Expanding OHDSI into Asia

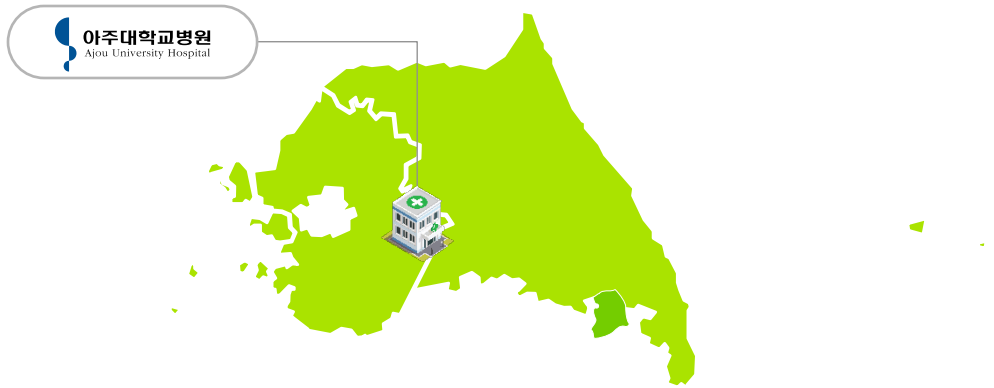
Mui Van Zandt, Hua Xu, PhD, Hui Lu PhD, Rae Woong Park, MD, PhD, Seng Chan You, MD, MS, Hee Hwang, MD, Sooyoung Yoo, PhD, Won Chul Cha. MD, Dong Kyung Chang, Tatsuo Hiramatsu, MD, PhD, Mengling Feng, PhD, Liu Lei PhD, Haoyan Cai

Joining the Journey

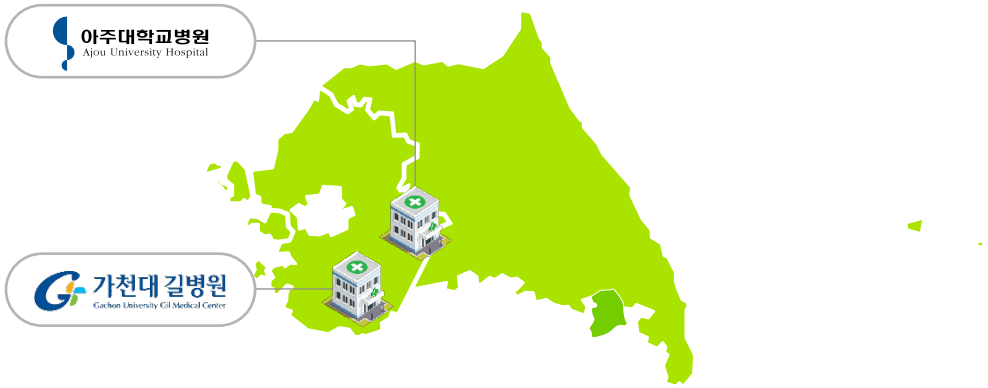

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

OHDSI Korea

CDM conversion of Ajou University EHR



CDM conversion of Gacheon University EHR



2014 2015 2016 2017 2018 2019

CDM conversion of National Health Insurance Service (NHIS) data

2014 2015 2016 2017 2018 2019

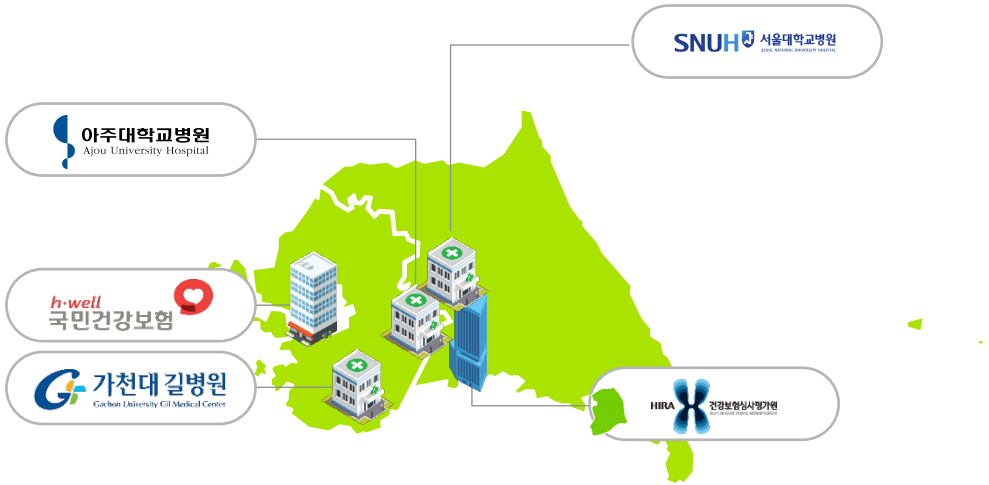
International Korea Symposium

1st OHDSI Data Governance Leadership Meeting

CDM conversion of Health Insurance Review & Assessment Service (HIRA)

2014 2015 2016 2017 2018 2019

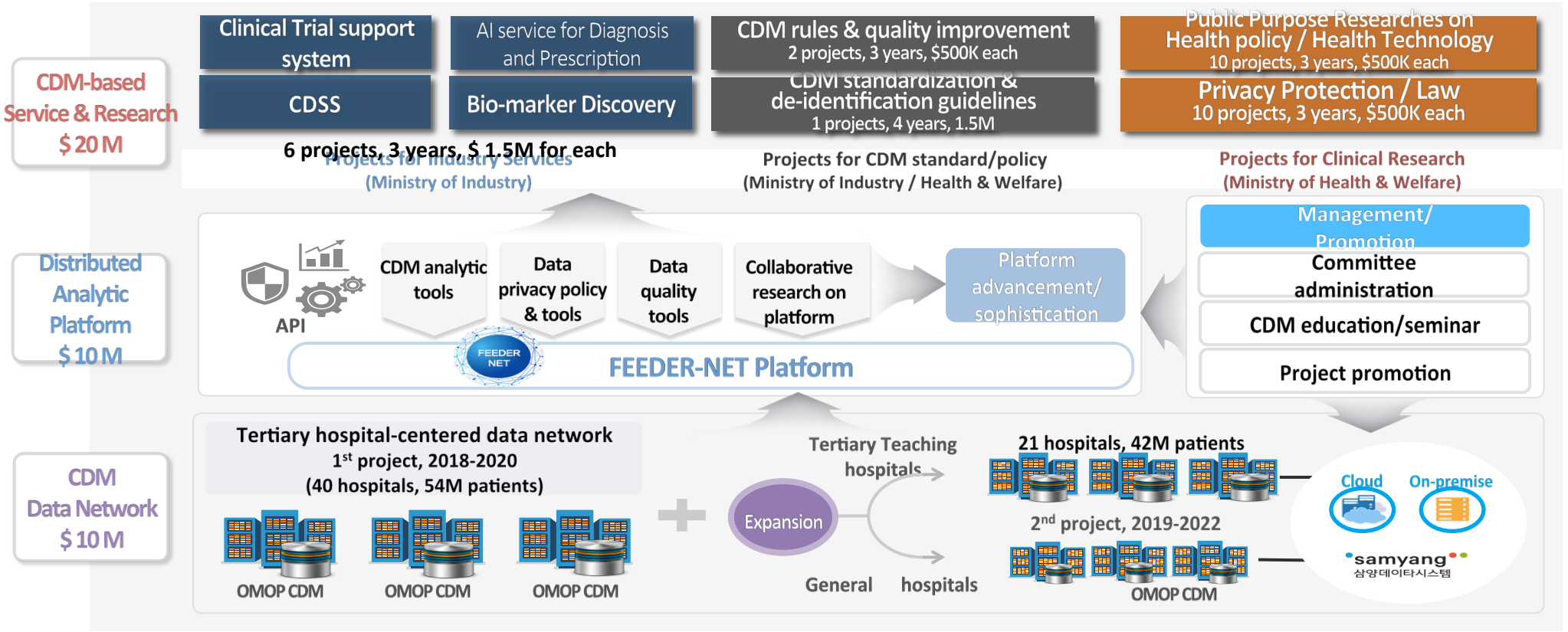
CDM conversion of Seoul National University Bundang Hospital



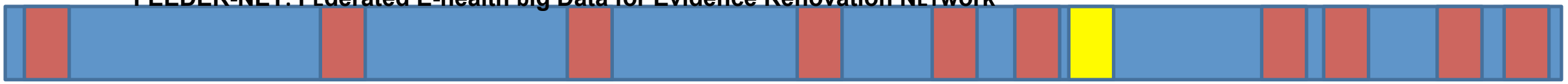
2014 2015 2016 2017 2018 2019

FEEDER-NET project launched

AJOU UNIVERSITY

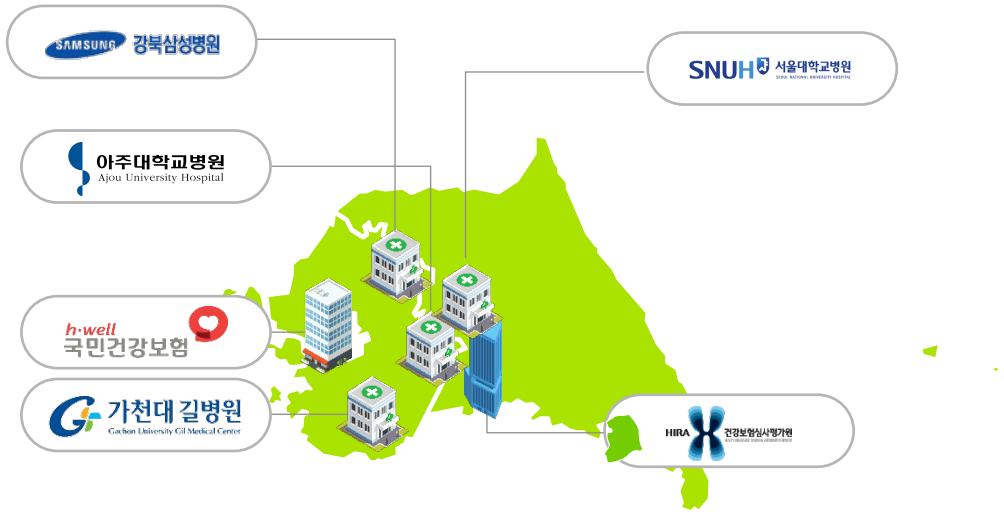


FEEDER-NET: FEderated E-health big Data for Evidence Renovation NETwork



2014 2015 2016 2017 2018 2019

CDM conversion of Samsung Medical University

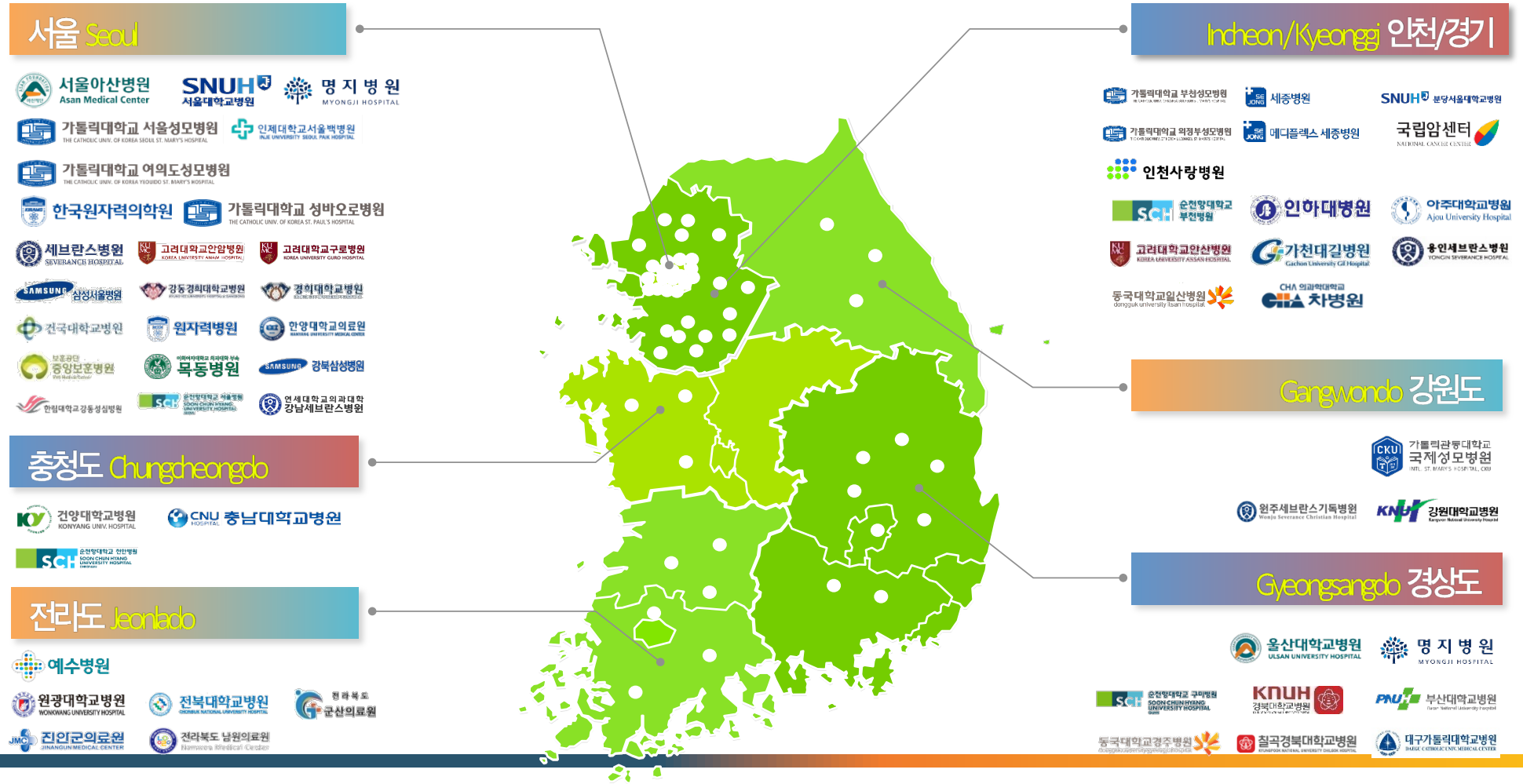


2014 2015 2016 2017 2018 2019

FEEDER-NET Data Network in Korea

Data Network of 60+ Hospitals, 98M Patients

70% of Tertiary Teaching Hospitals



Ajou University Datathon August 2019

2014 2015 2016 2017 2018 2019

Upcoming OHDSI Events

- OHDSI OMOP Tutorial
  - 2 days in October
- OHDSI Korea Symposium
  - December 12th – 14th

2014 2015 2016 2017 2018 2019


OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

OHDS China

OHDSI China Established

OHDSI China
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

https://ohdsichina.org

OHDSI China Symposium 2017

2016 2017 2018 2019

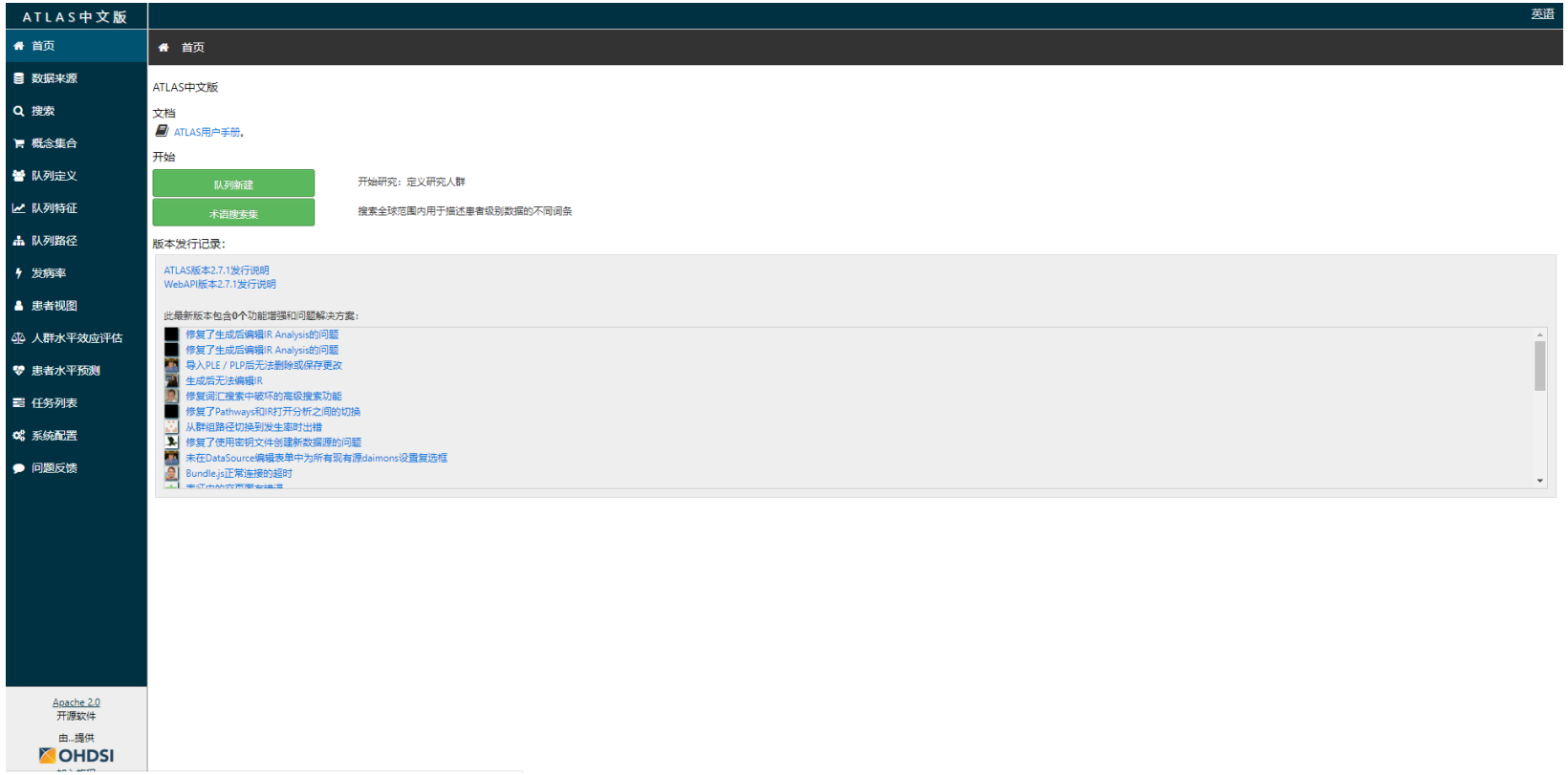
Shanghai Hackathon

2018 Symposium

Beijing Hackathon

2019 Symposium

Chinese Atlas



2016 2017 2018 2019

OMOP Conversion - Beijing-Tianjin-Hebei Psychiatry Alliance

Id	Name
1134	[China Study] Bipolar with antidepressant + antipsychotics/mood stabilizers + hospitalization - 365d prior and year 2013 after
1126	[China Study] Bipolar with antidepressant only and hospitalization - 365d prior and year 2013 after
1130	COPY OF: [China Study] Bipolar - 365d prior
1128	COPY OF: COPY OF: [China Study] Bipolar with antipsychotic or mood stabilizer - 365d prior and year 2013 after
1127	COPY OF: [China Study] Bipolar with antipsychotic or mood stabilizer - 365d prior and year 2013 after
1117	[China Study] Bipolar with antipsychotic or mood stabilizer - 365d prior and year 2013 after
1118	[China Study] Bipolar with antidepressant + antipsychotics/mood stabilizers - 365d prior and year 2013 after
1116	[China Study] Bipolar with antidepressant only - 365d prior and year 2013 after
1112	[China Study] Bipolar - 365d prior and year 2013 after, no exposure group
1125	[China Study] Bipolar with Prior Antidepressant - 365d prior and year 2013 after
1124	[China Study] Bipolar - 365d prior and year 2013 after without exit strategy for cohort pathways
1080	[China Study] Bipolar - 365d prior and year 2013 after
1082	[China Study] Bipolar with antidepressant - 365d prior and year 2013 after
1113	[China Study] antipsychotic use hms after bipolar diagnosis
1114	COPY OF: [China Study] antipsychotic use hms after bipolar diagnosis

