Large-scale Evidence Generation and Evaluation across a Network of Databases (**LEGEND**) Initiative

LEGEND: Principles and practice

Anna Ostropolets

on behalf of the LEGEND initiative

Towards Reliable Evidence …

Some current practices across the broader research community

Examining one target-comparator pair at a time

Not using appropriate methods to control for bias

Modify the design until significant results are found

Large-scale evidence generation across a network of databases (LEGEND)

* Pre-specified fixed design and dissemination of the results regardless of the estimates (avoid publication bias)
* Systematic process across all research questions
* Large-scale: looking at thousands of target-comparator pairs at a time
* Use of best practices: LSPS, extensive diagnostics, negative and positive controls

Some of the LEGEND Principles Step-by-Step

- 39 mono-drugs, 13 mono-classes
- 58 duo-drugs, 32 duo-classes
- 10,278 comparisons

	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

Select multiple target and comparator cohorts, for example, all drug in a drug class

↓

Carefully design the study, including sensitivity analyses

↓

Run on multiple databases

↓

Spend a lot of time on diagnostics: propensity score balance, covariate balance, calibration plots etc.

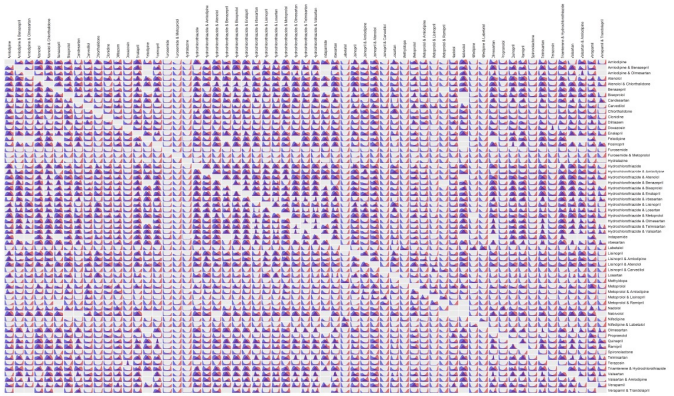
↓

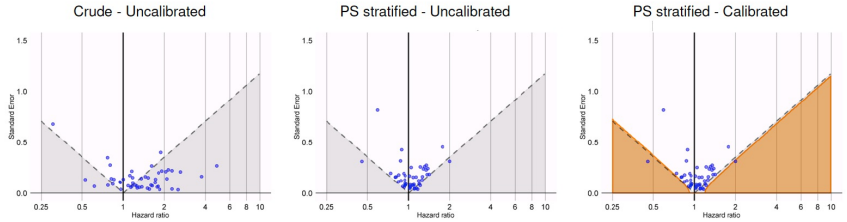
Publish all results

OHDSI

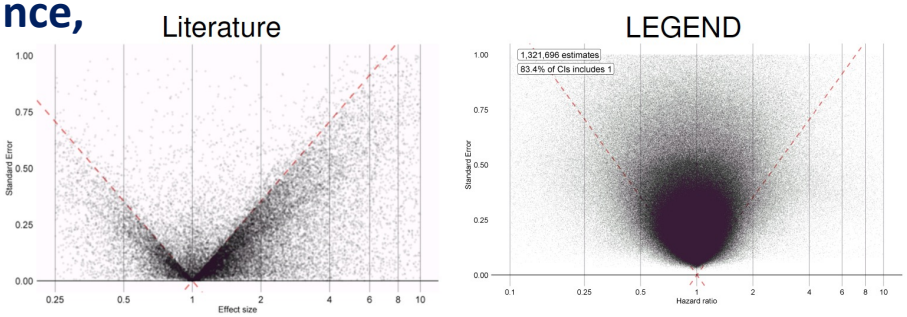
OHDSI Large-Scale Evidence Generation and Evaluation in a Network of Databases (LEGEND): Study of the Effects of Treatments for Hypertension

Version: 0.1





68% have $p < 0.05$ | 16% have $p < 0.05$ | 4% have $p < 0.05$



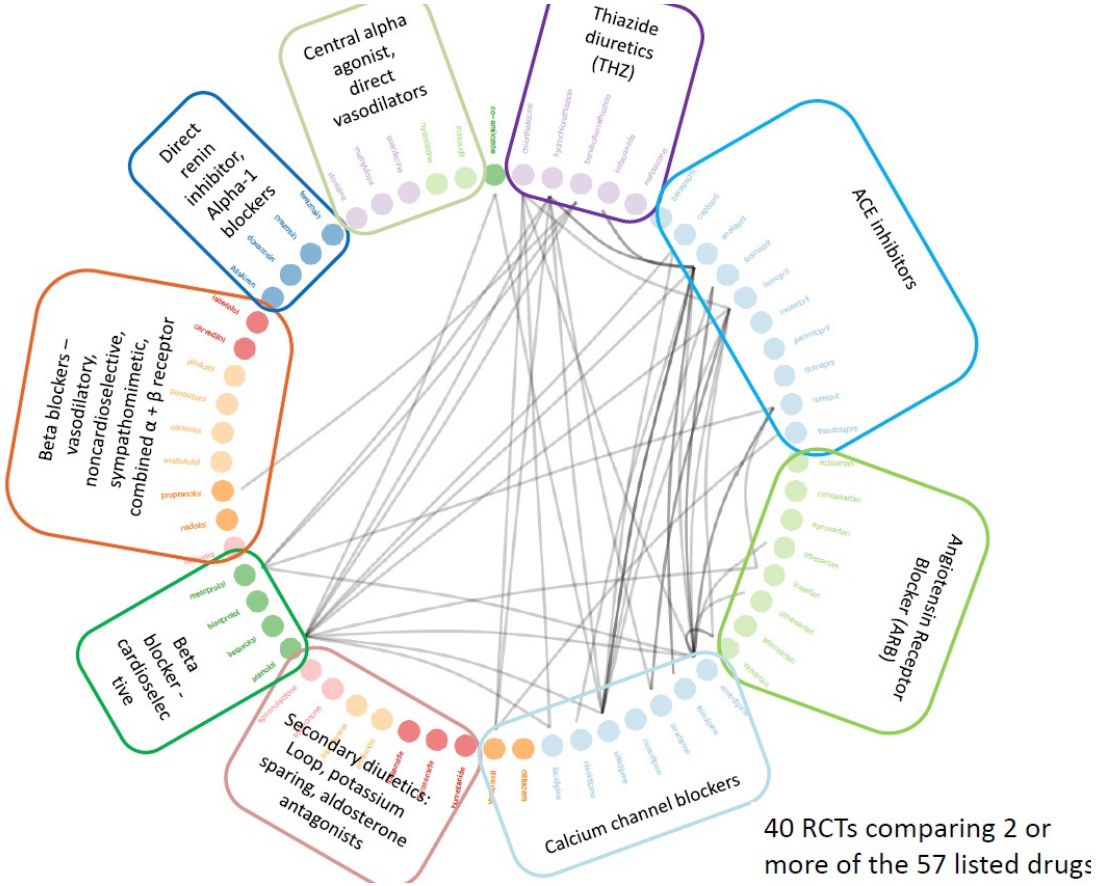
LEGEND-HTN: First-line antihypertensive treatments

RuiJun (Ray) Chen

on behalf of the LEGEND initiative

LEGEND-HTN Motivation

- Why?
  - New 2017, 2018 guidelines
  - Multiple recommended 1st-line drug classes
    - Thiazides, ACE inhibitors, ARBs, CCBs, B-blockers (ESC/ESH only)
  - Older RCTs, few direct comparisons
- Can we do better?



LEGEND-HTN Prior Publications

Main manuscript: class-level comparison, 55 outcomes, 9 databases

Suchard, et al. Published 2019 in *The Lancet*

Articles

Comprehensive comparative effectiveness and safety of first-line antihypertensive drug classes: a systematic, multinational, large-scale analysis

Marc A Suchard, Martijn J Schuemie, Harlan M Krumholz, Seng Chan You, RuiJun Chen, Nicole Pratt, Christian G Reich, Jon Duke, David Madigan, George Hripcsak, Patrick B Ryan

Summary

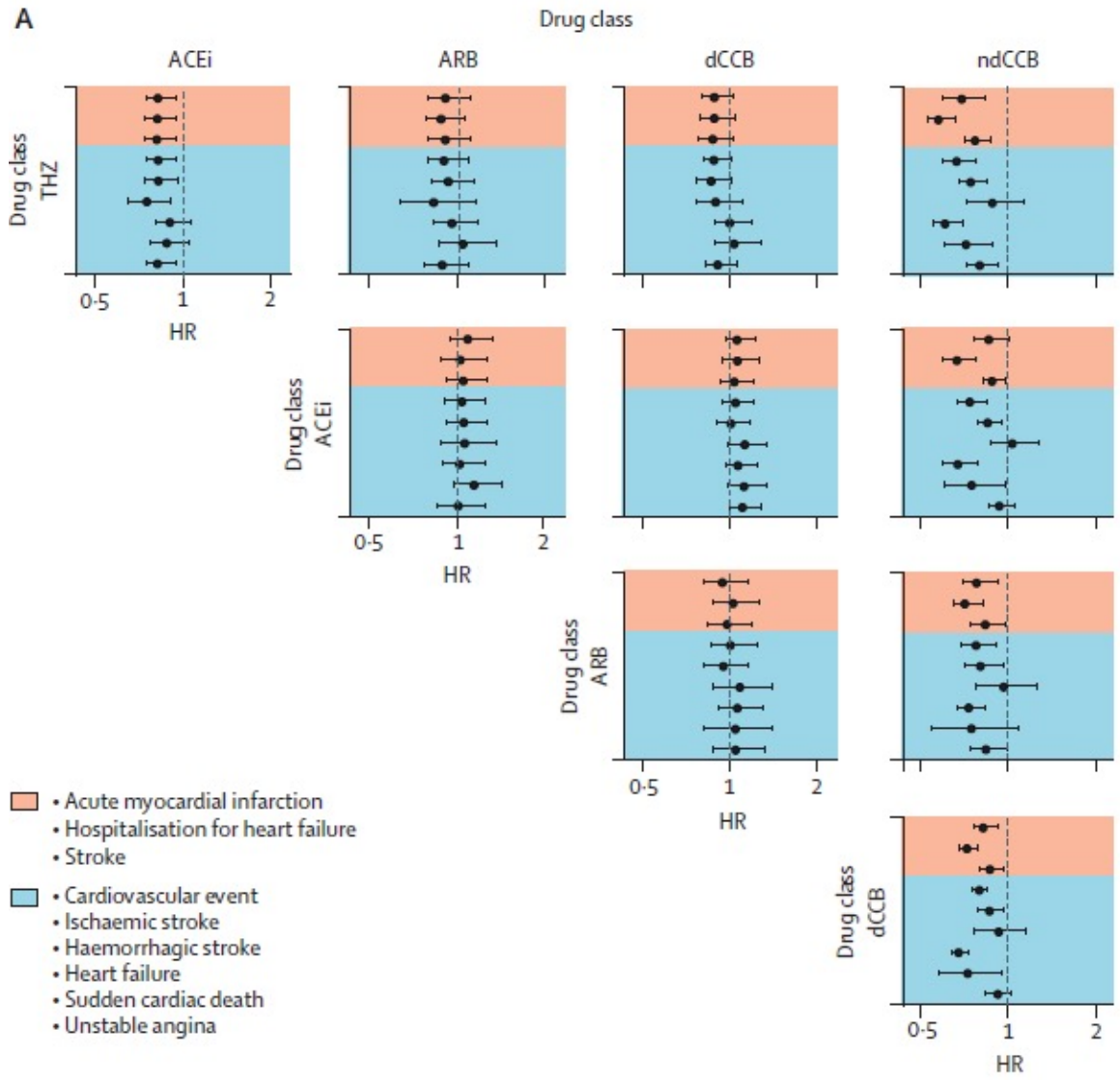
Background Uncertainty remains about the optimal monotherapy for hypertension, with current guidelines recommending any primary agent among the first-line drug classes thiazide or thiazide-like diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, dihydropyridine calcium channel blockers, and non-dihydropyridine calcium channel blockers, in the absence of comorbid indications. Randomised trials have not further refined this choice.

