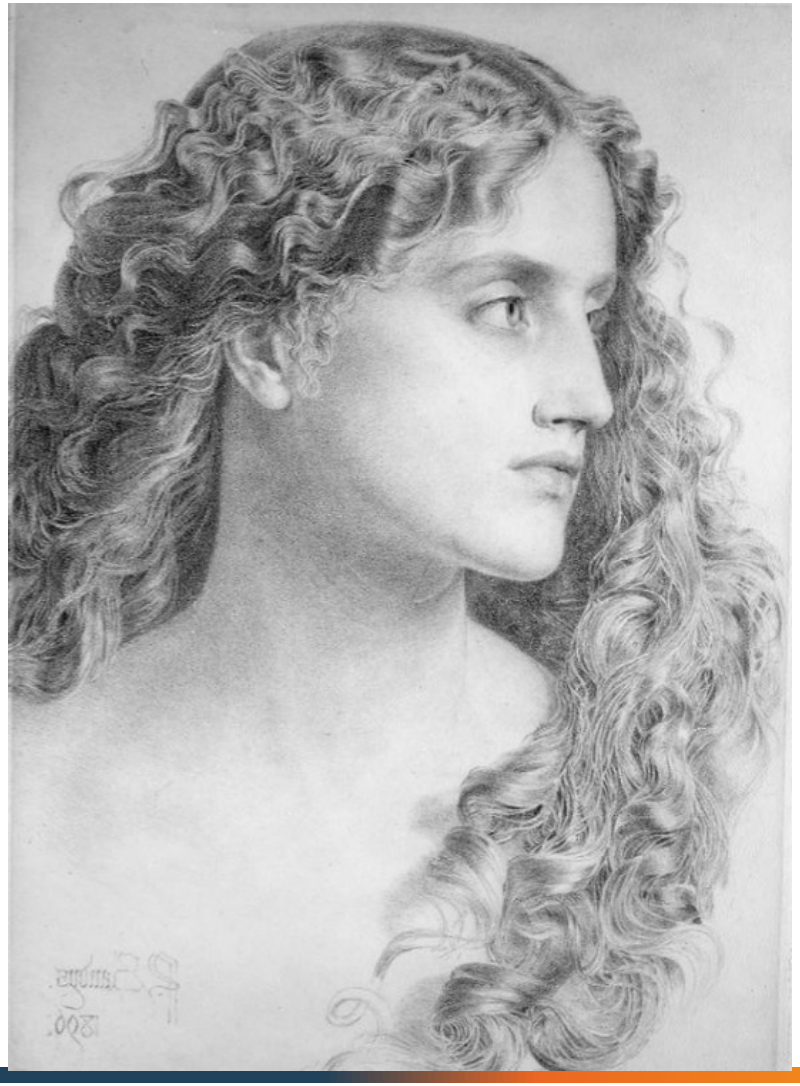


Enhanced Product Label



Enter PENELOPE

Personalized
Exploratory
Navigation &
Evaluation
Of
Labels for
Product
Effects



Geriatric use

Clinical studies of baclofen did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of KEMSTROâ¢ and observed closely.

Adverse Reactions

The most common adverse reaction during treatment with baclofen is transient drowsiness (10-63%). In one controlled study of 175 patients, transient drowsiness was observed in 63% of those receiving baclofen tablets compared to 36% of those in the placebo group. Other common adverse reactions are dizziness (5-15%), weakness (5-15%) and fatigue (2-4%). Others reported:

Neuropsychiatric: Confusion (1-11%), headache (4-8%), insomnia (2-7%); and, rarely, euphoria, excitement, depression, hallucinations, paresthesia, muscle pain, tinnitus, slurred speech, coordination disorder, tremor, rigidity, dystonia, ataxia, blurred vision, nystagmus, strabismus, miosis, mydriasis, diplopia, dysarthria, epileptic seizure.

Cardiovascular: Hypotension (0-9%). Rare instances of dyspnea, palpitation, chest pain, syncope.

Gastrointestinal: Nausea (4-12%), constipation (2-6%); and, rarely, dry mouth, anorexia, taste disorder, abdominal pain, vomiting, diarrhea, and positive test for occult blood in stool.

Genitourinary: Urinary frequency (2-6%); and, rarely, enuresis, urinary retention, dysuria, impotence, inability to ejaculate, nocturia, hematuria.

Other: Instances of rash, pruritus, ankle edema, excessive perspiration, weight gain, nasal congestion.

Some of the CNS and genitourinary symptoms may be related to the underlying disease rather than to drug therapy. The following laboratory tests have been found to be abnormal in a few patients receiving baclofen: increased SGOT, elevated alkaline phosphatase, and elevation of blood sugar.

