Learning Effective Treatment Pathways from Observational Data

A Multinational Cohort Study for Type 2 Diabetes

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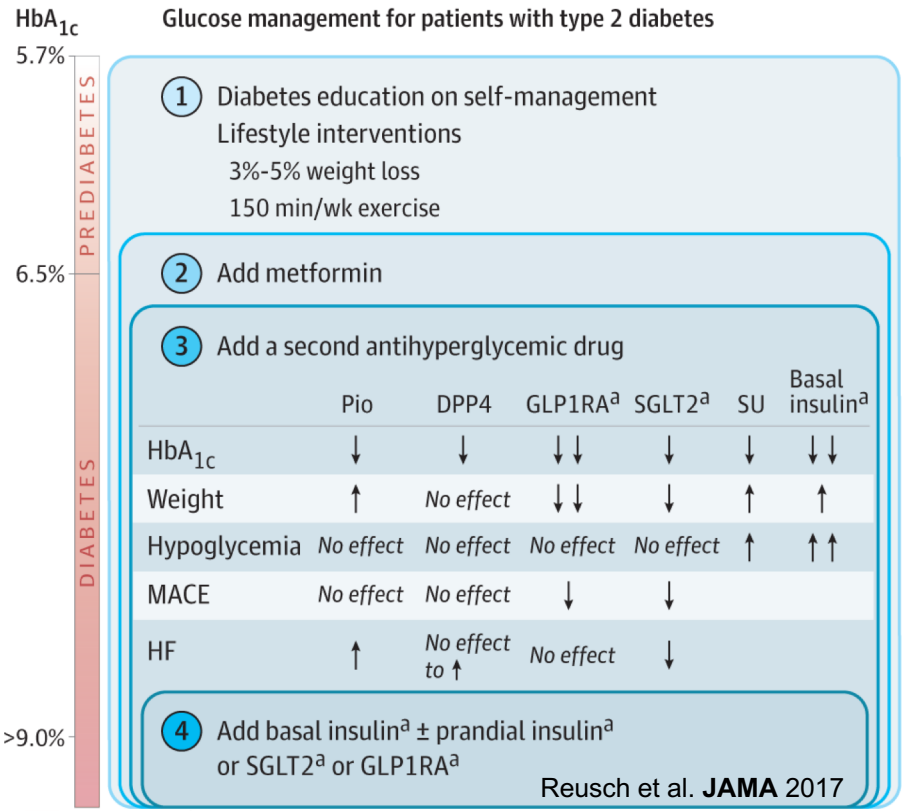
Stanford MEDICINE

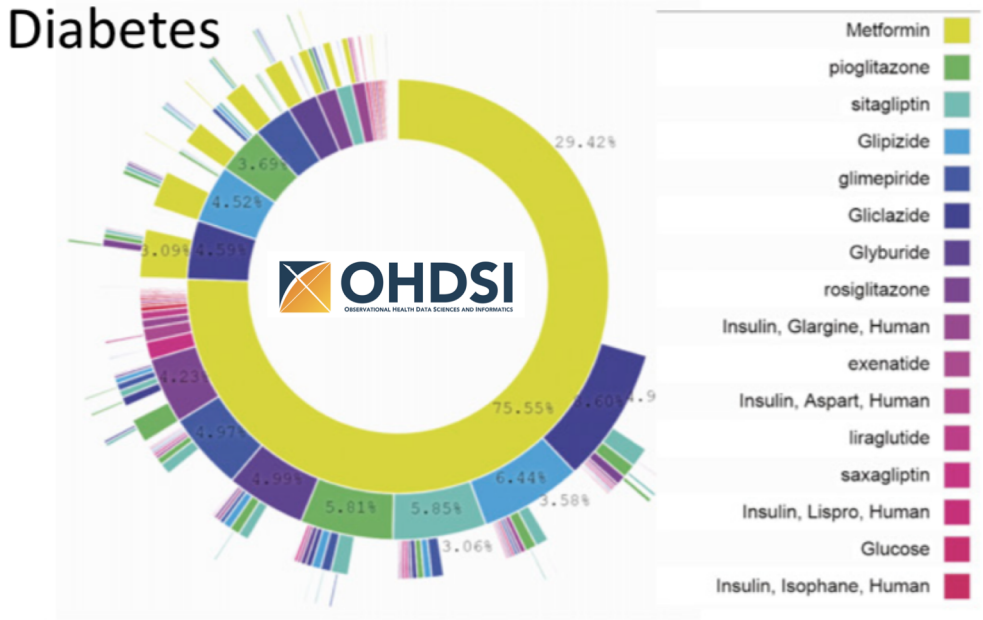
Diabetes

- 1.5 Million deaths in the year 2015.
- Global prevalence of 8.5% in the year 2014.
- Causes blindness, kidney failure, cardiovascular disorders, pregnancy complication and nerve damage.
- A chronic disease.