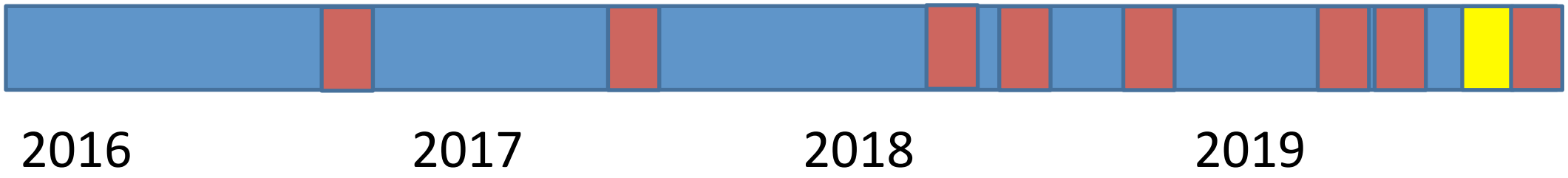
First network study using Chinese OMOP data

2016 2017 2018 2019

Fudan Tutorial August 2019

Upcoming OHDSI Events

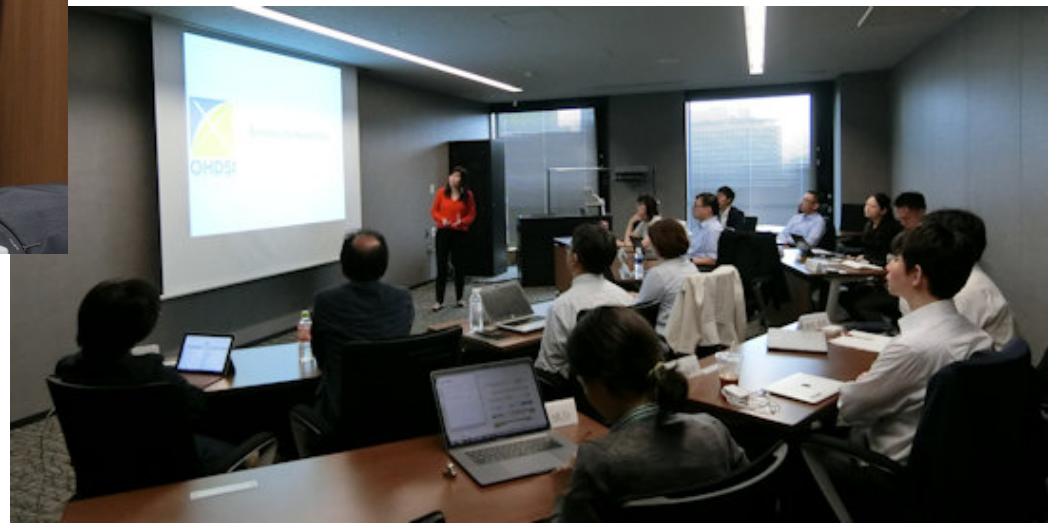
- OHDSI OMOP Tutorial
  - October 16th – 17th in Guangzhou
- OHDSI OMOP Half Day Tutorial
  - November 24th in Guangzhou




OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

OHDS Japan

OHDSI Japan Initial Meeting



2019 2020

OHDSI Japan 2nd Meeting

2019 2020

OHDSI Japan Working Groups

- OMOP CDM/ETL
- OMOP Vocabulary
- OHDSI Japan Promotions and Communications
- OHDSI Japan Forum

Upcoming OHDSI Events

- ETL Q&A workshop
  - TBD
- OHDSI Tutorials
  - TBD

OHDS Singapore

National University of Singapore

Clinical and survey data for type-2 diabetes cohort from Khoo Teck Puat Hospital, 5187 patients, 13th May 2019

Saw Swee Hock School of Public Health, type-2 diabetes cohort, 14,017 patients, 1st July 2019

Memorial Sloan Kettering Cancer Center

OMOP CDM Oncology Module at Work

Rimma Belenkaya, Michael Gurley, Christian Reich, Dmitry Dymshyts, Jeremy Warner, Robert Miller, Andrew Williams, RuiJun Chen

OHDSI Oncology WG

Memorial Sloan Kettering Cancer Center

Northwestern University

IMS Health & Quintiles are now IQVIA™

ODYSSEUS DATA SERVICES INC

VANDERBILT

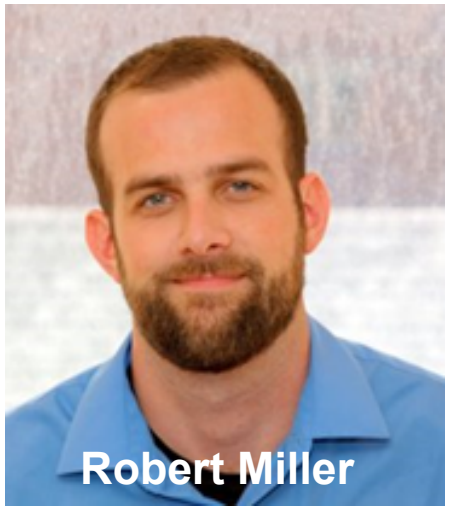
Tufts CTSI
Tufts Clinical and Translational Science Institute

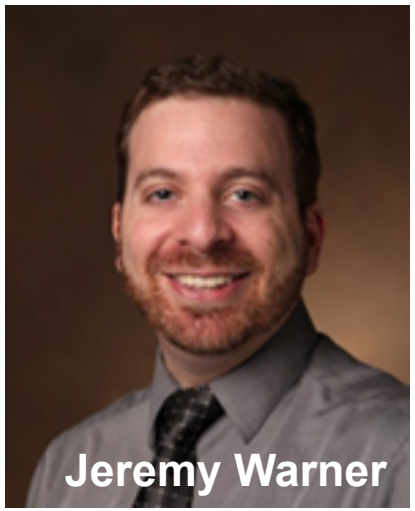
COLUMBIA
COLUMBIA UNIVERSITY DEPARTMENT OF BIOMEDICAL INFORMATICS


Michael Gurley

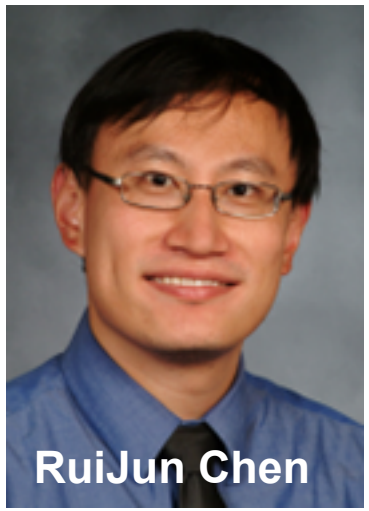

Christian Reich


Dmitry Dymshyts


Robert Miller


Jeremy Warner


Andrew Williams

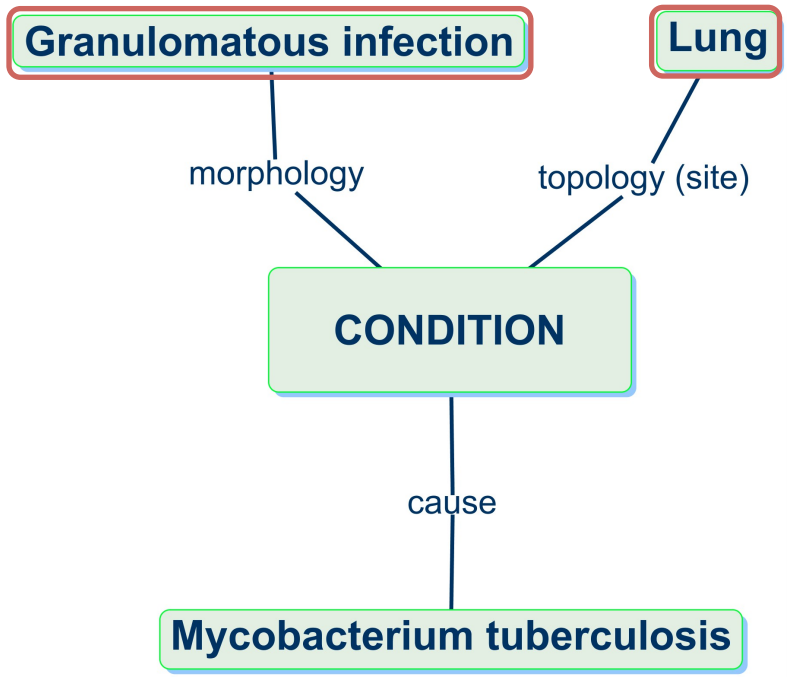

RuiJun Chen


Rimma Belenkaya

Challenges: Granularity

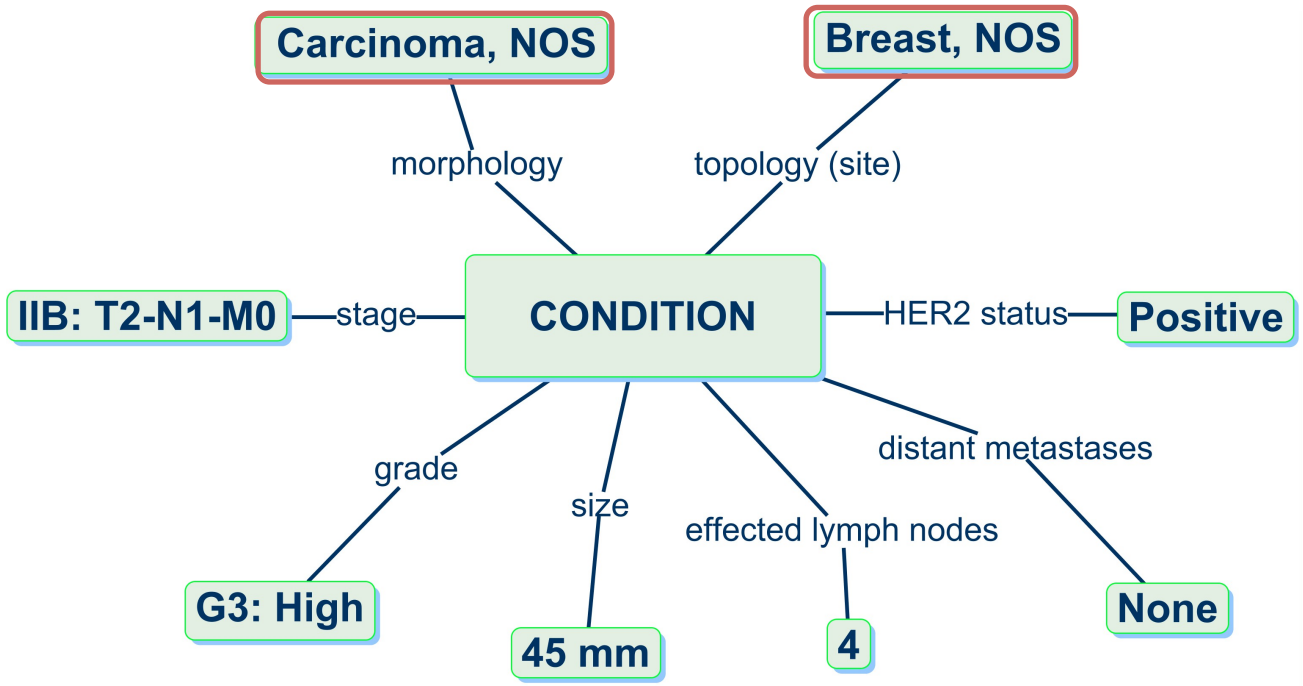
Normal Condition

Most normal conditions are defined by three main dimensions implicitly, plus some extra attributes



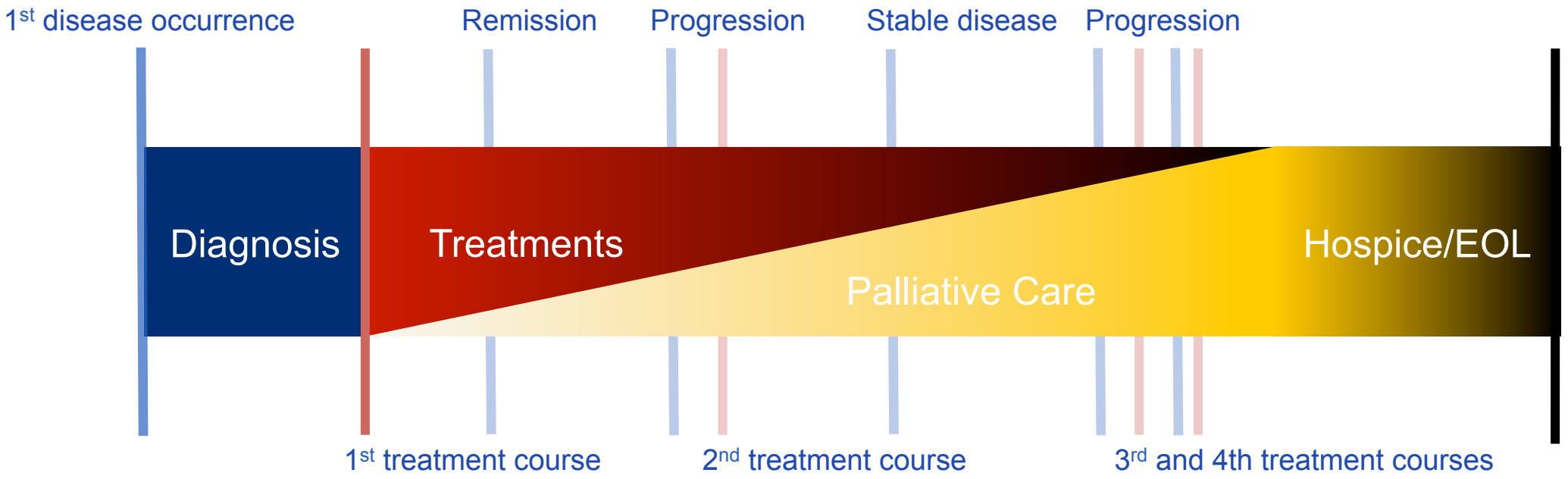
Cancer

- Cause is not known, but morphology and topology are detailed and explicit
- The many tumor attributes (modifiers) are also explicit and well defined



Challenges: Abstraction

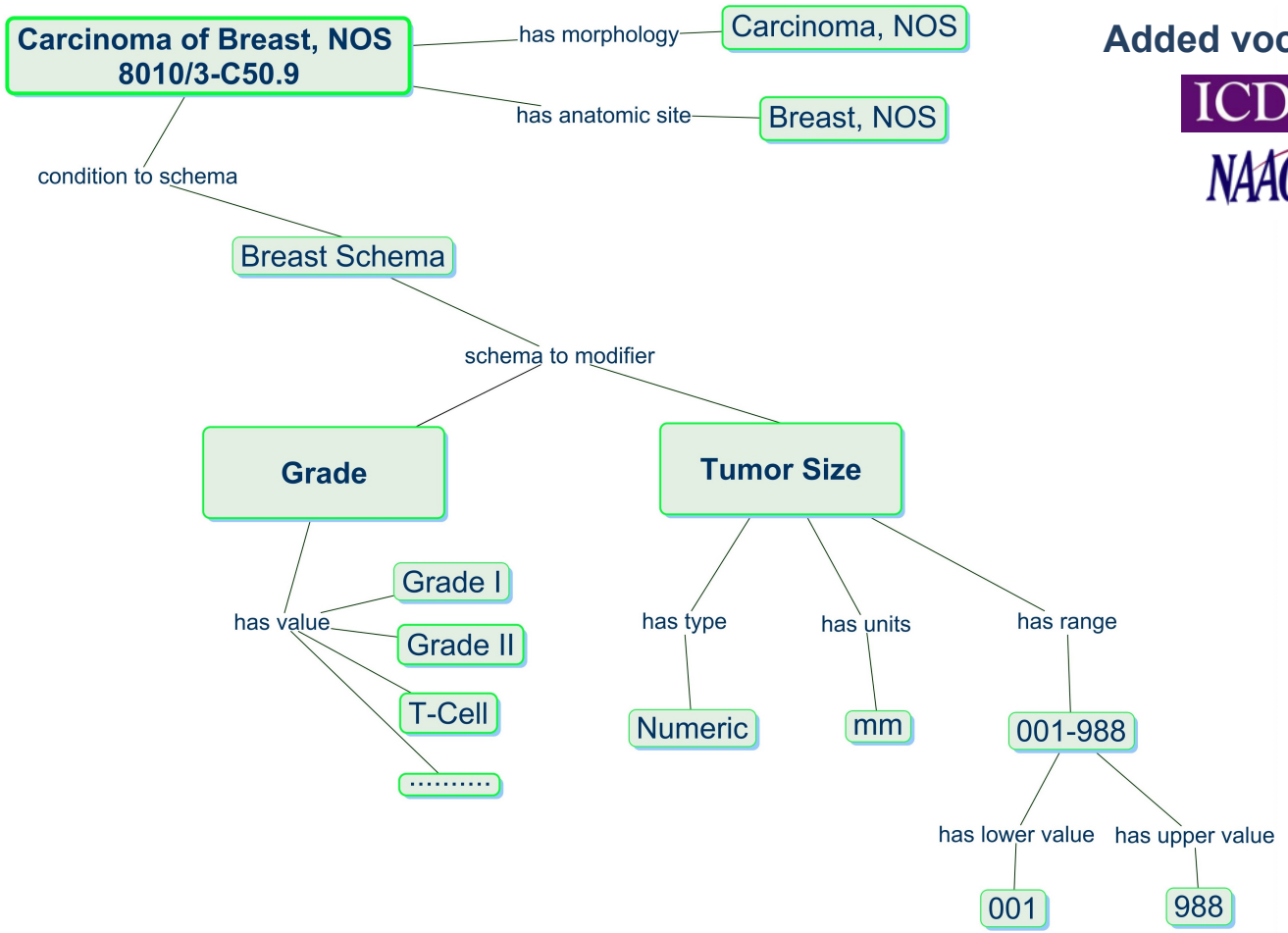
- Clinically and analytically relevant representation of cancer diagnoses, treatments, and outcomes requires data abstraction



  - Not readily available in the source data
  - Traditionally not supported in OMOP CDM

Solving Granularity Challenge

Cancer Diagnosis Model in the OMOP Vocabulary



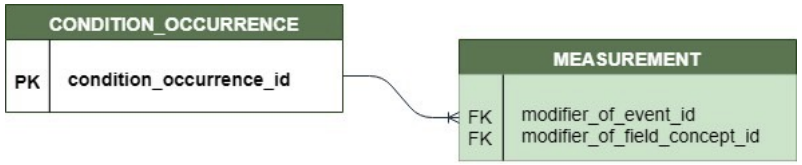
Added vocabularies:

ICD - O

NAACCR

Solving Granularity Challenge

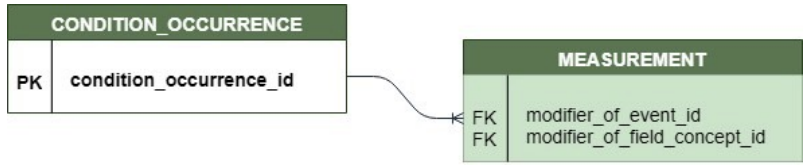
Cancer diagnosis representation in the OMOP CDM



- **Precoordinated concept** of cancer **Morphology + Site** is stored in **Condition_Occurrence**
- **Diagnostic modifiers** are stored in **Measurement** and **linked to** the **Condition_Occurrence** record