PENELOPE

- PENELOPE leverages OHDSI's evidence generation and curation tools to provide context to safety information on drug labels
- The nature of this context may differ for different stakeholders (e.g., providers, researchers, patients)

A Big Supporting Cast

ACHILLES:
Database profiling

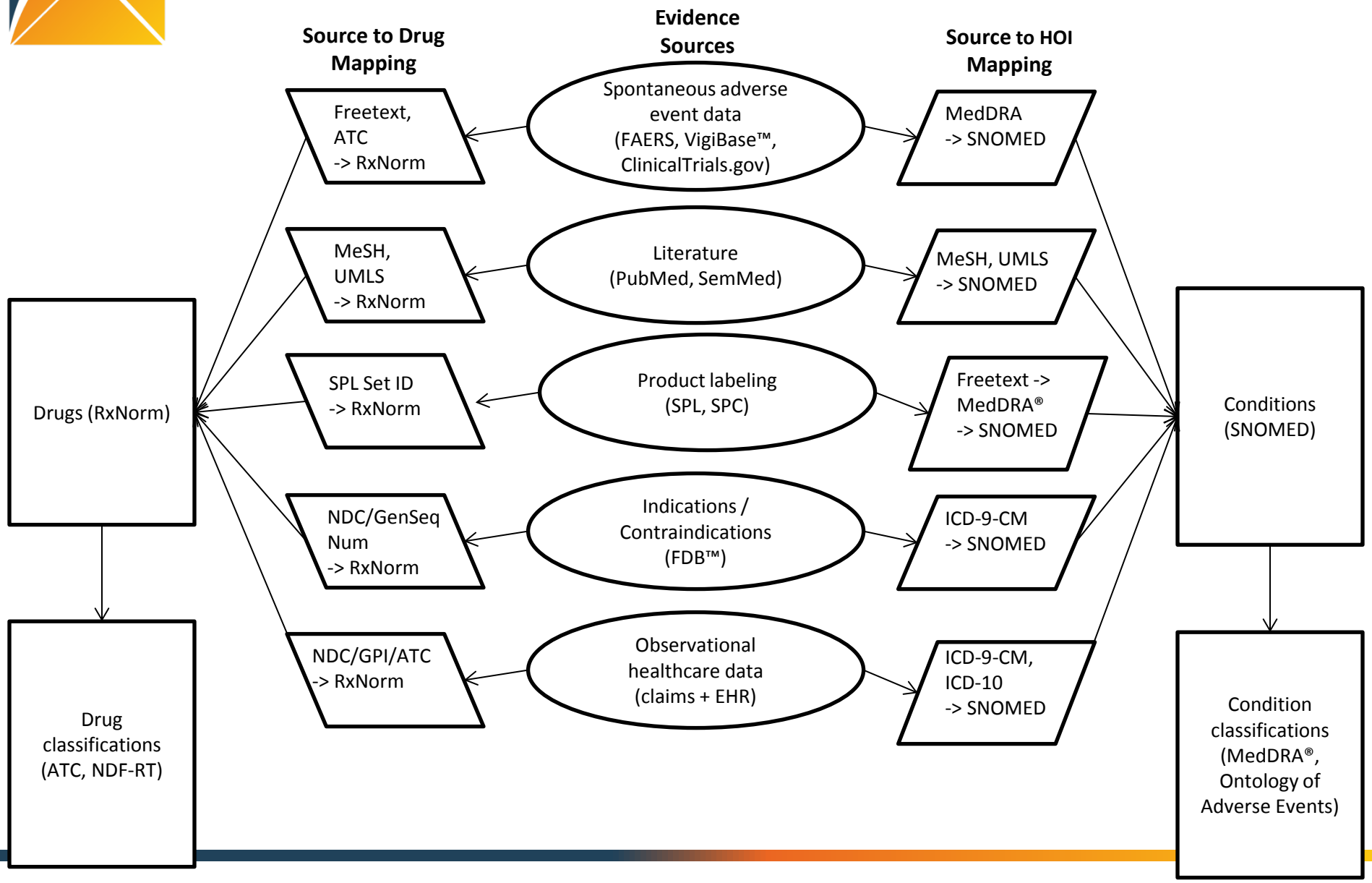
HERMES:
Vocabulary exploration

CIRCE:
Cohort definition

HERACLES:
Cohort characterization

LAERTES:
Drug-AE evidence base

LAERTES


Source to Drug Mapping
Evidence Sources
Source to HOI Mapping
Freetext, ATC -> RxNorm
Spontaneous adverse event data (FAERS, VigiBase™, ClinicalTrials.gov)
MedDRA -> SNOMED
MeSH, UMLS -> RxNorm
Literature (PubMed, SemMed)
MeSH, UMLS -> SNOMED
SPL Set ID -> RxNorm
Product labeling (SPL, SPC)
Freetext -> MedDRA® -> SNOMED
NDC/GenSeq Num -> RxNorm
Indications / Contraindications (FDB™)
ICD-9-CM -> SNOMED
NDC/GPI/ATC -> RxNorm
Observational healthcare data (claims + EHR)
ICD-9-CM, ICD-10 -> SNOMED
Drugs (RxNorm)
Drug classifications (ATC, NDF-RT)
Conditions (SNOMED)
Condition classifications (MedDRA®, Ontology of Adverse Events)

Penelope

zoloft

Sertraline

Evidence Explorer

Autonomic Nervous System Disorders–*Frequent:* impotence; *Infrequent:* flushing, increased saliva, cold clammy skin, mydriasis; *Rare:* pallor, glaucoma, priapism, vasodilation.

Body as a Whole–General Disorders–*Rare:* allergic reaction, allergy.

Cardiovascular–*Frequent:* palpitations, chest pain; *Infrequent:* hypertension, tachycardia, postural dizziness, postural hypotension, periorbital edema, peripheral edema, hypotension, peripheral ischemia, syncope, edema, dependent edema; *Rare:* precordial chest pain, substernal chest pain, aggravated hypertension, myocardial infarction, cerebrovascular disorder.

Central and Peripheral Nervous System Disorders–*Frequent:* hypertonia, hypoesthesia; *Infrequent:* twitching, confusion, hyperkinesia, vertigo, ataxia, migraine, abnormal coordination, hyperesthesia, leg cramps, abnormal gait, nystagmus, hypokinesia; *Rare:* dysphonia, coma, dyskinesia, hypotonia, ptosis, choreoathetosis, hyporeflexia.