Treatment Guidelines & Practice of Medicine in Type-2 Diabetes



Reusch et al. **JAMA** 2017

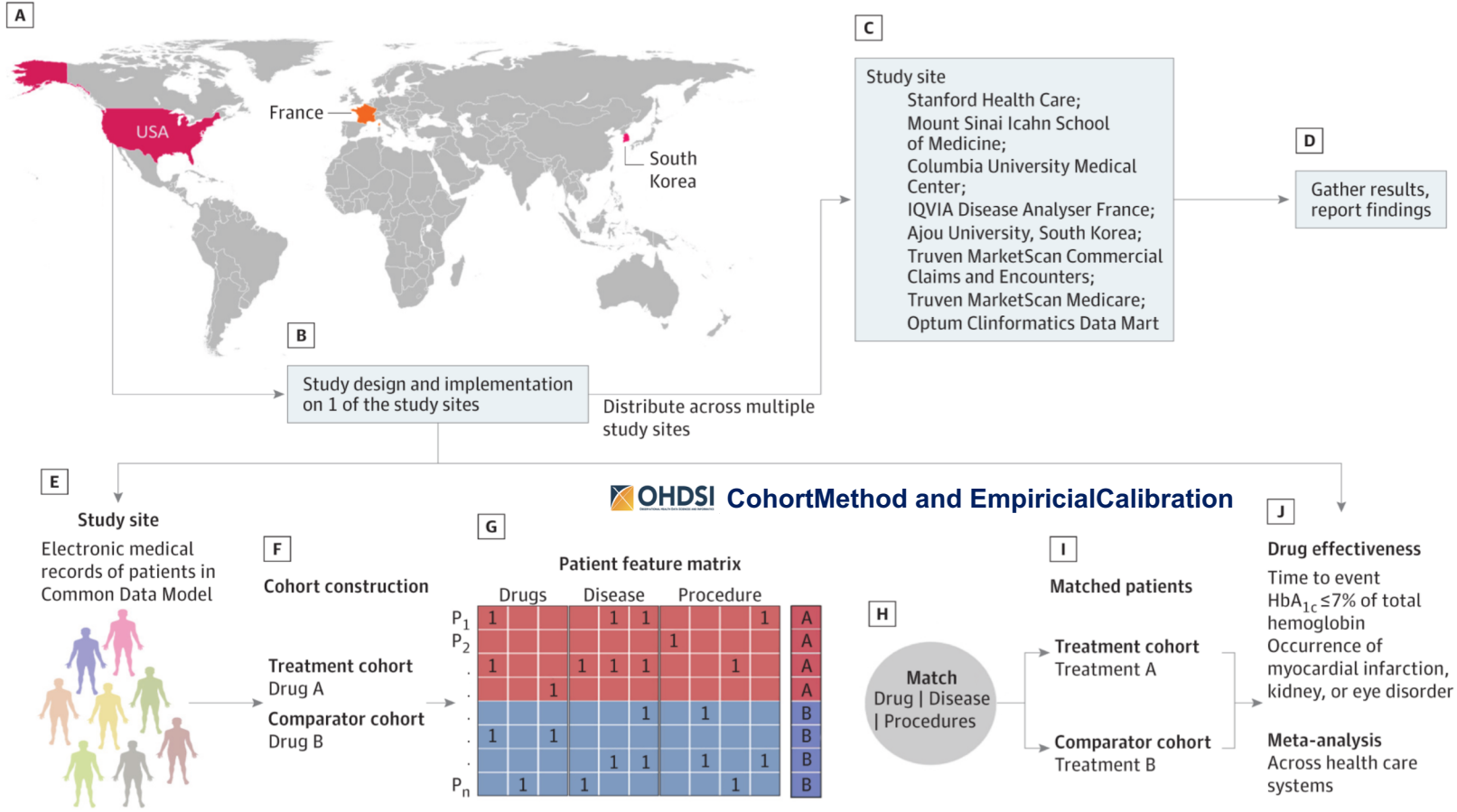


Hripcsak et al **PNAS** 2015

Which is the best second-line treatment to reduce HbA1c and prevent events related to myocardial infarction, kidney- and eye-disorders in patients with T2D?