Published Online
October 24, 2019
https://doi.org/10.1016/
S0140-6736(19)32317-7

LEGEND-HTN Prior Publications

Main manuscript

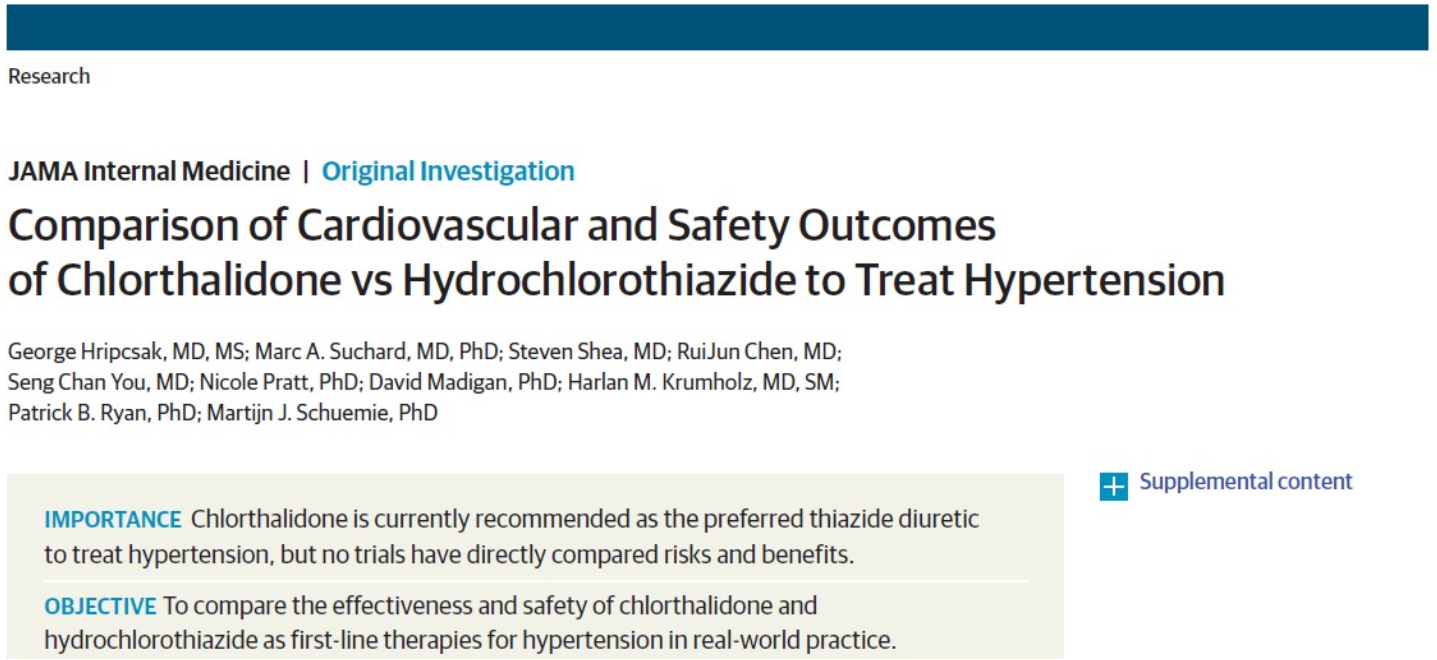
- 4.9M patients
- 22,000 calibrated, propensity-score adjusted HRs
- Thiazides better than ACE inhibitors for primary effectiveness outcomes
- Non-dihydropyridine CCBs inferior



LEGEND-HTN Prior Publications

Chlorthalidone vs HCTZ

- Chlorthalidone recommended as preferred thiazide diuretic
  - Longer half life
  - Used in trials
- HCTZ is most commonly prescribed thiazide
- No direct head-to-head comparisons (RCT in progress)
- Hripcsak, et al.
  Published 2020 in JAMA Internal Medicine



Research

JAMA Internal Medicine | Original Investigation

Comparison of Cardiovascular and Safety Outcomes of Chlorthalidone vs Hydrochlorothiazide to Treat Hypertension

George Hripcsak, MD, MS; Marc A. Suchard, MD, PhD; Steven Shea, MD; RuiJun Chen, MD; Seng Chan You, MD; Nicole Pratt, PhD; David Madigan, PhD; Harlan M. Krumholz, MD, SM; Patrick B. Ryan, PhD; Martijn J. Schuemie, PhD

Supplemental content

IMPORTANCE Chlorthalidone is currently recommended as the preferred thiazide diuretic to treat hypertension, but no trials have directly compared risks and benefits.

OBJECTIVE To compare the effectiveness and safety of chlorthalidone and hydrochlorothiazide as first-line therapies for hypertension in real-world practice.

LEGEND-HTN Prior Publications

Chlorthalidone vs HCTZ

- 3 databases with >2500 exposures
  - 730K patients
- No significant difference in effectiveness
- HCTZ with fewer renal and electrolyte abnormalities

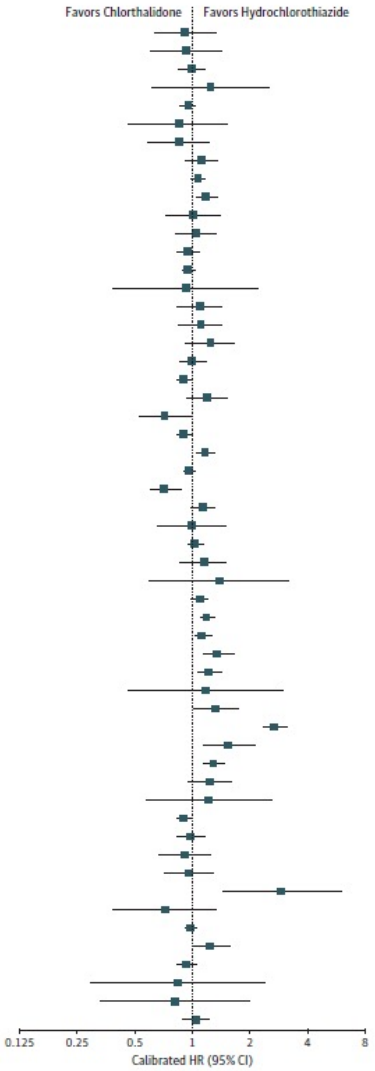
Figure 2. Homogeneity on Effectiveness

Source	Uncalibrated HR (95% CI)	Calibrated HR (95% CI)
CCAE	0.96 (0.70-1.29)	0.96 (0.72-1.29)
Optum	1.00 (0.76-1.28)	1.04 (0.81-1.33)
PanTher	1.10 (0.79-1.49)	1.00 (0.75-1.36)
Summary (I^2 <0.01)	1.01 (0.86-1.20)	1.00 (0.85-1.17)

Hazard ratios (HRs) and forest plot of the 3 databases and the meta-analysis for chlorthalidone vs hydrochlorothiazide on the composite cardiovascular disease outcome. The 3 databases showed excellent agreement. CCAE indicates Commercial Claims and Encounters Database.