Solving Granularity Challenge

Cancer diagnosis representation in the OMOP CDM



- **Precoordinated concept** of cancer **Morphology + Site** is stored in **Condition_Occurrence**
- **Diagnostic modifiers** are stored in **Measurement** and **linked to** the **Condition_Occurrence** record

Example of cancer diagnosis in the OMOP CDM

Histology+Site diagnosis in **Condition_Occurrence**

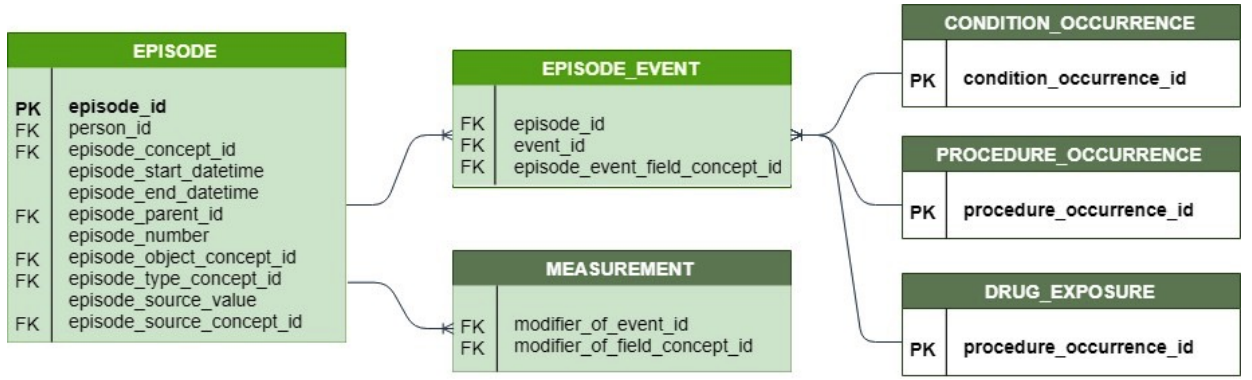
condition_occurrence_id	123456789	
person_id	1	
condition_concept_id	**4116071**	← **SNOMED concept 'Carcinoma of breast'**
condition_start_datetime	June 9, 2019	
condition_type_concept_id	32535	
condition_source_value	**8010/3-C50.9**	← **Precoordinated concept of ICD-O Histology & Site**
condition_source_concept_id	44505310	

Grade modifier in **Measurement**

measurement_id	567890	
person_id	1	
measurement_datetime	June 9, 2019	
measurement_concept_id	**35918640**	← **NAACCR concept 'Grade Pathological'**
measurement_date	June 9, 2019	
value_as_concept_id	**35922509**	← **NAACCR concept 'G3: High combined histologic grade (unfavorable); SBR score of 8-9 points'**
measurement_type_concept_id	32534	← **OMOP concept 'Tumor registry'**
measurement_source_value	3844	← **NAACCR code for 'Grade Pathological'**
measurement_source_concept_id	35918640	← **NAACCR concept 'Grade Pathological'**
value_source_value	breast@3844@3	← **NAACCR code for 'G3: High combined histologic grade (unfavorable); SBR score of 8-9 points'**
modifier_of_event_id	**123456789**	← **Value of the respective condition record condition_occurrence_id**
modifier_field_concept_id	**1147127**	← **Concept for 'condition_occurrence.condition_occurrence_id'**

Solving Abstraction Challenge

Disease and treatment episodes in the OMOP CDM

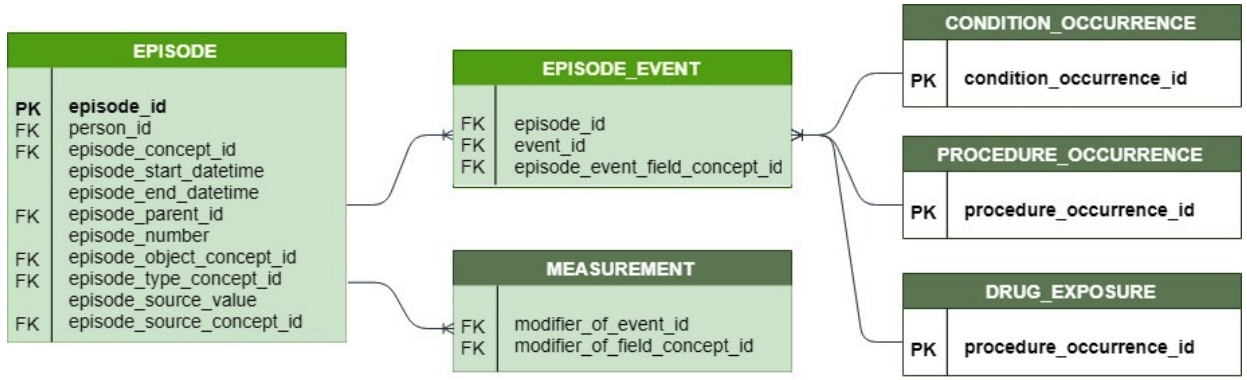


Added vocabularies:

HemOnc.org

Solving Abstraction Challenge

Disease and treatment episodes in the OMOP CDM



Added vocabularies:

HemOnc.org

Example of disease and treatment episodes in the Episode table

'First occurrence'-of-*'Carcinoma of breast'*

episode_id	12345
person_id	1
episode_concept_id	**32528**
episode_start_datetime	June 9, 2019
episode_object_concept_id	**4116071**
episode_type_concept_id	32535

- episode_concept_id: **OMOP concept 'First disease occurrence'**
- episode_object_concept_id: **SNOMED concept 'Carcinoma of breast'**
- episode_type_concept_id: **OMOP concept 'Tumor registry'**

'Treatment regimen'-of-*' Carboplatin and Paclitaxel'*

episode_id	12346
person_id	1
episode_concept_id	**32531**
episode_start_datetime	July 9, 2019
episode_parent_id	12345
episode_object_concept_id	35804255
episode_type_concept_id	32545

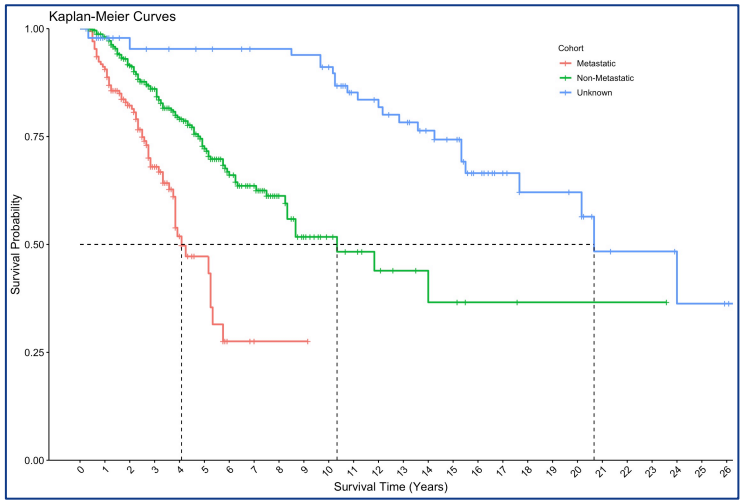
- episode_concept_id: **OMOP concept 'Treatment Regimen'**
- episode_start_datetime: **Foreign key to the disease Episode record**
- episode_parent_id: **HemOnc concept 'Carboplatin and Paclitaxel'**
- episode_object_concept_id: **OMOP concept 'Episode algorithmically derived from EHR'**

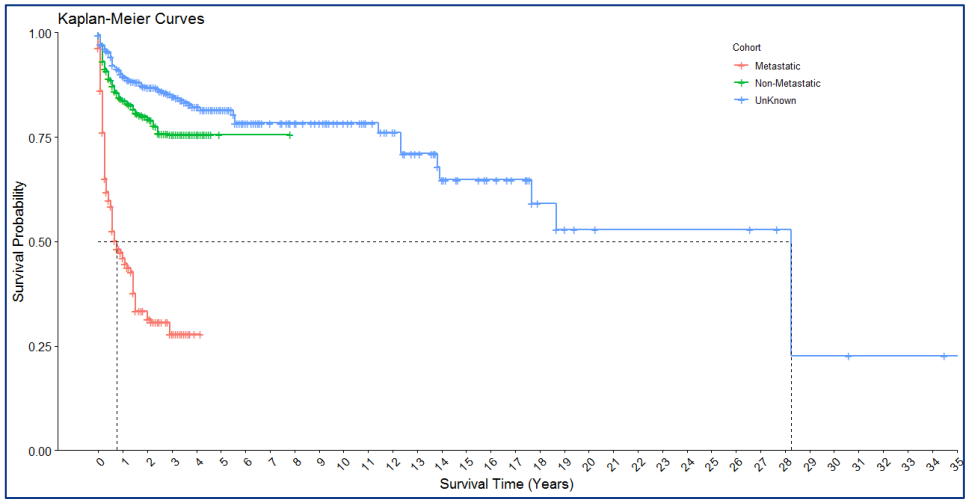
Testing

- Developed **vocabulary-driven ETL** for data conversion from Tumor Registry
- **Converted EHR** and **Tumor Registry data** from four participating institutions
- Tested **clinical characterization use cases**
  - Survival from initial diagnosis
  - Time from diagnosis to treatment
  - High-level treatment course for 1st cancer occurrence
  - Derivation of chemotherapy regimens from atomic drugs

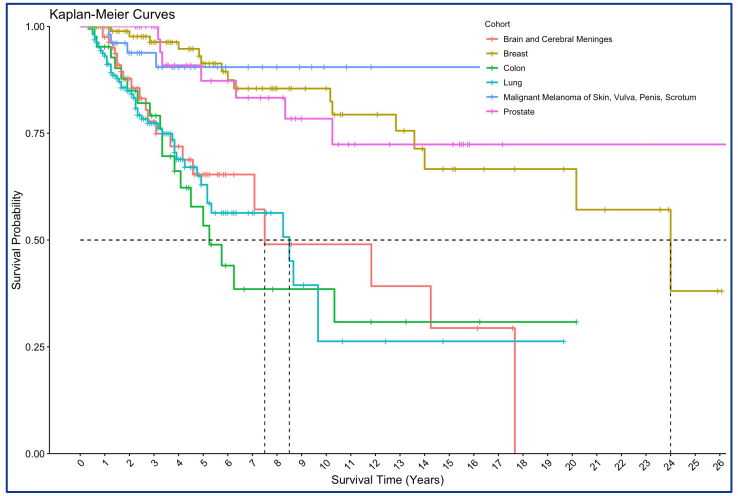
Survival from diagnosis

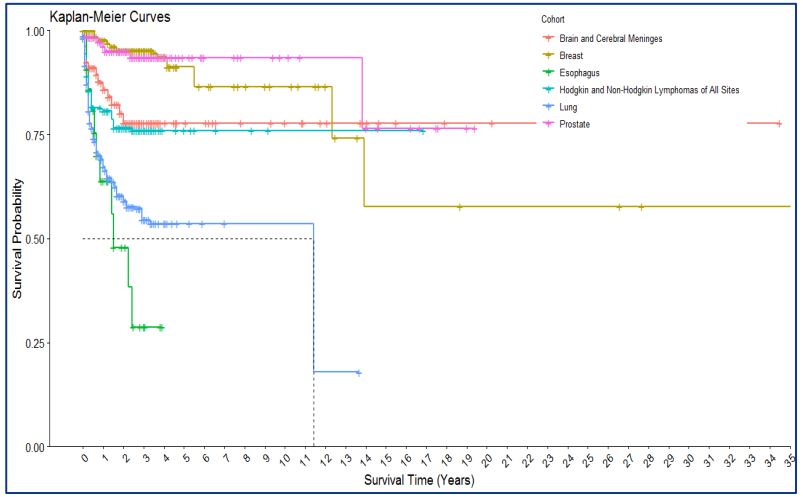
Metastatic vs. Non-metastatic cancers





Six most prevalent cancers





Join the Effort!

- **CDM and Vocabulary Work**
  - Adding domains for genomics, imaging and outcomes
  - Improving ICD-O-3 to SNOMED mapping precision
  - Mapping of NAACCR data dictionary to SNOMED
- **Oncology-specific THEMIS conventions**
- **ETL**
  - Validation
  - Conventions and algorithms for fusing tumor registry and EHR data on the same patient
- **Use-case-driven algorithms for**
  - identifying & characterizing cancer populations
  - identifying treatment pathways and disease progression
  - predicting disease progression

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Charles Bailey, Children's Hospital of Philadelphia, US
Scott Campbell, University of Nebraska, US
Rachel Chee, IQVIA, Great Britain
Mark Danese, Outcome Insights, US
Asieh Golozar, Regeneron, US
George Hripcsak, Columbia University, US
Ben May, Columbia University, US
Maxim Moinat, The Hyve, Netherlands
Anna Ostropolets, Columbia University, US
Meera Patel, MSK, US
Joseph Plasek, Aurora, US
Gurvaneet Randhawa, NCI, US
Donna Rivera, NIH, US
Mitra Rocca, FDA, US
Anastasios Siapos, IQVIA , Great Britain
Firas Wehbe, Northwestern University, US
Seng Chan You, Ajou University School of Medicine, Korea

Thank you!


OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Thank you!

FAIR Phenotyping with APHRODITE

Juan M. Banda[1] , Andrew Williams[2], Mehr Kashyap[3], Martin G. Seneviratne[3], Aaron Potvien[4], Jon Duke[4], Nigam H. Shah[3]

[1]Department of Computer Science, Georgia State University, Atlanta GA 30303

[2]Tufts Medical Center, Boston MA 02111

[3]Center for Biomedical Informatics Research, Stanford University, Stanford CA 94305

[4]Georgia Tech Research Institute, Atlanta GA 30308

Georgia State University

The Need

- The common failure to reproduce published results has created an atmosphere of crisis even in disciplines where precise measurement and tight experimental control are the norm
- There is even more reason for vigilance in disciplines that must manage lower degrees of measurement accuracy and experimental control
- One response to this crisis has been the emergence of open science principles that publicly expose the process of defining hypotheses, data selection and development, study design and analytic choices

The solution

SCIENTIFIC DATA

Comment | OPEN | Published: 15 March 2016

The FAIR Guiding Principles for scientific data management and stewardship

Mark D. Wilkinson, Michel Dumontier, IJsbrand Jan Aalbersberg, Gabrielle Appleton, Myles Axton, Arie Baak, Niklas Blomberg, Jan-Willem Boiten, Luiz Bonino da Silva Santos, Philip E. Bourne, Jildau Bouwman, Anthony J. Brookes, Tim Clark, Mercè Crosas, Ingrid Dillo, Olivier Dumon, Scott Edmunds, Chris T. Evelo, Richard Finkers, Alejandra Gonzalez-Beltran, Alasdair J.G. Gray, Paul Groth, Carole Goble, Jeffrey S. Grethe, Jaap Heringa, Peter A.C 't Hoen, Rob Hooft, Tobias Kuhn, Ruben Kok, Joost Kok, Scott J. Lusher, Maryann E. Martone, Albert Mons, Abel L. Packer, Bengt Persson, Philippe Rocca-Serra, Marco Roos, Rene van Schaik, Susanna-Assunta Sansone, Erik Schultes, Thierry Sengstag, Ted Slater, George Strawn, Morris A. Swertz, Mark Thompson, Johan van der Lei, Erik van Mulligen, Jan Velterop, Andra Waagmeester, Peter Wittenburg, Katherine Wolstencroft, Jun Zhao & Barend Mons ✉ - Show fewer authors

Scientific Data **3**, Article number: 160018 (2016) | Download Citation ⭳

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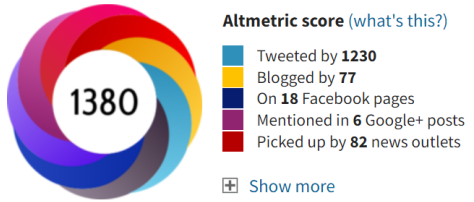
Total citations

Online attention



This Altmetric score means that the article is:

- in the 99th percentile (ranked 76th) of the 264,573 tracked articles of a similar age in all journals
- in the 1st percentile (ranked 1st) of the 1 tracked articles of a similar age in *Scientific Data*

Georgia State University

Rapid adoption of principles:

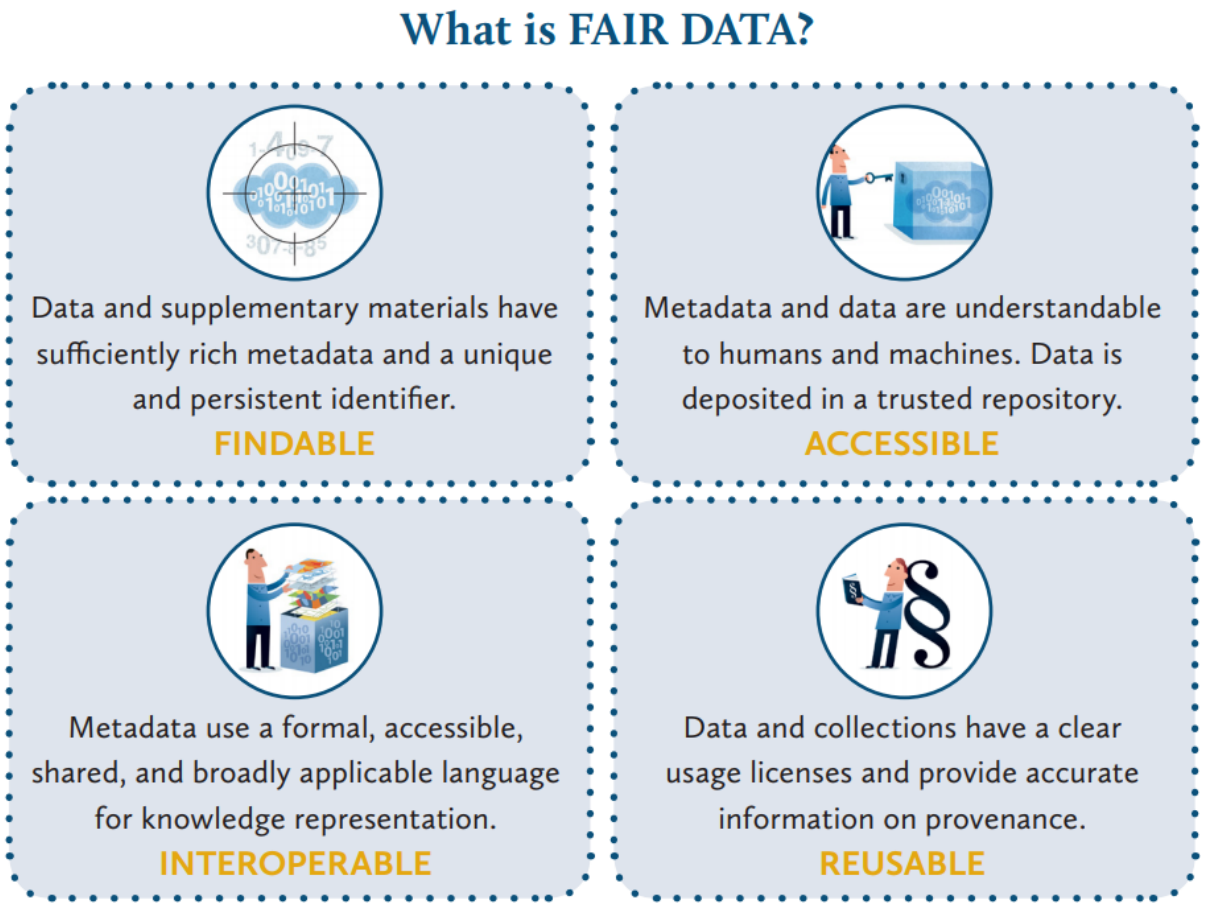
Progress towards the European Open Science Cloud

News item | 01-12-2017 | 18:00

Germany and the Netherlands establish office for the GO FAIR Initiative / France joins

What does it mean to be FAIR?