Our Approach to Understand Effectiveness of Second-line Treatment in T2D within OHDSI Framework

JAMA Network | Open
Vashisht et al. 2018



Total Number of Patients

Across Eight Healthcare Systems

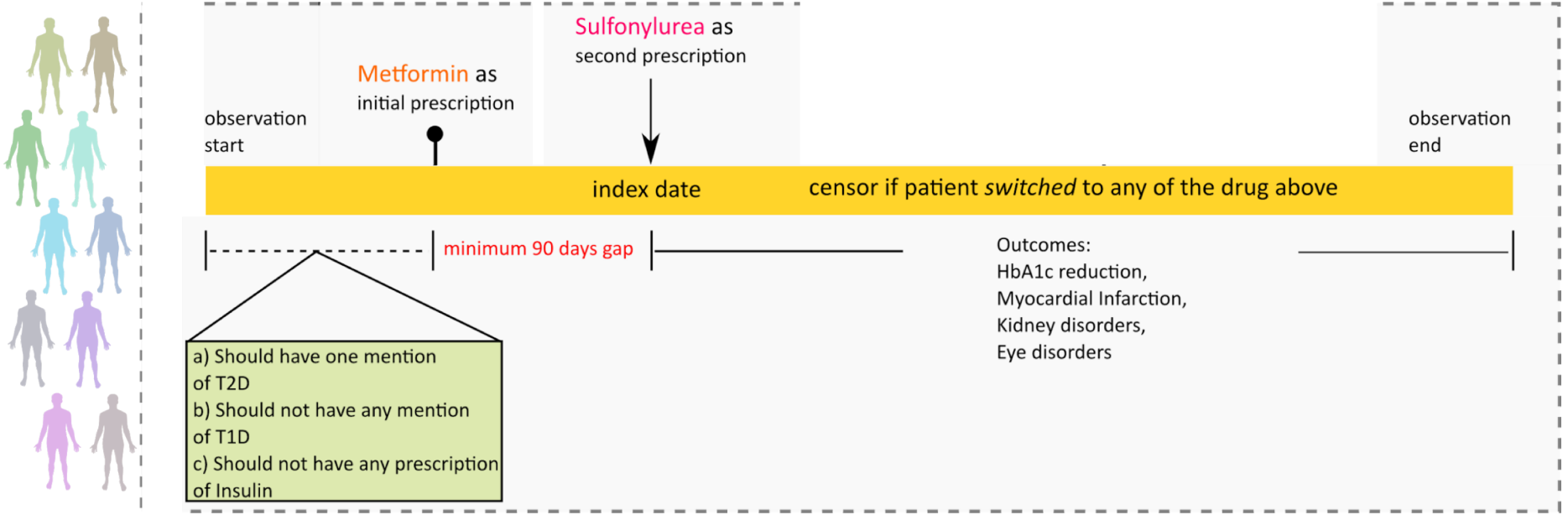
Table 1. Patient-Level Characteristics Across Data Sources

Data Source	No. of Patients	%		Time, y		
		Female	Male	Start	End	Total
Truven MarketScan Commercial Claims and Encounters	135 249 219	51.1	48.2	2000	2017	7
Columbia University Medical Center	5 405 830	55.9	43.7	1985	2016	31
IQVIA Disease Analyzer France	9 949 909	52.3	47.1	1997	2016	19
Truven MarketScan Medicare Supplemental and Coordination of Benefits	9 825 381	55.3	44.6	2000	2017	7
Mount Sinai	1 941 454	56.1	43.7	1979	2014	35
Optum Clinformatics Data Mart	79 604 449	50.5	49.4	2000	2017	7
Ajou University School of Medicine, South Korea	2 275 118	48	52	1994	2015	21
Stanford Health Care	2 307 445	54.3	45.4	2007	2017	10
Total No. of patients	246 558 805	51.5	48.5			

