



Observational Health Data Sciences and Informatics (OHDSI)

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Observational Health Data Sciences and Informatics (OHDSI, as “Odyssey”)

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

A multi-stakeholder, interdisciplinary, international collaborative with a coordinating center at Columbia University



OHDSI's global research community



- >200 collaborators from 25 different countries
- Experts in informatics, statistics, epidemiology, clinical sciences
- Active participation from academia, government, industry, providers
- Currently records on about 500 million unique patients in >100 databases

<http://ohdsi.org/who-we-are/collaborators/>



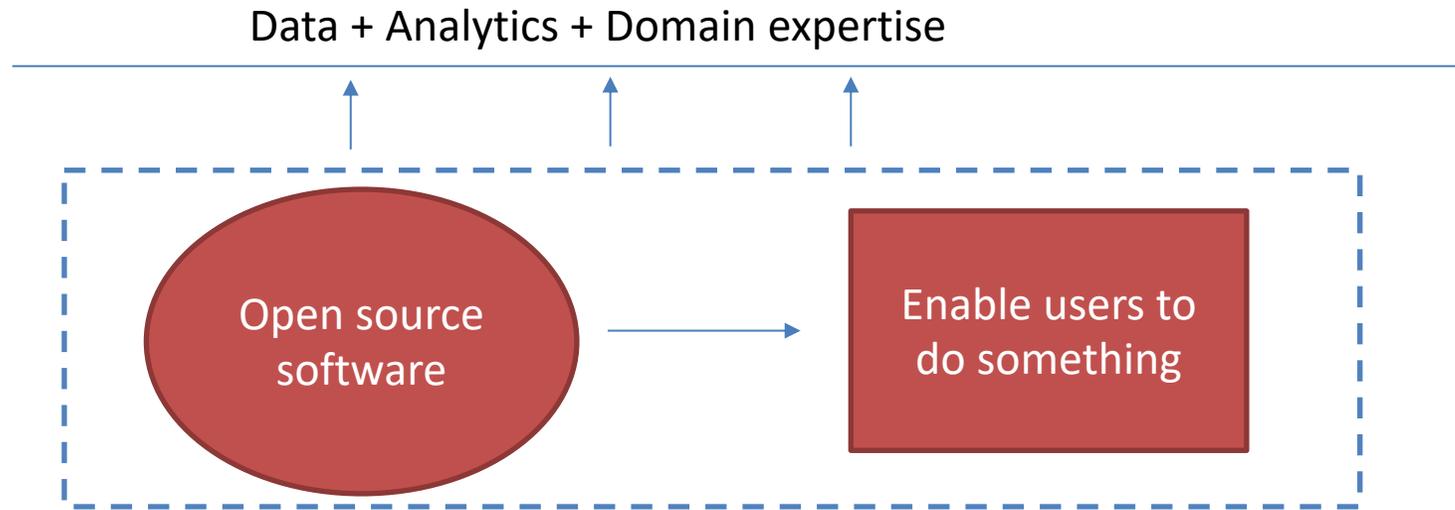
Evidence OHDSI seeks to generate from observational data

- **Clinical characterization - tally**
 - Natural history: Who has diabetes, and who takes metformin?
 - Quality improvement: What proportion of patients with diabetes experience complications?
- **Population-level estimation - cause**
 - Safety surveillance: Does metformin cause lactic acidosis?
 - Comparative effectiveness: Does metformin cause lactic acidosis more than glyburide?
- **Patient-level prediction - predict**
 - Precision medicine: Given everything you know about me, if I take metformin, what is the chance I will get lactic acidosis?
 - Disease interception: Given everything you know about me, what is the chance I will develop diabetes?