- **FAIR**
- Findable,
- Accessible,
- Interoperable,
- Reusable.



https://libereurope.eu/wp-content/uploads/2017/12/LIBER-FAIR-Data.pdf

What are we proposing?

Anatomy of an APHRODITE FAIR phenotype definition

A phenotype definition will be **Findable**

- To address the need to have a persistent global unique resource identifier (URI) for each phenotype definition version, we have utilized GitHub unique commit hash value to identify each individual phenotype definition version

- The OHDSI Gold Standard Phenotype Library workgroup has defined and created an additional abstraction layer over the phenotype definitions available as a R Shiny App

A phenotype definition will be **Accessible**

- The phenotype definition, generation script, and metadata will be retrievable by their identifier using any regular web browser or the application layer of the phenotype library

- By using a publicly and freely available resource such as GitHub, we offer better accessibility than placing the definitions on an institutional server

A phenotype definition will be **Interoperable**

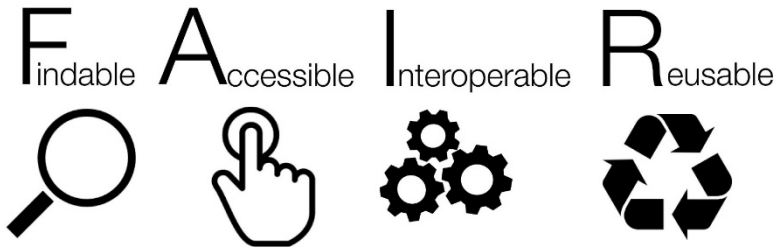
- We will leverage the OMOP CDM and associated vocabularies to solve the major obstacle to interoperability across sites. Our phenotype definitions' metadata will use JSON for knowledge representation and ease of machine readability

- When developing phenotyping definitions based on prior publications, or when a publication is generated from a definition generated from our pipeline, we will include all proper URI's to the publications in question

A phenotype definition will be **Re-usable**

- Currently APHRODITE definitions are easily shareable and re-usable for other sites. We have added meta-data elements related to software, CDM, and vocabulary versions, as well as a plurality of accurate and relevant attributes to guarantee re-usability
- All the publicly available phenotypes will be released under relevant open source licenses, details of which will be attached to the definition's meta-data
- Site and researcher information will be recorded as well as relevant publications in allowing fully traceable provenance for each definition

Questions?



Improving the FAIRness of digital resources will increase their quality and their potential for reuse

@micheldumontier::RDA:2018-01-31

Want to help? reach out: @drjmbanda or jbanda@gsu.edu

OHDSI-enabled distributed network analysis for clinical trial feasibility: a collaborative case study to inform a pediatrics randomized trial.

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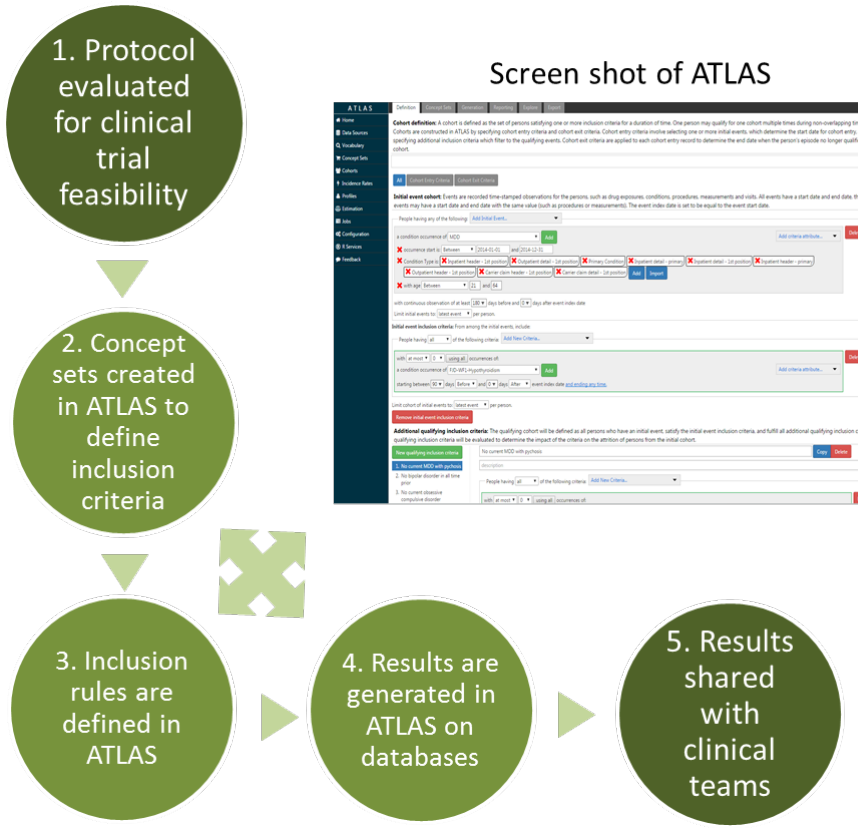
Clinical trial feasibility, what is it and why is this important?

Clinical trial feasibility analyses address operational questions, provide insight in overall population eligibility, impact protocol design, and can potentially avoid protocol amendments for a clinical trial.



Case study: Pediatric patients with Type II diabetes

This study presents a two-site (U.S. claims networks and hospital network) analysis using the OHDSI toolset (OMOP common data model (CDM) and ATLAS) to conduct clinical trial feasibility based on the protocol for an ongoing phase III randomized study to investigate the efficacy and safety of canagliflozin in a type II diabetic pediatric population.

Conducting feasibility with de-identified claims data in ATLAS

1. Find appropriate databases

Databases: IBM MarketScan® Commercial Database (CCAE), IBM MarketScan® Multi-State Medicaid Database (MDCD) and Optum© De-Identified Clinformatics® Data Mart Database – Socio-Economic Status (SES) (Optum SES)

2. Set index criteria

Patients aged 10-17 with a Type II diabetes diagnosis; with at least 365 days of enrollment time; an additional Type II diabetes diagnosis prior to index and limited evidence of Type I diabetes.

Conducting feasibility with de-identified claims data

Protocol specified 31 eligibility criteria from various data domains (10 conditions, 7 measurements, 5 drug, 5 administrative, 2 procedures, 1 observation, 1 demographic). Of the 31 criteria, 18 could be evaluated in the US claims databases

709 patients satisfy the index criteria with 487 patients (68.69%) matching all criteria implemented in CCAE

Collaboration with PEDSnet

PEDSnet contains electronic health records from 7 of the nation's largest pediatric health systems, covering outpatient and inpatient care. Data has been transformed to the CDM, and can be addressed using ATLAS.

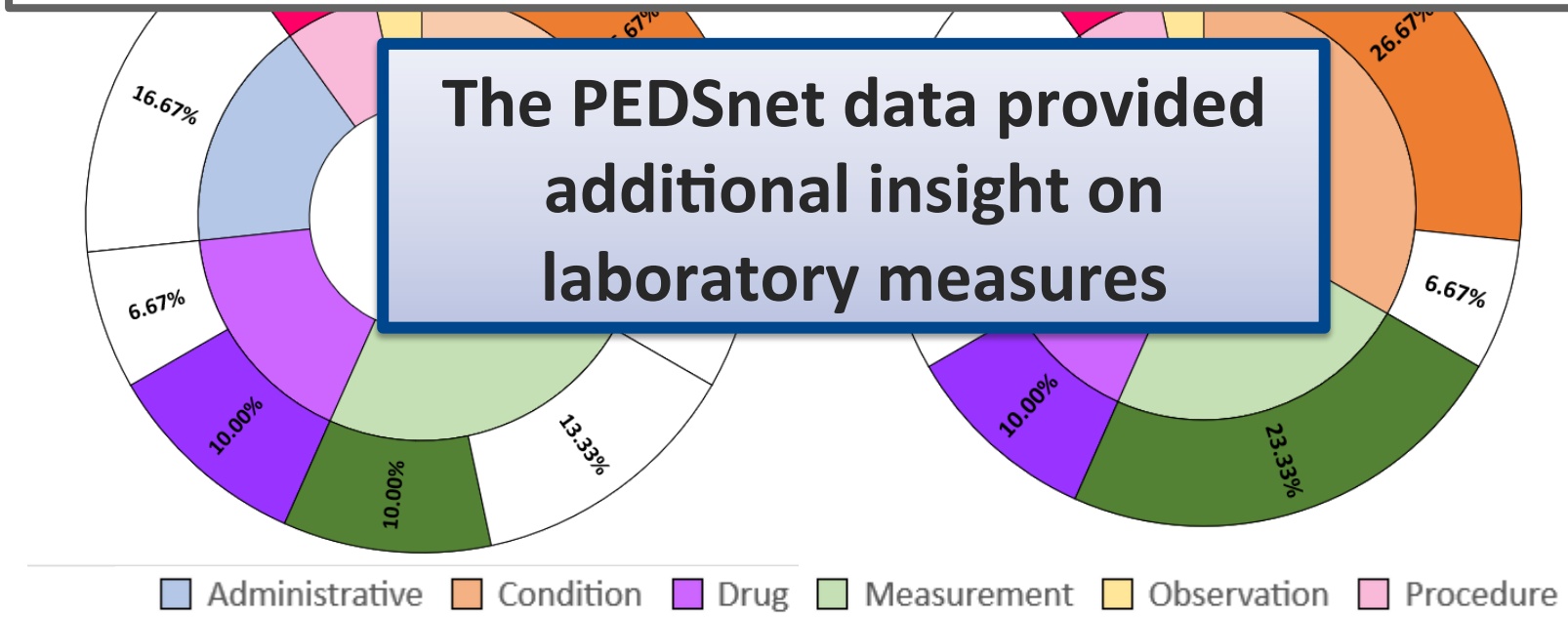
We spent a day together and were able to solely use ATLAS and share JSON to start the process of conducting similar feasibility—without sharing patient level data, or re-entering code sets!

What did we find?

Measurable criteria

Conditions, procedures, observations are measured similarly from both the claims dataset and PEDSnet

The PEDSnet data provided additional insight on laboratory measures



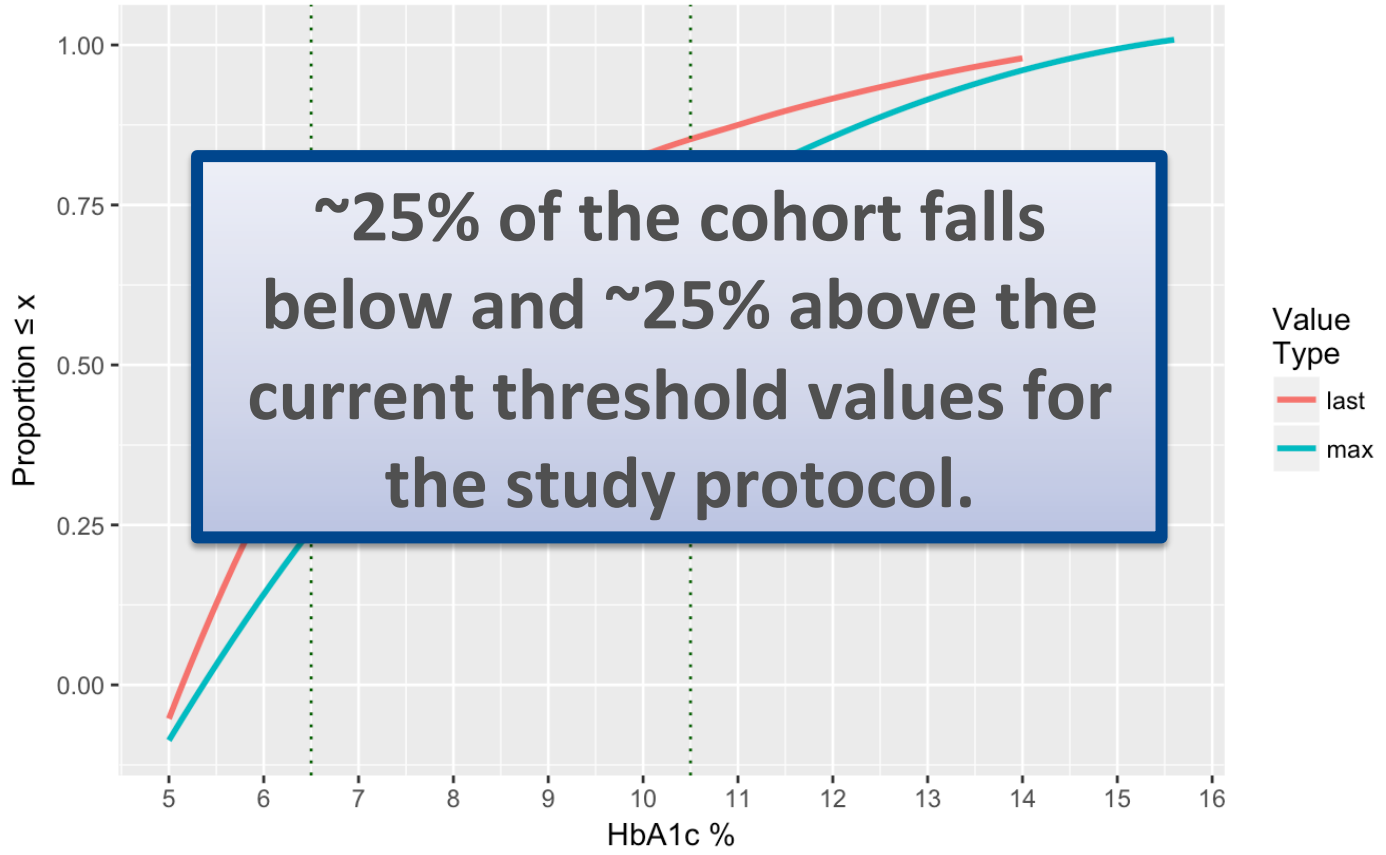
What did we find?

Measurable criteria

- No single criteria affected the protocol more than 10% of the population in either dataset (IBM CCAE & PEDSnet).
- The biggest drop-off in patients was with criteria in regarding anti-convulsant medications, prior history of type I diabetes, severe hypoglycemia or seizure or loss of consciousness 6 months prior to and including index and prior diagnosis of diabetic ketoacidosis.

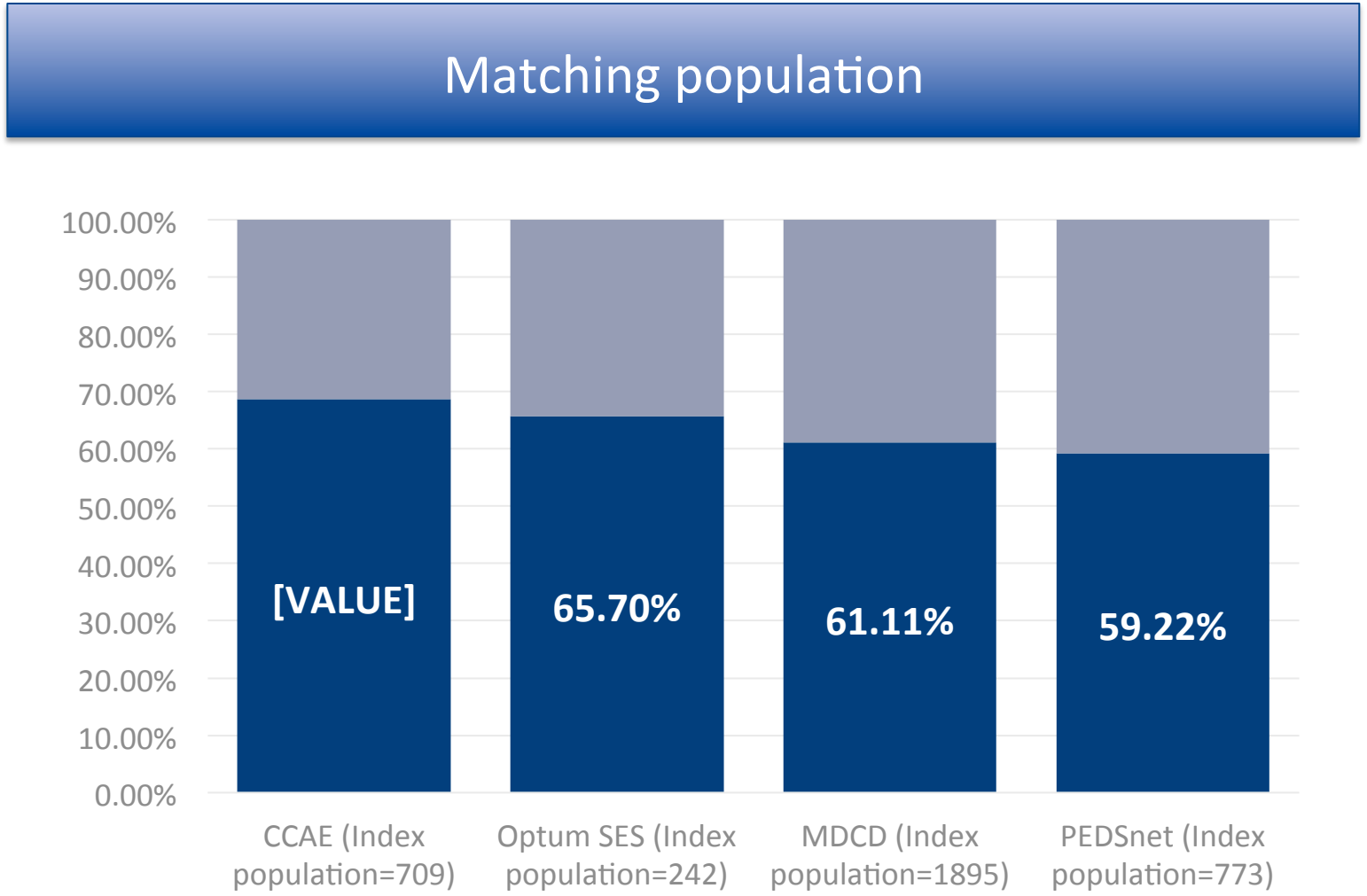
What did we find?

Criteria thresholds



~25% of the cohort falls below and ~25% above the current threshold values for the study protocol.

What did we find?



Feasibility to patient recruitment

- By utilizing the OHDSI framework and ATLAS we are able to conduct multi-site feasibility in real- time with real world evidence that can meaningfully inform clinical trial design and aid in recruitment and enrollment of eligible populations.

- Clinical trial inclusion criteria can often, but not always, be evaluated in observational data and by the extension of including a pediatric network that contain possible sites for enrollment we can further validate the exercise of feasibility and its role in clinical development and patient recruitment.