Rule Based Cohort Construction from EHRs

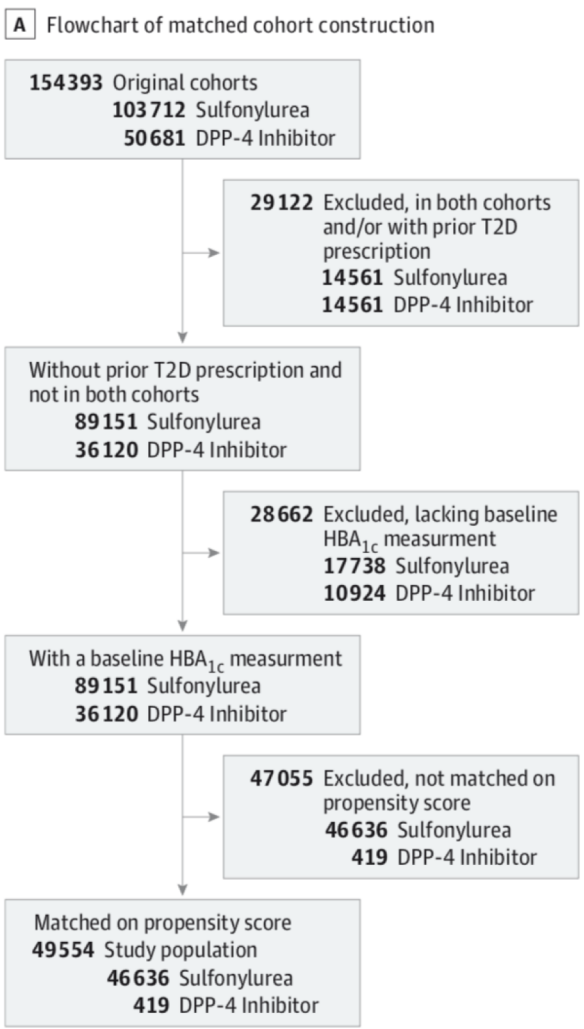
Second line treatments: Sulfonylureas, DPP4-Inhibitors and Thiazolidinediones.

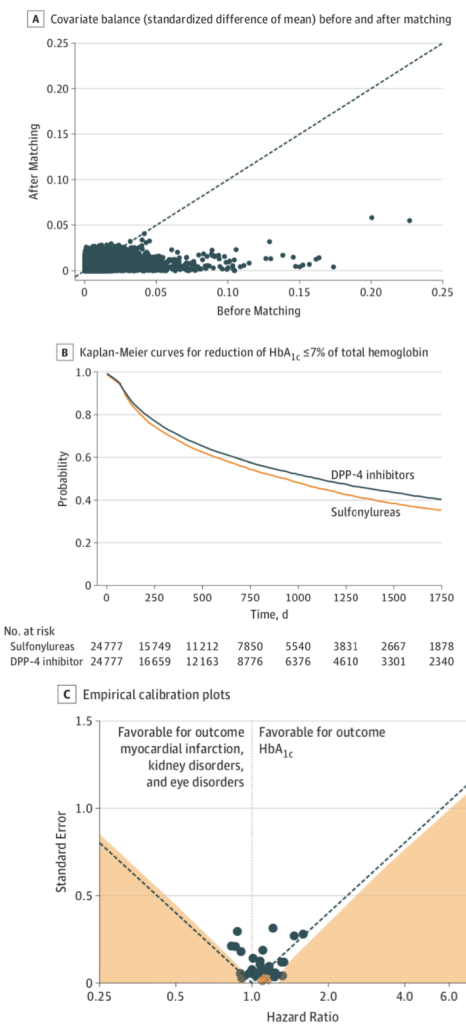
Outcome: Reduction in HbA1c <= 7%, myocardial infarction, kidney- and eye-disorders.