Open Science

Open science



Standardized, transparent workflows

Database summary

Cohort definition

Cohort summary

Compare cohorts

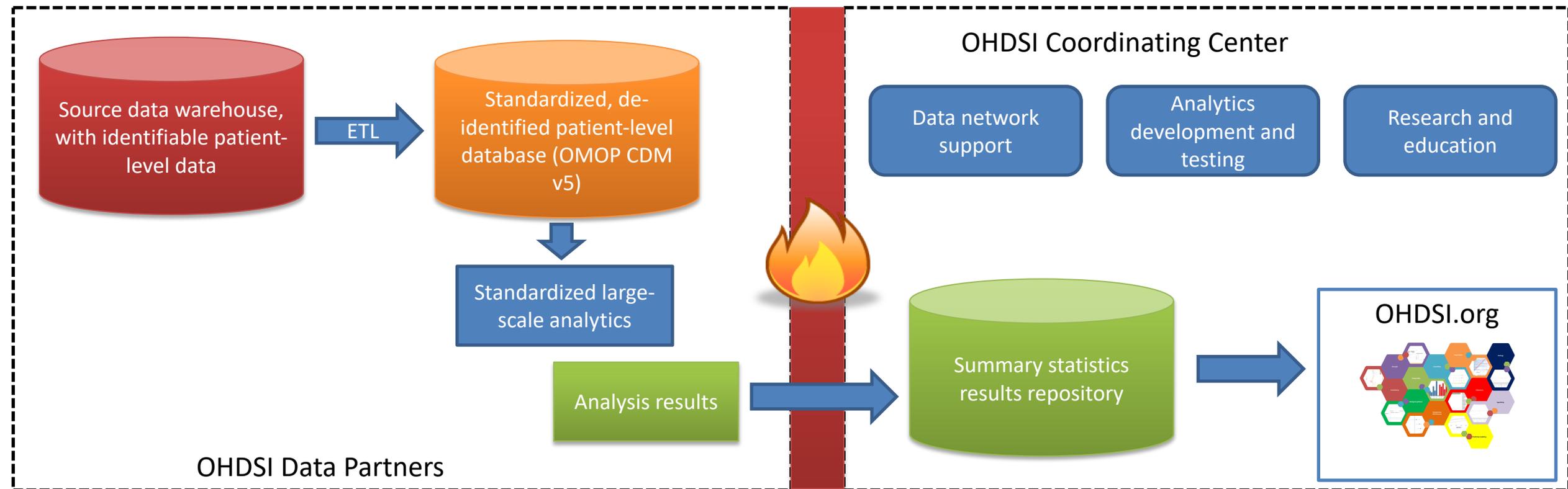
Exposure-outcome
summary

Effect estimation &
calibration

Compare
databases



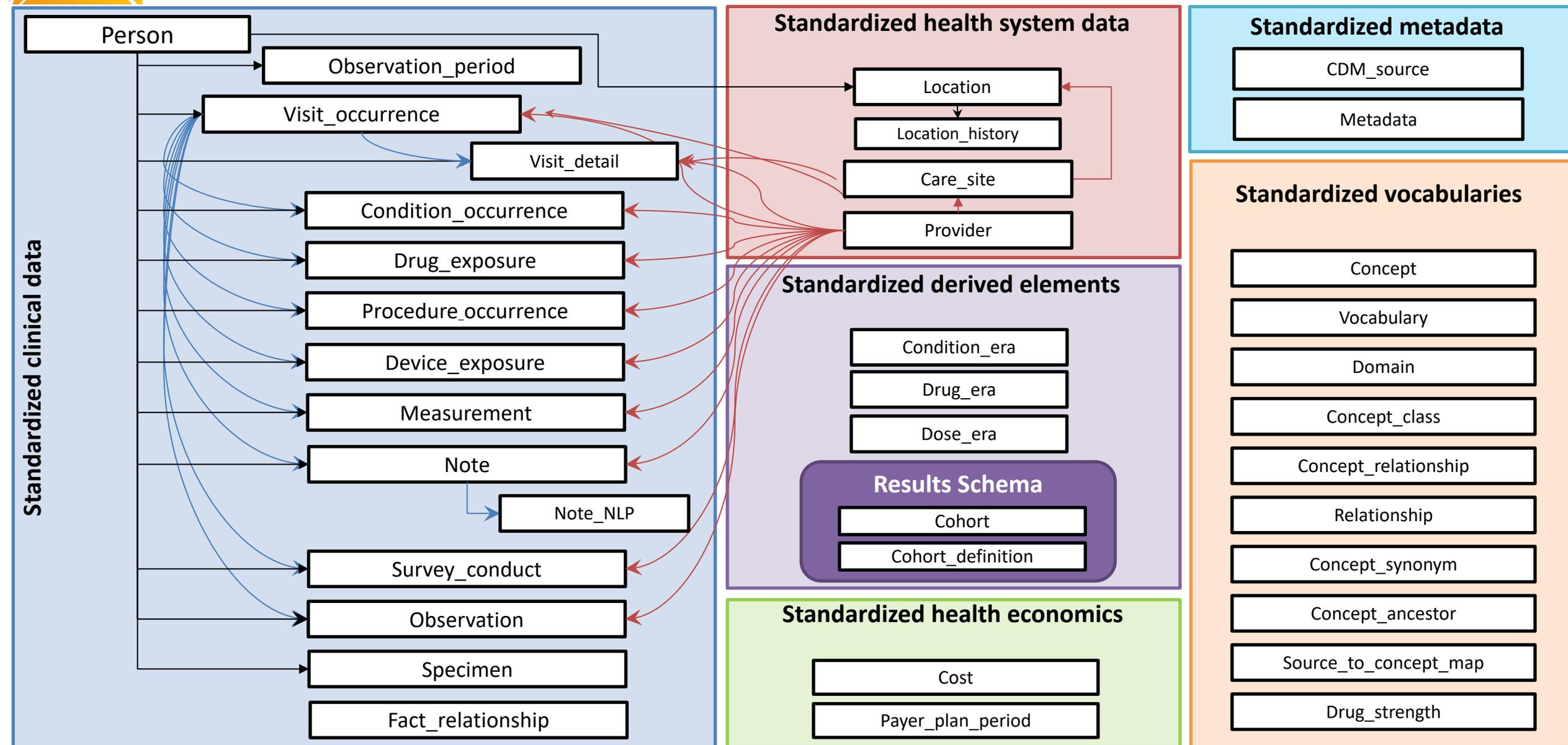
How OHDSI Works





Deep information model

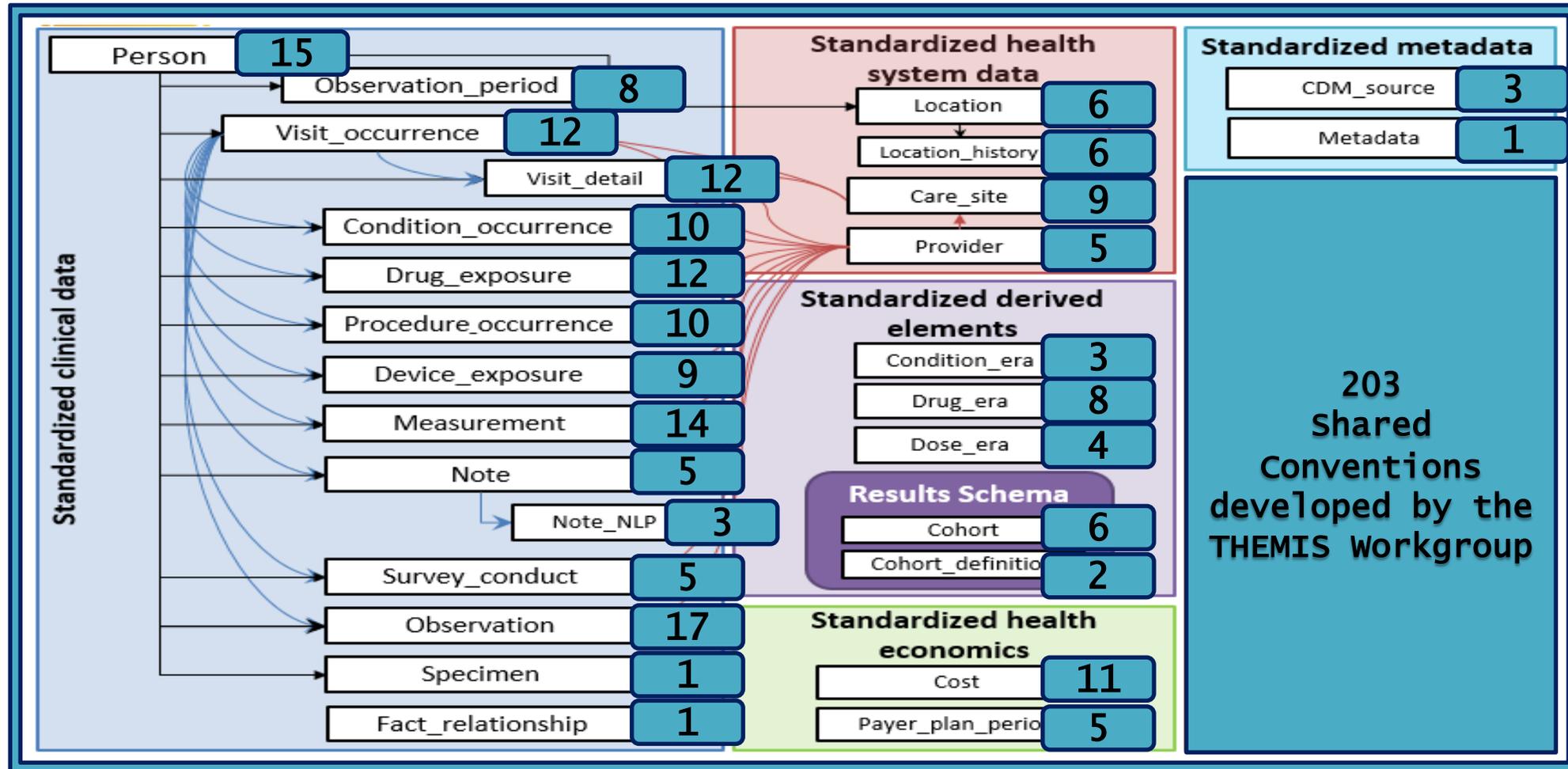
OMOP CDM Version 6





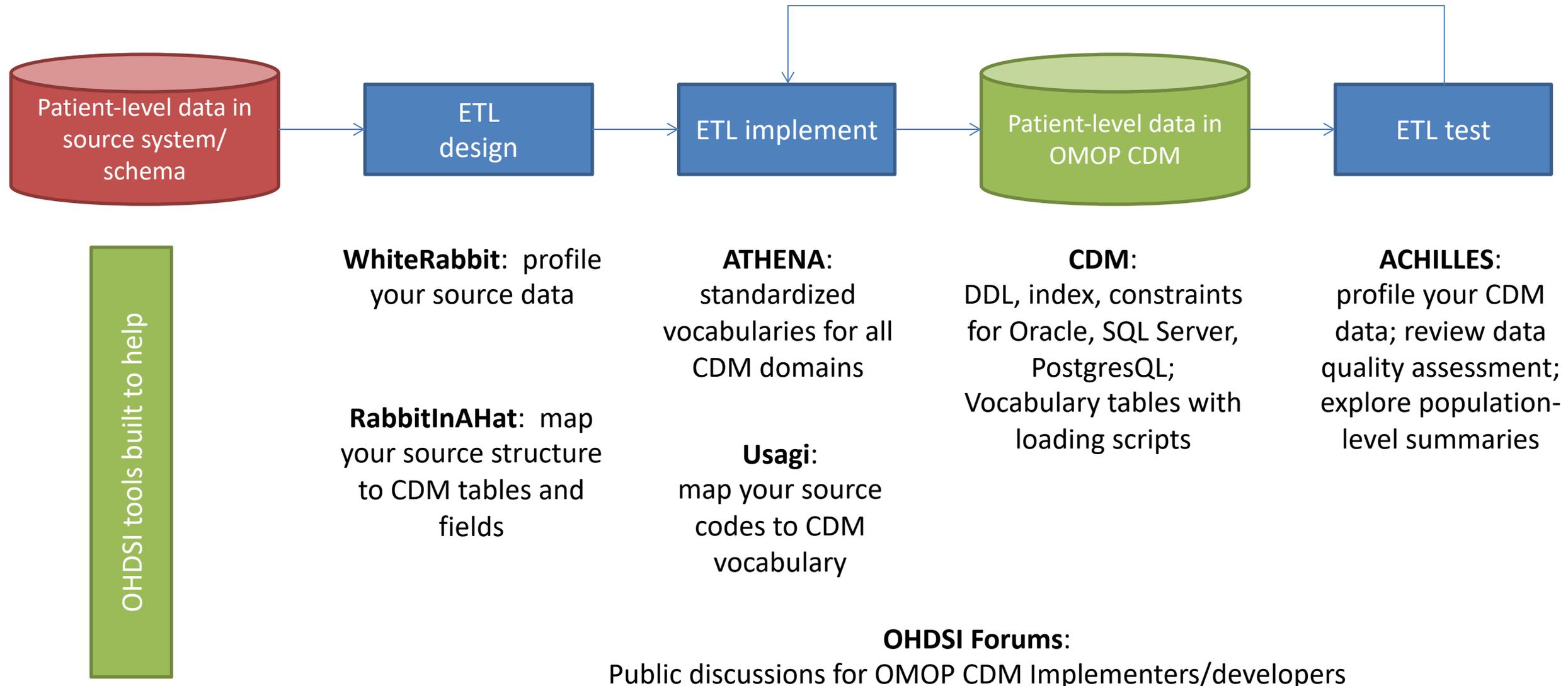
Standardized conventions

OHDSI adjusting to experience





Preparing your data for analysis



OHDSI tools built to help



ACHILLES Heel Data Curation

Data Quality Messages

Search:

Show / hide columns

Message Type

▲ Message



ERROR	101-Number of persons by age, with age at first observation period; should not have age < 0, (n=848)
ERROR	103 - Distribution of age at first observation period (count = 1); min value should not be negative
ERROR	114-Number of persons with observation period before year-of-birth; count (n=851) should not be > 0
ERROR	206 - Distribution of age by visit_concept_id (count = 7); min value should not be negative
ERROR	301-Number of providers by specialty concept_id; 224 concepts in data are not in correct vocabulary (Specialty)
ERROR	400-Number of persons with at least one condition occurrence, by condition_concept_id; 115 concepts in data are not in correct vocabulary (SNOMED)
ERROR	406 - Distribution of age by condition_concept_id (count = 753); min value should not be negative



ATLAS to build, visualize, and analyze cohorts

— People having any of the following: **Add Primary Criteria...**

a condition occurrence of **Delivery**

Add Criterion...

Delete

X occurrence start is: **Between** 2005-01-01 and 2013-12-31

X with age **Between** 18 and 55

X with a gender of: **X FEMALE** **Add** **Import**

with observation at least **180** days prior and **365** days after index

Limit primary events to: **All Events** per person.

For people matching the Primary Criteria, include:

— People having **All** of the following criteria: **Add New Criteria...**

with **At Least** **1** occurrences of:

Add Criterion...

a condition occurrence of **Depression**

occurring between **0** days **Before** and **180** days **After** index

Delete Criteria

and with **At Most** **0** occurrences of:

Add Criterion...

a condition occurrence of **Depression**

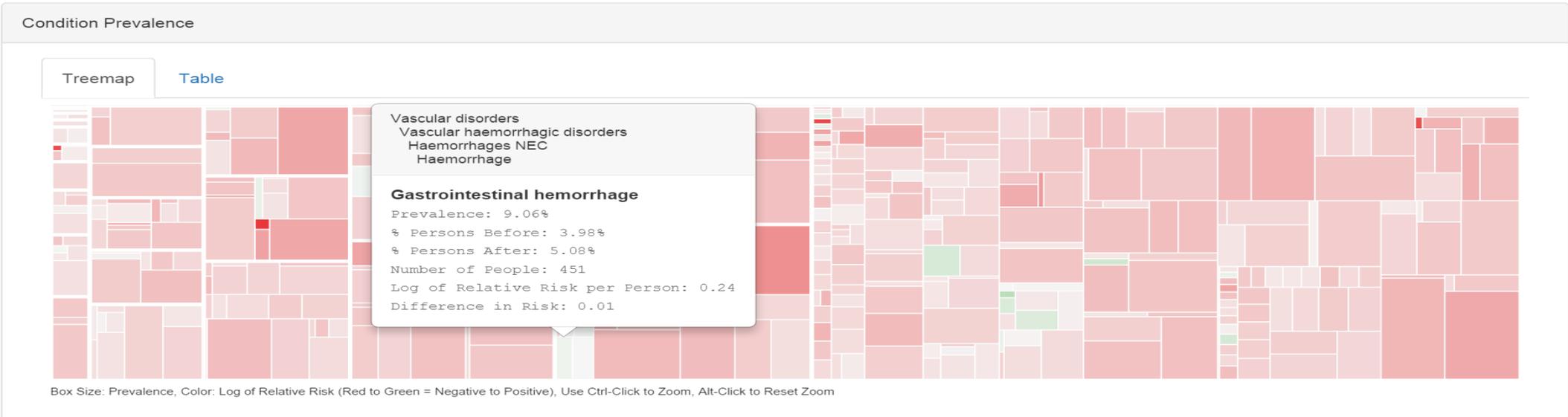
occurring between **All** days **Before** and **0** days **After** index

Delete Criteria



Characterize the cohorts of interest

Matching Population: MiniSentinel replication - warfarin new users



Drug Exposures

Drugs by Index

Heracles Heel

Measurements

Observation Periods

Observations

Person

Procedures

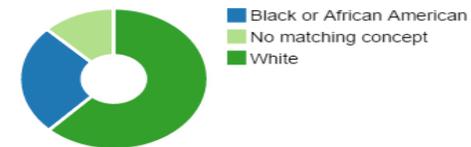
Procedures by Index

Visits

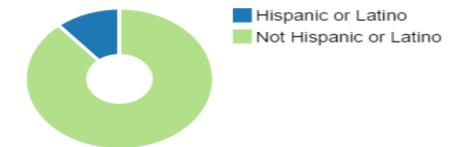
Population by Gender ↓



Population by Race ↓



Population by Ethnicity ↓





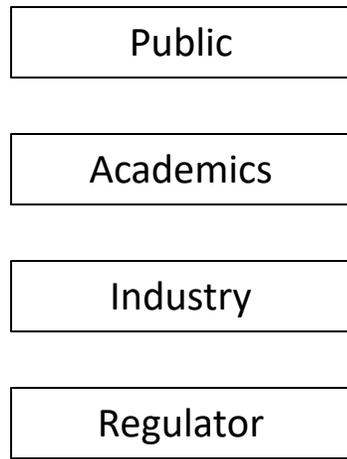
OHDSI in Action

- Characterization



Treatment Pathways

Global stakeholders



Evidence



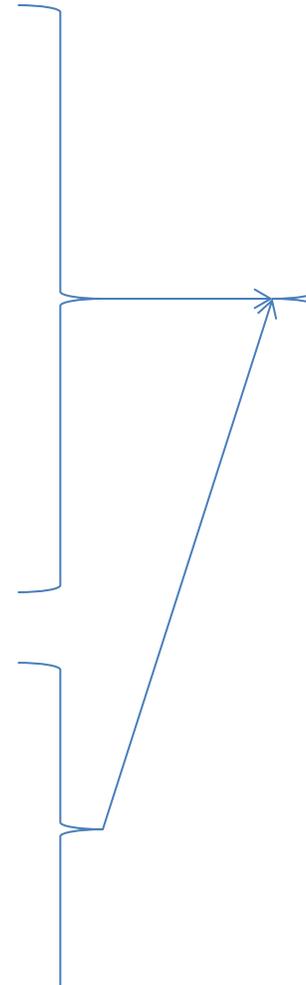
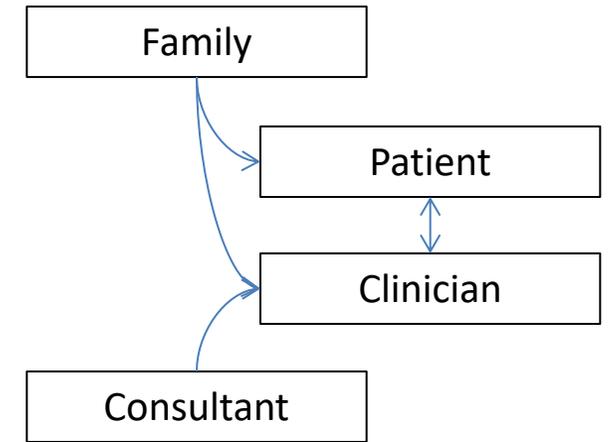
Conduits



Inputs



Local stakeholders





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



OHDSI participating data partners

Abbre- viation	Name	Description	Population, millions
AUSOM	Ajou University School of Medicine	South Korea; inpatient hospital EHR	2
CCAЕ	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