Figure 3. Forest Plot of Safety and Effectiveness Outcomes

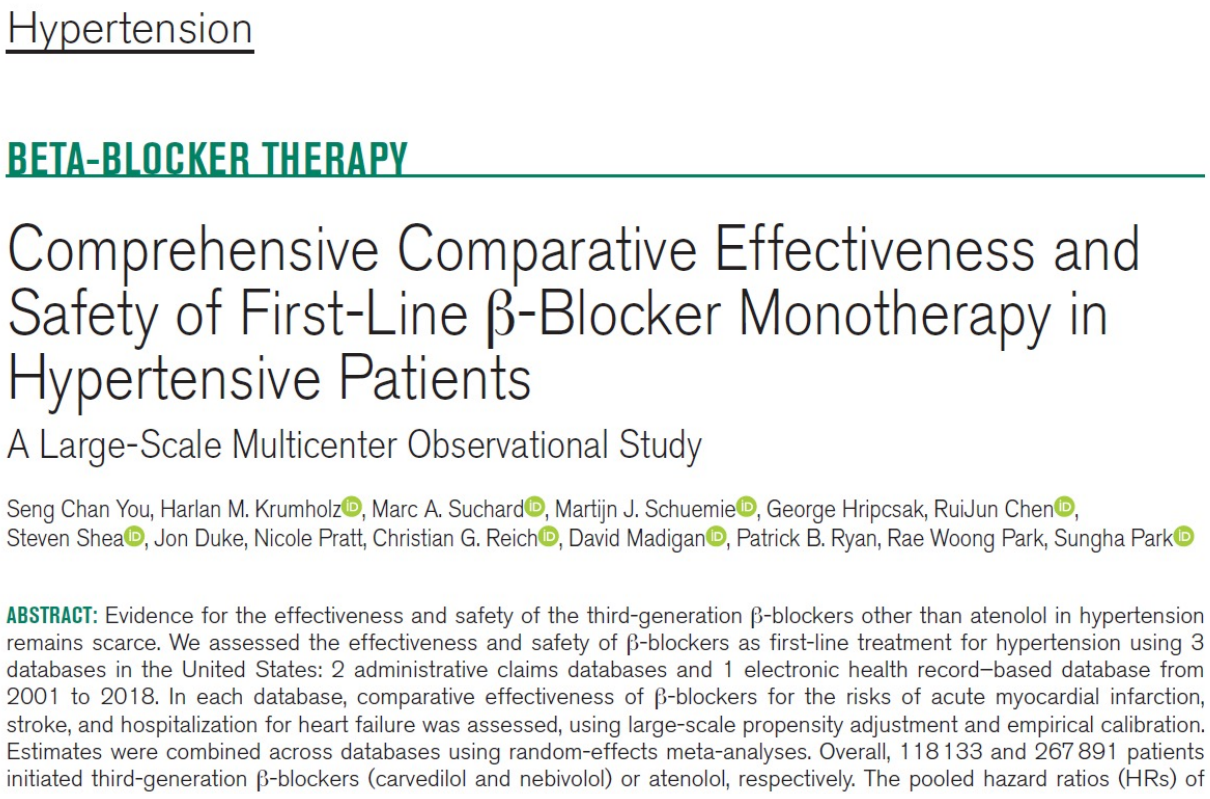
Source	Calibrated HR (95% CI)
Acute myocardial infarction	0.92 (0.64-1.31)
All-cause mortality	0.93 (0.61-1.42)
Cardiovascular event	1.00 (0.85-1.17)
Cardiovascular-related mortality	1.24 (0.62-2.51)
Chest pain or angina	0.94 (0.87-1.03)
Sudden cardiac death	0.85 (0.47-1.52)
Unstable angina	0.85 (0.59-1.23)
Bradycardia	1.12 (0.93-1.35)
Cardiac arrhythmia	1.07 (0.99-1.15)
Syncope	1.19 (1.07-1.33)
Heart failure	1.01 (0.73-1.40)
Hospitalization for heart failure	1.05 (0.82-1.34)
Fall	0.95 (0.84-1.08)
Headache	0.95 (0.89-1.02)
Hemorrhagic stroke	0.92 (0.39-2.18)
Ischemic stroke	1.09 (0.84-1.42)
Stroke	1.10 (0.86-1.41)
Transient ischemic attack	1.23 (0.93-1.64)
Vertigo	1.01 (0.87-1.17)
Anxiety	0.91 (0.85-0.98)
Decreased libido	1.19 (0.95-1.51)
Dementia	0.73 (0.54-0.98)
Depression	0.91 (0.84-0.99)
Impotence	1.18 (1.07-1.30)
Abdominal pain	0.97 (0.91-1.02)
Abnormal weight gain	0.73 (0.61-0.86)
Abnormal weight loss	1.14 (0.99-1.31)
Acute pancreatitis	0.99 (0.66-1.48)
Diarrhea	1.04 (0.95-1.14)
Gastrointestinal bleeding	1.14 (0.87-1.50)
Hepatic failure	1.38 (0.60-3.15)
Nausea	1.09 (0.99-1.20)
Type 2 diabetes mellitus	1.21 (1.12-1.30)
Vomiting	1.14 (1.04-1.25)
Acute renal failure	1.37 (1.15-1.63)
Chronic kidney disease	1.24 (1.09-1.42)
End-stage renal disease	1.17 (0.47-2.94)
Hyperkalemia	1.34 (1.03-1.74)
Hypokalemia	2.72 (2.38-3.12)
Hypomagnesemia	1.57 (1.16-2.12)
Hyponatremia	1.31 (1.16-1.47)
Hypotension	1.23 (0.95-1.60)
Measured renal dysfunction	1.23 (0.58-2.60)
Anemia	0.91 (0.84-0.98)
Malignant neoplasm	0.99 (0.84-1.17)
Neutropenia or agranulocytosis	0.91 (0.67-1.23)
Thrombocytopenia	0.96 (0.72-1.29)
Anaphylactoid reaction	2.96 (1.46-5.97)
Angioedema	0.72 (0.39-1.32)
Cough	0.98 (0.93-1.04)
Gout	1.27 (1.02-1.57)
Rash	0.93 (0.84-1.04)
Rhabdomyolysis	0.83 (0.29-2.37)
Vasculitis	0.81 (0.33-1.98)
Venous thromboembolic events	1.05 (0.90-1.22)



LEGEND-HTN Prior Publications

Beta blockers

- ACC/AHA guidelines no longer recommend beta blockers
- Heterogeneous
  - 3rd generation beta blockers have greater vasodilatory effects
- Few direct comparisons vs atenolol or other classes
- You et al.
  Published 2021 in Hypertension



Hypertension

BETA-BLOCKER THERAPY

Comprehensive Comparative Effectiveness and Safety of First-Line β-Blocker Monotherapy in Hypertensive Patients

A Large-Scale Multicenter Observational Study

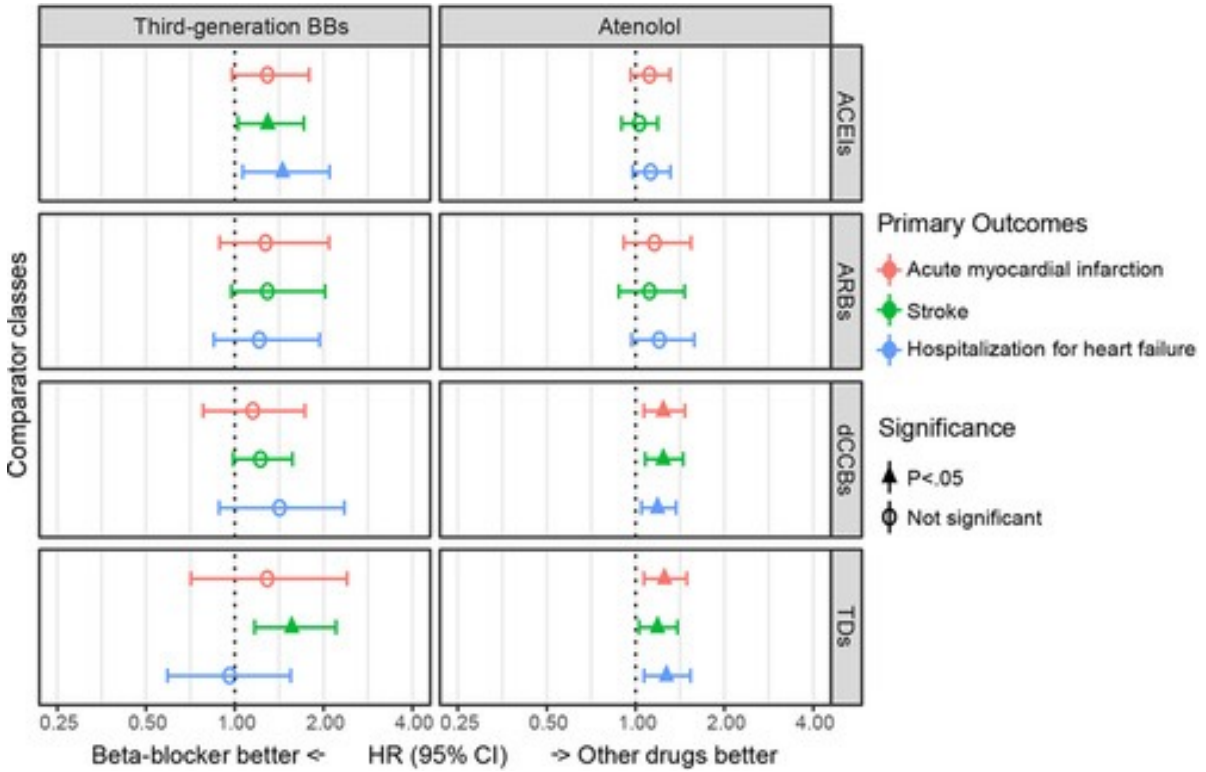
Seng Chan You, Harlan M. Krumholz, Marc A. Suchard, Martijn J. Schuemie, George Hripcsak, RuiJun Chen, Steven Shea, Jon Duke, Nicole Pratt, Christian G. Reich, David Madigan, Patrick B. Ryan, Rae Woong Park, Sungha Park

ABSTRACT: Evidence for the effectiveness and safety of the third-generation β-blockers other than atenolol in hypertension remains scarce. We assessed the effectiveness and safety of β-blockers as first-line treatment for hypertension using 3 databases in the United States: 2 administrative claims databases and 1 electronic health record–based database from 2001 to 2018. In each database, comparative effectiveness of β-blockers for the risks of acute myocardial infarction, stroke, and hospitalization for heart failure was assessed, using large-scale propensity adjustment and empirical calibration. Estimates were combined across databases using random-effects meta-analyses. Overall, 118 133 and 267 891 patients initiated third-generation β-blockers (carvedilol and nebivolol) or atenolol, respectively. The pooled hazard ratios (HRs) of