- **By assessing the impact of protocol implementation on the proportion of patients from a clinical trial with the OHDSI framework provides an avenue to understand feasibility of a population as well as a path to recruit patients from data networks.**

Acknowledgements

Thank you to all of our collaborators

Hanieh Razzaghi & Dr. Charlie Bailey and PEDSNET

Patrick Ryan and Janssen

Comparing 102 psychotropic drug regimens for diabetes mellitus risk

Anastasiya Nestsiarovich, MD, PhD
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Department of Internal Medicine
Center for Global Health

September 16, 2019

Research team:

- **University of New Mexico**
  - **Christophe Lambert,** PhD – Center for Global Health, DoIM; Translational Informatics
  - **Annette Crisanti**, PhD – Dept. of Psychiatry and Behavioral Sciences
  - **Mauricio Tohen**, MD, DrPH, MBA – Chair, Dept. of Psychiatry and Behavioral Sciences
  - **Stuart Nelson**, MD – Health Sciences Library; Translational Informatics; DoIM
  - **Yiliang Zhu**, PhD – Epidemiology, Biostatistics, and Preventive Medicine; DoIM
  - **Tudor Oprea**, MD, PhD – Division Chief, Translational Informatics; DoIM
  - **Mark Unruh**, MD – Chair, DoIM
  - **Douglas Perkins**, PhD – Director, Center for Global Health; DoIM

- **UCLA**
  - Berit Kerner, MD
- **New Mexico Behavioral Health Institute**
  - Nathaniel Hurwitz, MD
- **TwoFoldChange consulting**
  - Aurélien Mazurie, PhD
- **Iterative Consulting**
  - Daniel Cannon

Data source

- IBM MarketScan® administrative claims database (2003-2015)
  - Commercially insured patients
  - De-identified information on 932,815 US patients with ≥2 BD diagnoses
  - Visits, diagnoses, procedures, medications, lab orders
  - Data transformed to **OMOP Common Data Model**
- Data hosted by UNM HSC CTSC on high-performance server

Manuscripts:

- Published:
  - A Nestsiarovich, B Kerner, A J Mazurie, D C Cannon, N G Hurwitz, Y Zhu, S J Nelson, T I Oprea, M L Unruh, AS Crisanti, M Tohen, DJ Perkins, CG Lambert. **Comparison of 71 bipolar disorder pharmacotherapies for kidney disorder risk: The potential hazards of polypharmacy. Journal of Affective disorders.** 2019 Jan; 252:201-2011.
  - Nestsiarovich A, Mazurie AJ, Hurwitz NG, Kerner B, Nelson SJ, Crisanti AS, Tohen M, Krall RL, Perkins DJ, Lambert CG. **Comprehensive comparison of monotherapies for psychiatric hospitalization risk in bipolar disorders.** Bipolar Disord. 2018 Dec;20(8):761-771.

- Accepted for publication:
  - Praveen Kumar, Anastasiya Nestsiarovich, Stuart J. Nelson, Berit Kerner, Douglas J. Perkins, Christophe G. Lambert. **Imputation and characterization of uncoded self-harm in major mental illness using machine learning**. JAMIA journal (accepted 05 Sept. 2019).

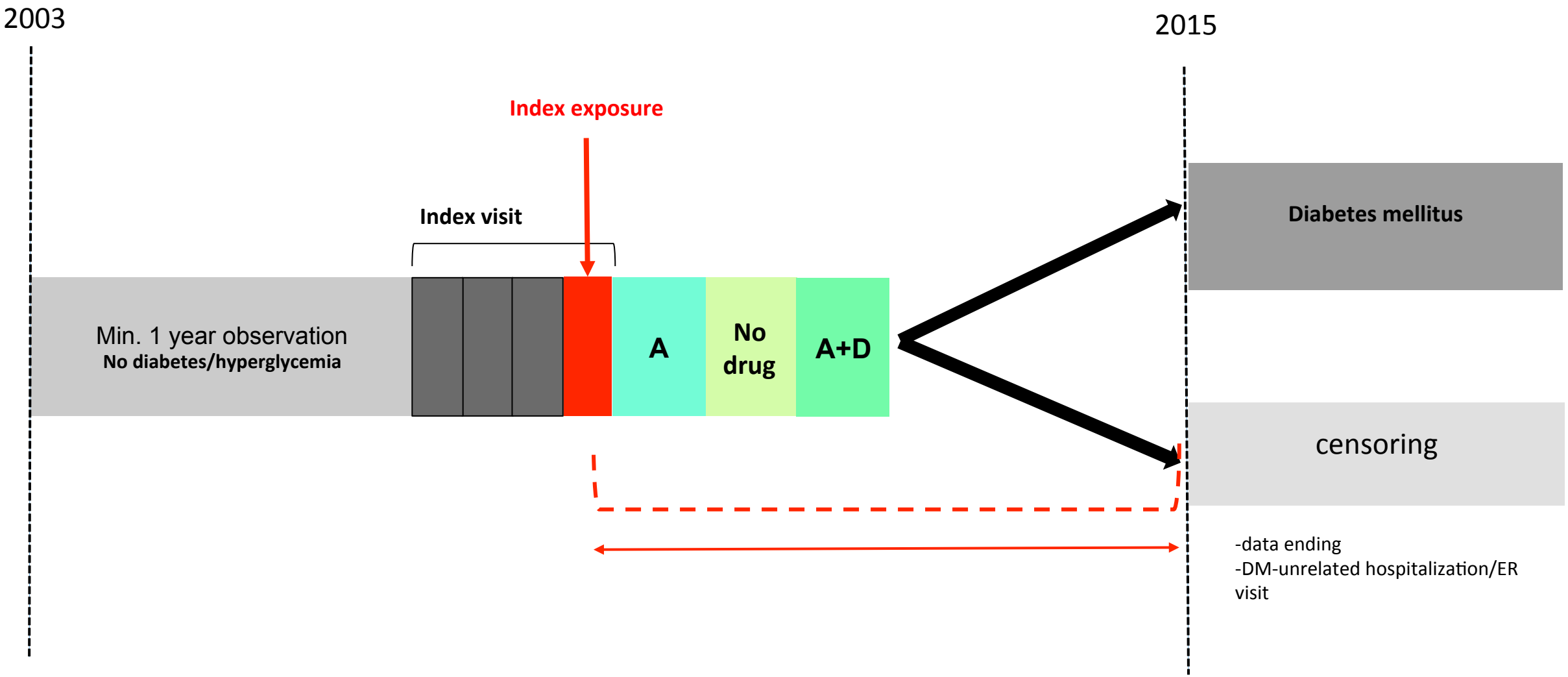
- **Under review:**
  - Anastasiya Nestsiarovich, Berit Kerner, Aurélien J. Mazurie, Daniel C. Cannon, Nathaniel G. Hurwitz, Yiliang Zhu, Stuart J. Nelson, Tudor I. Oprea, Annette S. Crisanti, Mauricio Tohen, Douglas J. Perkins, Christophe G. Lambert, Ph.D. **Diabetes mellitus risk for 102 drugs and drug combinations used in patients with bipolar disorder.** Psychoneuropharmacology (submitted 27 Aug 2019).

Design and analysis:

- **Inclusion criteria:**
  - Age **18-64** years
  - **≥2 ICD codes for BD** (296.[0-1]*, 296.[4-8]*, F30*, F31*) during 2003-2015.
  - **Received BD medication(s)** at least once following the index visit

- **Exclusion criteria:**
  - **Diagnosis** of schizophrenia, schizoaffective disorder, chronic delusional disorders, intellectual disabilities, autism spectrum disorders, mental illness of organic origin, or Parkinson's disease at any time during the observation period
  - Received **anti-dementia drugs** at any time point
  - Received **insulin or were diagnosed with any glucose metabolism-related disorder**, including DM and pancreatic disorders, prior to index exposure

Design:


2003
2015
Index exposure
Index visit
Min. 1 year observation
No diabetes/hyperglycemia
A
No drug
A+D
Diabetes mellitus
censoring
-data ending
-DM-unrelated hospitalization/ER visit

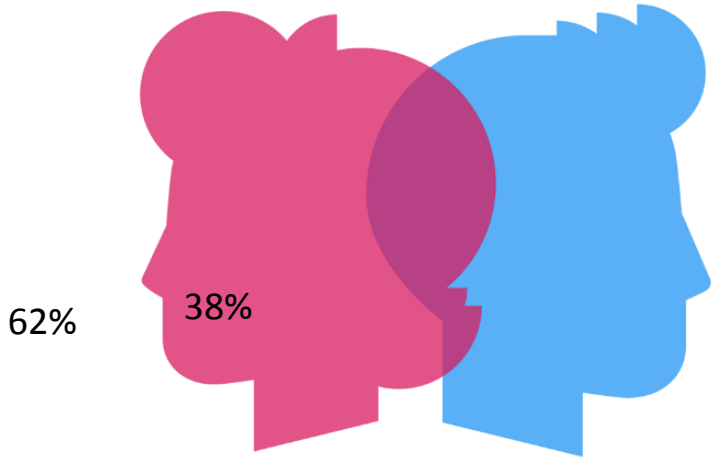
Design and analysis:

- Drug regimen: ≥ 1000 treatment intervals, ≥5 DM outcomes.
  - 659 regimens →19 monotherapies + 83 combinations
  - **Individual** therapies: lithium, MSAs, SGAs, TGA
  - **Classes**: FGAs, antidepressants
  - **Multi-class** polypharmacies: 2, 3, and 4+ classes

- Cox regression model with time-varying covariates
  - 102 regimens **with "no drug" as a reference**
  - 85 pre-treatment covariates

Diabetes mellitus (DM) study: results

- Total: 565,253 adults fit criteria
- 4.1% had a new DM (N=22,951).
- Annual incidence of new-onset DM 3.09% (general US population 0.32-0.88%)
  - mean of **342.7 days** (median 136) after the index visit
  - **741,573 years** of observation under the drug regimens studied



Diabetes mellitus regression analysis

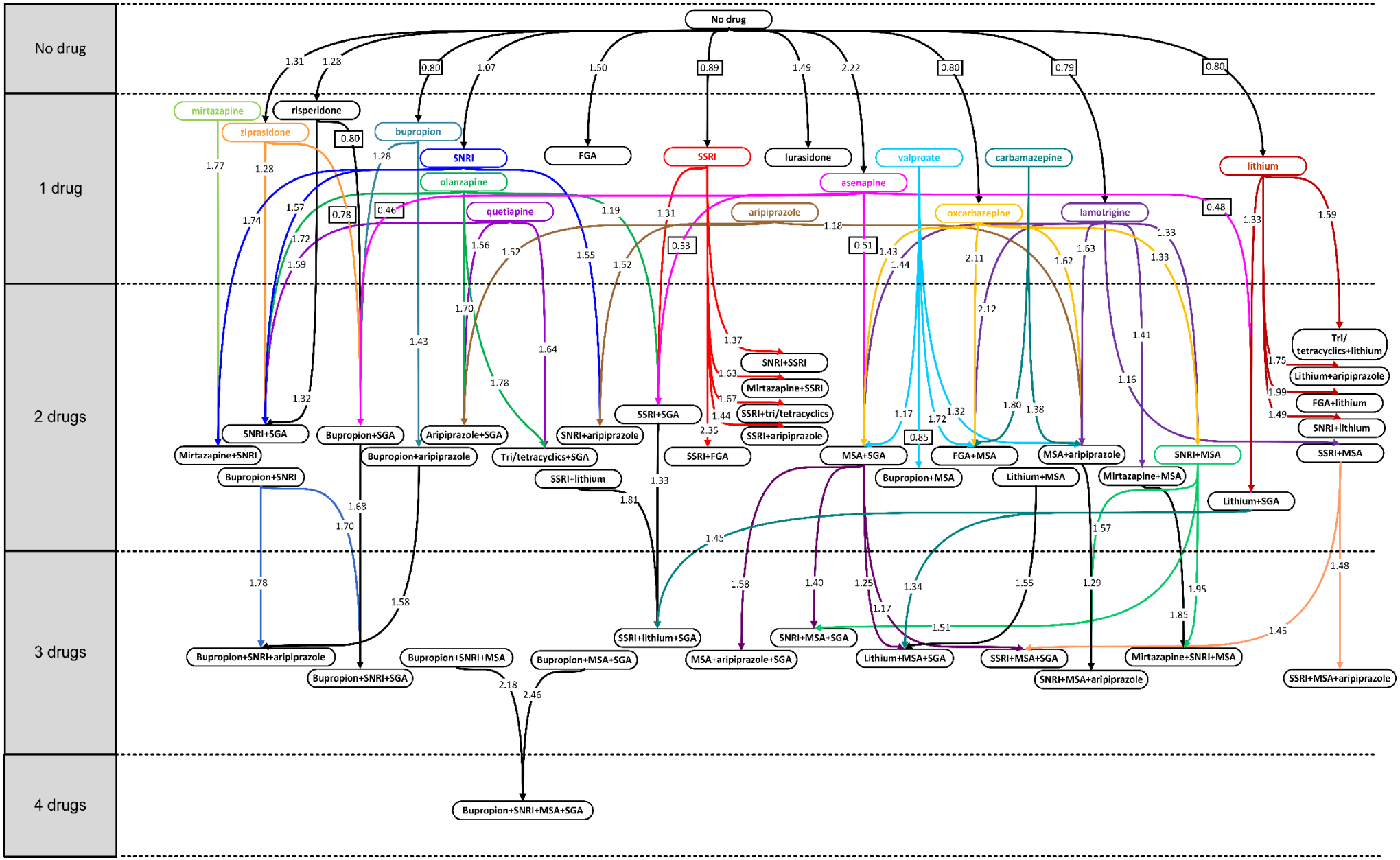
39 regimens had HR>1 with p<0.05

Covariate	HR	p-value	Lower limit 95%CI	Upper limit 95%CI	N-patients	N-intervals
Drug regimens						
NDRI+SNRI+MSA+SGA	2.37	5.38×10^{-6}	1.62	3.46	941	1,533
Uncommon monotherapy	2.32	2.47×10^{-3}	1.33	4.04	521	876
asenapine monotherapy	2.22	2.70×10^{-4}	1.43	3.43	1,579	2,385
SSRI+MSA+TGA+SGA	2.18	3.64×10^{-3}	1.27	3.72	809	1,151
SSRI+FGA	2.09	3.42×10^{-5}	1.46	2.97	1,073	1,601
SNRI+SSRI+TGA	2.08	6.16×10^{-3}	1.22	3.56	736	1,012
NASSA+SNRI+MSA	2.07	3.74×10^{-3}	1.25	3.41	716	1,032
NASSA+SNRI	1.86	3.05×10^{-3}	1.22	2.82	1,396	1,972
MSA+TGA+SGA	1.81	4.04×10^{-4}	1.29	2.52	2,339	3,693
NDRI+SNRI+TGA	1.79	1.46×10^{-3}	1.24	2.58	1,187	2,007
multiSGA	1.77	2.04×10^{-4}	1.30	2.40	3,368	4,733
SNRI+SSRI+MSA+SGA	1.74	4.65×10^{-2}	1.00	3.03	889	1,293
Tri/tetracyclics+SGA	1.73	1.66×10^{-2}	1.09	2.75	1,113	1,655
NDRI+SNRI+SGA	1.71	1.15×10^{-3}	1.23	2.38	1,722	2,812
FGA+MSA	1.68	2.44×10^{-4}	1.27	2.24	1,869	3,056
SNRI+SGA	1.68	6.12×10^{-24}	1.52	1.86	18,655	31,326
SNRI+lithium+TGA	1.68	8.55×10^{-2}	0.92	3.07	715	1,095
SNRI+MSA+TGA	1.66	6.85×10^{-7}	1.35	2.03	4,374	7,432
SNRI+TGA	1.66	3.51×10^{-12}	1.43	1.91	10,089	16,880
TGA+SGA	1.66	1.48×10^{-3}	1.21	2.27	3,535	5,148
Polypharmacy2	1.60	6.67×10^{-5}	1.27	2.03	3,832	6,516
SNRI+MSA+SGA	1.59	2.33×10^{-11}	1.39	1.83	9,670	16,562
FGA+lithium	1.59	1.96×10^{-3}	1.18	2.15	1,015	1,865
SSRI+lithium+SGA	1.55	6.08×10^{-5}	1.25	1.93	4,729	7,989
FGA mono-class therapy	1.50	4.20×10^{-4}	1.19	1.89	3,817	6,337

Diabetes mellitus regression analysis (cont.)

Covariate	HR	p-value	Lower limit 95%CI	Upper limit 95%CI	N-patients
SSRI+MSA	**0.92**	**1.67 x10^{-2}**	**0.85**	**0.99**	**68,565**
NASSA+TGA	0.90	8.13 x10^{-1}	0.37	2.20	750
SSRI mono-class therapy	**0.89**	**2.12 x10^{-5}**	**0.84**	**0.94**	**144,353**
NDRI+lithium+MSA	0.88	5.83 x10^{-1}	0.56	1.38	1,929
NDRI+SSRI+MSA	0.88	2.08 x10^{-1}	0.72	1.08	8,300
NDRI+lithium	0.86	2.14 x10^{-1}	0.68	1.09	5,769
SSRI+lithium	**0.86**	**3.31 x10^{-2}**	**0.74**	**0.99**	**15,068**
NDRI+lithium+SGA	0.84	4.59 x10^{-1}	0.52	1.35	1,714
NDRI+MSA	**0.83**	**1.36 x10^{-3}**	**0.75**	**0.93**	**27,347**
NDRI+SSRI	**0.83**	**2.05 x10^{-2}**	**0.70**	**0.97**	**15,861**
lithium monotherapy	**0.80**	**2.39 x10^{-9}**	**0.74**	**0.86**	**54,944**
NDRI (bupropion only) monotherapy	**0.80**	**4.29 x10^{-6}**	**0.72**	**0.88**	**50,277**
oxcarbazepine monotherapy	**0.80**	**6.89 x10^{-3}**	**0.67**	**0.94**	**18,009**
lamotrigine monotherapy	**0.79**	**1.16 x10^{-3}**	**0.75**	**0.85**	**121,730**
NDRI+SSRI+lithium	0.77	3.05 x10^{-1}	0.46	1.29	1,533
NASSA+NDRI	0.73	4.77 x10^{-1}	0.30	1.78	759
NDRI+lithium+MSA+SGA	0.66	3.05 x10^{-1}	0.29	1.49	706
NASSA+MSA+SGA	0.57	1.63 x10^{-1}	0.25	1.28	1,021

Multi-drug analysis



Conclusions:

1. DM risk varied **3-fold** among different regimens.
2. **Lower DM risk** for lithium, lamotrigine, oxcarbazepine, and bupropion monotherapies, SSRI mono-class therapy, and bupropion- and SSRI-containing drug combinations.
3. **Psychotropic polypharmacy** was often associated with higher risk of DM compared to monotherapies.
4. The majority of **antipsychotic-**containing regimens were associated with a significantly higher risk of DM versus “No drug”.