Characterizing treatment pathways at scale using the OHDSI network

George Hripcsak^{a,b,c,1}, Patrick B. Ryan^{c,d}, Jon D. Duke^{c,e}, Nigam H. Shah^{c,f}, Rae Woong Park^{c,g}, Vojtech Huser^{c,h}, Marc A. Suchard^{c,i,j,k}, Martijn J. Schuemie^{c,d}, Frank J. DeFalco^{c,d}, Adler Perotte^{a,c}, Juan M. Banda^{c,l}, Christian G. Reich^{c,l}, Lisa M. Schilling^{c,m}, Michael E. Matheny^{c,n,o}, Daniella Meeker^{c,p,q}, Nicole Pratt^{c,r}, and David Madigan^{c,s}

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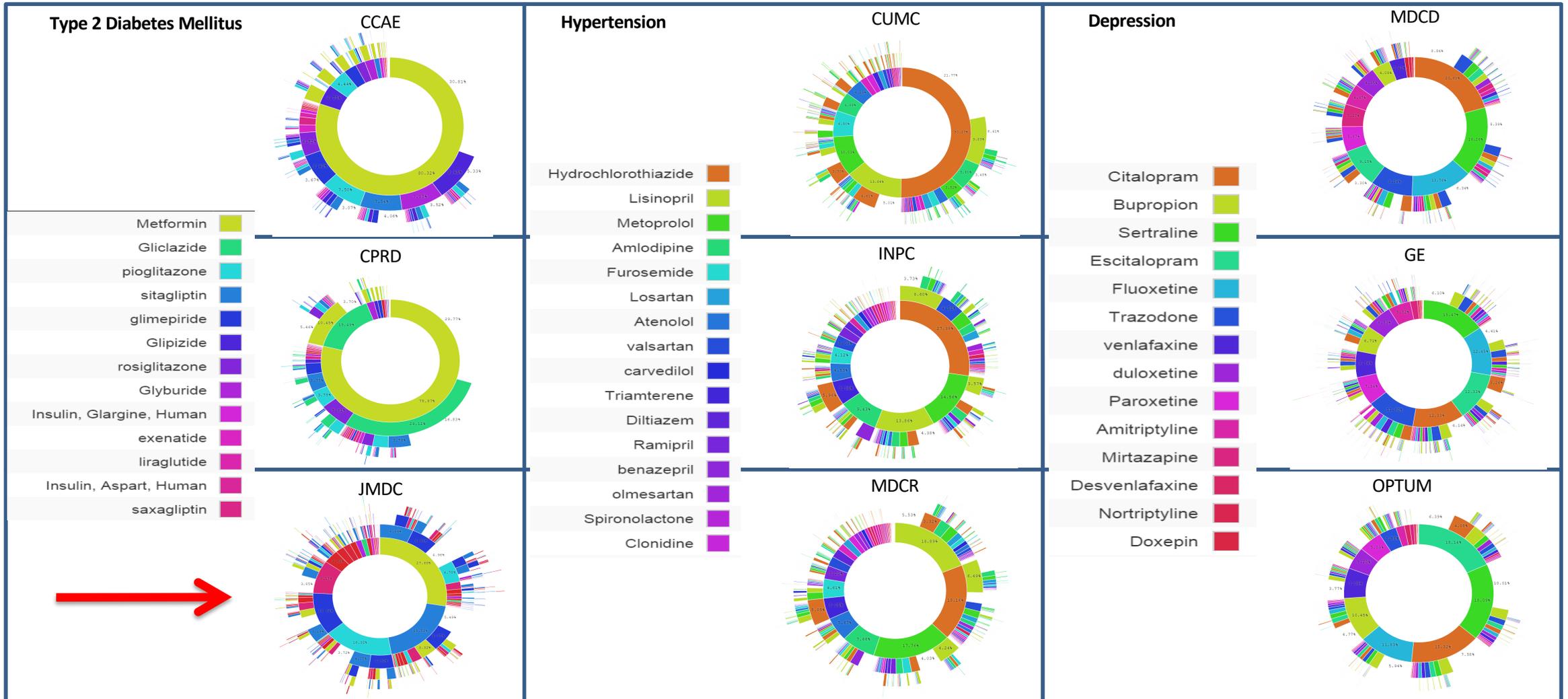
Edited by Richard M. Shiffrin, Indiana University, Bloomington, IN, and approved April 5, 2016 (received for review June 14, 2015)

Observational research promises to complement experimental research by providing large, diverse populations that would be infeasible for an experiment. Observational research can test its own clinical hypotheses, and observational studies also can contribute to the design of experiments and inform the generalizability of experimental research. Understanding the diversity of populations

Without sufficiently broad databases available in the first stage, randomized trials are designed without explicit knowledge of actual disease status and treatment practice. Literature reviews are restricted to the population choices of previous investigations, and pilot studies usually are limited in scope. By exploiting the ClinicalTrials.gov national trial registry (9) and electronic health



Population-level heterogeneity across systems, and patient-level heterogeneity within systems





Conclusions: Network research

- It is feasible to encode the world population in a single data model
- Generating evidence is feasible
- Stakeholders willing to share results
- Able to accommodate vast differences in privacy and research regulation



howoften.org

- Incidence of side effects
- Any drug on the world market
- Any condition
- Absolute risk
 - Not causal
(Characterization)
- On the Internet



How Often...

How often do patients get a condition after starting a drug?

Which drug are you interested in?

Which condition are you interested in?

[Go »](#) [Clear](#)

What this does

Use this tool to look up the proportion of people starting a drug who are newly diagnosed with a condition within 1 year of starting the drug. You can search for a specific drug-condition incidence by entering your drug and condition of interest in the fields above. Or, you can browse a list of conditions of potential interest by leaving the condition field blank, and you'll be shown conditions listed on the drug's product label.

What this does not do

This tool **does not** demonstrate that a drug causes a condition (i.e., that the condition is a side effect of the drug). Instead, for example, the condition may be part of the reason you are taking the drug, or the condition may just be common in the population.

This tool provides the overall observed risk in a population, but does not provide the attributable risk due to drug exposure. The results provided are raw unadjusted numbers for each diagnosis. The data made available through this site are for informational purposes only and are not a substitute for professional medical advice or services. You should not use this information for comparing drugs or making decisions related to diagnosing or treating a medical or health condition; instead, please consult a physician or healthcare professional in all matters related to your health.



OHDSI in Action

OHDSI is not just a data model
→ Methods development

What is the quality of the current evidence from observational analyses?



ORIGINAL CONTRIBUTION

JAMA

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
Christian C. Abnet, PhD
Marie M. Cantwell, PhD
Liam J. Murray, MD

Context Use of oral bisphosphonates has increased dramatically and elsewhere. Esophagitis is a known adverse effect of these drugs, and recent reports suggest a link between bisphosphonate use and esophageal cancer. This has not been robustly investigated.

Objective To investigate the association between bisphosphonate use and esophageal cancer.

Design, Setting, and Participants Data were extracted from the UK General Practice Research Database (GPRD) between 1995 and 2008. The study included 41 826 members in each cohort (81% were aged 11.4 years). One hundred sixteen esophageal or gastric cancers occurred in the bisphosphonate cohort and 115 (72%) in the control cohort. The incidence of esophageal and gastric cancer was 1.14 per 1000 person-years of risk in both the bisphosphonate and control cohorts. The incidence of esophageal cancer alone in the bisphosphonate cohort was 0.44 per 1000 person-years of risk, respectively. The incidence of esophageal and gastric cancer combined between the bisphosphonate and control cohorts was 0.96 (95% confidence interval [CI], 0.77-1.49). There was no difference in risk of cancer by duration of bisphosphonate intake.

Conclusion Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer.

Key Words: bisphosphonates, esophageal cancer, gastric cancer, observational study, UK General Practice Research Database

Abbreviations: GPRD, General Practice Research Database; CI, confidence interval

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BMJ

RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,¹ Gabriela Czanner, statistician,¹ Gillian Reeves, statistical epidemiologist,¹ Joanna Watson, epidemiologist,¹ Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,² Valerie Beral, professor of cancer epidemiology¹

ABSTRACT

Objective To examine the hypothesis that risk of oesophageal, but not of gastric or colorectal, cancer is increased in users of oral bisphosphonates.

Design Nested case-control analysis within a primary care cohort of about 6 million people in the UK, with prospectively recorded information on prescribing of bisphosphonates.

Setting UK General Practice Research Database cohort.
Participants Men and women aged 40 years or over—2954 with oesophageal cancer, 2018 with gastric cancer, and 10 641 with colorectal cancer, diagnosed in 1995-2005; five controls per case matched for age, sex, general practice, and observation time.

Main outcome measures Relative risks for incident invasive cancers of the oesophagus, stomach, and colorectum, adjusted for smoking, alcohol, and body mass index.

Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In Europe and North America, the incidence of oesophageal cancer at age 60-79 is typically 1 per 1000 population over five years, and this is estimated to increase to about 2 per 1000 with five years' use of oral bisphosphonates.

INTRODUCTION

Adverse gastrointestinal effects are common among people who take oral bisphosphonates for the prevention and treatment of osteoporosis; they range from dyspepsia, nausea, and abdominal pain to erosive oesophagitis and oesophageal ulcers.¹ Recent case reports have suggested a possible increase in the risk of oesophageal cancer with use of such bisphosphonate preparations.² We report here on the relation between prospectively recorded prescribing information for

August 2010: "Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer"

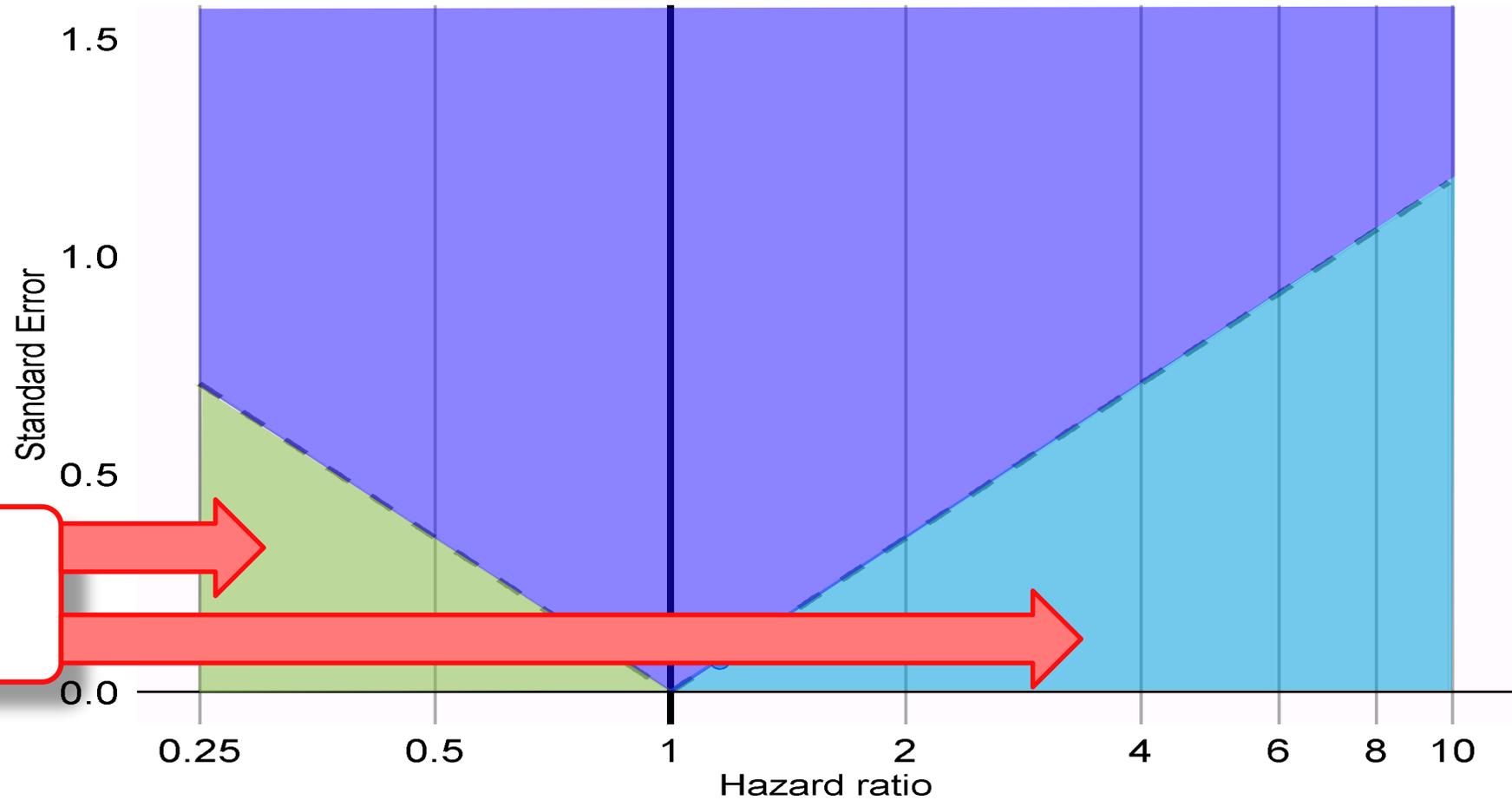
Sept 2010: "In this large nested case-control study within a UK cohort [General Practice Research Database], we found a significantly increased risk of oesophageal cancer in people with previous prescriptions for oral bisphosphonates"

corticosteroids. Cancers of the stomach and colorectum were not associated with prescription of bisphosphonate: relative risks for one or more versus no prescriptions were 0.87 (0.64 to 1.19) and 0.87 (0.77 to 1.00). The specificity

style data. General Practice Research Database prescription data have been shown to be virtually complete, and the data on incidence of cancer (based on hospital records) are around 95% valid and