LEGEND-HTN Prior Publications

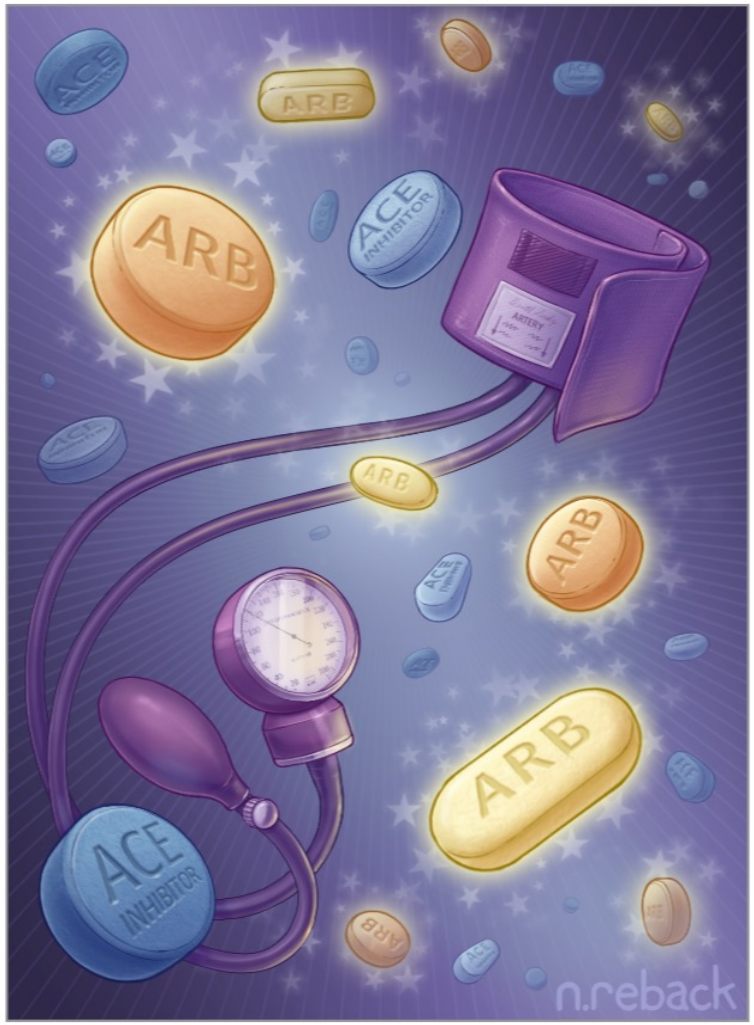
Beta blockers

- 3 databases with >2500 exposures
  - 380K patients
- No significant difference in effectiveness between 3rd generation BBs and atenolol
- Higher risk for stroke with 3rd generation BBs vs ACE-I's or thiazide diuretics



LEGEND-HTN ACE Inhibitors vs ARBs

- Equally recommended 1st-line therapies
- Act along the same physiologic pathway
- Despite some known side effects, ACEs are much more commonly used than ARBs
- Few existing head-to-head studies



LEGEND-HTN ACE Inhibitors vs ARBs

- 8 databases with >2500 exposures
- 2.3M patients initiating treatment with ACE-I
- 674K patients initiating with ARBs
- No significant difference in primary outcomes

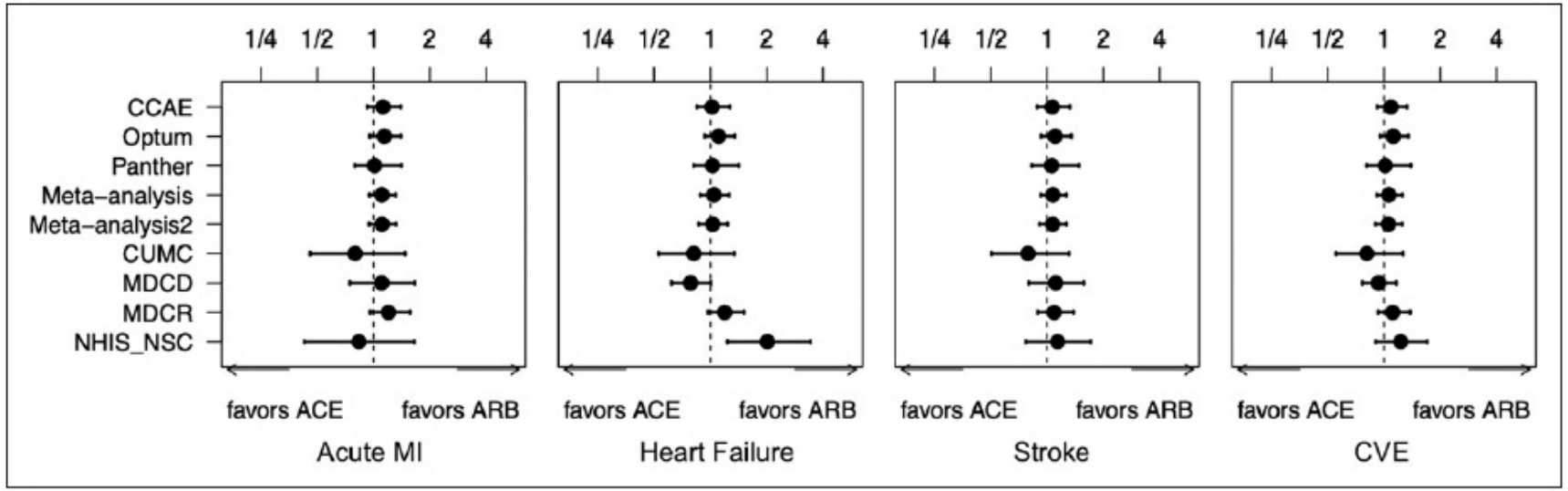
Hypertension

ANTIHYPERTENSIVE TREATMENT

Comparative First-Line Effectiveness and Safety of ACE (Angiotensin-Converting Enzyme) Inhibitors and Angiotensin Receptor Blockers

A Multinational Cohort Study

RuiJun Chen, Marc A. Suchard, Harlan M. Krumholz, Martijn J. Schuemie, Steven Shea, Jon Duke, Nicole Pratt, Christian G. Reich, David Madigan, Seng Chan You, Patrick B. Ryan, George Hripcsak



LEGEND-HTN ACE Inhibitors vs ARBs

- 51 secondary and safety outcomes
- ARBs with better safety profile
  - Lower risk of cough, angioedema, pancreatitis, and GI bleeding
  - Cough and angioedema remain significant even with Bonferroni correction

Outcome	HR (95% CI)	*P* value	Calibrated HR (95% CI)	Calibrated *P* value
Abdominal pain	1.00 (0.96–1.03)	0.87	1.01 (0.88–1.19)	0.87
Abnormal weight gain	0.82 (0.79–0.86)	<0.01	0.84 (0.74–0.98)	0.04
Abnormal weight loss	1.18 (1.11–1.25)	<0.01	1.18 (1.01–1.41)	0.04
Acute pancreatitis	1.32 (1.09–1.60)	<0.01	1.32 (1.04–1.70)	0.02
Acute renal failure	1.13 (1.08–1.18)	<0.01	1.14 (0.98–1.35)	0.10
Anaphylactoid reaction	1.31 (1.00–1.72)	0.05	1.31 (0.98–1.79)	0.07
Anemia	0.96 (0.92–0.99)	0.02	0.97 (0.84–1.14)	0.76
Angioedema	3.53 (2.99–4.16)	<0.01	3.31 (2.55–4.51)	<0.01
Anxiety	0.98 (0.95–1.00)	0.03	0.99 (0.86–1.16)	0.91
Bradycardia	0.96 (0.86–1.08)	0.52	0.98 (0.82–1.18)	0.84
Cardiac arrhythmia	0.96 (0.91–1.02)	0.22	0.98 (0.84–1.15)	0.82
Chest pain or angina	0.99 (0.97–1.01)	0.23	1.00 (0.87–1.17)	0.92
Chronic kidney disease	1.00 (0.93–1.08)	0.98	1.01 (0.87–1.20)	0.84
Cough	1.32 (1.23–1.42)	<0.01	1.32 (1.11–1.59)	<0.01
Decreased libido	0.96 (0.90–1.03)	0.29	0.98 (0.84–1.16)	0.83
Dementia	1.12 (1.06–1.18)	<0.01	1.13 (0.97–1.34)	0.14
Depression	1.02 (0.99–1.05)	0.20	1.03 (0.90–1.21)	0.65
Diarrhea	1.06 (1.02–1.09)	<0.01	1.07 (0.92–1.25)	0.40
End stage renal disease	0.87 (0.62–1.20)	0.39	0.88 (0.63–1.25)	0.50
Fall	1.09 (0.99–1.19)	0.10	1.04 (0.89–1.22)	0.61
Gastrointestinal bleed	1.18 (1.11–1.25)	<0.01	1.18 (1.01–1.41)	0.04
Gout	1.00 (0.97–1.04)	0.83	1.02 (0.88–1.19)	0.81

LEGEND-HTN: Dual combination therapy for treatment escalation

Yuan Lu

on behalf of the LEGEND initiative

Study Objective

As an extension of the LEGEND-HTN initiative, we aim to conduct a large-scale observational study within the OHDSI collaborative community to characterize real-world utilization of dual antihypertensive combination therapies for treatment escalation among people with hypertension.

Twelve Exposure Cohorts

Cohort #	1st Drug	2nd Drug
1	ACEi/ARB	CCB
2	CCB	ACEi/ARB
3	ACEi/ARB	Diuretic
4	Diuretic	ACEi/ARB
5	ACEi/ARB	Beta-blocker
6	Beta-blocker	ACEi/ARB
7	CCB	Diuretic
8	Diuretic	CCB
9	CCB	Beta-blocker
10	Beta-blocker	CCB
11	Diuretic	Beta-blocker
12	Beta-blocker	Diuretic

Data Sources

Data Source	Data Type	Country/District	Time Period	No. of Patients
IQVIA LPD Australia	EHR	Australia	2006-2020	3,101,500
ePBRN SWSLHD 2019 Linked Dataset (ePBRN SWSLHD)	EHR	Australia	2012-2019	139,346
Ajou University School of Medicine (AUSOM)	EHR	Korea	1995-2019	3,109,677
Kyung Hee University Hospital (KHMC)	EHR	Korea	2008-2018	2,010,456
Khoo Teck Puat Hospital (KTPH)	EHR	Singapore	2010-2016	290,074
National University Hospital (NUH)	EHR	Singapore	2015-2018	750,270
China Jiangsu Province Hospital (CJSPH)	EHR	China	2005-2015	6,230,000
Taiwan Taipei Medical University Clinical Research Database (TMUCRD)	EHR	Taiwan	2004-2020	3,659,572
IQVIA US Ambulatory EMR	EHR	United States	2006-2020	78,526,000
IQVIA LPD France	EHR	France	1994-2020	18,118,000
IQVIA LPD Italy	EHR	Italy	2004-2020	2,209,600

Together, the committed data sources cover:
118 millions patients in 8 countries and districts

