Drawing reproducible conclusions from observational clinical data with 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 registered collaborators, 2500 forum participants 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/
Paucity of evidence
A tiny fraction of potential questions have answers

All health outcomes of interest
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”
Evaluate observational research

- Effect size
- Standard error
- Not significant
- Protect
- Harm
- P = 0.05
Observational research results in literature

85% of exposure-outcome pairs have $p < 0.05$

Not significant

Protect

Harm

29,982 estimates
11,758 papers

Schuemie, Phil Trans A, 2018
Publication bias

- Literature
- Simulation of ideal research

p=0.01
p=0.05
Over-optimism of p-values and CIs

• Look at four published studies
  – Use 50 negative controls to assess CI
• “95%” CIs cover only 30%, 47%, 60%, 88%

Schuemie, PNAS 2018
Consequences

- Overcall positive results
- Throw negative ones away

- Conflicting, unreliable evidence
- Too little evidence and what is there is poor
  - Woody Allen: "Boy, the food at this place is really terrible."
  - "Yeah, I know; and such small portions."
  - It’s just observational research
OHDSI is Open Science

Open science

Data + Analytics + Domain expertise

Generate evidence

Open source software

Enable users to do something

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 v6) → Standardized large-scale analytics → Analysis results → Summary statistics results repository → OHDSI.org

OHDSI Coordinating Center
- Data network support
- Analytics development and testing
- Research and education

OHDSI Data Partners

OHDSI.org
Deep information model
OMOP CDM Version 6

Standardized health system data
- Location
- Location_history
- Care_site
- Provider

Standardized derived elements
- Condition_era
- Drug_era
- Dose_era

Results Schema
- Cohort
- Cohort_definition

Standardized health economics
- Cost
- Payer_plan_period

Standardized metadata
- CDM_source
- Metadata

Standardized vocabularies
- Concept
- Vocabulary
- Domain
- Concept_class
- Concept_relationship
- Relationship
- Concept_synonym
- Concept_ancestor
- Source_to_concept_map
- Drug_strength

Standardized clinical data
- Person
  - Observation_period
  - Visit_occurrence
    - Visit_detail
  - Condition_occurrence
  - Drug_exposure
  - Procedure_occurrence
  - Device_exposure
  - Measurement
  - Note
    - Note_NLP
  - Survey_conduct
  - Observation
  - Specimen
  - Fact_relationship
Extensive international vocabularies
Standardized conventions
Need more than vocabulary and schema
Tools to help you map data

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
Usagi: map your source codes to CDM vocabulary
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 Forums:
Public discussions for OMOP CDM Implementers/developers

http://github.com/OHDSI
Data Quality: ACHILLES Heel

<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>
Tools for analytics: CYCLOPS

• Cyclic Coordinate Descent for Logistic, Poisson and Survival Analysis
  – Open source toolkit
  – 100 million cases x million columns
  – regularized regression
  – R library written in C
  – No one else can do this scale
ATLAS to build, visualize, and analyze cohorts

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
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?
Characterization

• Treatment pathways
  – How are patients currently treated?
T2DM: All databases

Treatment pathways for diabetes on 240M patients in 5 countries, 12 databases

Only drug

First drug

Second drug

Table:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>29.42%</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>4.62%</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>3.69%</td>
</tr>
<tr>
<td>Glipizide</td>
<td>4.52%</td>
</tr>
<tr>
<td>Glimepiride</td>
<td>3.09%</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>3.58%</td>
</tr>
<tr>
<td>Glyburide</td>
<td>5.1%</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>5.81%</td>
</tr>
<tr>
<td>Insulin, Glargine, Human</td>
<td>5.85%</td>
</tr>
<tr>
<td>Exenatide</td>
<td>4.99%</td>
</tr>
<tr>
<td>Insulin, Aspart, Human</td>
<td>4.97%</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>3.59%</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>4.28%</td>
</tr>
<tr>
<td>Insulin, Lispro, Human</td>
<td>4.09%</td>
</tr>
<tr>
<td>Glucose</td>
<td>8.60%</td>
</tr>
<tr>
<td>Insulin, Isophane, Human</td>
<td>6.06%</td>
</tr>
</tbody>
</table>
Treatment pathways
Heterogeneity within and across health systems