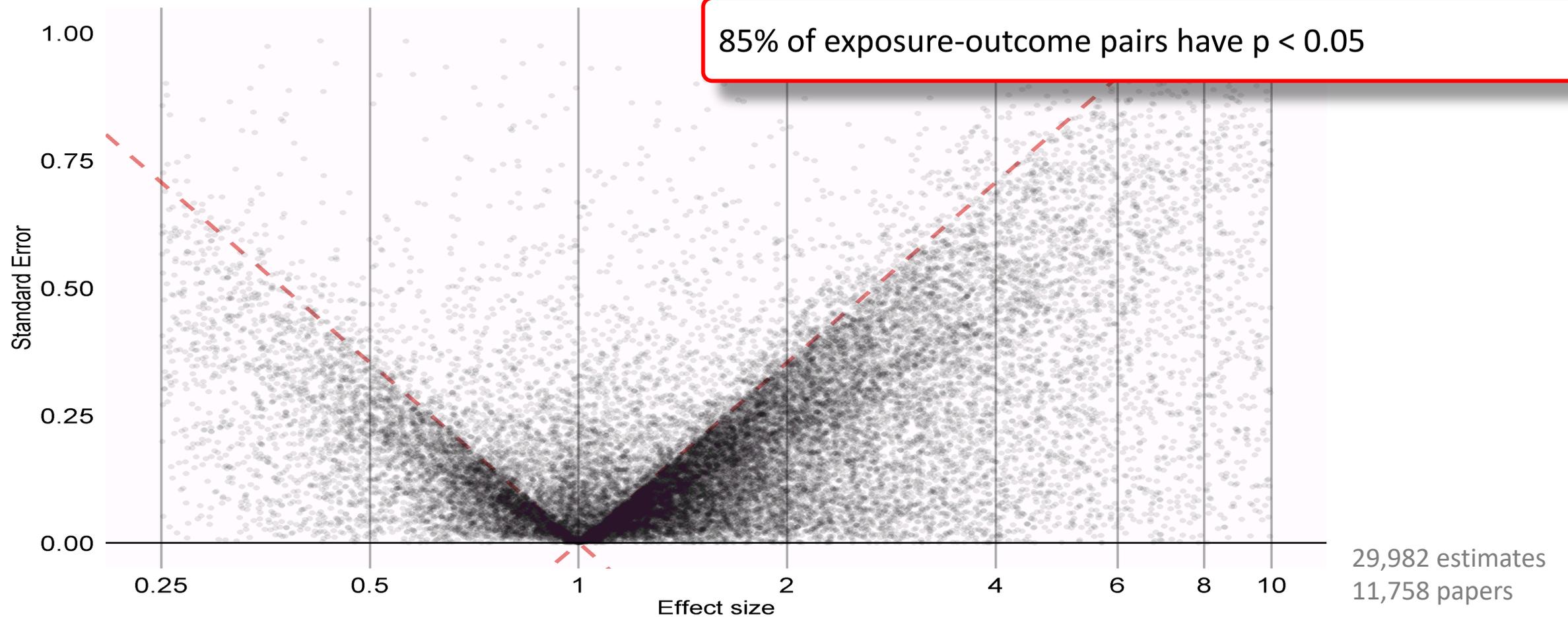
Standard error vs effect size



Statistically significant



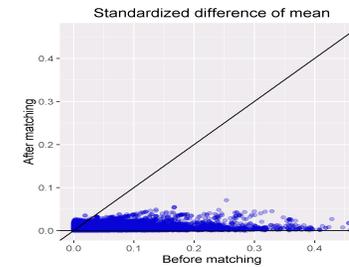
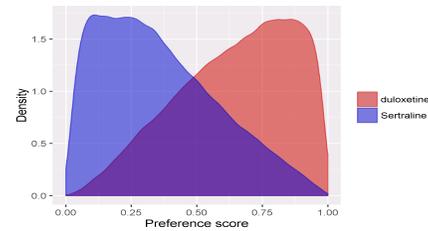
Observational research results in literature



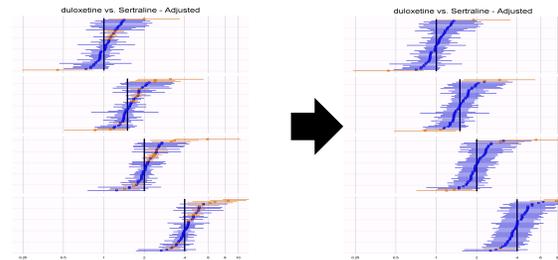
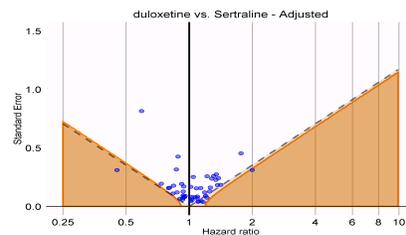


Addressing reproducibility

1. Propensity stratification with *systematic* variable selection: measured confounding



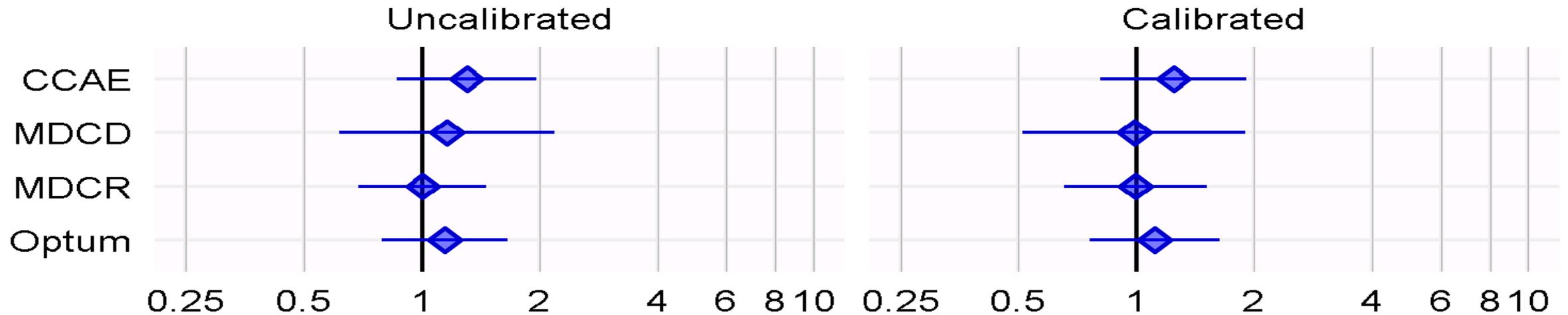
2. Confidence interval calibration using negative controls: unmeasured confounding





Addressing reproducibility

3. **Multiple** databases, locations, practice types



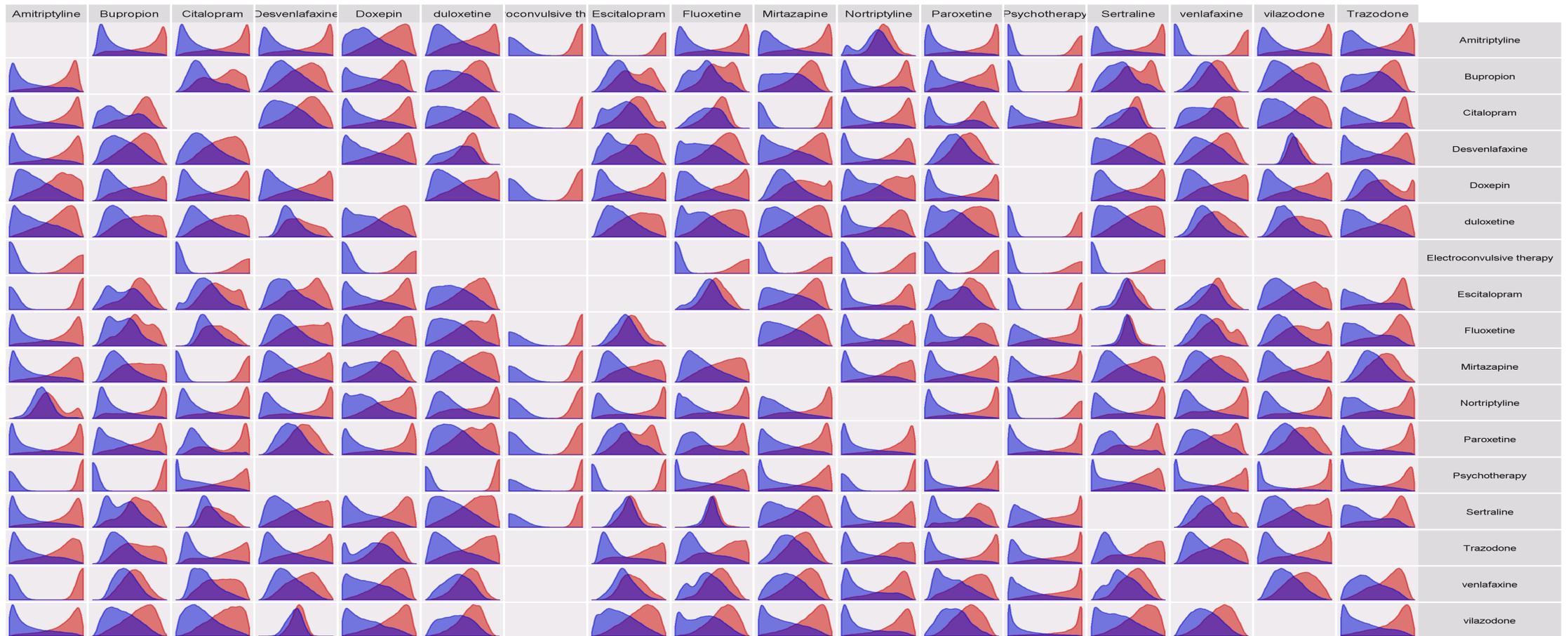
4. Publish **all** hypotheses, code, parameters, runs