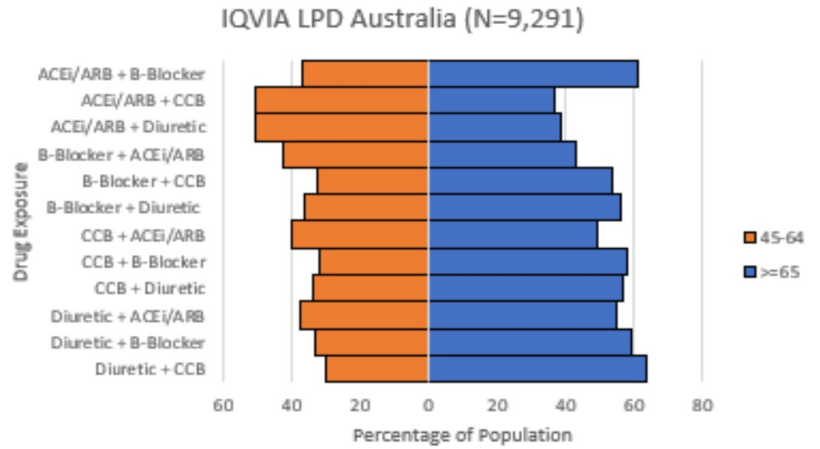
Patient Counts for 12 Exposure Cohorts

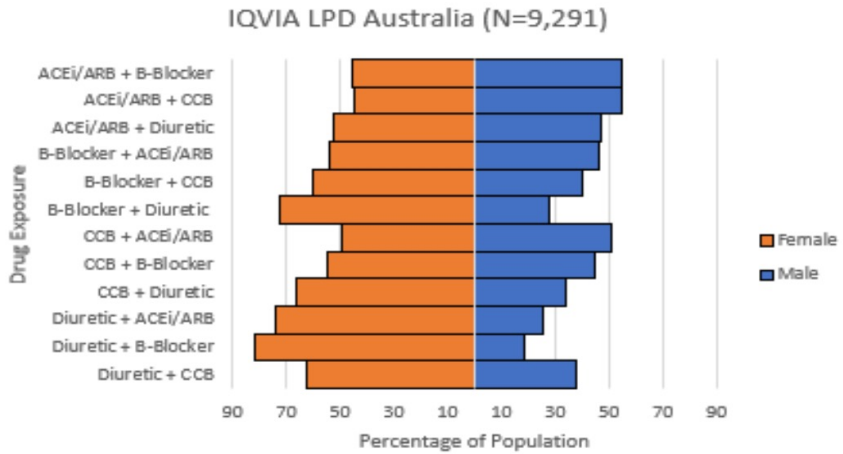
Cohort #	Dual combination	Data Sources										
		Australia		Korea		Singapore		China	Taiwan	France	Italy	United States
		Australia LPD	ePBRN SWSLHD	Ajou University	KHMC	KTPH	NUH	Jiangsu	TMUCRD	France LPD	Italy LPD	US AmbEMR
1	ACEi/ARB + Beta-blocker	1,184	268	392	49	105	144	46	1,464	11,236	11,844	110,579
2	ACEi/ARB + CCB	4,254	698	1,216	147	216	439	3,127	2,812	22,523	14,628	95,284
3	ACEi/ARB + Diuretic	2,066	508	474	12	16	31	111	8	22,399	16,988	123,940
4	Beta-blocker + ACEi/ARB	717	210	386	98	68	128	26	2,357	11,116	8,264	106,380
5	Beta-blocker + CCB	159	54	614	199	97	243	19	2,484	5,972	2,755	41,388
6	Beta-blocker + Diuretic	27	17	51	10	5	7	1	1	4,316	2,967	36,303
7	CCB + ACEi/ARB	1,339	246	1,487	191	191	133	3,312	5,015	15,749	5,841	54,297
8	CCB + Beta-blocker	190	41	814	217	120	101	34	2,518	3,866	2,475	30,593
9	CCB + Diuretic	74	28	259	15	11	6	78	4	1,660	1,103	21,108
10	Diuretic + ACEi/ARB	251	94	154	2	8	7	114	-	3,281	5,749	84,275
11	Diuretic + Beta-blocker	27	14	43	5	1	8	-	-	779	1,929	27,422
12	Diuretic + CCB	50	25	139	6	4	7	140	-	1,097	1,539	22,568

Cohort Characterization by Age and Sex

- Younger patients were more likely to be prescribed ACEi/ARB then a CCB or a diuretic compared with older patients.

- Women were more likely to be prescribed diuretics then an ACEi/ARB or a CCB compared with men.





Treatment Pathways

- Large variations treatment pathways across countries

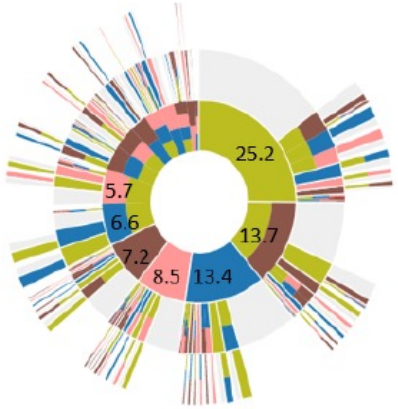
IQVIA US AmbEMR

Target Cohort

[APAC HTN] APAC overall population

- Target cohort count: 6,000,244
- Persons with pathways count: 5,166,727
- Persons with pathways portion: 86.1%

[APAC HTN] ACEi/ARB use after hypertension diagnosis
[APAC HTN] Diuretic use after hypertension diagnosis
[APAC HTN] CCB use after hypertension diagnosis
[APAC HTN] Beta-blocker use after hypertension diagnosis



IQVIA Italy LPD

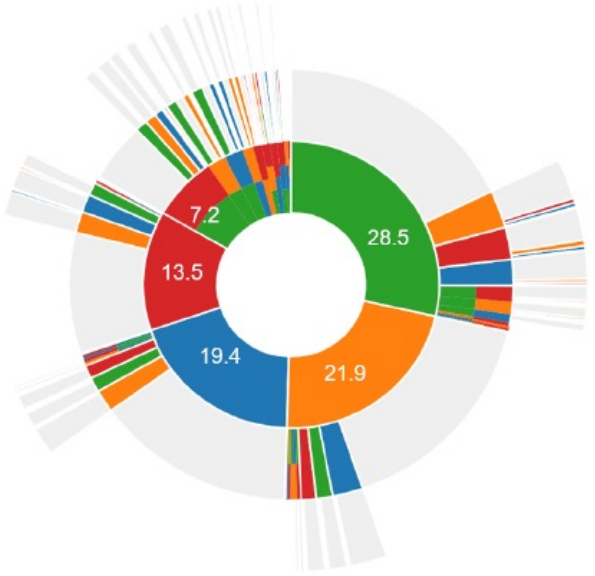
Target Cohort

[APAC HTN] APAC overall population

- Target cohort count: 535,157
- Persons with pathways count: 283,301
- Persons with pathways portion: 52.9%

Event Cohorts

[APAC HTN] Beta-blocker use after hypertension diagnosis
[APAC HTN] CCB use after hypertension diagnosis
[APAC HTN] ACEi/ARB use after hypertension diagnosis
[APAC HTN] Diuretic use after hypertension diagnosis



Main Findings and Lessons Learned

- Large variation in the transition between monotherapy and dual combination therapy for hypertension across countries and by demographic groups.

Main Findings and Lessons Learned

- Large variation in the transition between monotherapy and dual combination therapy for hypertension across countries and by demographic groups.

- Future research is needed to identify what dual combinations work best for which patients.

Main Findings and Lessons Learned

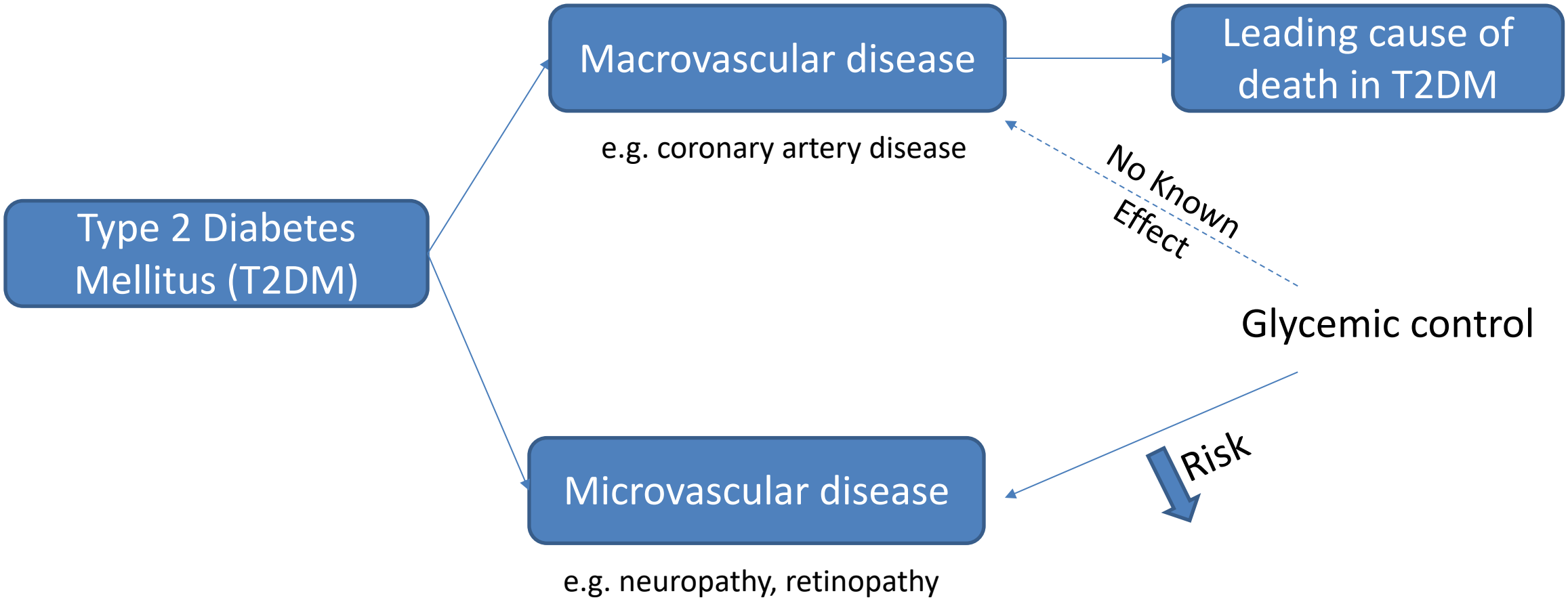
- Large variation in the transition between monotherapy and dual combination therapy for hypertension across countries and by demographic groups.
- Future research is needed to identify what dual combinations work best for which patients.
- Using LEGEND principles can help mobilize collaboration with OHDSI data partners, but substantial effort was required to ensure data quality and alignment of methods across data sources.

