Observational Health Data Sciences and Informatics (OHDSI)

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Medical Informatics Services, NewYork-Presbyterian
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

http://ohdsi.org
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

Data + Analytics + Domain expertise

Open source software

Enable users to do something

Generate evidence

Standardized, transparent workflows

Database summary → Cohort definition → Cohort summary → Compare cohorts → Exposure-outcome summary → Effect estimation & calibration → Compare databases
How OHDSI Works

Source data warehouse, with identifiable patient-level data → ETL → Standardized, de-identified patient-level database (OMOP CDM v5) → Standardized large-scale analytics → Analysis results → OHDSI Coordinating Center

OHDSI Coordinating Center

Data network support
Analytics development and testing
Research and education

Summary statistics results repository → OHDSI.org

OHDSI Data Partners
Extensive vocabularies
Standardized conventions

OHDSI adjusting to experience

Shared Conventions developed by the THEMIS Workgroup
Preparing your data for analysis

Patient-level data in source system/schema → ETL design → ETL implement → Patient-level data in OMOP CDM → ETL test

WhiteRabbit: profile your source data
RabbitInAHat: map your source structure to CDM tables and fields

ATHENA: standardized vocabularies for all CDM domains

CDM: DDL, index, constraints for Oracle, SQL Server, PostgresQL; Vocabulary tables with loading scripts

ACHILLES: profile your CDM data; review data quality assessment; explore population-level summaries

OHDSI tools built to help

Usagi: map your source codes to CDM vocabulary

OHDSI Forums: Public discussions for OMOP CDM Implementers/developers

http://github.com/OHDSI
<table>
<thead>
<tr>
<th>Message Type</th>
<th>Message</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERROR</td>
<td>101-Number of persons by age, with age at first observation period; should not have age &lt; 0, (n=848)</td>
</tr>
<tr>
<td>ERROR</td>
<td>103 - Distribution of age at first observation period (count = 1); min value should not be negative</td>
</tr>
<tr>
<td>ERROR</td>
<td>114-Number of persons with observation period before year-of-birth; count (n=851) should not be &gt; 0</td>
</tr>
<tr>
<td>ERROR</td>
<td>206 - Distribution of age by visit_concept_id (count = 7); min value should not be negative</td>
</tr>
<tr>
<td>ERROR</td>
<td>301-Number of providers by specialty concept_id; 224 concepts in data are not in correct vocabulary (Specialty)</td>
</tr>
<tr>
<td>ERROR</td>
<td>400-Number of persons with at least one condition occurrence, by condition_concept_id; 115 concepts in data are not in correct vocabulary (SNOMED)</td>
</tr>
<tr>
<td>ERROR</td>
<td>406 - Distribution of age by condition_concept_id (count = 753); min value should not be negative</td>
</tr>
</tbody>
</table>
ATLAS to build, visualize, and analyze cohorts

---

- People having any of the following: **Add Primary Criteria...**
  - A condition occurrence of: **Delivery**
  - Occurrence start is: **Between** 2005-01-01 and 2013-12-31
  - With age **Between** 18 and 55
  - With a gender of: **Female**
  - 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:
    - A condition occurrence of: **Depression**
    - Occurring between **0** days **Before** and **180** days **After** index
  - And with **At Most** **0** occurrences of:
    - A condition occurrence of: **Depression**
    - Occurring between **All** days **Before** and **0** days **After** index

---
Characterize the cohorts of interest
OHDSI in Action

• Characterization
Treatment Pathways

Global stakeholders
- Public
- Academics
- Industry
- Regulator

Evidence
- RCT, Obs

Conduits
- Social media
- Lay press
- Literature
- Guidelines
- Advertising
- Formulary
- Labels

Inputs
- Indication
- Feasibility
- Cost
- Preference

Local stakeholders
- Family
- Patient
- Clinician
- Consultant

Local stakeholders
- Patient
- Clinician
- Consultant
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
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Name</th>
<th>Description</th>
<th>Population, millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUSOM</td>
<td>Ajou University School of Medicine</td>
<td>South Korea; inpatient hospital EHR</td>
<td>2</td>
</tr>
<tr>
<td>CCAE</td>
<td>MarketScan Commercial Claims and Encounters</td>
<td>US private-payer claims</td>
<td>119</td>
</tr>
<tr>
<td>CPRD</td>
<td>UK Clinical Practice Research Datalink</td>
<td>UK; EHR from general practice</td>
<td>11</td>
</tr>
<tr>
<td>CUMC</td>
<td>Columbia University Medical Center</td>
<td>US; inpatient EHR</td>
<td>4</td>
</tr>
<tr>
<td>GE</td>
<td>GE Centricity</td>
<td>US; outpatient EHR</td>
<td>33</td>
</tr>
<tr>
<td>INPC</td>
<td>Regenstrief Institute, Indiana Network for Patient Care</td>
<td>US; integrated health exchange</td>
<td>15</td>
</tr>
<tr>
<td>JMDC</td>
<td>Japan Medical Data Center</td>
<td>Japan; private-payer claims</td>
<td>3</td>
</tr>
<tr>
<td>MDCD</td>
<td>MarketScan Medicaid Multi-State</td>
<td>US; public-payer claims</td>
<td>17</td>
</tr>
<tr>
<td>MDCR</td>
<td>MarketScan Medicare Supplemental and Coordination of</td>
<td>US; private and public-payer claims</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Benefits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPTUM</td>
<td>Optum ClinFormatics</td>
<td>US; private-payer claims</td>
<td>40</td>
</tr>
<tr>
<td>STRIDE</td>
<td>Stanford Translational Research Integrated Database</td>
<td>US; inpatient EHR</td>
<td>2</td>
</tr>
<tr>
<td>HKU</td>
<td>Hong Kong University</td>
<td>Hong Kong; EHR</td>
<td>1</td>
</tr>
</tbody>
</table>
Characterizing treatment pathways at scale using the OHDSI network