Disorders of Skin and Appen

Let's Take a Look!

ivity reaction, maculopapular rash; *Rare:* follic ration, pustular rash.

Endocrine Disorders–*Rare:* e

Gastrointestinal Disorders–*Frequent:* appetite increased; *Infrequent:* dysphagia, tooth caries aggravated, eructation, esophagitis, gastroenteritis; *Rare:* melena, glossitis, gum hyperplasia, hiccup, stomatitis, tenesmus, colitis, diverticulitis, fecal incontinence, gastritis, rectum hemorrhage, hemorrhagic peptic ulcer, proctitis, ulcerative stomatitis, tongue edema, tongue ulceration.

General–*Frequent:* back pain, asthenia, malaise, weight increase; *Infrequent:* fever, rigors, generalized edema; *Rare:* face edema, aphthous stomatitis.

Hearing and Vestibular Disorders–*Rare:* hyperacusis, labyrinthine disorder.

Hematopoietic and Lymphatic–*Rare:* anemia, anterior chamber eye hemorrhage.

Liver and Biliary System Disorders–*Rare:* abnormal hepatic function.

Metabolic and Nutritional Disorders–*Infrequent:* thirst; *Rare:* hypoglycemia, hypoglycemia reaction.

Musculoskeletal System Disorders–*Frequent:* myalgia; *Infrequent:* arthralgia, dystonia, arthrosis, muscle cramps, muscle weakness.

Psychiatric Disorders–*Frequent:* yawning, other male sexual dysfunction, other female sexual dysfunction; *Infrequent:* depression, amnesia, paroniria, teeth-grinding, emotional lability, apathy, abnormal dreams, euphoria, paranoid reaction, hallucination, aggressive reaction, aggravated depression, delusions; *Rare:* withdrawal syndrome, suicide ideation, libido increased, somnambulism, illusion.

PENELOPE - it takes a community!

Anthony Sena
Janssen

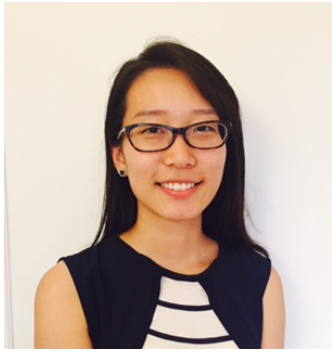
Frank DeFalco
Janssen

Rich Boyce
UPitt

Matt Levine
Columbia

Hamed Abedtash
Indiana U

Wen Zhang
UPitt



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Join the journey

Interested in OHDSI?

Questions or comments?