Limitations of the study:

- Non-randomized assignment of patients to treatment groups,
- No data were available prior to insurance enrollment data or 2003 (baseline risk for DM could differ)
- Unmeasured indication or other biases could remain that distort drug risk estimates for DM (family history, ethnicity, lifestyle).
- No correction was made for the number of drugs of interest used prior, current drug dosage, route of administration, or release mechanism.
- "No drug" chosen as a comparator - indication bias can exist

Poster #77

Global collaborative research through OHDSI network:

Net Clinical Benefit of Ticagrelor compared to Clopidogrel in patients with Acute Coronary Syndrome following Percutaneous Coronary Intervention

Seng Chan You[1]; Yeunsook Rho[2]; Jiwoo Kim2; Anastasios Siapos[3]; Ajit Londhe[4]; Jaehyeong Cho[5]; Jimyung Park[5]; Martijn Schuemie[4]; Marc A Suchard, MD, PhD[6,7]; David Madigan PhD8; George Hripcsak MD[9]; Christian G. Reich3; Patrick B. Ryan[4]; Rae Woong Park, MD, PhD[1,5]; Harlan M. Krumholz, MD[10]

[1]Department of Biomedical Informatics, Ajou University School of Medicine, Suwon, Korea; [2]Health Insurance Review and Assessment Service, Wonju, Korea; [3]IQVIA, Durham, USA; [4]Janssen Research and Development, Titusville, USA; [5]Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, Korea; [6]Department of Biostatistics, Fielding School of Public Health, University of California, Los Angeles, CA, USA; [7]Department of Biomathematics, David Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA; [8]Department of Statistics, Columbia University, New York, NY, USA; [9]Medical Informatics Services, New York-Presbyterian Hospital, New York, NY, USA; [10]Yale University School of Medicine, USA

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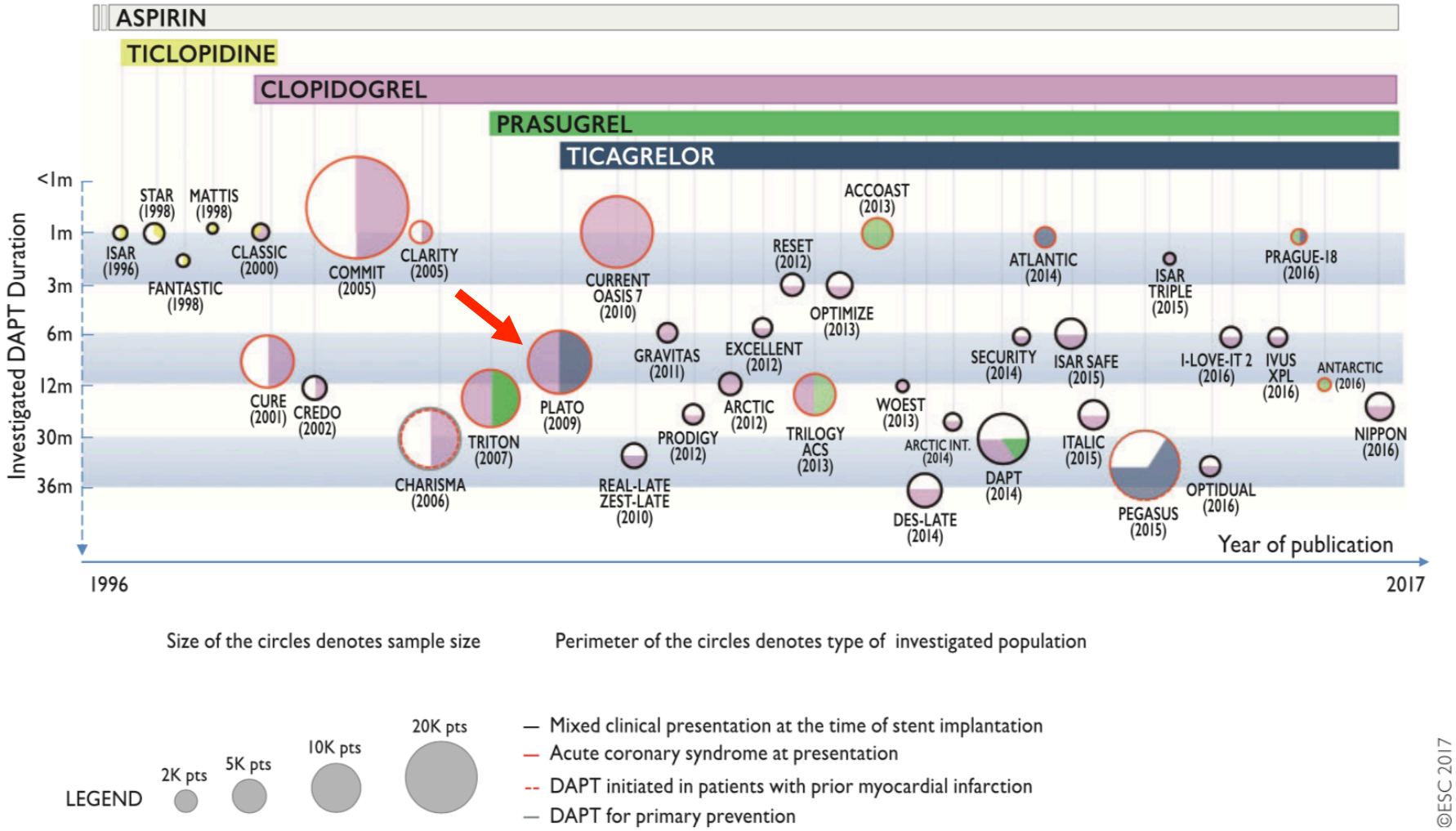
Disclosures

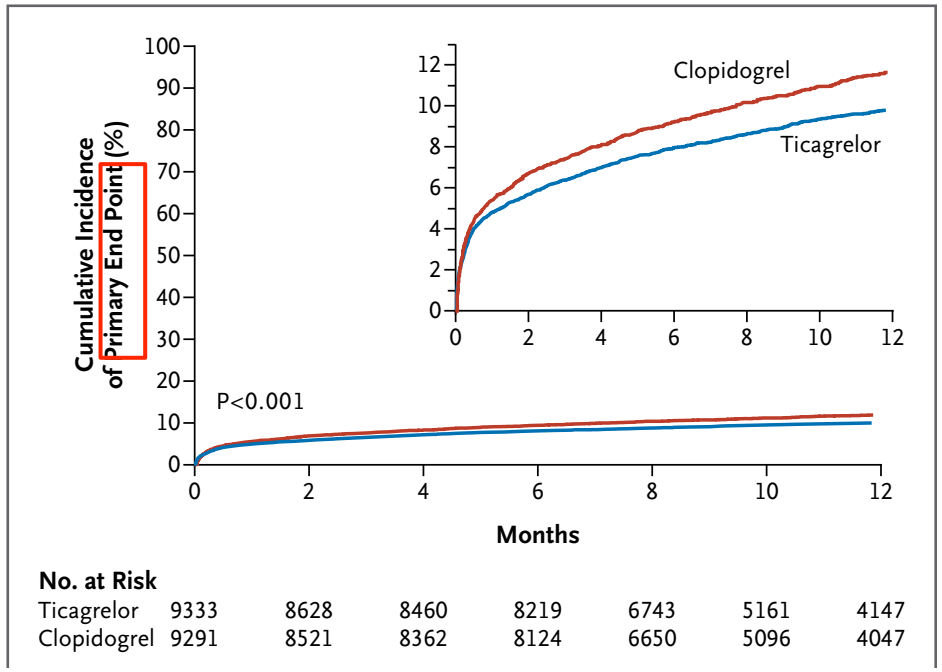
- Potential Conflict of interests
  - Dr. Ryan, Dr. Schuemie, and Ajit Londhe are employees of Janssen Research & Development, a subsidiary of Johnson & Johnson. Dr. Reich and Mr. Siapos are employees of IQVIA. Neither Janssen nor IQVIA had input in the design, execution, interpretation of results or decision to publish.
- Source of Funding
  - This work was supported by the Bio Industrial Strategic Technology Development Program (20001234) funded By the Ministry of Trade, Industry & Energy (MOTIE, Korea) and a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea [grant number: HI16C0992]

History of **D**ual **A**nti**P**latelet **T**herapy (DAPT) in patients with coronary artery disease



2017 ESC DAPT guideline

PLATelet inhibition and patient **O**utcomes (PLATO) Trial



End Point	Ticagrelor Group	Clopidogrel Group	Hazard or Odds Ratio for Ticagrelor Group (95% CI)†	P Value
Primary safety end points — no./total no. (%)				
Major bleeding, study criteria	961/9235 (11.6)	929/9186 (11.2)	1.04 (0.95–1.13)	0.43
Major bleeding, TIMI criteria‡	657/9235 (7.9)	638/9186 (7.7)	1.03 (0.93–1.15)	0.57
Bleeding requiring red-cell transfusion	818/9235 (8.9)	809/9186 (8.9)	1.00 (0.91–1.11)	0.96
Life-threatening or fatal bleeding, study criteria	491/9235 (5.8)	480/9186 (5.8)	1.03 (0.90–1.16)	0.70
Fatal bleeding	20/9235 (0.3)	23/9186 (0.3)	0.87 (0.48–1.59)	0.66
Nonintracranial fatal bleeding	9/9235 (0.1)	21/9186 (0.3)		0.03
Intracranial bleeding	26/9235 (0.3)	14/9186 (0.2)	1.87 (0.98–3.58)	0.06
Fatal	11/9235 (0.1)	1/9186 (0.01)		0.02
Nonfatal	15/9235 (0.2)	13/9186 (0.2)		0.69
Secondary safety end points — no./total no. (%)				
Non–CABG-related major bleeding, study criteria	362/9235 (4.5)	306/9186 (3.8)	1.19 (1.02–1.38)	0.03
Non–CABG-related major bleeding, TIMI criteria	221/9235 (2.8)	177/9186 (2.2)	1.25 (1.03, 1.53)	0.03
CABG-related major bleeding, study criteria	619/9235 (7.4)	654/9186 (7.9)	0.95 (0.85–1.06)	0.32
CABG-related major bleeding, TIMI criteria	446/9235 (5.3)	476/9186 (5.8)	0.94 (0.82–1.07)	0.32
Major or minor bleeding, study criteria	1339/9235 (16.1)	1215/9186 (14.6)	1.11 (1.03–1.20)	0.008
Major or minor bleeding, TIMI criteria‡	946/9235 (11.4)	906/9186 (10.9)	1.05 (0.96–1.15)	0.33
Dyspnea — no./total no. (%)				
Any	1270/9235 (13.8)	721/9186 (7.8)	1.84 (1.68–2.02)	<0.001
Requiring discontinuation of study treatment	79/9235 (0.9)	13/9186 (0.1)	6.12 (3.41–11.01)	<0.001

Primary End Point: Vascular death, myocardial infarction and stroke

Wallentin et al., *NEJM*, 2009

Current clinical guideline for DAPT in ACS solely based on PLATO trial

Recommendations	Class[a]	Level[b]
In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin[c] is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contraindications.[20]	I	B

2017 ESC/EACTS DAPT guideline

Recommendations for Specific $P2Y_{12}$ Inhibitors

COR	LOE	RECOMMENDATIONS
IIa	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation and in patients with NSTE-ACS treated with medical therapy alone (without revascularization), it is reasonable to use ticagrelor in preference to clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy (53,71,72).

2016 ACC/AHA DAPT guideline

PLATO trial did not demonstrate superiority of Ticagrelor in North America and Asia

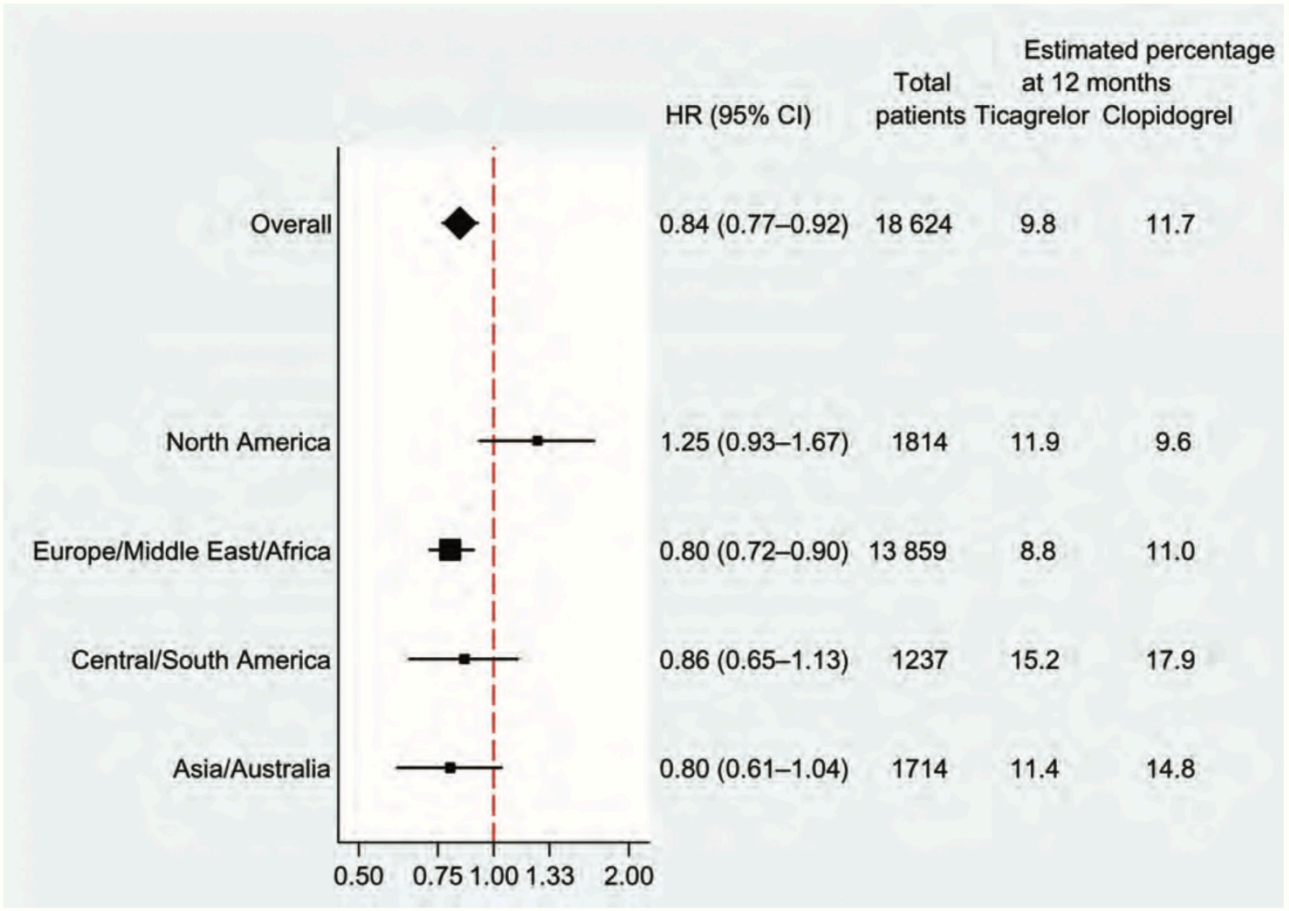


Figure 1 Estimated treatment effects by geographic region for the primary endpoint (CV death, MI, or stroke) of the PLATO trial (hazard ratios with 95% CIs, interaction *P*-value 0.05).

Pocock et al., *EHJ*, 2013

Objectives

- Compare risk of **net adverse clinical event** (**NACE**) between ticagrelor and clopidogrel in patients with Acute Coronary Syndrome (ACS) following percutaneous coronary intervention (PCI) through OHDSI network.

Method: Study Population

- Inclusion Criteria
  - Adults (>=20 yrs) who initiated ticagrelor or clopidogrel due to acute coronary syndrome (ACS) and undertook percutaneous coronary intervention (PCI)
- Exclusion Criteria
  - Prior history of stroke or gastrointestinal bleeding
  - Use of prasugrel or opposing drug within previous 30 days from index date

Method: Outcome

Primary endpoint: Net Adverse Clinical Event (NACE)

- Composite of recurrent myocardial infarction, any revascularization, ischemic stroke, intracranial hemorrhage, or gastrointestinal bleeding

Secondary endpoint

- Ischemic Event
  - Recurrent myocardial infarction
  - Any revascularization (PCI + CABG)
  - Ischemic stroke
- Hemorrhagic Event (major bleeding)
  - Intracranial hemorrhage
  - Gastrointestinal bleeding
- Overall death
- Dyspnea (Positive control)

Method: Statistical Analysis

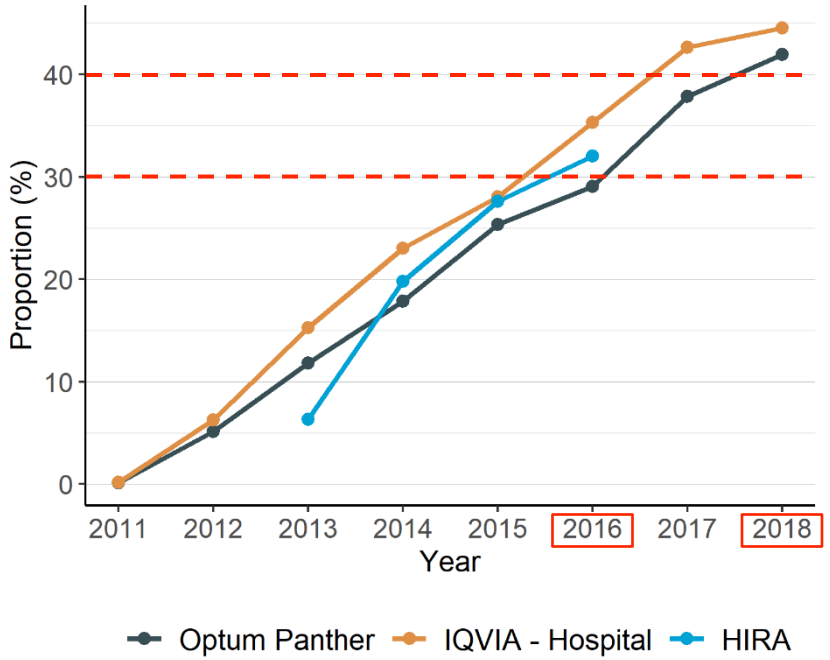
- Primary analysis
  - Time windows: From 1 day to 365 days after the index date
  - Unconditioned Cox regression after 1-to-1 PS matching
- Sensitivity analyses
  - Time windows
    - On-treatment
    - 5-year
  - Statistical analysis
    - 1-to-1 PS matching with blanking period of outcome (28 days)
    - Variable-ratio PS matching
    - PS stratification
- Assessment of systemic errors
  - 96 Negative controls

Method

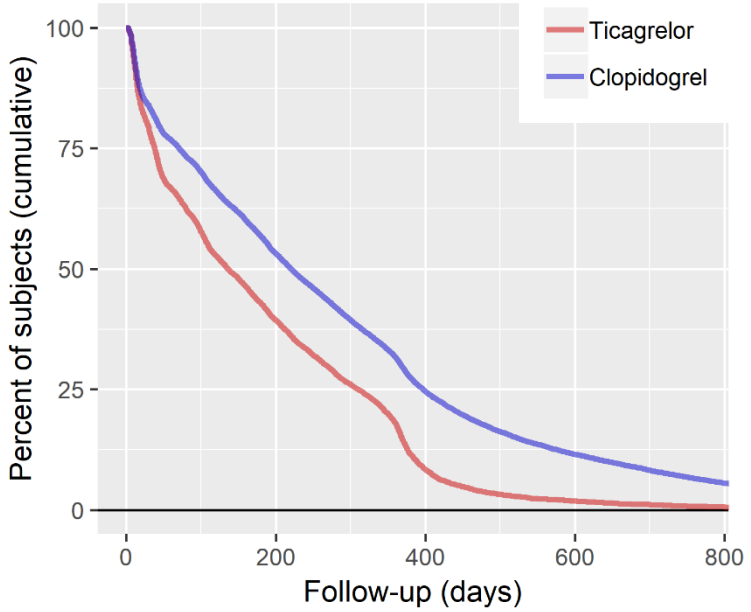
- Data source
  - **Optum Pan-Therapeutics (PanTher) : USA, EHR (86M)**
  - **IQVIA's Hospital data : USA, EHR (85M)**
  - **HIRA: South Korea, Nationwide Claim for patients undertaking PCI (0.4M)**