Study Population & Analysis

Example: comparison of Sulfonylureas vs DPP4-Inhibitors for Outcome reduction in HbA1c <= 7% using CohortMethod and EmpiricalCalibration

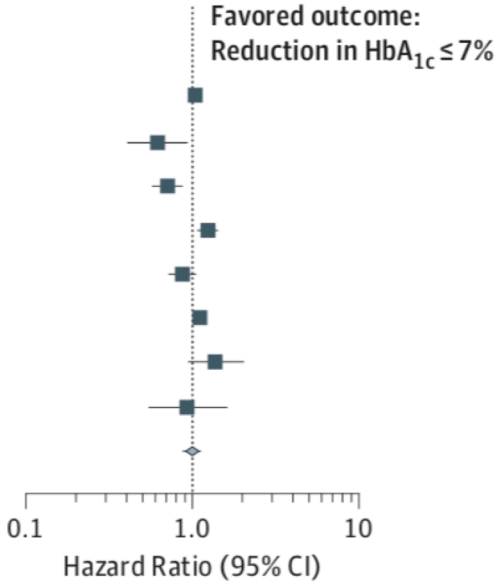




Treatment Effectiveness

Sulfonylurea(T) vs DPP4-Inhibitors(C)

Source	No. of Patients	Hazard Ratio (95% CI)
Truven MarketScan Commercial Claims and Encounters	10011	1.04 (0.98-1.09)
Columbia University Medical Center	205	0.62 (0.41-0.91)
IQVIA, France	774	0.71 (0.58-0.86)
Truven MarketScan Medicare	1661	1.24 (1.09-1.40)
Mount Sinai	880	0.87 (0.73-1.04)
Optum	24777	1.11 (1.08-1.15)
Ajou University School of Medicine, South Korea	567	1.38 (0.95-2.02)
Sanford University	98	0.93 (0.55-1.57)
Summary, $I^2 = 84.2\%$		0.99 (0.89-1.10)



Results across healthcare systems are summarize using random effect meta-analysis approach.

Summary Estimates

Table 2. Consensus Hazard Ratio (HR) Estimates for Primary and Secondary Outcomes After Meta-Analysis[a]

Outcome	Sulfonylureas (T) vs DPP-4 Inhibitors (C)	Sulfonylureas (T) vs Thiazolidinediones (C)	DPP-4 Inhibitors (T) vs Thiazolidinediones (C)
Reduction of HbA_{1c} ≤7%	0.99 (0.89-1.10)	1.06 (0.96-1.16)	1.08 (0.96-1.21)
Myocardial infarction	1.12 (1.02-1.24)	1.07 (0.92-1.24)	1.10 (0.96-1.25)
Kidney disorders	1.07 (0.97-1.19)	1.02 (0.91-1.13)	1.02 (0.97-1.07)
Eye disorders	1.15 (1.11-1.19)	1.05 (1.00-1.09)	0.96 (0.92-1.01)

DPP4-Inhibitors compared to Sulfonylureas when prescribed after Metformin **appears to have lower hazard** of **Myocardial Infarction** and **Eye Disorders** in patient with Type-2 diabetes.

Limitations of the Study

Confounders

- We did not considered actual values of lab results but just the presences or absence of the laboratory test ordered for the patient - for example, we did not consider the actual blood pressure of the patient, but relied on if the blood pressure was measured.

- We did not consider other factors such as the socio economic status of the patients that might confound the analysis - this information is often not reported in EHR setting.

Meta Analysis

- There was considerable amount of heterogeneity in the meta-analysis of few of the comparisons - there could be numerous reasons for the source of heterogeneity, which were beyond the scope of our study to quantify.

Conclusion

1. DPP4-Inhibitors compared to Sulfonylureas when prescribed after Metformin have lower observed hazards of Myocardial Infarction and Eye related disorders.

2. Large-Scale observational data within OHDSI framework can be utilized to address clinical question and generate real world evidence at scale where RCTs are infeasible to conduct.

3. OHDSI framework enables the generation of clinical evidence in a matter of a day compared to a randomized trial, which might take years to execute with staggering cost.

4. Our analysis is an example of initial steps towards building a learning healthcare system.

7 Steps to Conduct a Network Study within OHDSI Framework

1. Decide a clinical question of interest.
2. Assess if your question belong to ***'descriptive', 'population level estimation' or 'patient level classification/prediction'*** framework of problem solving.
3. Build a **deep understanding** of amazing OHDSI tools (ATLAS, CohortMethod, PLP etc.)
4. Write a study protocol and **share** it with the community for the feedback. Be **very open** to feedback, changes and suggestions – often lot of them, which is good. (modified by James Weaver).
5. Attend any of the **OHDSI meeting**: Face to Face or OHDSI symposium and talk to community members. Go with questions.
6. Execute your study and **share the results** with the community.
7. Request other members of OHDSI community to execute your study – **they are a gem of people**.

Thank You Amazing Team OHDSI