`URL ~ 1000`



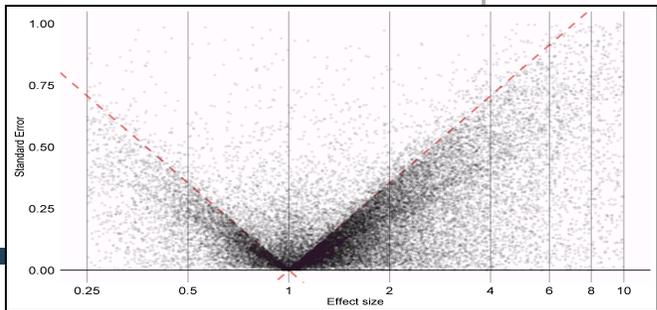
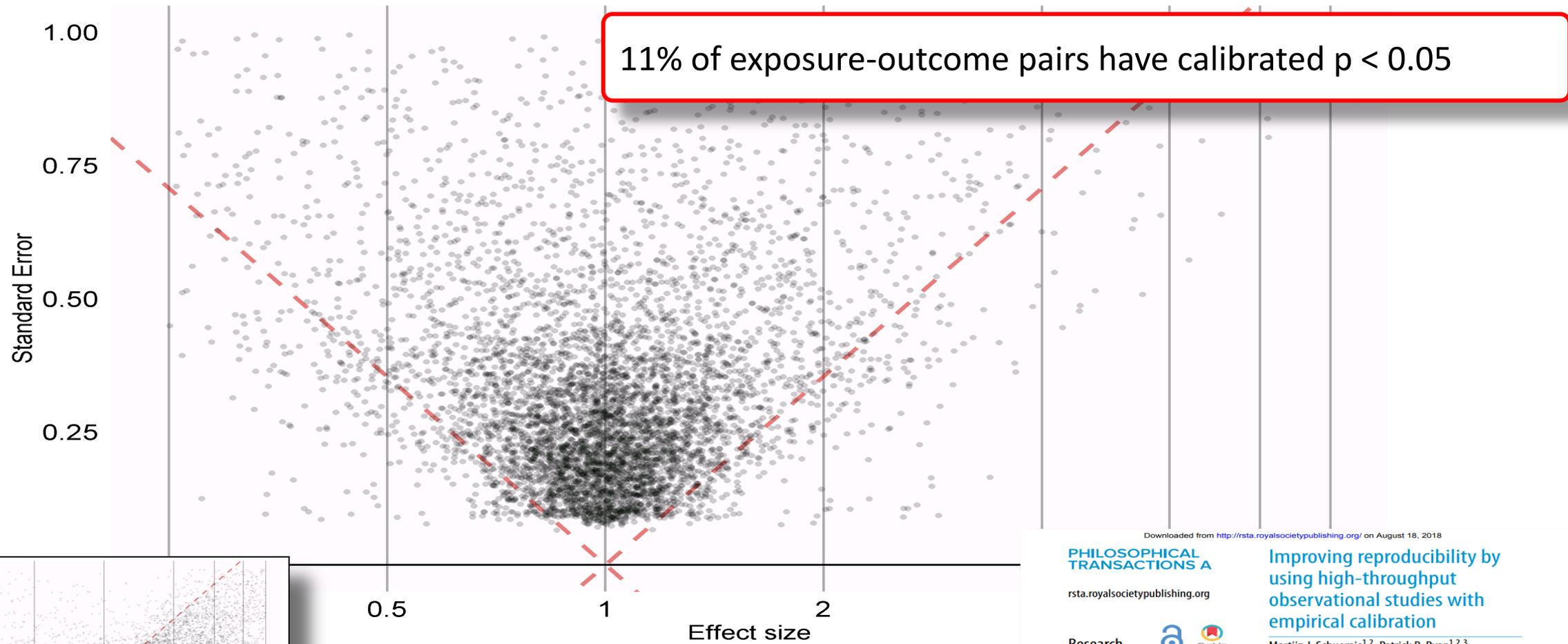
Addressing reproducibility

5. Carry out on aligned hypotheses at scale





Estimates are in line with expectations



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PHILOSOPHICAL
TRANSACTIONS A

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Research



Cite this article: Schuemie MJ, Ryan PB, Hripcsak G, Madigan D, Suchard MA. 2018 Improving reproducibility by using high-throughput observational studies with empirical calibration. *Phil. Trans. R. Soc. A* **376**: 20170356. <http://dx.doi.org/10.1098/rsta.2017.0356>

Accepted: 8 May 2018

Improving reproducibility by using high-throughput observational studies with empirical calibration

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¹Observational Health Data Sciences and Informatics (OHDSI), New York, NY 10032, USA

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³Department of Biomedical Informatics, Columbia University Medical Center, New York, NY 10032, USA



OHDSI LEGEND Hypertension Study

OHDSI is not just a data model
Not just methods development
→ Evidence generation



What's in a guideline?

Clinical Practice Guideline: Executive Summary

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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Jeff D. W... , PhD, FAHA##

56 pages
containing

106 recommendations

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8.1.6. Choice of Initial Medication

Recommendation for Choice of Initial Medication

References that support the recommendation are summarized in **Online Data Supplement 27** and **Systematic Review Report**.

COR	LOE	Recommendation
I	A ^{SR}	1. For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. ^{S8.1.6-1,S8.1.6-2}

SR indicates systematic review.

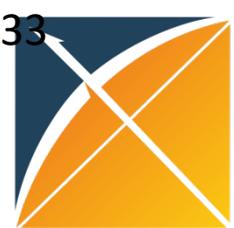


Table 18. Oral Antihypertensive Drugs

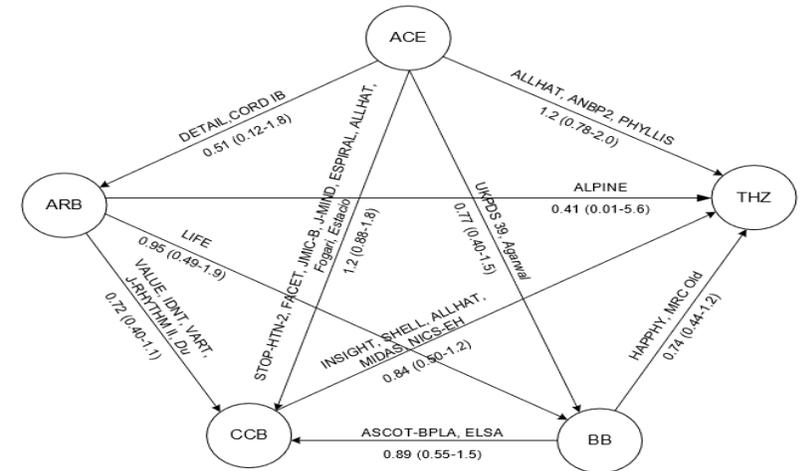
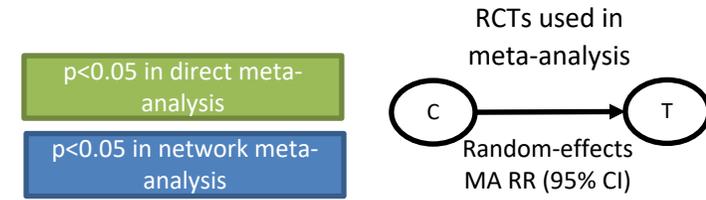
Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Primary agents				
Thiazide or thiazide-type diuretics	Chlorthalidone	12.5–25	1	<ul style="list-style-type: none"> Chlorthalidone is preferred on the basis of prolonged half-life and proven trial reduction of CVD. Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. Use with caution in patients with history of acute gout unless patient is on uric acid–lowering therapy.
	Hydrochlorothiazide	25–50	1	
	Indapamide	1.25–2.5	1	
	Metolazone	2.5–10	1	
ACE inhibitors	Benazepril	10–40	1 or 2	<ul style="list-style-type: none"> Do not use in combination with ARBs or direct renin inhibitor. There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K⁺ supplements or K⁺-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema. ACE inhibitors. Avoid in pregnancy.
	Captopril	12.5–150	2 or 3	
	Enalapril	5–40	1 or 2	
	Fosinopril	10–40	1	
	Lisinopril	10–40	1	
	Moexipril	7.5–30	1 or 2	
	Perindopril	4–16	1	
	Quinapril	10–80	1 or 2	
	Ramipril	2.5–10	1 or 2	
Trandolapril	1–4	1		
ARBs	Azilsartan	40–80	1	<ul style="list-style-type: none"> Do not use in combination with ACE inhibitors or direct renin inhibitor. There is an increased risk of hyperkalemia in those on K⁺ supplements or K⁺-sparing diuretics. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema. Patients with a history of angioedema with ACE inhibitors can receive an ARB 1–2 weeks after ACE inhibitor is discontinued. Avoid in pregnancy.
	Candesartan	8–32	1	
	Eprosartan	600–800	1 or 2	
	Irbesartan	150–300	1	
	Losartan	50–100	1 or 2	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–320	1	
CCB—dihydropyridines	Amlodipine	2.5–10	1	<ul style="list-style-type: none"> Avoid use in patients with HFrEF; amlodipine may be used if required. felodipine may be used if required. They are associated with dose-related edema, which is more common in women.
	Felodipine	5–10	1	
	Isradipine	5–10	2	
	Nicardipine SR	5–20	1	
	Nifedipine LA	60–120	1	
	Nisoldipine	30–90	1	
CCB—nondihydropyridines	Diltiazem SR	180–360	2	<ul style="list-style-type: none"> Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. Do not use in patients with HFrEF. There are drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).
	Diltiazem ER	120–480	1	
	Verapamil IR	40–80	3	
	Verapamil SR	120–480	1 or 2	
	Verapamil-delayed onset ER (various forms)	100–480	1 (in the evening)	

Only **29** different drugs in **5** different classes to choose from!

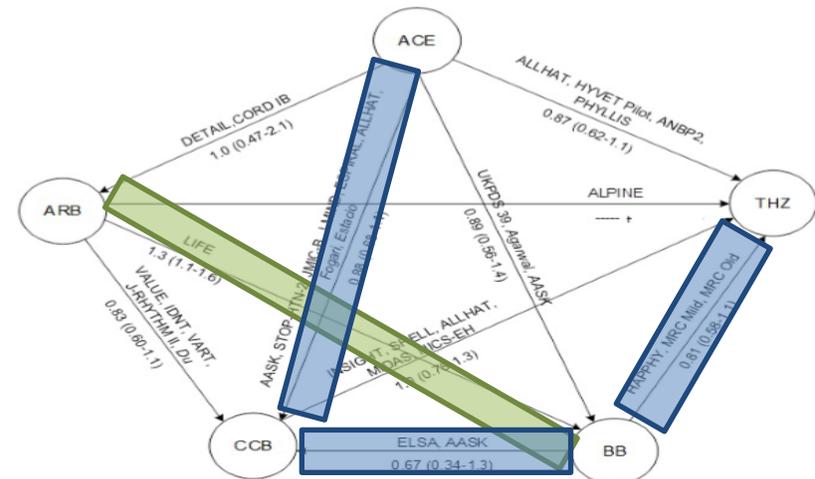
Distinguished from **28** drugs in **12** other classes that are classified as potential secondary agents (including Beta Blockers)



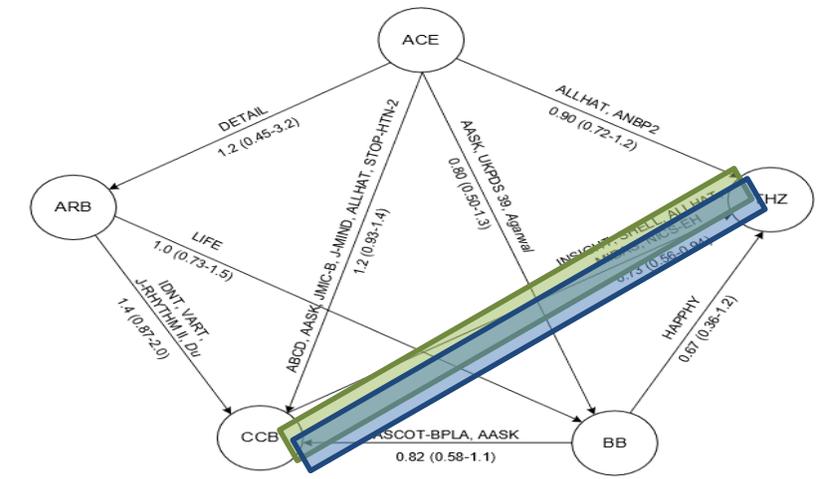
RCT evidence about comparative effectiveness for cardiovascular outcomes



Myocardial infarction



Stroke



Heart failure

- 8/10 DMA comparisons cannot rule out possibility of 2x risk

- 1/10 DMA comparisons cannot rule out possibility of 2x risk

- 4/10 DMA comparisons cannot rule out possibility of 2x risk



58 outcomes of interest

Abdominal pain	Dementia	Ischemic stroke
Abnormal weight gain	Depression	Kidney disease
Abnormal weight loss	Diarrhea	Malignant neoplasm
Acute myocardial infarction	Edema	Measured renal dysfunction
Acute pancreatitis	End stage renal disease	Nausea
Acute renal failure	Fall	Neutropenia or agranulocytosis
All-cause mortality	Gastrointestinal bleeding	Rash
Anaphylactoid reaction	Gout	Rhabdomyolysis
Anemia	Headache	Stroke
Angioedema	Heart failure	Sudden cardiac death
Anxiety	Hemorrhagic stroke	Syncope
Bradycardia	Hepatic failure	Thrombocytopenia
Cardiac arrhythmia	Hospitalization with heart failure	Transient ischemic attack
Cardiovascular disease	Hospitalization with preinfarction syndrome	Type 2 diabetes mellitus
Cardiovascular-related mortality	Hyperkalemia	Vasculitis
Chest pain or angina	Hypokalemia	Venous thromboembolic events
Chronic kidney disease	Hypomagnesemia	Vertigo
Coronary heart disease	Hyponatremia	Vomiting
Cough	Hypotension	
Decreased libido	Impotence	