LEGEND-T2DM: Second-line antihyperglycemic treatment protocol

Rohan Khera

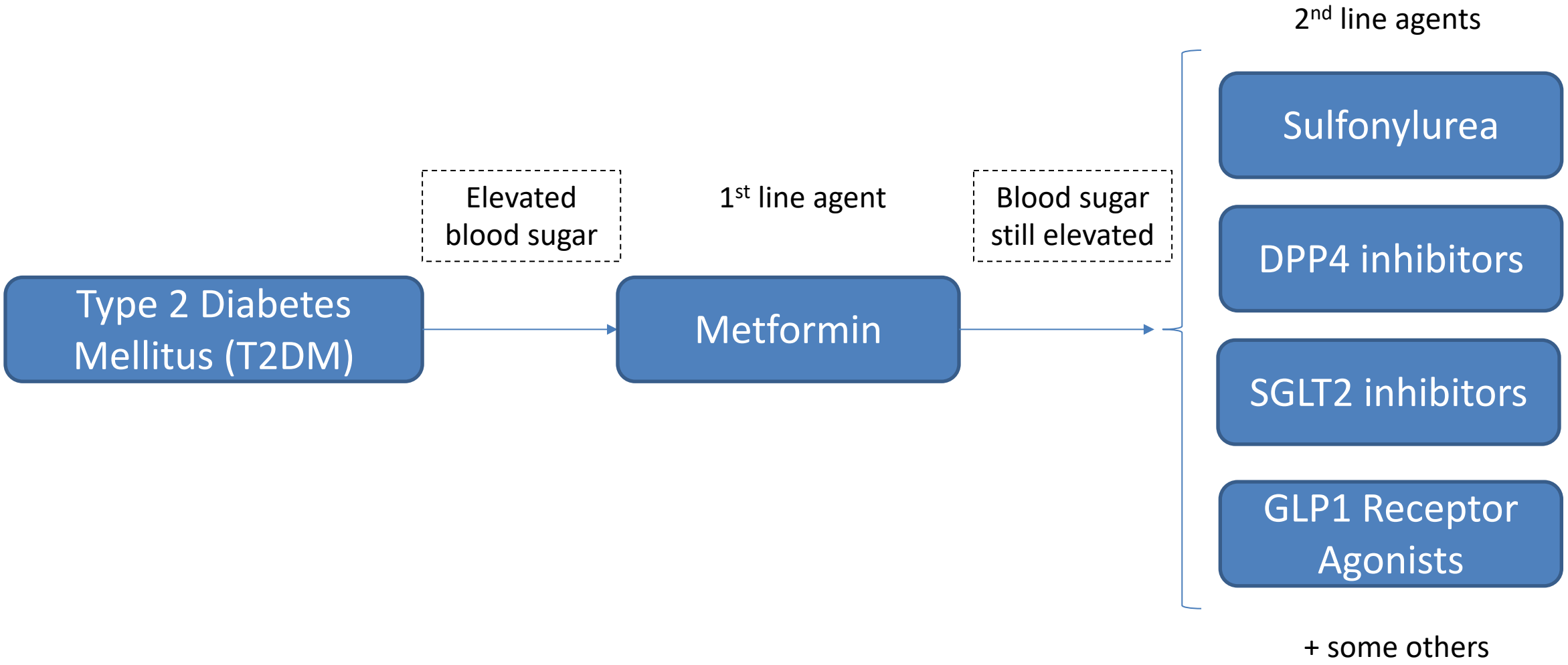
on behalf of the LEGEND initiative

What is the Motivation for LEGEND-T2DM?



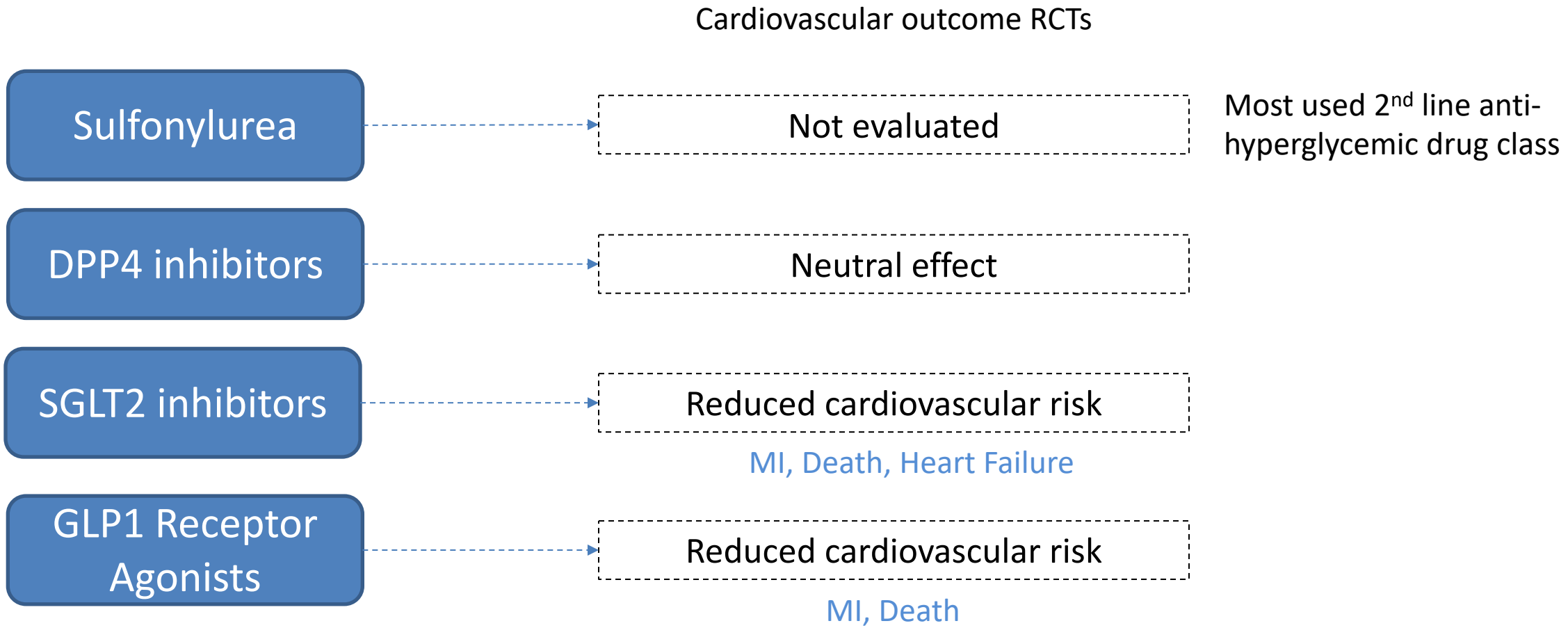
What is the Motivation for LEGEND-T2DM?

Several treatment strategies



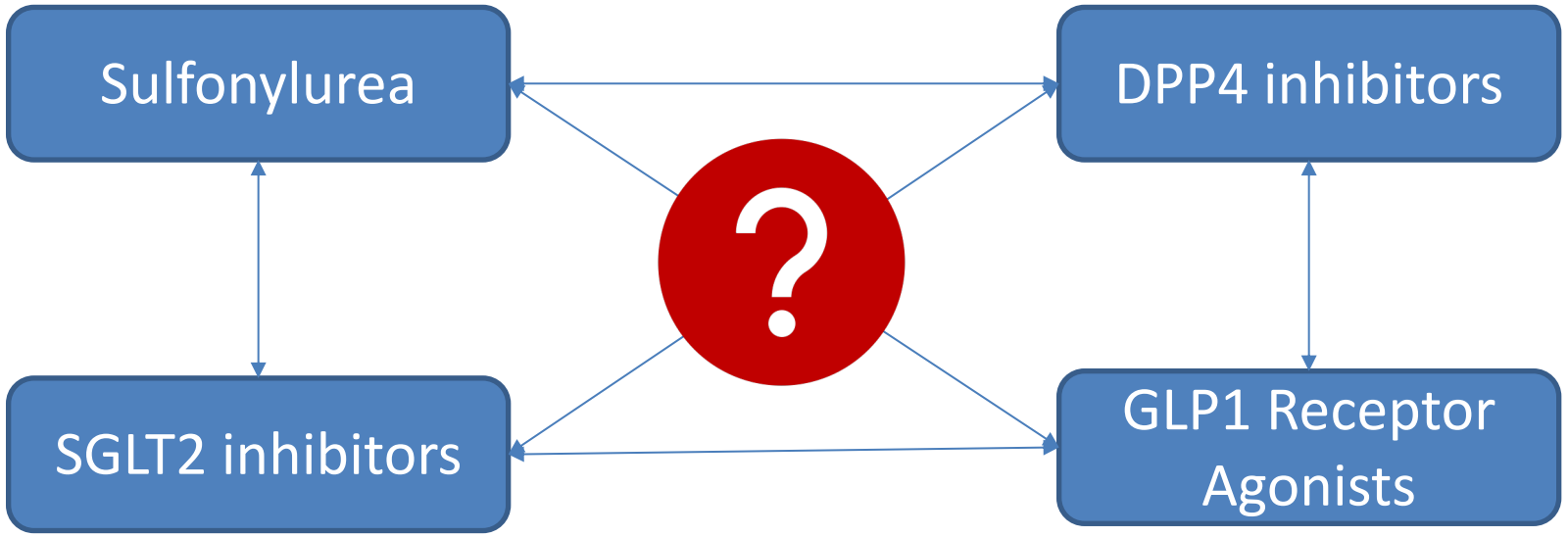
What is the Motivation for LEGEND-T2DM?

Variable evidence for cardiovascular efficacy for agents



What is the Motivation for LEGEND-T2DM?

Unknown cardiovascular effects of agents relative to each other



Critical need for evidence to improve choice between drug classes

What is the Motivation for LEGEND-T2DM?