25% of HTN patients were on a unique pathway

Hripcsak, PNAS 2016
Population-level estimation

- Causality
1. Address confounding that is measured
   • Propensity stratification
   • Systematic (not manual) variable selection
     • Balance 58,285 variables ("Table 1")

After stratification on the propensity score, all 58,285 covariates have standardized difference of mean < 0.1

Tian, Int J Epi 2018
OHDSI Reproducible research

2. Unmeasured (residual) confounding
   - Confidence interval calibration
     - Adjust for all uncertainty, not just sampling
   - Many (50-100) negative controls
     - Unique to OHDSI (PNAS)

After calibration, 4% have $p < 0.05$ (was 16%)

Schuemie, PNAS 2018
OHDSI Reproducible research

3. Multiple databases, locations, practice types
   • Exploit international OHDSI network
OHDSI Reproducible research

4. Open: publish all
   • Hypotheses
   • Code
   • Parameters
   • Runs
Generating evidence for US FDA

Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System (FAERS) between October - December 2015

| Keppra (levetiracetam) tablet, oral solution, injection | Angioedema | FDA is evaluating the need for regulatory action. |

- Protocol completed, code tested, study announced
  - 7 sites ran the code on 10 databases (5 claims / 5 EHR)
  - 59,367 levetiracetam patients, 74,550 phenytoin patients

- No difference detected with small confidence interval
- Accepted essentially without revision
  - Add word to title, move diagram from supplement to body

Duke, Epilepsia 2017
5. Carry out on aligned hypotheses at large scale
OHDSI Reproducible research

• Full diagnostics at each step
  – Tells us if this a result we can trust
Estimates are in line with expectations

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

Mirtazapine vs. Citalopram
Constipation
Database: Truven MDCD

Calibrated HR = 0.90 (0.70 – 1.12)
Large-scale estimation

• Not “data-dredging”!
  – Data-dredging is not about what you do but about what you *throw out*
    • This can’t be done for literature

• One-off studies
  – Wouldn’t it be best to optimize each study?
    • Never get 10 or 100 parameters right
  – Cannot study its operating characteristics
    • End up in today’s situation
OHDSI LEGEND Hypertension Study