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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
• Incidence of side effects
• Any drug on the world market
• Any condition
• Absolute risk
  • Not causal
    (Characterization)
• On the Internet
OHDSI is not just a data model → Methods development
What is the quality of the current evidence from observational analyses?

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.”
Standard error vs effect size

Statistically significant
Observational research results in literature

85% of exposure-outcome pairs have p < 0.05

29,982 estimates
11,758 papers
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

[Graph showing different databases and their results in uncalibrated and calibrated states]
Addressing reproducibility

5. Carry out on aligned hypotheses at scale
Estimates are in line with expectations

11% of exposure-outcome pairs have calibrated p < 0.05
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


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

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56 pages containing 106 recommendations
### 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.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>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</td>
</tr>
</tbody>
</table>

SR indicates systematic review.
Table 18. Oral Antihypertensive Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Usual Dose, Range (mg/d)*</th>
<th>Daily Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary agents</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazide or</td>
<td>Chlorthalidone</td>
<td>12.5–25</td>
<td>1</td>
<td>Chlorthalidone is preferred on the basis of prolonged half-life and proven trial reduction of CVD.</td>
</tr>
<tr>
<td>thiazide-type</td>
<td>Hydrochlorothiazide</td>
<td>25–50</td>
<td>1</td>
<td>Monitor for hyponatremia and hypokalemia, uric acid and calcium levels.</td>
</tr>
<tr>
<td>diuretics</td>
<td>Indapamide</td>
<td>1.25–2.5</td>
<td>1</td>
<td>Use with caution in patients with history of acute gout unless patient is on uric acid-lowering therapy.</td>
</tr>
<tr>
<td></td>
<td>Metolazone</td>
<td>2.5–10</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>ACE inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benazepril</td>
<td>10–40</td>
<td></td>
<td>1 or 2</td>
<td>Do not use in combination with ARBs or direct renin inhibitor.</td>
</tr>
<tr>
<td>Captopril</td>
<td>12.5–150</td>
<td></td>
<td>2 or 3</td>
<td>There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K⁺ supplements or K⁺-sparking drugs.</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5–40</td>
<td></td>
<td>1 or 2</td>
<td>There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis.</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>10–40</td>
<td></td>
<td>1</td>
<td>Do not use if patient has history of angioedema with ACE inhibitors.</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10–40</td>
<td></td>
<td>1</td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td>Moexipril</td>
<td>7.5–30</td>
<td></td>
<td>1 or 2</td>
<td>Do not use in combination with ARBs or direct renin inhibitor.</td>
</tr>
<tr>
<td>Perindopril</td>
<td>4–16</td>
<td></td>
<td>1</td>
<td>There is an increased risk of hyperkalemia in those on K⁺ supplements or K⁺-sparking drugs.</td>
</tr>
<tr>
<td>Quinapril</td>
<td>10–80</td>
<td></td>
<td>1 or 2</td>
<td>There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis.</td>
</tr>
<tr>
<td>Ramipril</td>
<td>2.5–10</td>
<td></td>
<td>1 or 2</td>
<td>Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive 6 weeks after ACE inhibitor is discontinued.</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1–4</td>
<td></td>
<td>1</td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td><strong>ARBs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azilsartan</td>
<td>40–80</td>
<td></td>
<td>1</td>
<td>Do not use in combination with ARBs or direct renin inhibitor.</td>
</tr>
<tr>
<td>Candesartan</td>
<td>6–32</td>
<td></td>
<td>1</td>
<td>There is an increased risk of hyperkalemia in those on K⁺ supplements or K⁺-sparking drugs.</td>
</tr>
<tr>
<td>Eprosartan</td>
<td>600–800</td>
<td></td>
<td>1 or 2</td>
<td>There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis.</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>150–500</td>
<td></td>
<td>1</td>
<td>Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive 6 weeks after ACE inhibitor is discontinued.</td>
</tr>
<tr>
<td>Losartan</td>
<td>50–100</td>
<td></td>
<td>1 or 2</td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td>Olmesartan</td>
<td>20–40</td>
<td></td>
<td>1</td>
<td>Do not use if patient has history of angioedema with ARBs.Patients with a history of angioedema with an ACE inhibitor can receive 6 weeks after ACE inhibitor is discontinued.</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>20–80</td>
<td></td>
<td>1</td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td>Valsartan</td>
<td>80–320</td>
<td></td>
<td>1</td>
<td>Avoid use in patients with HFrEF; amlodipine may be used if required. They are associated with dose-related side effects which is more common in women.</td>
</tr>
<tr>
<td><strong>CCB—dihydropyridines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5–10</td>
<td></td>
<td>1</td>
<td>Avoid routine use with beta blockers because of increased risk of bradycardia and heart block.</td>
</tr>
<tr>
<td>Felodipine</td>
<td>5–10</td>
<td></td>
<td>1</td>
<td>Do not use in patients with HFrEF.</td>
</tr>
<tr>
<td>Isradipine</td>
<td>5–10</td>
<td></td>
<td>2</td>
<td>There are drug interactions with dihydrazine and verapamil (CYP3A4 major substrate and moderate inhibitor).</td>
</tr>
<tr>
<td>Nicardipine SR</td>
<td>5–20</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nifedipine LA</td>
<td>60–120</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nisoldipine</td>
<td>30–90</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>CCB—nondihydropyridines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem SR</td>
<td>180–360</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Diltiazem ER</td>
<td>120–480</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Verapamil IR</td>
<td>40–80</td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Verapamil SR</td>
<td>120–480</td>
<td></td>
<td>1 or 2</td>
<td></td>
</tr>
<tr>
<td>Verapamil-delayed onset ER (various forms)</td>
<td>100–480</td>
<td>1 (in the evening)</td>
<td>1</td>
<td>Do not use in patients with HFrEF.</td>
</tr>
<tr>
<td>Distinguished from 28 drugs in 12 other classes that are classified as potential secondary agents (including Beta Blockers).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hypertension 2018
• 40 randomized trials
• Most decisions are “expert opinion”
RCT evidence about comparative effectiveness for cardiovascular outcomes