Unknown cardiovascular effects of agents relative to each other

Goals of LEGEND-T2DM

Evaluate relative cardiovascular effectiveness and safety of 2nd line anti-hyperglycemic drug classes

Assess relative cardiovascular effectiveness and safety of individual 2nd line anti-hyperglycemic agents across classes

LEGEND-T2DM: Emerging best practices

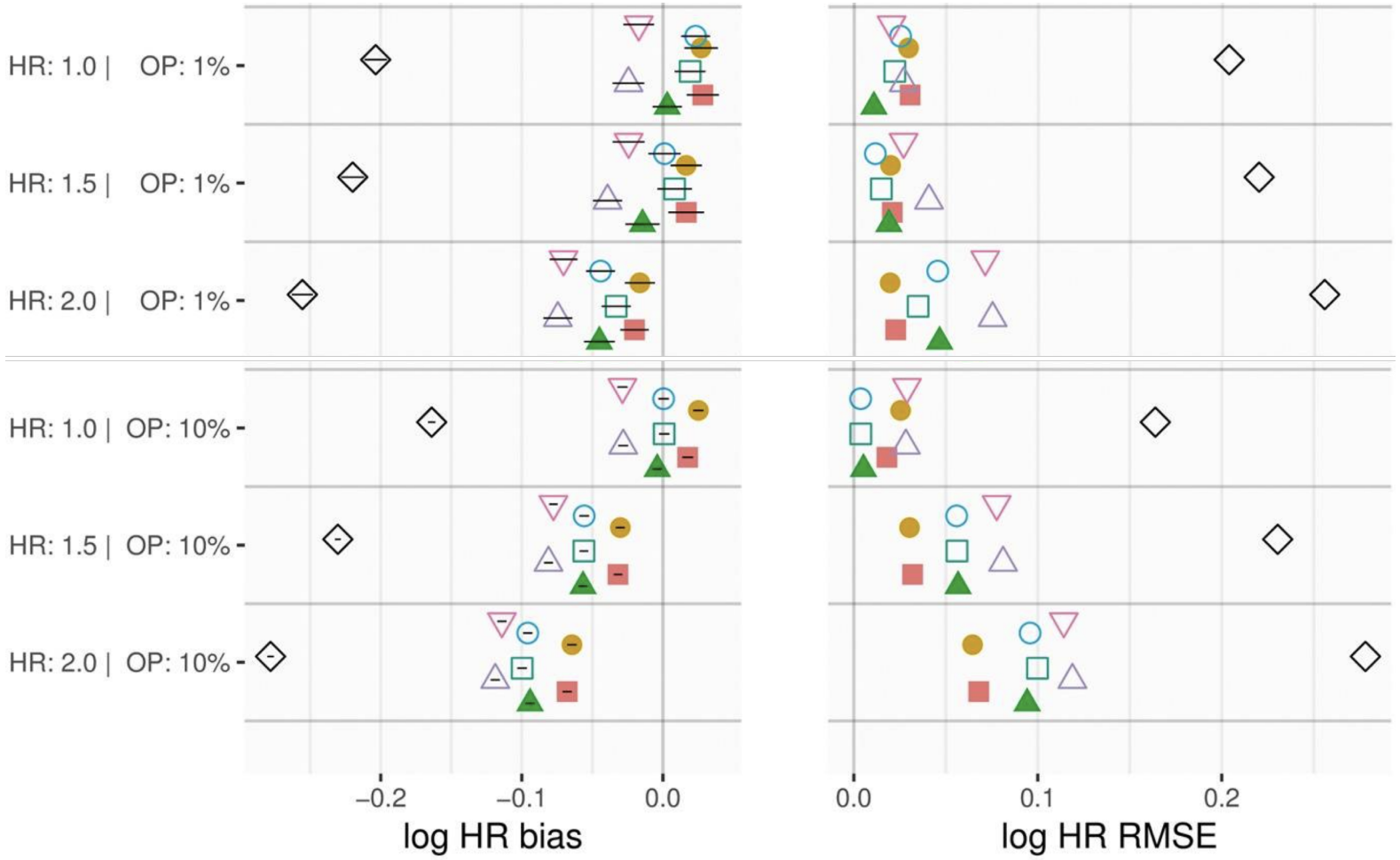
Aki Nishimura and Fan Bu

on behalf of the LEGEND initiative

Methodological gaps in realizing LEGEND objectives

- Improved causal inference for survival outcomes
- Evidence synthesis of federated data sources

Causal inference on survival outcomes



Non-linearity / non-collapsibility of Cox model causes *bias* toward null.

Causal inference on survival outcomes

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December 1984

Biased estimates of treatment effect in randomized experiments with nonlinear regressions and omitted covariates

M. H. GAIL, S. WIEAND, S. PIANTADOSI

Biometrika, Volume 71, Issue 3, December 1984, Pages 431–444, https://doi-org.proxy1.library.jhu.edu/10.1093/biomet/71.3.431
Published: 01 December 1984 **Article history**

Springer Link

Published: 18 January 2013

On collapsibility and confounding bias in Cox and Aalen regression models

Torben Martinussen & Stijn Vansteelandt

Lifetime Data Analysis **19**, 279–296 (2013) | Cite this article

Causal inference on survival outcomes

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Peter C. Austin, Elizabeth A. Stuart,

First published: 06 August 2015 | https://doi-org.proxy1.library.jhu.edu/10.1002/sim.6602 |
Citations: 32

onfounding bias in Cox
odels

Torben Martinussen & Stijn Vansteelandt

Lifetime Data Analysis **19**, 279–296 (2013) | Cite this article

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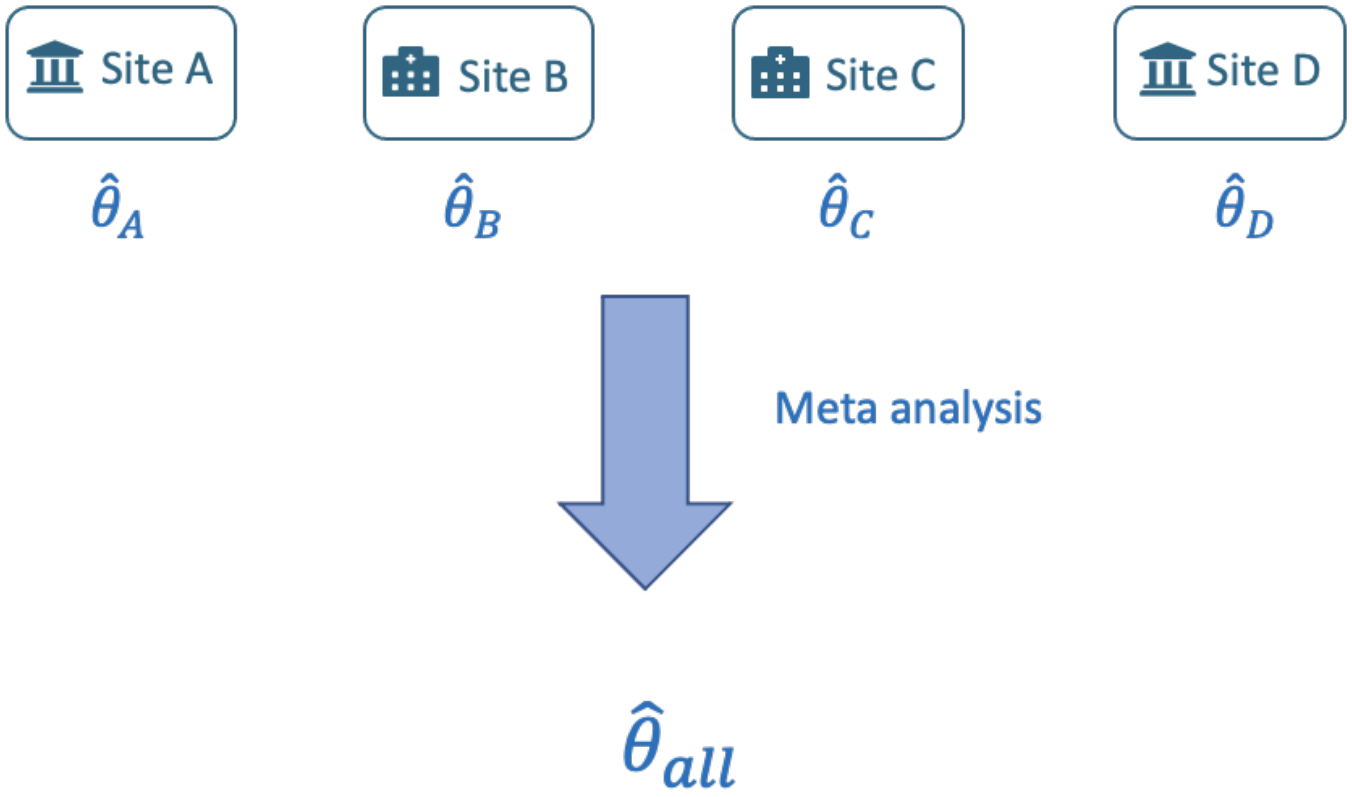
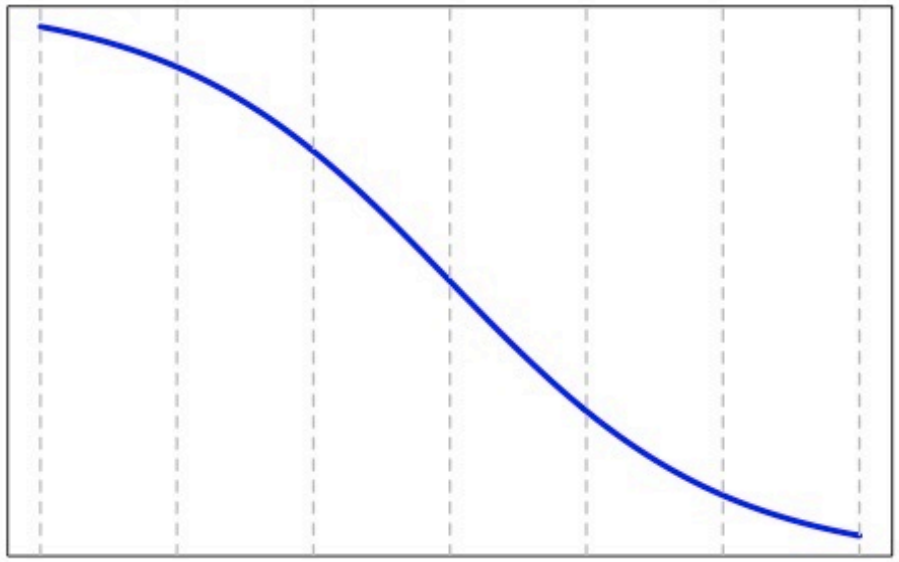
Evidence synthesis: traditional method