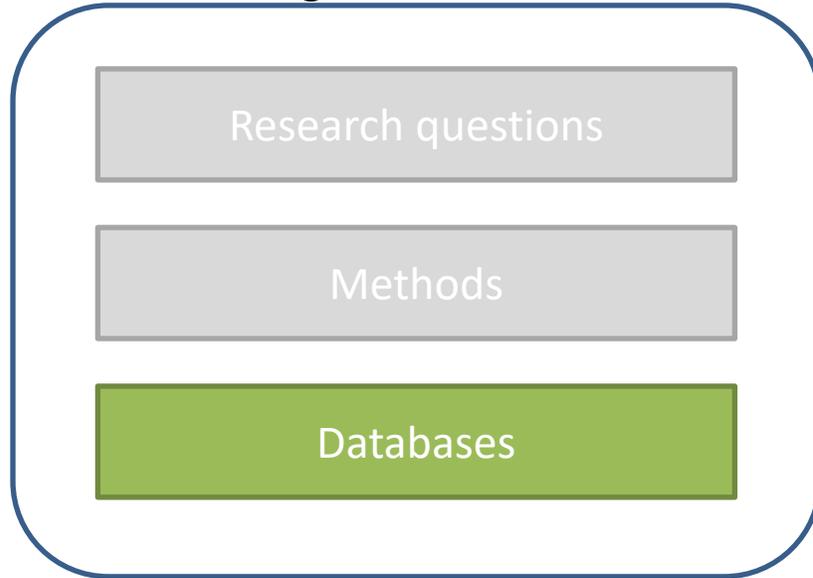


76 negative controls

Abnormal cervical smear
Abnormal pupil
Abrasion and/or friction burn of trunk without infection
Absence of breast
Absent kidney
Acid reflux
Acquired hallux valgus
Acquired keratoderma
Acquired trigger finger
Acute conjunctivitis
Amputated foot
Anal and rectal polyp
Burn of forearm
Calcaneal spur
Cannabis abuse
Cervical somatic dysfunction
Changes in skin texture
Chondromalacia of patella
Cocaine abuse
Colostomy present
Complication due to Crohn's disease
Contact dermatitis
Contusion of knee
Crohn's disease
Derangement of knee
Difficulty sleeping
Disproportion of reconstructed breast
Effects of hunger
Endometriosis
Epidermoid cyst
Feces contents abnormal
Foreign body in orifice
Ganglion cyst
Genetic predisposition
Hammer toe
Hereditary thrombophilia
Herpes zoster without complication
High risk sexual behavior
Homocystinuria
Human papilloma virus infection
Ileostomy present
Impacted cerumen
Impingement syndrome of shoulder region
Ingrowing nail
Injury of knee
Irregular periods
Kwashiorkor
Late effect of contusion
Late effect of motor vehicle accident
Leukorrhea
Macular drusen
Melena
Nicotine dependence
Noise effects on inner ear
Nonspecific tuberculin test reaction
Non-toxic multinodular goiter
Onychomycosis due to dermatophyte
Opioid abuse
Passing flatus
Postviral fatigue syndrome
Presbyopia
Problem related to lifestyle
Psychalgia
Ptotic breast
Regular astigmatism
Senile hyperkeratosis
Somatic dysfunction of lumbar region
Splinter of face, without major open wound
Sprain of ankle
Strain of rotator cuff capsule
Tear film insufficiency
Tobacco dependence syndrome
Vaginitis and vulvovaginitis
Verruca vulgaris
Wrist joint pain
Wristdrop

Databases

Evidence generation



- US insurance databases
 - IBM® MarketScan® CCAE
 - IBM® MarketScan® MDCD
 - IBM® MarketScan® MDCR
 - Optum® Clinformatics®
- Japanese insurance database
 - Japan Medical Data Center
- Korean national insurance database
 - NHIS-NSC
- US EHR databases
 - Columbia University Medical Center
 - Optum® PANTHER®
- German EHR database
 - QuintilesIMS Disease Analyzer (DA) Germany



Ajou University



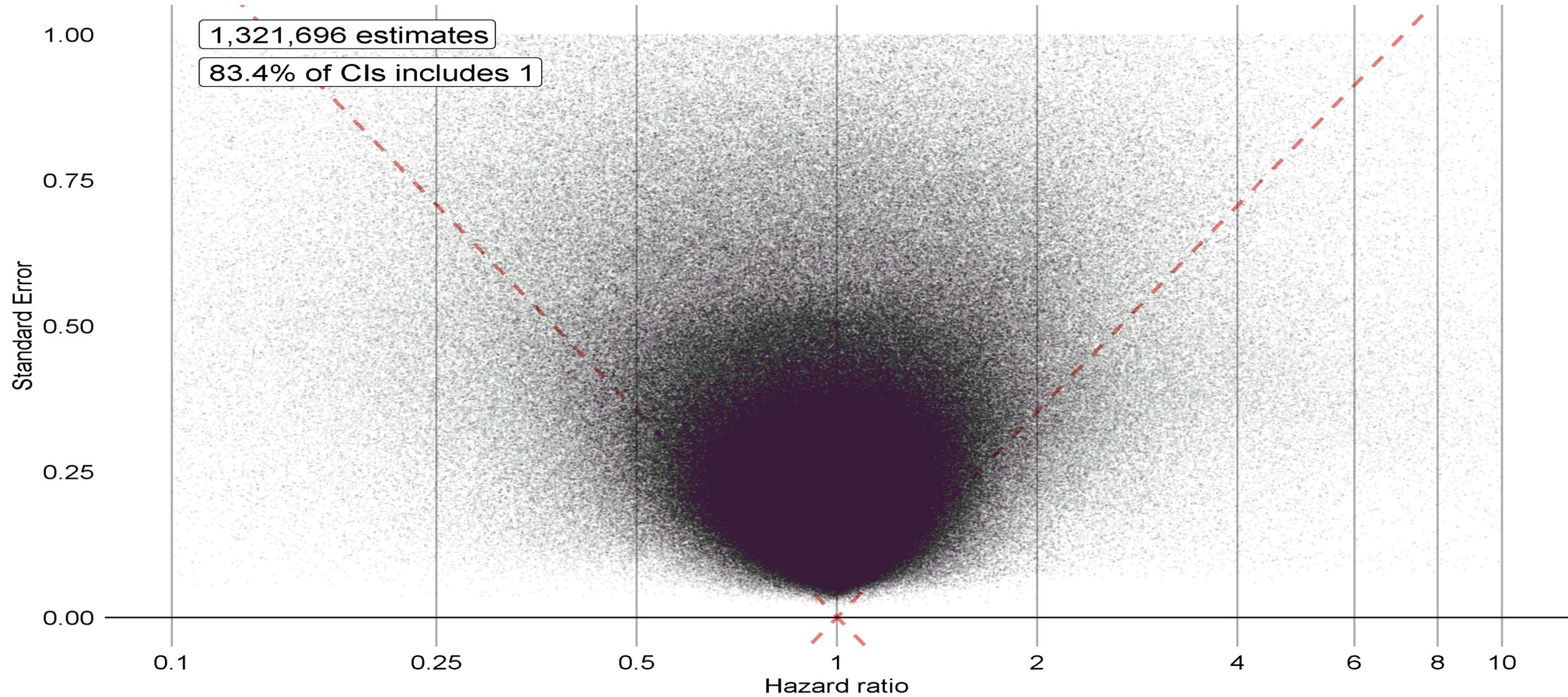
Columbia University

Comparisons of hypertension treatments

	Theoretical	Observed (n > 2,500)
Single ingredients	58	39
Single ingredient comparisons	$58 * 57 = 3,306$	1,296
Single drug classes	15	13
Single class comparisons	$15 * 14 = 210$	156
Dual ingredients	$58 * 57 / 2 = 1,653$	58
Single vs duo drug comparisons	$58 * 1,653 = 95,874$	3,810
Dual classes	$15 * 14 / 2 = 105$	32
Single vs duo class comparisons	$15 * 105 = 1,575$	832
Duo vs duo drug comparisons	$1,653 * 1,652 = 2,730,756$	2,784
Duo vs duo class comparisons	$105 * 104 = 10,920$	992
...
Total comparisons	2,843,250	10,278
Outcomes of interest	58	58
Target-comparator-outcomes	$2,843,250 * 58 = 164,908,500$	587,020