• What becomes possible?
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>Primary agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazide or thiazide-type diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorothalidone</td>
<td>12.5–25</td>
<td>1</td>
<td></td>
<td>Chlorothalidone is preferred on the basis of its prolonged half-life and proven trial results for CVD.</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>25–50</td>
<td>1</td>
<td></td>
<td>Monitor for hyponatremia and hypokalemia, uric acid and calcium levels.</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25–2.5</td>
<td>1</td>
<td></td>
<td>Use with caution in patients with history of acute gout unless patient is on uric acid–lowering therapy.</td>
</tr>
<tr>
<td>Metolazone</td>
<td>2.5–10</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benazepril</td>
<td>10–40</td>
<td>1 or 2</td>
<td></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>2 or 3</td>
<td></td>
<td>There is an increased risk of hyperkalemia, especially in patients with CKD or those on K⁺ supplements or K⁺-sparing drugs.</td>
</tr>
<tr>
<td>Enalapril</td>
<td>5–40</td>
<td>1 or 2</td>
<td></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>1</td>
<td></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>1</td>
<td></td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td>Moexipril</td>
<td>7.5–30</td>
<td>1 or 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perindopril</td>
<td>4–16</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quinapril</td>
<td>10–80</td>
<td>1 or 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td>2.5–10</td>
<td>1 or 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1–4</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azilsartan</td>
<td>40–80</td>
<td>1</td>
<td></td>
<td>Do not use in combination with ACE inhibitors or direct renin inhibitor.</td>
</tr>
<tr>
<td>Candesartan</td>
<td>8–32</td>
<td>1</td>
<td></td>
<td>There is an increased risk of hyperkalemia in CKD or those on K⁺ supplements or K⁺-sparing drugs.</td>
</tr>
<tr>
<td>Eprosartan</td>
<td>600–800</td>
<td>1 or 2</td>
<td></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>150–300</td>
<td>1</td>
<td></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 an ARB beginning 5 weeks after ACE inhibitor is discontinued.</td>
</tr>
<tr>
<td>Losartan</td>
<td>50–100</td>
<td>1 or 2</td>
<td></td>
<td>Avoid in pregnancy.</td>
</tr>
<tr>
<td>Olmesartan</td>
<td>20–40</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telmisartan</td>
<td>20–80</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valsartan</td>
<td>80–320</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCE—dihydropyridines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5–10</td>
<td>1</td>
<td></td>
<td>Avoid use in patients with HFrEF; amlodipine or felodipine may be used if required.</td>
</tr>
<tr>
<td>Felodipine</td>
<td>5–10</td>
<td>1</td>
<td></td>
<td>They are associated with dose-related peptic ulcer disease, which is more common in women than men.</td>
</tr>
<tr>
<td>Isradipine</td>
<td>5–10</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicardipine SR</td>
<td>5–20</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine LA</td>
<td>60–120</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nisoldipine</td>
<td>30–90</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCE—nondihydropyridines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem SR</td>
<td>180–360</td>
<td>2</td>
<td></td>
<td>Avoid routine use with beta blockers because of increased risk of bradycardia and heart block.</td>
</tr>
<tr>
<td>Diltiazem ER</td>
<td>120–480</td>
<td>1</td>
<td></td>
<td>Do not use in patients with HFrEF.</td>
</tr>
<tr>
<td>Verapamil IR</td>
<td>40–80</td>
<td>3</td>
<td></td>
<td>There are drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).</td>
</tr>
<tr>
<td>Verapamil SR</td>
<td>120–480</td>
<td>1 or 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil-delayed onset ER (various forms)</td>
<td>100–480</td>
<td>1 (in the evening)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Evidence to support the guideline

- 40 randomized trials
- Only 11% of recommendations based on RCT
- Most decisions are “expert opinion”
## 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>
</tr>
<tr>
<td>Dual ingredients</td>
<td>58 * 57 / 2 = 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>
</tr>
<tr>
<td>Dual classes</td>
<td>15 * 14 / 2 = 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>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Total comparisons</td>
<td>2,843,250</td>
<td>10,278</td>
</tr>
<tr>
<td>Outcomes of interest</td>
<td>58</td>
<td>58</td>
</tr>
<tr>
<td>Target-comparator-outcomes</td>
<td>2,843,250 * 58 = 164,908,500</td>
<td>587,020</td>
</tr>
</tbody>
</table>
Each hypothesis a fully executed trial
Not all comparisons are valid
Legend: Knowledge base for hypertension

Head-to-head HTN drug comparisons

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

- Comparisons: 10,278
- $N = 3502 - [212K] - 1.9M$
First-line agents: comparisons from LEGEND

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

**RCTs**

<table>
<thead>
<tr>
<th></th>
<th>ACEIs</th>
<th>ARBs</th>
<th>cBBs</th>
<th>dCCBs</th>
<th>TZDs</th>
</tr>
</thead>
<tbody>
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<td>ACEIs</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>cBBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dCCBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TZDs</td>
<td></td>
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</tr>
</tbody>
</table>

**LEGEND**

<table>
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<th>ARBs</th>
<th>cBBs</th>
<th>dCCBs</th>
<th>TZDs</th>
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<tr>
<td>dCCBs</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>TZDs</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

Composite (MI, HF, stroke) outcome in meta-analysis
Prescriptions are not written at the class-level; must choose an individual drug for the patient.