- Each site produces point estimate for effect size
- Use meta-analysis (e.g., random effect model) to combine estimates
- End result is an overall estimate



But there might be issues

Rare events with small or zero counts

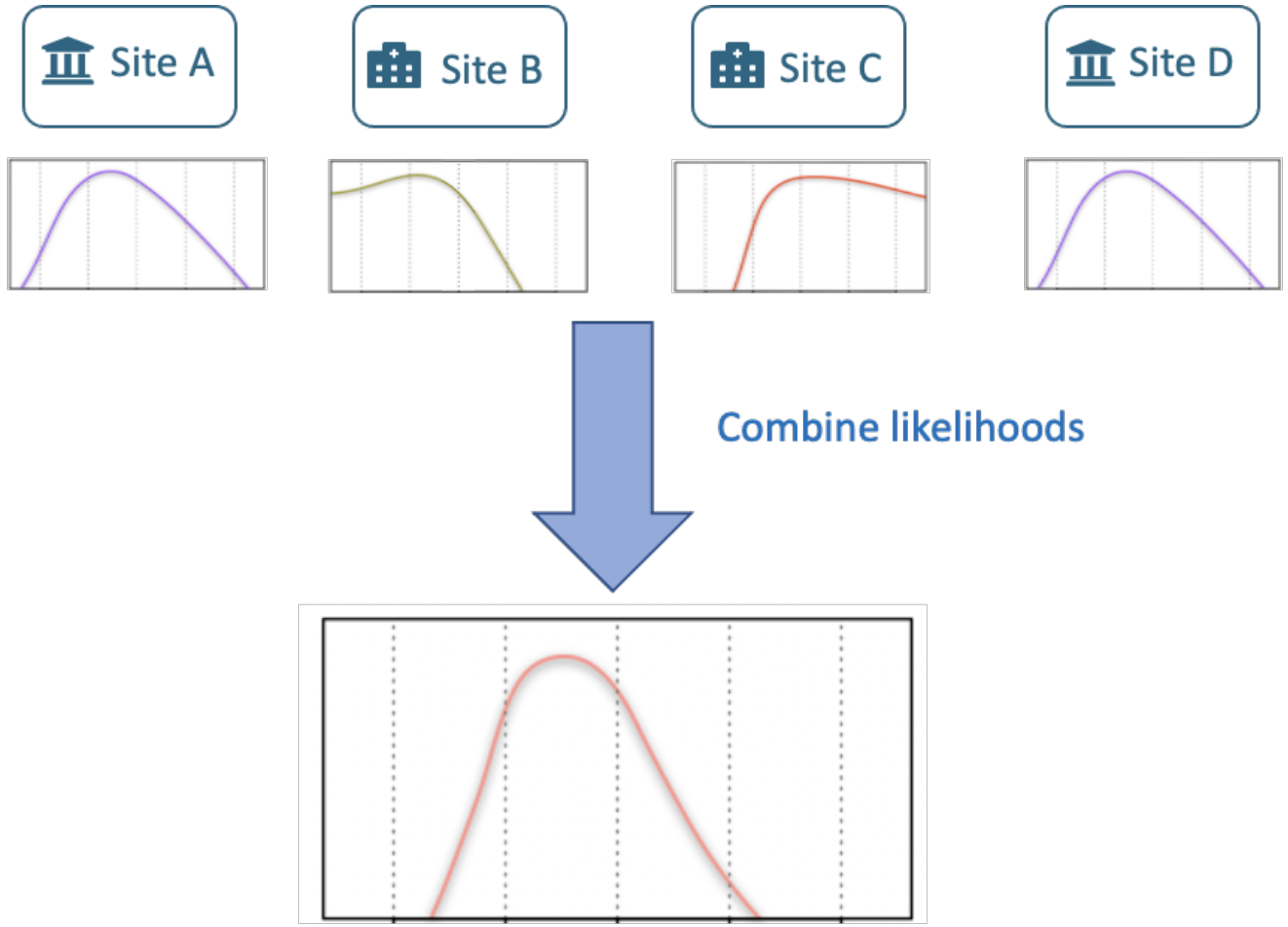


Likelihood monotonic:
no optimality!

- no MLE, no confidence interval
- traditional method discards such data sites

Evidence synthesis: emerging alternative

- Instead of summary statistics
- Each site produces a likelihood
- Likelihood: profile of full evidence
- Use Bayesian or numerical methods to "combine" likelihoods
- End result is an overall likelihood profile



Challenges and emerging & future work

- Small or zero counts (monotonic individual likelihoods)
  - need better likelihood approximations or better combination algorithms (e.g., Schuemie et al., 2021; Duan et al., 2020)

- Systematic errors (common in observational data)
  - calibration using negative (& positive) controls (e.g., Mulgrave et al., 2020)

- Community-level confounding
  - possible solution with mixture models or latent factor models

LEGEND-T2DM: How to get involved?

Marc Suchard

on behalf of the LEGEND initiative

LEGEND-T2DM Kick-off!

- ENCePP EU PAS Register #43551

- Preliminary exposure and outcome cohort diagnostics:
  - Large US claims data sources: **CCAE**, **MDCR**, **MDCD**
  - Large US EHR data sources: **VA**, **OptumEHR**
  - US academic EHR data sources: **Columbia**, **Hopkins**
  - Int'l EHR data sources: **NUS (Singapore)**

- Formal study start date: 1 Nov 2021 !!

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Comment on this paper

RESEARCH PROTOCOL: Large-scale evidence generation and evaluation across a network of databases for type 2 diabetes mellitus

Rohan Khera, Martijn J Scheumie, Yuan Lu, Anna Ostropolets, Ruijun Chen, George Hripcsak, Patrick B Ryan, Harlan M Krumholz, Marc A Suchard

doi: https://doi.org/10.1101/2021.09.27.21264139

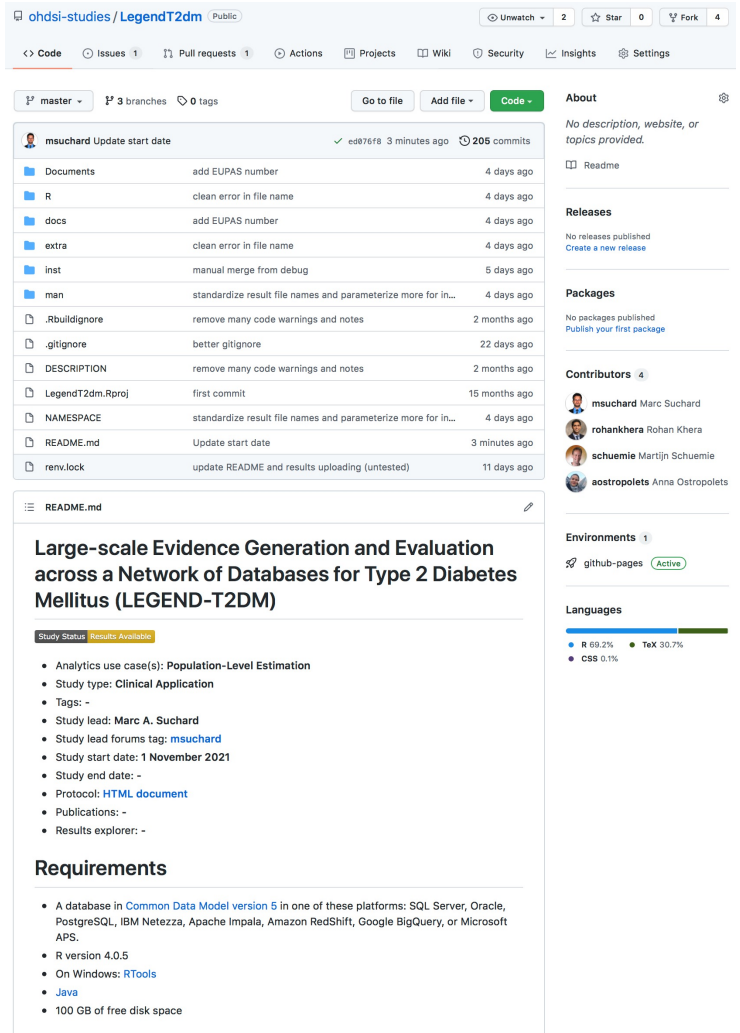
This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract | Full Text | Info/History | Metrics | Preview PDF

Abstract

Background Therapeutic options for type 2 diabetes mellitus (T2DM) have expanded over the last decade with the emergence of sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP1) receptor agonists, which reduced the risk of major cardiovascular events in randomized controlled trials (RCTs). Cardiovascular evidence for older second-line agents, such as sulfonylureas, and direct head-to-head comparisons, including with dipeptidyl peptidase 4 (DPP4) inhibitors, are lacking, leaving a critical gap in our understanding of the relative effects of T2DM agents on cardiovascular risk and on patient-centered safety outcomes.

LegendT2dm Study Package



- Distributed as an OHDSI Network study R package from github.com
  - OMOP CDM v5 and R 4.0.5
  - README.md
  - renv / dockerfile
- Cohort characterization is ready for execution across our network
- Please contribute as a ***data partner***

LEGENDary Resources

- Team:
  - Fan Bu
  - Ray Chen
  - George Hripcsak
  - Rohan Khera
  - Harlan Krumholz
  - Kelly Li
  - Yuan Lu
  - Evan Minty
  - Aki Nishimura
  - Anna Ostropolets
  - Patrick Ryan
  - Martijn Schuemie
  - Marc Suchard

- Join us:
  - 2nd/4th/5th Thursday of each month at 12p ET

- Links:
  - Study protocol: **https://ohdsi-studies.github.io/LegendT2dm/Protocol.html**
  - Study package: **https://github.com/ohdsi-studies/LegendT2dm**

- Contact to participate: **Marc Suchard** (Teams) or **msuchard@ohdsi.org**