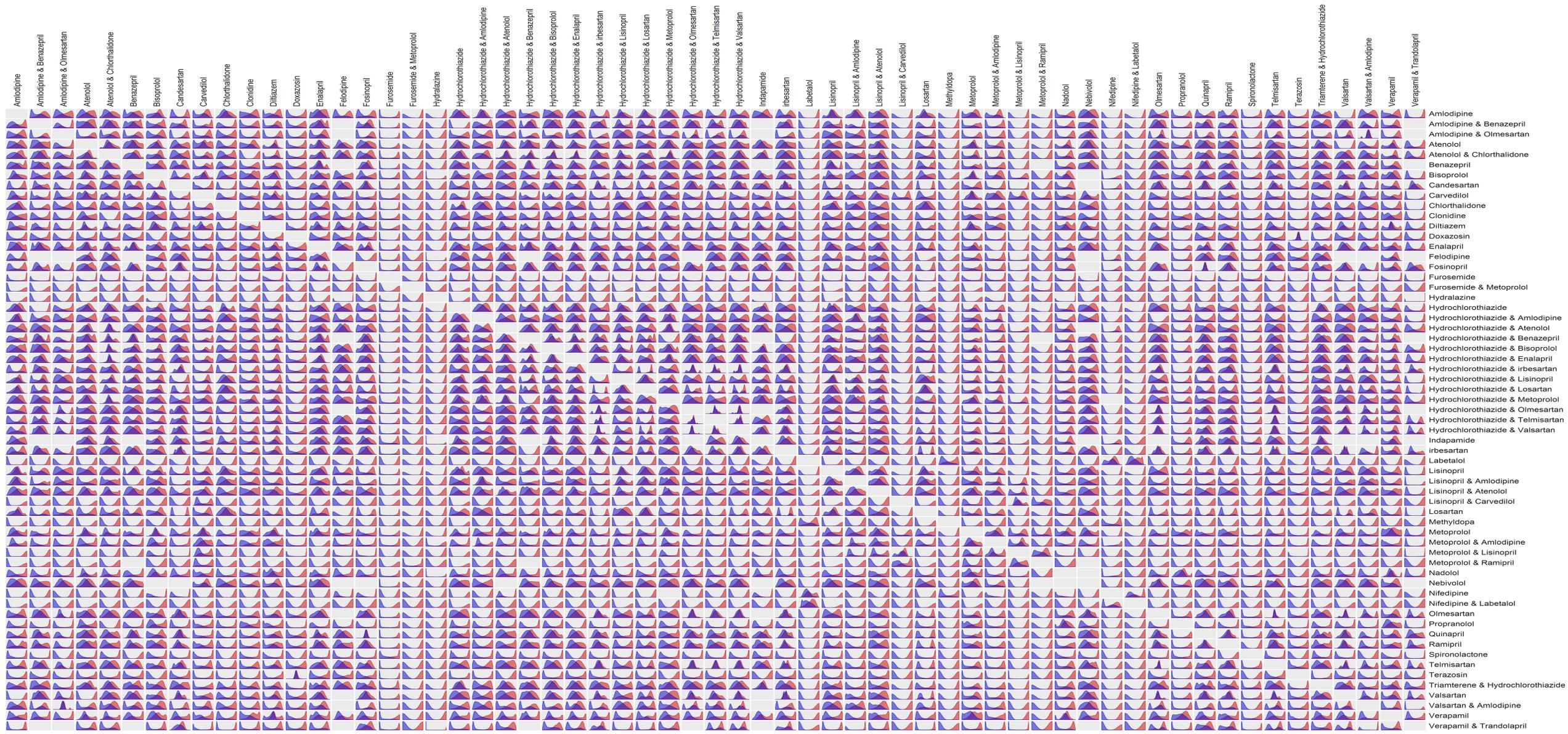


LEGEND results



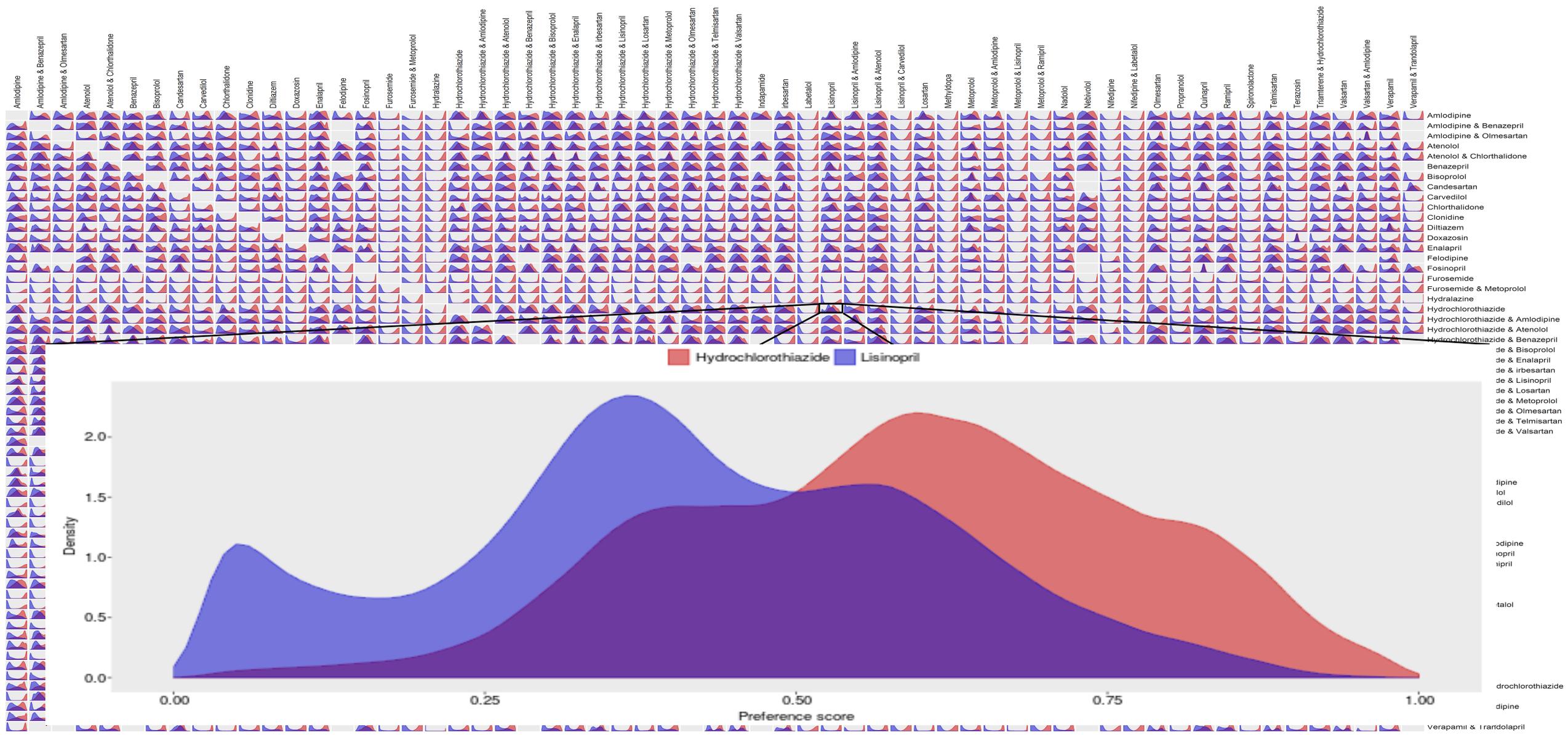


Not all comparisons are valid

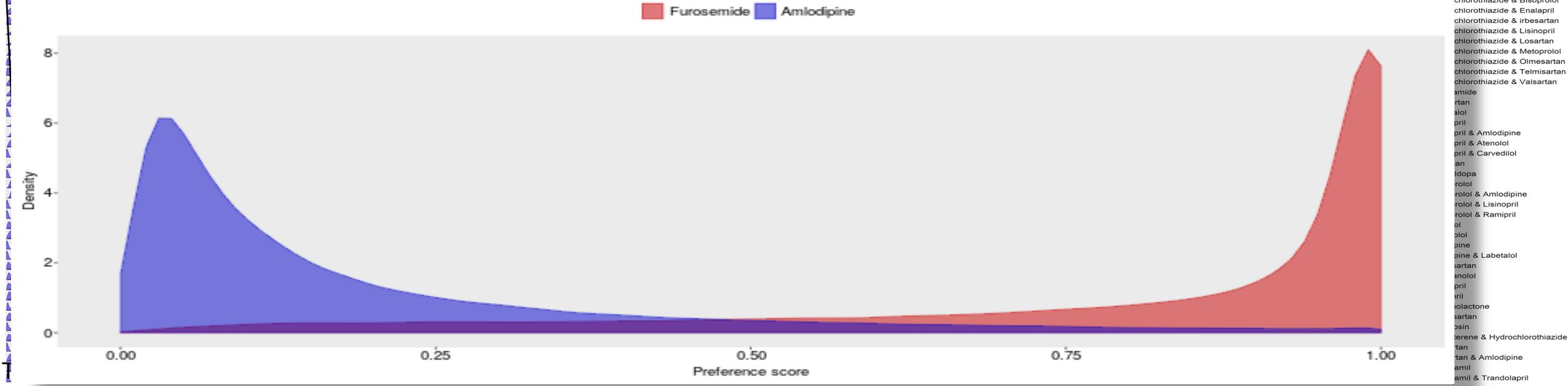
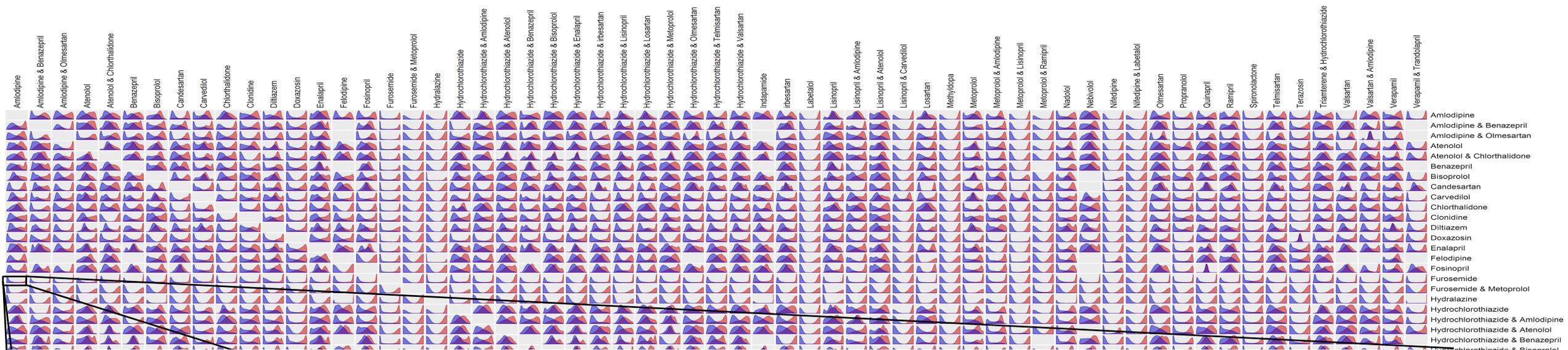




Not all comparisons are valid



Not all comparisons are valid

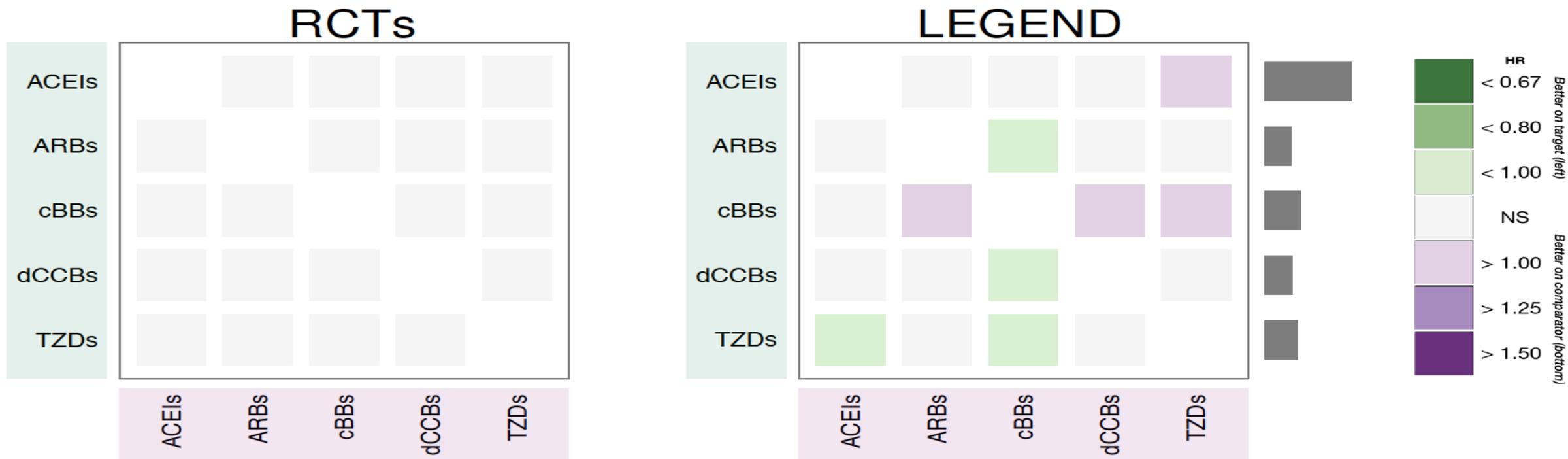


- Amlodipine
- Amlodipine & Benazepril
- Amlodipine & Olmesartan
- Atenolol
- Atenolol & Chlorthalidone
- Benazepril
- Bisoprolol
- Candesartan
- Carvedilol
- Chlorthalidone
- Clonidine
- Diltiazem
- Doxazosin
- Enalapril
- Felodipine
- Fosinopril
- Furosemide
- Furosemide & Metoprolol
- Hydralazine
- Hydrochlorothiazide
- Hydrochlorothiazide & Amlodipine
- Hydrochlorothiazide & Atenolol
- Hydrochlorothiazide & Benazepril
- Hydrochlorothiazide & Bisoprolol
- Hydrochlorothiazide & Enalapril
- Hydrochlorothiazide & Irbesartan
- Hydrochlorothiazide & Lisinopril
- Hydrochlorothiazide & Losartan
- Hydrochlorothiazide & Metoprolol
- Hydrochlorothiazide & Olmesartan
- Hydrochlorothiazide & Telmisartan
- Hydrochlorothiazide & Valsartan
- Indapamide
- Irbesartan
- Labelalol
- Lisinopril
- Lisinopril & Amlodipine
- Lisinopril & Atenolol
- Lisinopril & Carvedilol
- Losartan
- Methyldopa
- Metoprolol
- Metoprolol & Amlodipine
- Metoprolol & Lisinopril
- Metoprolol & Ramipril
- Nadolol
- Nebivololol
- Nifedipine
- Nifedipine & Labetalol
- Olmesartan
- Propranolol
- Quinapril
- Ramipril
- Spirinolactone
- Telmisartan
- Terazosin
- Triamterene & Hydrochlorothiazide
- Valsartan
- Valsartan & Amlodipine
- Verapamil
- Verapamil & Trandolapril