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

Composite (MI, HF, stroke) outcome in meta-analysis
### Risk estimates and meta-analysis across LEGEND databases:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Data source</th>
<th>HR</th>
<th>LB</th>
<th>UB</th>
<th>P</th>
<th>Cal.HR</th>
<th>Cal.LB</th>
<th>Cal.UB</th>
<th>Cal.P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS stratification, on-treatment</td>
<td>CCAE</td>
<td>0.65</td>
<td>0.33</td>
<td>1.14</td>
<td>0.17</td>
<td>0.66</td>
<td>0.37</td>
<td>1.19</td>
<td>0.18</td>
</tr>
<tr>
<td>PS stratification, on-treatment</td>
<td>Meta-analysis</td>
<td>0.79</td>
<td>0.54</td>
<td>1.16</td>
<td>0.24</td>
<td>0.61</td>
<td>0.56</td>
<td>1.17</td>
<td>0.30</td>
</tr>
<tr>
<td>PS stratification, on-treatment</td>
<td>Optum</td>
<td>0.90</td>
<td>0.52</td>
<td>1.44</td>
<td>0.67</td>
<td>0.93</td>
<td>0.57</td>
<td>1.53</td>
<td>0.82</td>
</tr>
<tr>
<td>PS stratification, on-treatment</td>
<td>Panther</td>
<td>0.98</td>
<td>0.05</td>
<td>5.06</td>
<td>0.99</td>
<td>0.91</td>
<td>0.26</td>
<td>3.42</td>
<td>0.96</td>
</tr>
</tbody>
</table>

*Showing 1 to 4 of 4 entries*

#### Table 1a. Number of subjects, follow-up time (in years), number of outcome events, and event incidence rate (IR) per 1,000 patient years (PY) in the target (Chlorthalidone) and comparator (Hydrochlorothiazide) group after stratification, as well as the minimum detectable relative risk (MDRR). Note that the IR does not account for any stratification.

<table>
<thead>
<tr>
<th>Target subjects</th>
<th>Comparator subjects</th>
<th>Target years</th>
<th>Comparator years</th>
<th>Target events</th>
<th>Comparator events</th>
<th>Target IR (per 1,000 PY)</th>
<th>Comparator IR (per 1,000 PY)</th>
<th>MDRR</th>
<th>i²</th>
</tr>
</thead>
<tbody>
<tr>
<td>25,566</td>
<td>528,202</td>
<td>14,047</td>
<td>339,516</td>
<td>&lt;32</td>
<td>819</td>
<td>&lt;2.28</td>
<td>2.41</td>
<td>&gt;1.58</td>
<td>0.00</td>
</tr>
</tbody>
</table>
CTD vs. HCTZ: safety profile

- Safety favors HCTZ – electrolyte imbalance
- CTD is more potent, longer half-life
Clinical lessons for hypertension

• OHDSI evidence concordant with RCT meta-analysis
  – Where RCTs exist
  – Larger samples, more diversity, narrower confidence intervals

• Largely supports US guideline
  – First line drugs superior to second
  – Beta blockers not first line (unlike European)

• ACE inhibitors inferior to thiazide diuretics
  – 48% of world starts on ACEi
  – Avoid 1.3 cardiovascular events per 1000 patients (HR = 0.84)
  – Accepted to Lancet
OHDSI open results

- data.ohdsi.org (500K studies)
Conclusions

• It is feasible to create an enormous international research network
• Sites willing to participate despite privacy ...
• Nearing 1/10th world population
• Completely open: Data model, methods, tools
• Concrete approach to address the credibility crisis
• **Must change the way we do observational research**
  – Large scale to measure and improve reproducibility
Upcoming meetings

• 2019 OHDSI Symposium
  – 15-17 September 2019
  – Near Washington, DC
    • Bethesda, Maryland, USA
  – No registration fee

• 2020 European OHDSI Symposium
  – 27-29 March 2020
  – University of Oxford, UK