Proportion of ticagrelor across years and drug adherence in Korea

Proportion of Ticagrelor user among whole study population

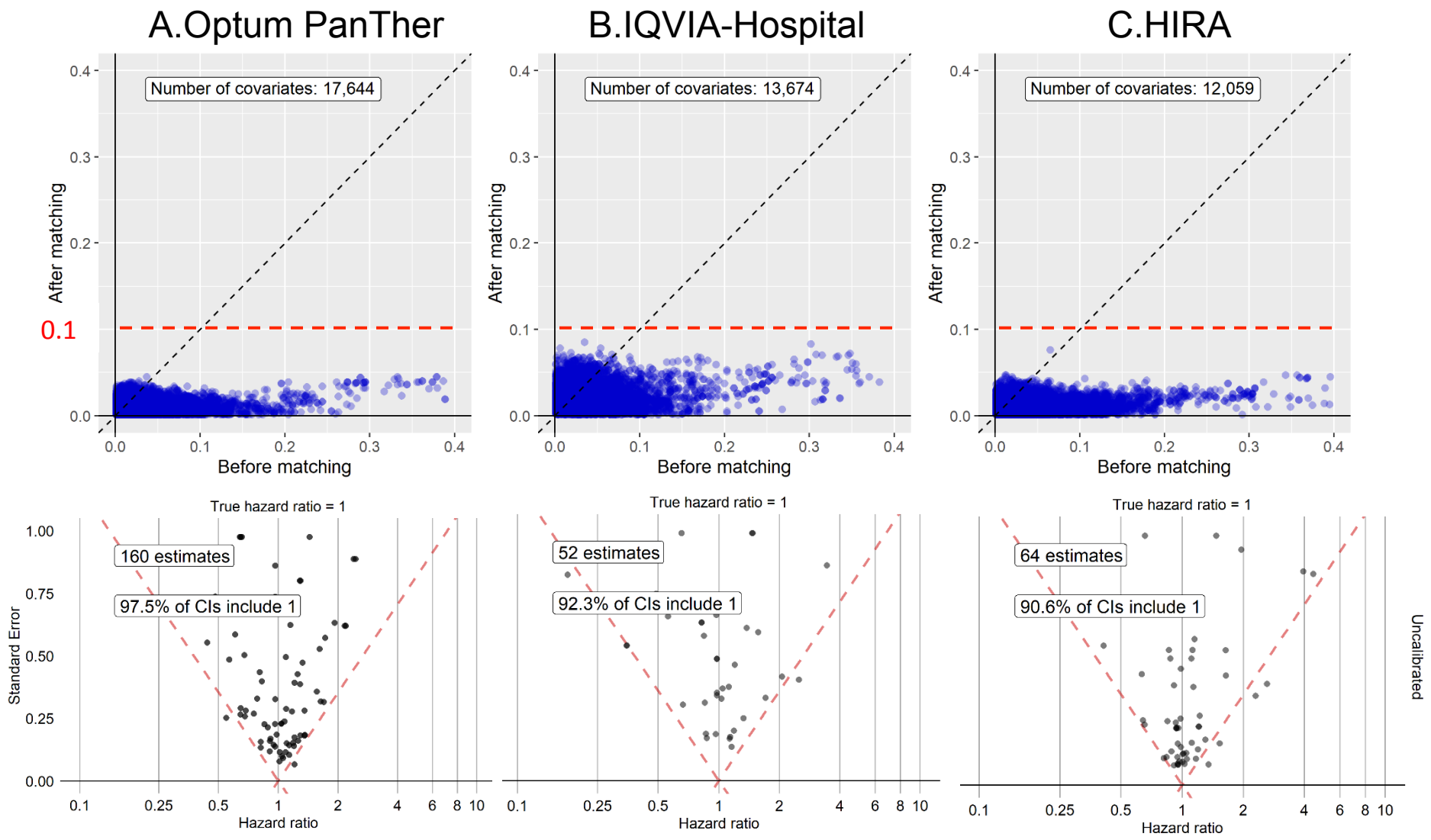


Days of continuation of ticagrelor and clopidogrel

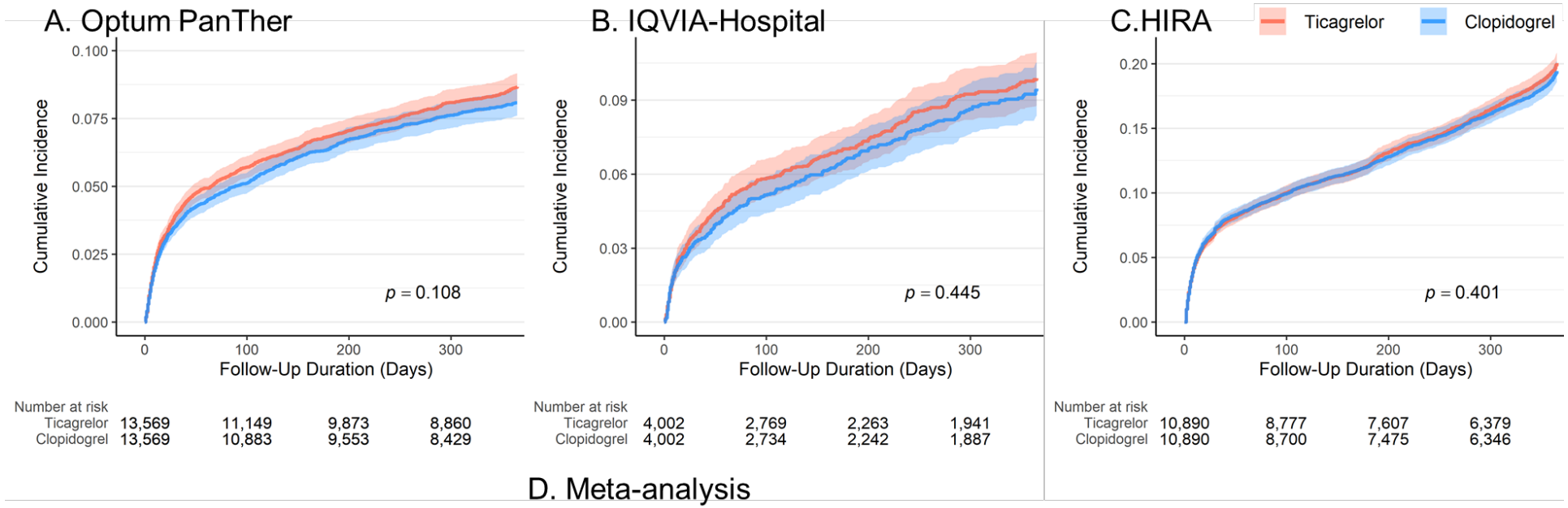


Days of Drug Continuation	1Q	Median	3Q
Ticagrelor	38	132	363
Clopidogrel	78	232	566

Balance before and after PS matching and Systematic error control

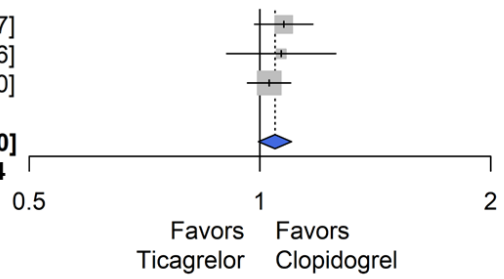


Primary endpoint: 1-year NACE

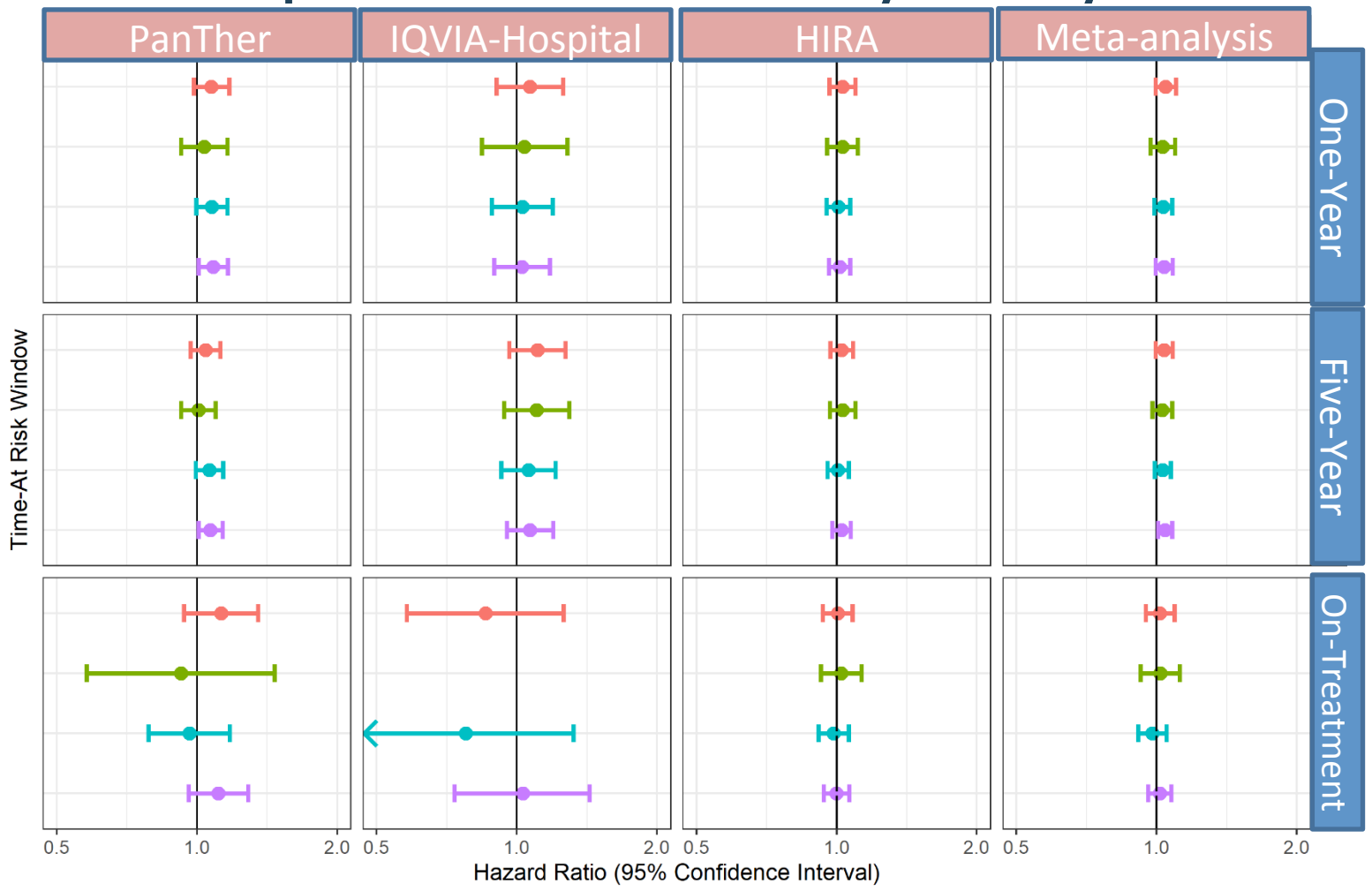


D. Meta-analysis

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	1,057	13,569	968	1.07	[0.98; 1.17]
IQVIA - Hospital	4,002	299	4,002	276	1.07	[0.90; 1.26]
HIRA	10,890	1,881	10,890	1,817	1.03	[0.96; 1.10]
Overall	**28,461**	**3,237**	**28,461**	**3,061**	**1.05**	**[1.00; 1.10]**
Heterogeneity: I^2 = 0.0%						***P* = 0.074**



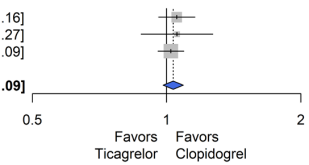
Consistency in the results of the primary endpoint in sensitivity analyses



A. Ischemic event

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	919	13,569	859	1.05	[0.96; 1.16]
IQVIA - Hospital	4,002	234	4,002	218	1.06	[0.88; 1.27]
HIRA	10,890	1,771	10,890	1,720	1.02	[0.96; 1.09]
Overall	**28,461**	**2,924**	**28,461**	**2,797**	**1.03**	**[0.98; 1.09]**

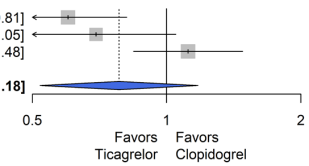
Heterogeneity: I^2 = 0.0%



B. Ischemic stroke

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	68	13,569	110	0.60	[0.44; 0.81]
IQVIA - Hospital	4,002	39	4,002	55	0.69	[0.46; 1.05]
HIRA	10,890	104	10,890	92	1.12	[0.84; 1.48]
Overall	**28,461**	**211**	**28,461**	**257**	**0.78**	**[0.52; 1.18]**

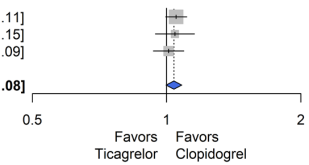
Heterogeneity: I^2 = 78.5%



C. Recurrent acute MI

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	2,685	13,569	2,547	1.05	[1.00; 1.11]
IQVIA - Hospital	4,002	783	4,002	746	1.04	[0.94; 1.15]
HIRA	10,890	1,270	10,890	1,249	1.01	[0.93; 1.09]
Overall	**28,461**	**4,738**	**28,461**	**4,542**	**1.04**	**[1.00; 1.08]**

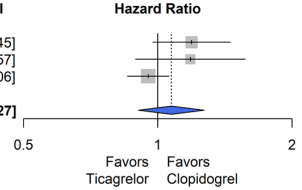
Heterogeneity: I^2 = 0.0%



D. Any revascularization

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	215	13,569	177	1.19	[0.98; 1.45]
IQVIA - Hospital	4,002	106	4,002	88	1.18	[0.89; 1.57]
HIRA	10,890	657	10,890	681	0.95	[0.86; 1.06]
Overall	**28,461**	**978**	**28,461**	**946**	**1.07**	**[0.90; 1.27]**

Heterogeneity: I^2 = 59.8%



E. Hemorrhagic event

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	190	13,569	147	1.26	[1.01; 1.56]
IQVIA - Hospital	4,002	73	4,002	66	1.09	[0.78; 1.52]
HIRA	10,890	218	10,890	173	1.25	[1.02; 1.52]
Overall	**28,461**	**481**	**28,461**	**386**	**1.22**	**[1.07; 1.40]**

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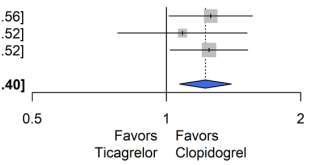
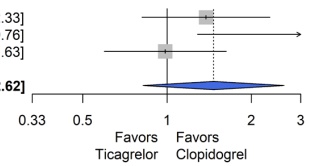


F. Hemorrhagic stroke

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	34	13,569	24	1.38	[0.81; 2.33]
IQVIA - Hospital	4,002	18	4,002	5	3.54	[1.29; 9.76]
HIRA	10,890	31	10,890	31	0.99	[0.60; 1.63]
Overall	**28,461**	**83**	**28,461**	**60**	**1.47**	**[0.82; 2.62]**

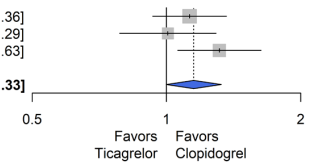
Heterogeneity: I^2 = 59.8%



G. GI bleeding

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	230	13,569	199	1.13	[0.93; 1.36]
IQVIA - Hospital	4,002	126	4,002	123	1.01	[0.79; 1.29]
HIRA	10,890	194	10,890	146	1.31	[1.06; 1.63]
Overall	**28,461**	**550**	**28,461**	**468**	**1.15**	**[1.00; 1.33]**

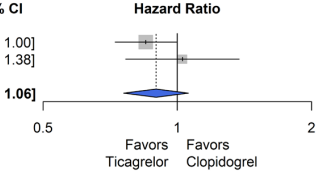
Heterogeneity: I^2 = 23.6%



H. Overall death

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	288	13,569	332	0.85	[0.73; 1.00]
IQVIA - Hospital	4,002	92	4,002	88	1.03	[0.77; 1.38]
Overall	**17,571**	**380**	**17,571**	**420**	**0.90**	**[0.76; 1.06]**

Heterogeneity: I^2 = 19.7%



I. Dyspnea

Source	Ticagrelor Total	Ticagrelor Event	Clopidogrel Total	Clopidogrel Event	HR	95% CI
Optum Panther	13,569	3,597	13,569	2,969	1.23	[1.17; 1.29]
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HIRA	10,890	816	10,890	728	1.12	[1.01; 1.23]
Overall	**28,461**	**4,889**	**28,461**	**4,097**	**1.19**	**[1.13; 1.26]**

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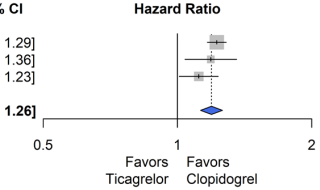

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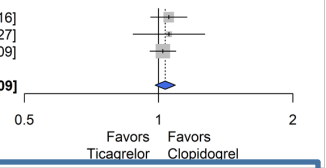

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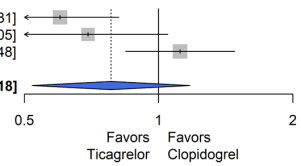

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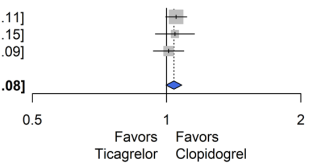

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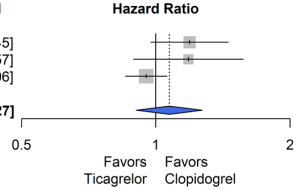

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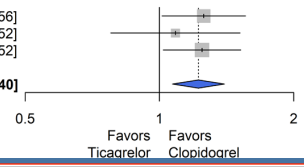

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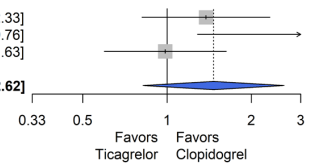

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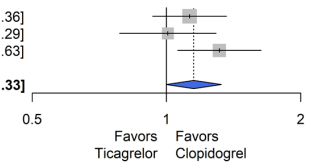

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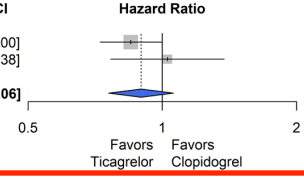

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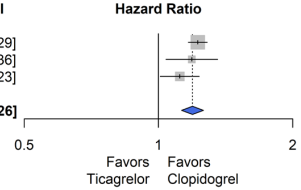

Summary

- There appears to be **no significant difference** in **1-year NACE risk between ticagrelor and clopidogrel** users with ACS following PCI
- The findings for primary endpoint were consistent across sensitivity analyses
- **Ticagrelor** is associated with **higher risk of hemorrhagic events and dyspnea**.