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

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

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

Reboussin et al., Hypertension 2018
# 58 outcomes of interest

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

- **US insurance databases**
  - IBM® MarketScan® CCAE
  - IBM® MarketScan® MDCD
  - IBM® MarketScan® MDCR
  - Optum® Clininformatics®

- **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
## Comparisons of hypertension treatments

<table>
<thead>
<tr>
<th></th>
<th>Theoretical</th>
<th>Observed (n &gt; 2,500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single ingredients</td>
<td>58</td>
<td>39</td>
</tr>
<tr>
<td>Single ingredient comparisons</td>
<td>58 * 57 = 3,306</td>
<td>1,296</td>
</tr>
<tr>
<td>Single drug classes</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Single class comparisons</td>
<td>15 * 14 = 210</td>
<td>156</td>
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<tr>
<td>Dual ingredients</td>
<td>1,653</td>
<td>58</td>
</tr>
<tr>
<td>Single vs duo drug comparisons</td>
<td>58 * 1,653 = 95,874</td>
<td>3,810</td>
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<tr>
<td>Dual classes</td>
<td>105</td>
<td>32</td>
</tr>
<tr>
<td>Single vs duo class comparisons</td>
<td>15 * 105 = 1,575</td>
<td>832</td>
</tr>
<tr>
<td>Duo vs duo drug comparisons</td>
<td>1,653 * 1,652 = 2,730,756</td>
<td>2,784</td>
</tr>
<tr>
<td>Duo vs duo class comparisons</td>
<td>105 * 104 = 10,920</td>
<td>992</td>
</tr>
</tbody>
</table>

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

1,321,696 estimates
83.4% of CIs includes 1
Not all comparisons are valid
Not all comparisons are valid
Not all comparisons are valid
Efficacy outcome: **myocardial infarction**, heart failure, stroke

<table>
<thead>
<tr>
<th>RCTs</th>
<th>LEGEND</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEIs</td>
<td>&lt; 0.67</td>
</tr>
<tr>
<td>ARBs</td>
<td>&lt; 0.80</td>
</tr>
<tr>
<td>cBBs</td>
<td>&lt; 1.00</td>
</tr>
<tr>
<td>dCCBs</td>
<td>NS</td>
</tr>
<tr>
<td>TZDs</td>
<td>&gt; 1.00</td>
</tr>
<tr>
<td>ACEIs</td>
<td>&gt; 1.25</td>
</tr>
<tr>
<td>ARBs</td>
<td>&gt; 1.50</td>
</tr>
</tbody>
</table>

Data source: meta-analysis, $\sim 1 - 2M$ 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
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 1\textsuperscript{st}-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 is supports all part of the evidence generation process and generates evidence
Join the journey

http://ohdsi.org