First-line agents: comparisons from LEGEND

Efficacy outcome: **myocardial infarction**, heart failure, stroke

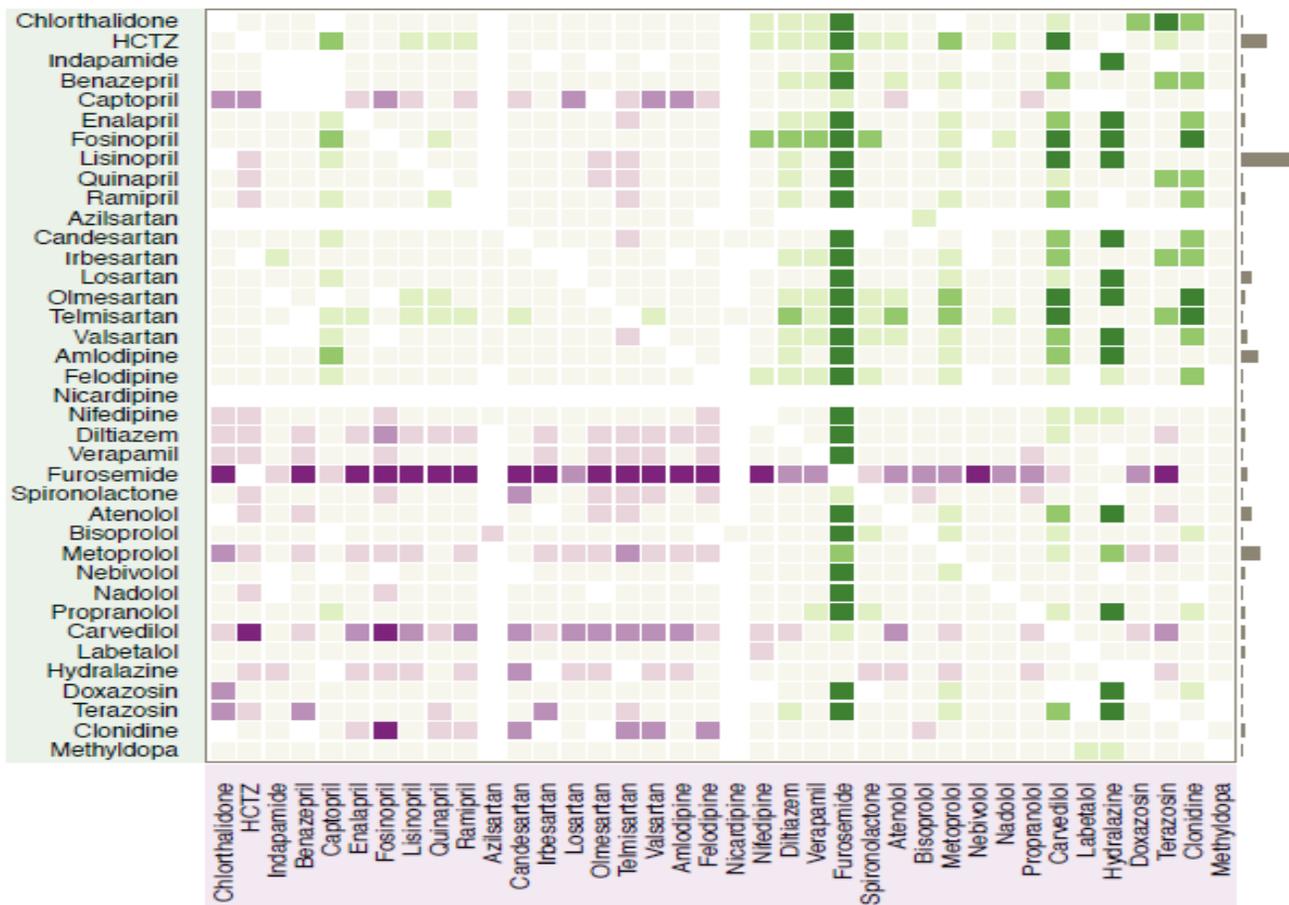


Data source: meta-analysis, ~ 1 – 2M total patients per study

- Beta blockers underperform alternatives
- Unexpected: TZDs > ACEIs. Reliable?



Cardiovascular efficacy by drug



Prescriptions are not written at the class-level; must choose an individual drug for the patient

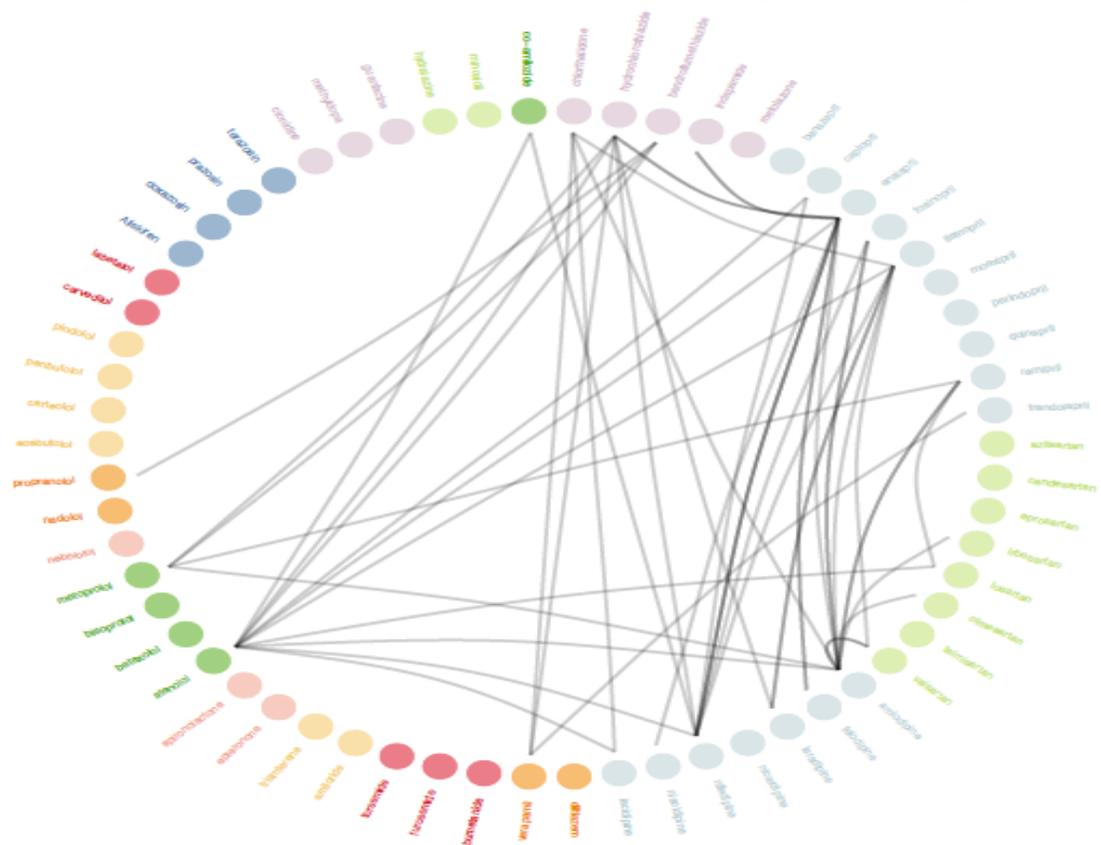
- 1st-line > 2nd-line
- Some within-class differences failed diagnostics, e.g. captopril

Composite (MI, HF, stroke) outcome in meta-analysis

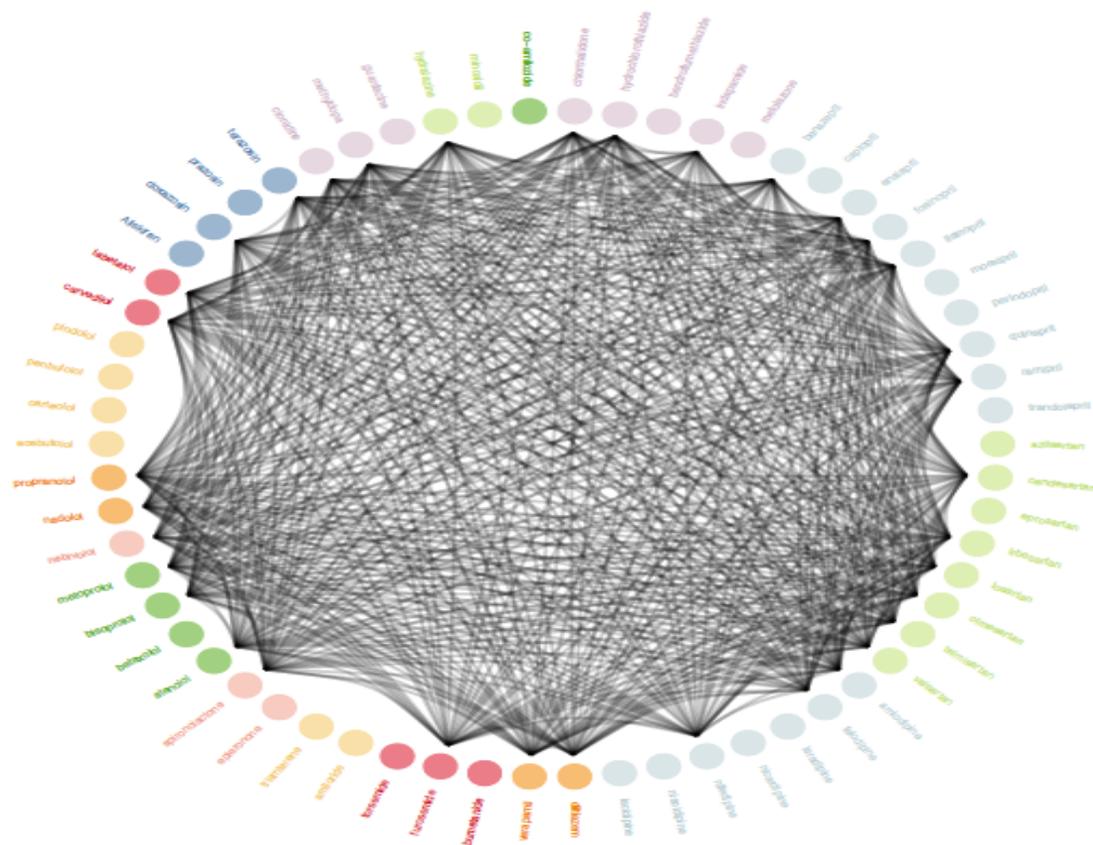


LEGEND knowledge base for hypertension

Head-to-head HTN drug comparisons



- Trials: 40
- $N = 102 - [1148] - 33K$



- Comparisons: 10,278
- $N = 3502 - [212K] - 1.9M$



Clinical lessons for hypertension

LEGEND evidence is concordant with RCTs:

- Where RCT results exist, but many unanswered questions remains
- More outcomes, comparisons, data sources

Not all 1st-line agents are equivalent:

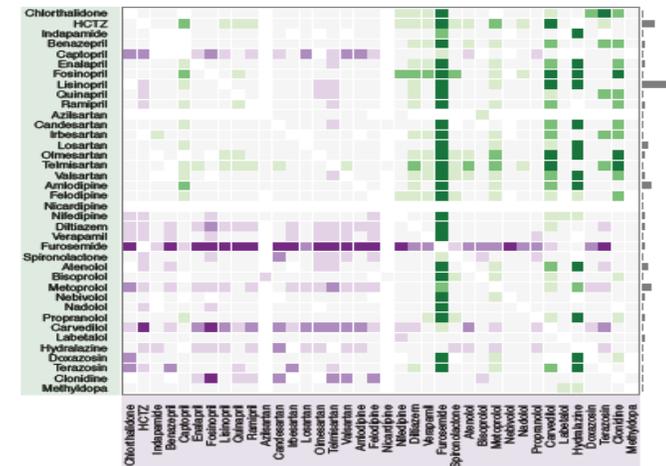
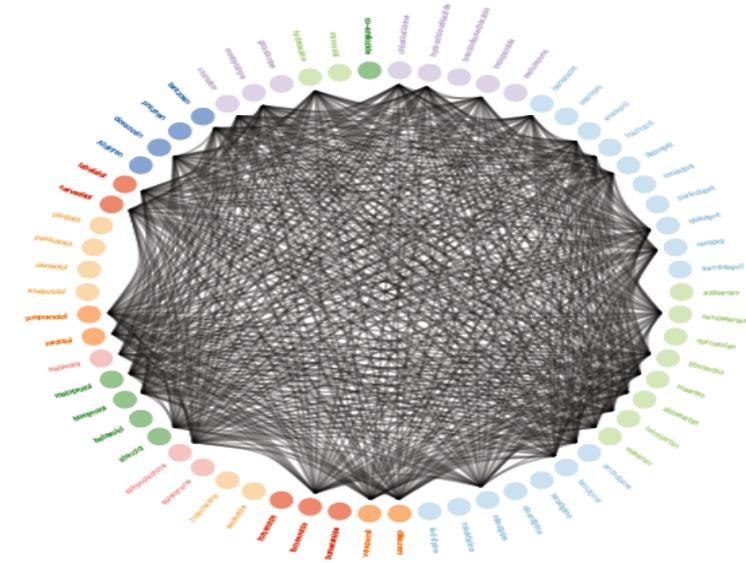
- ↓ BBs, TZDs > ACEIs

Combo-therapy initiation:

- ↓ evidence that combo-therapy is better
- Evidence of ↑ safety risk

DCP trial prediction:

- CTD vs. HCTZ – no efficacy difference





Conclusions

- It is feasible to create an enormous international research network
- Sites will volunteer to run studies
- Completely open
 - Data model, methods, tools
- Concrete approach to address the credibility crisis
- OHDSI supports all part of the evidence generation process and generates evidence



Join the journey

<http://ohdsi.org>