Thank You
for your time

Delivering on-demand evidence via an informatics consultation service

Alison Callahan PhD

Research Scientist, Stanford University School of Medicine

OHDSI Symposium 2019

Acknowledgements

Informatics Consult team


Saurabh Gombar


Alison Callahan


Vladimir Polony


Ken Jung


Nigam Shah


Robert Harrington


Rob Tibshirani


Trevor Hastie

Stanford Health Care partners


David Entwistle


Tip Kim


Christopher Sharp

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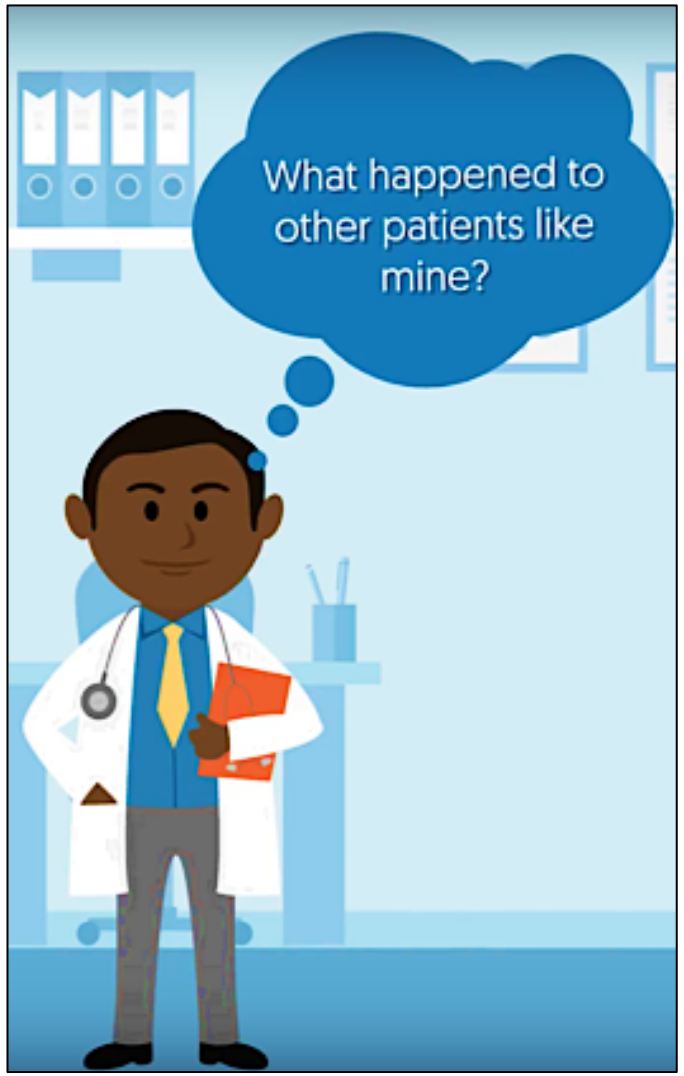
The Green Button Service



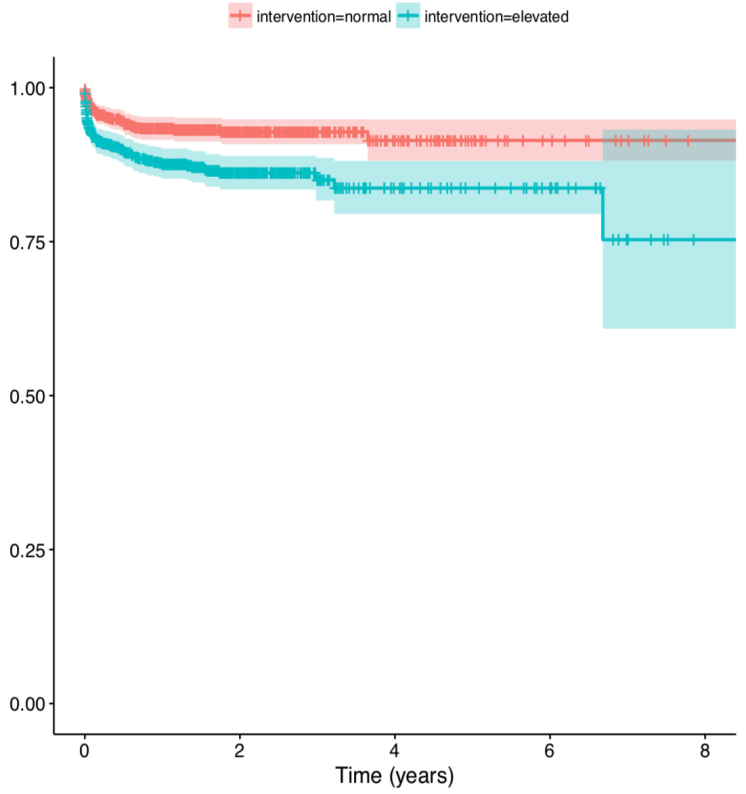
Given a specific case, provides a report summarizing similar patients in Stanford's clinical data warehouse, the common treatment choices made, and the observed outcomes.

An institutional review board approved study (IRB # 39709).

http://greenbutton.stanford.edu

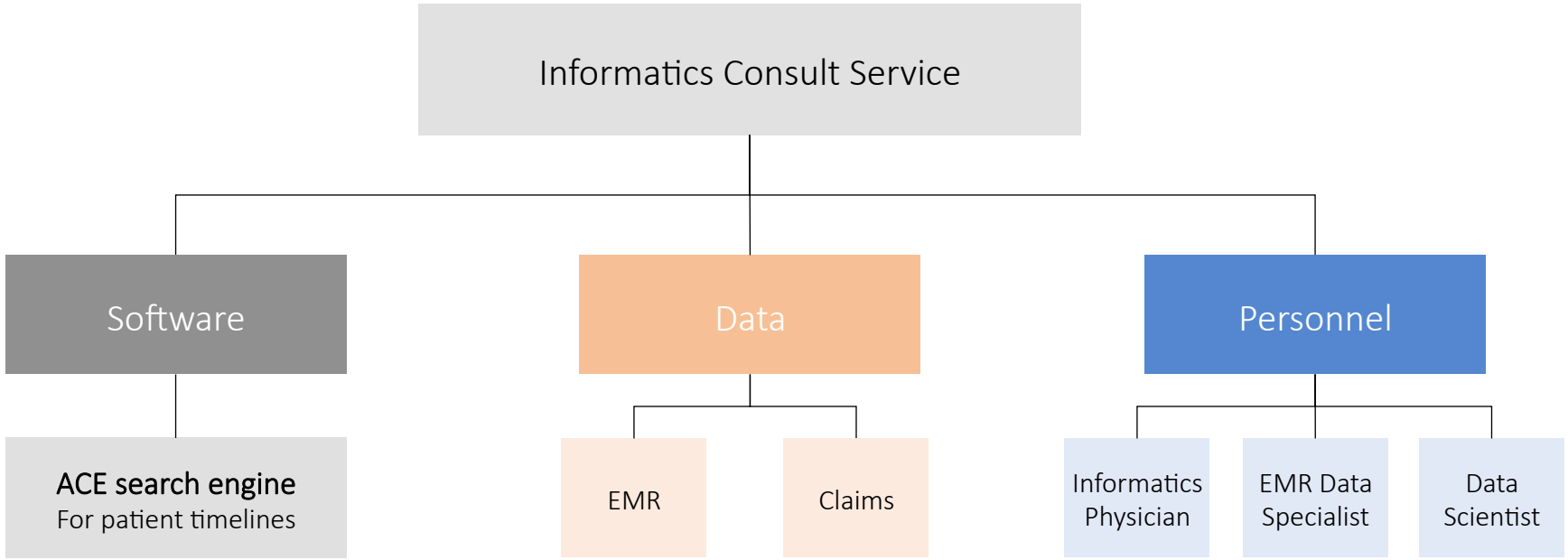
An example report

Mildly elevated serum free light chains and subsequent malignancy

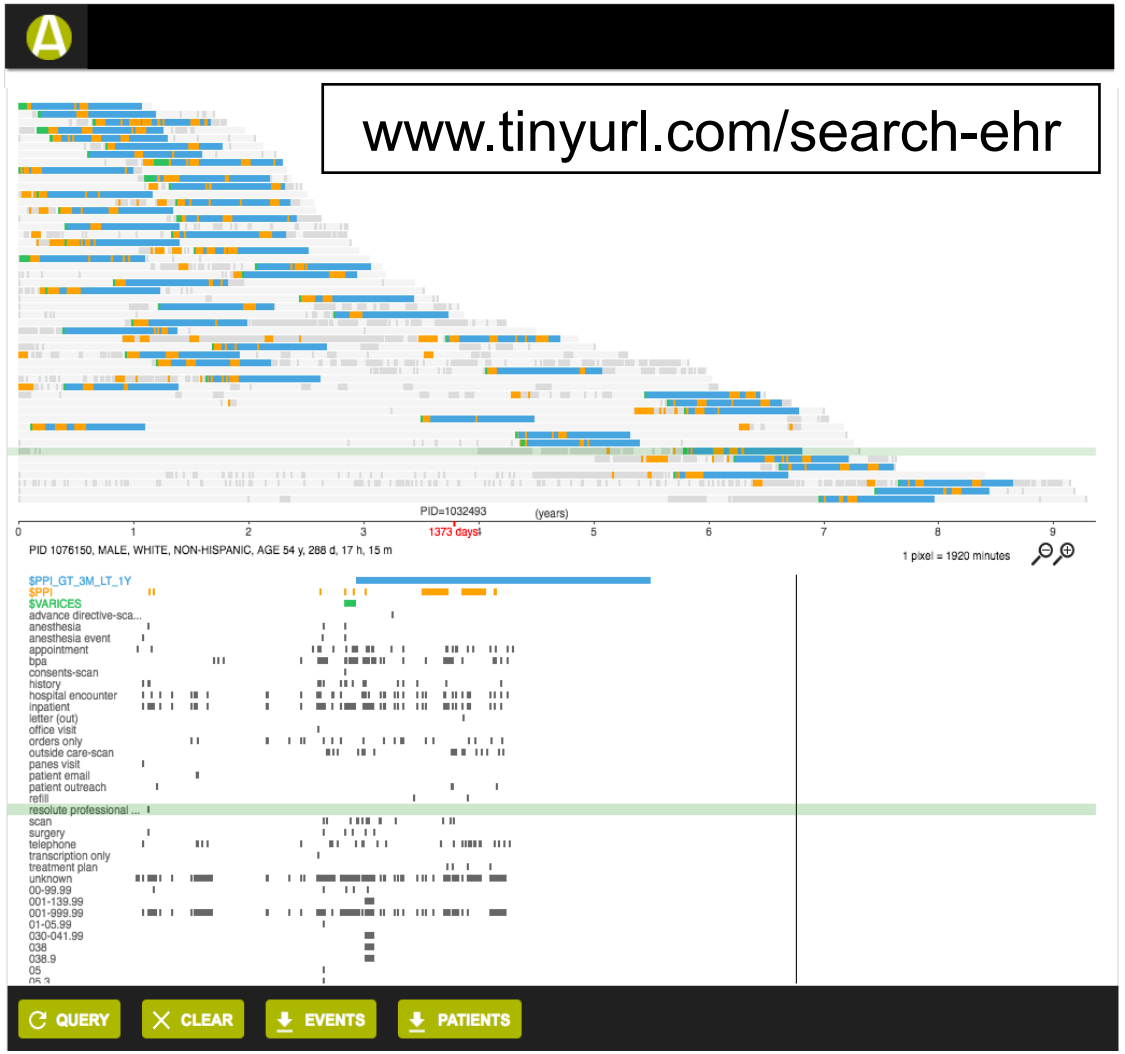


	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$	chisq	pvalue
normal	760	49	73.365	8.092	16.413	16.4	5.09e-05
elevated	760	96	71.635	8.287	16.413	16.4	5.09e-05

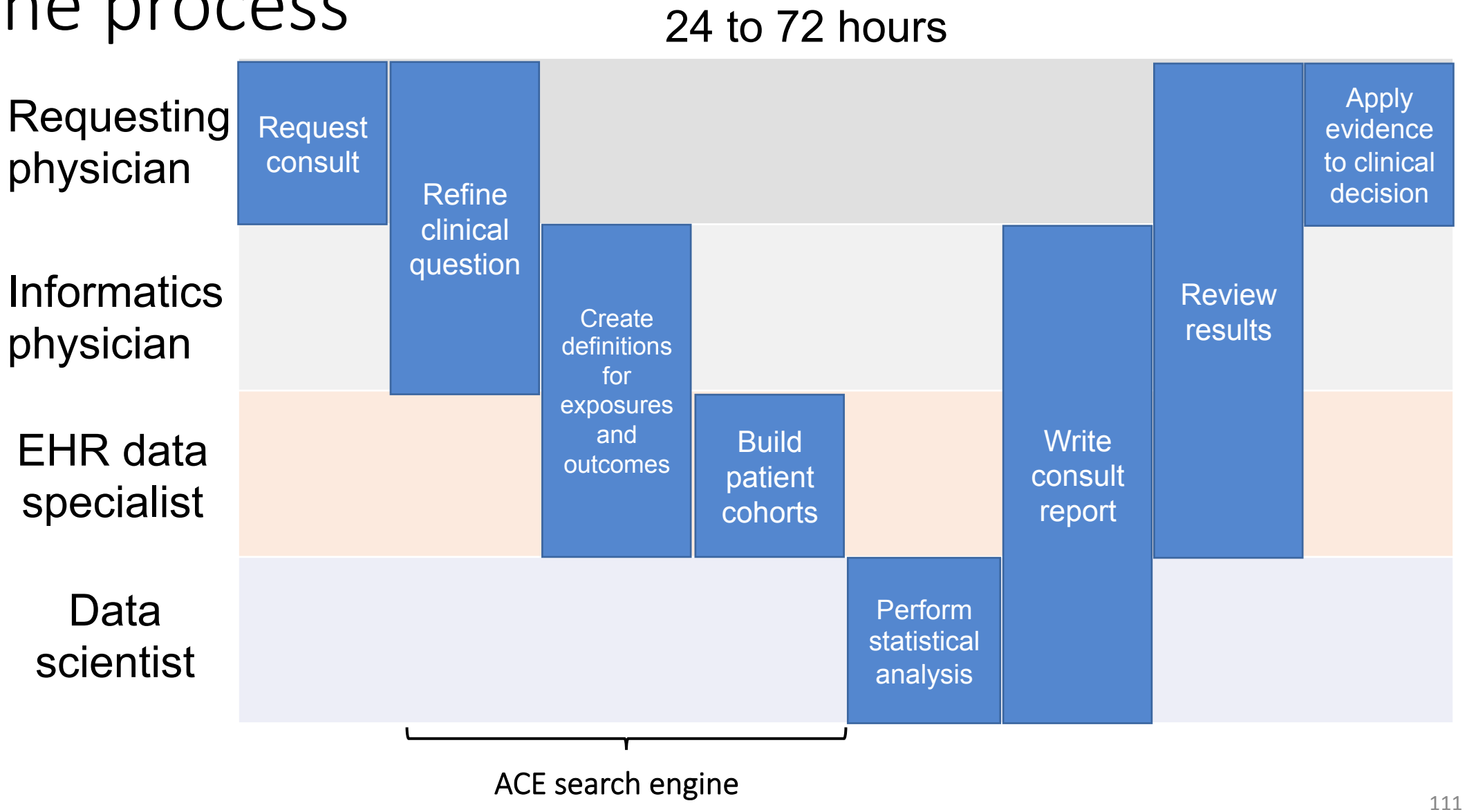
Service = software, data, and personnel



The ACE search engine



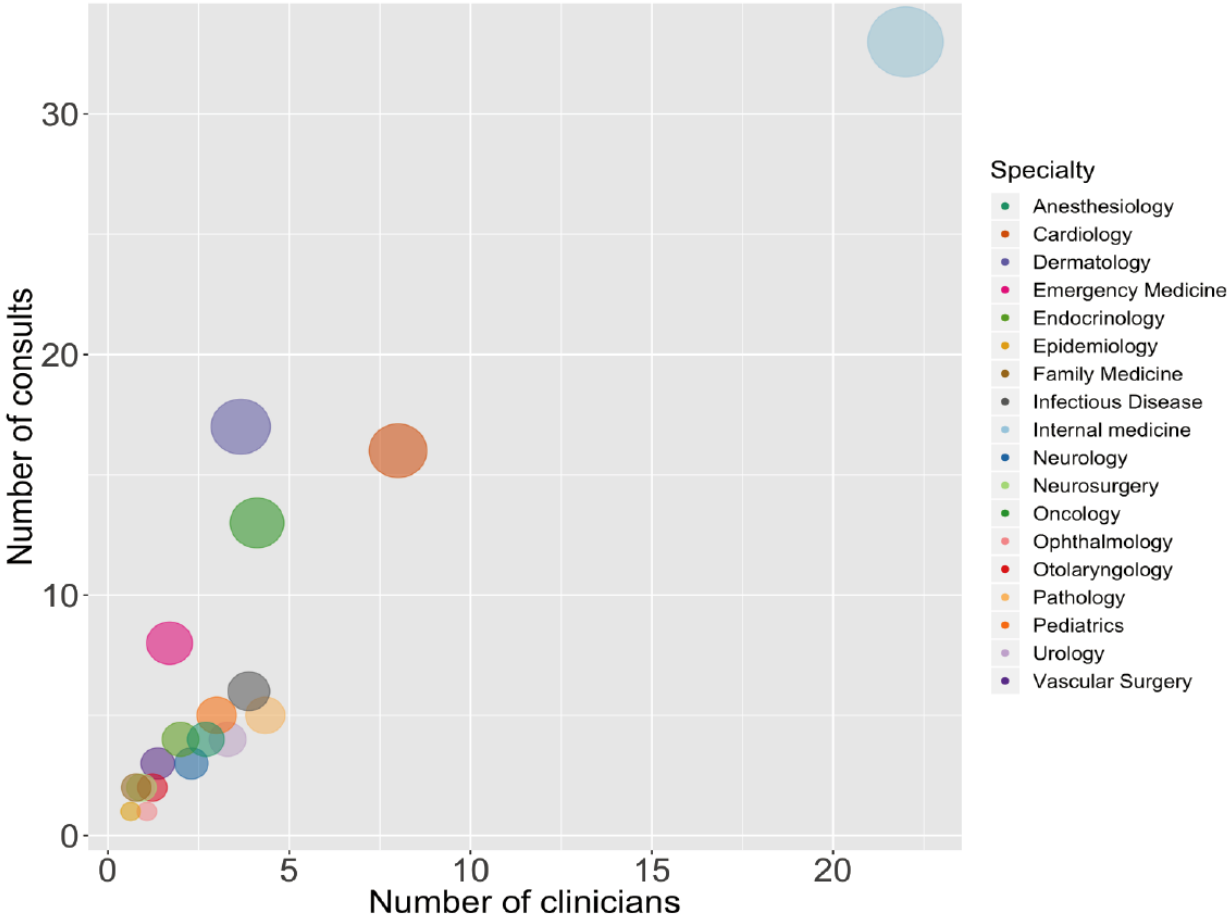
The process


24 to 72 hours
Requesting physician
Informatics physician
EHR data specialist
Data scientist
Request consult
Refine clinical question
Create definitions for exposures and outcomes
Build patient cohorts
Perform statistical analysis
Write consult report
Review results
Apply evidence to clinical decision
ACE search engine

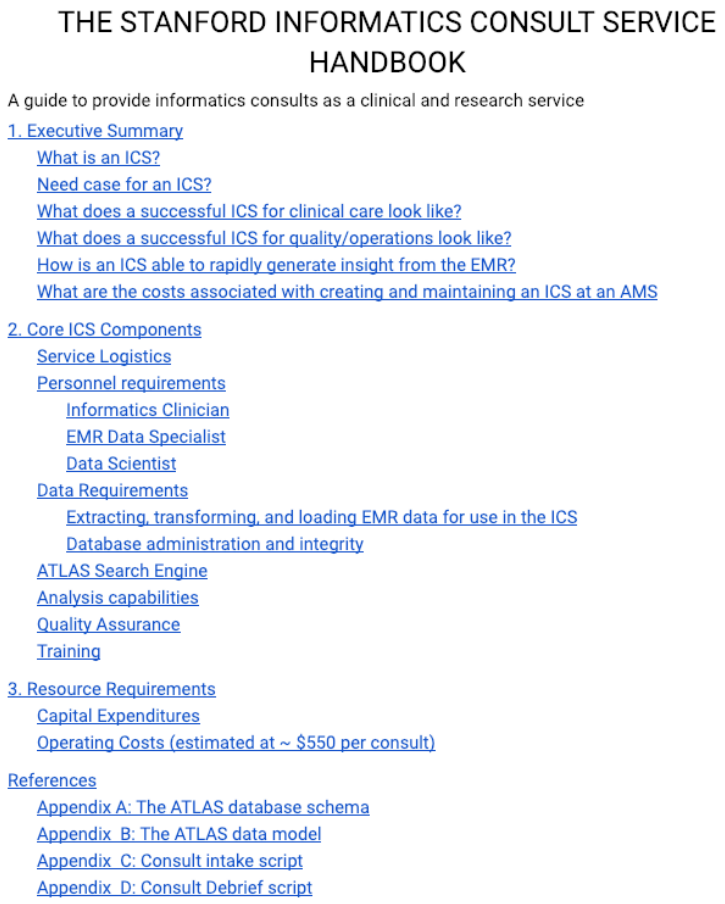
What we do to not be wrong

- Use CohortMethod's data diagnostics
- Use negative controls for empirical calibration
- E-values to quantify the degree of confounding that can produce the observed effect
- Ask the question using multiple datasets
- Schedule an in-person debrief

Learning from the first 150 consults



Deploying the service at your site



THE STANFORD INFORMATICS CONSULT SERVICE HANDBOOK

A guide to provide informatics consults as a clinical and research service

- Data in OHDSI CDM
- Institutional support
- Data science expertise
- Marketing
- A process to sanity-check the data and consult findings

http://greenbutton.stanford.edu

Ask me about the next phase of our study on measuring utility, and deploying the Green Button at Stanford Health Care