



# The Journey to Reliable Evidence- Update

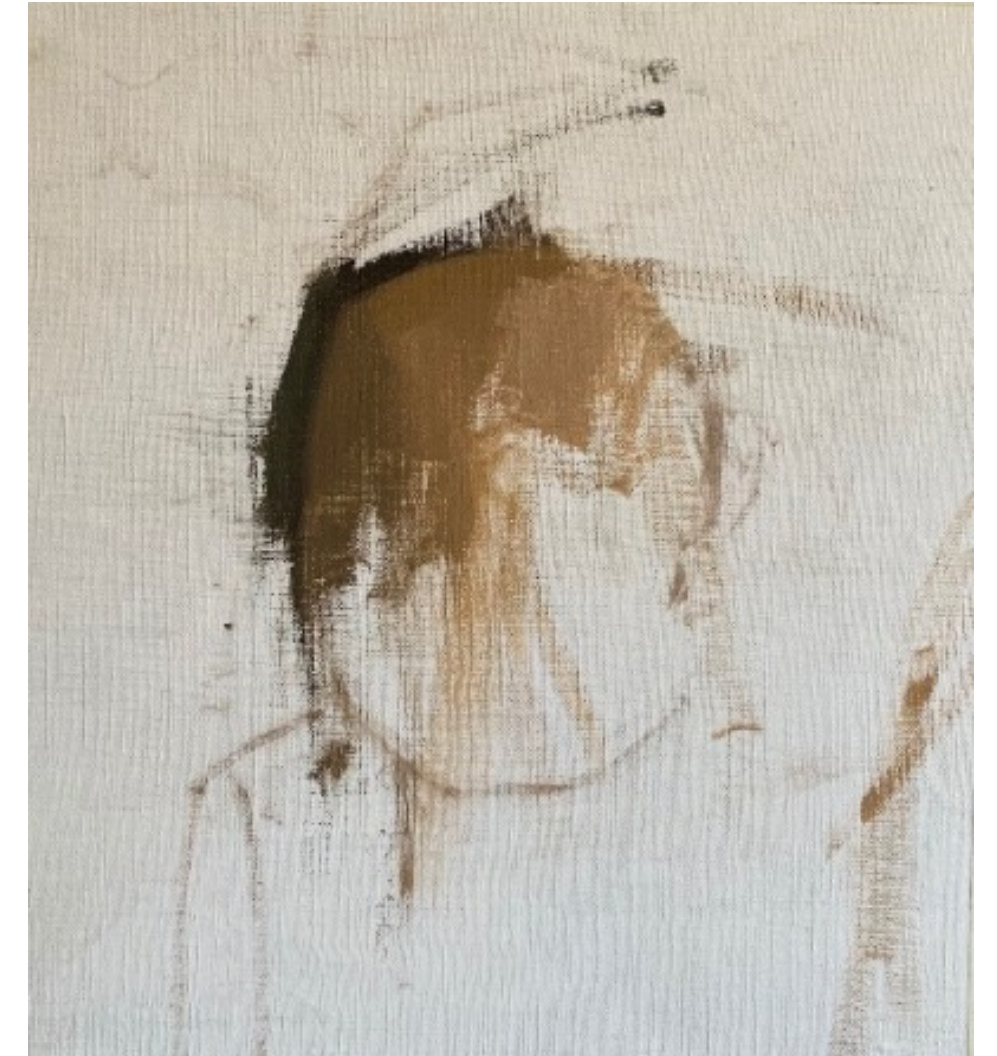
OHDSI Community call- March 2022

Asieh Golozar







# Original Study



Diabetes Care Volume 44, June 2021 1

 Check for updates



## Glucagon-Like Peptide 1 Receptor Agonists and Chronic Lower Respiratory Disease Exacerbations Among Patients With Type 2 Diabetes

Yasser Albogami,<sup>1,2,3</sup> Kenneth Cusi,<sup>4</sup> Michael J. Daniels,<sup>5</sup> Yu-Jung J. Wei,<sup>1,2</sup> and Almut G. Winterstein<sup>1,2</sup>

Diabetes Care 2021;44:1–9 | <https://doi.org/10.2337/DC20-1794>

EMERGING THERAPIES: DRUGS AND REGIMENS



# Fully Reproduced Study

Same data + same analysis

Plus

- Diagnostics
- Sensitivity analyses
- Different data
- Different population
- Different geography
- Different methods
- Meta-analysis



Hans Holbein the Younger  
Portrait of an English Dame  
1540-43





# OHDSI Reproducibility Service

A team of experts available on-demand to provide consults to execute this systematic process



David Madigan



Christian Reich



Kristin Kostka



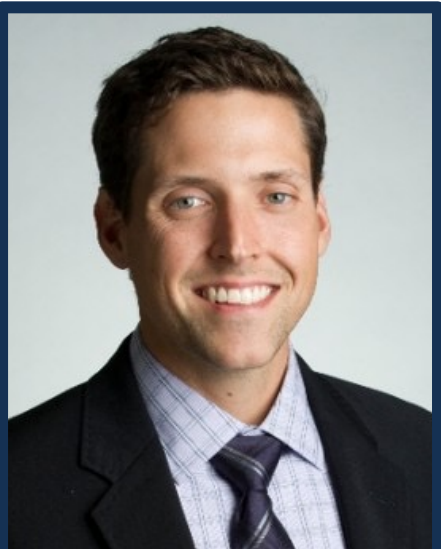
Brianne Olivieri-Mui



Andrew Williams



Asieh Golozar



Justin Manjourides





# What is a good candidate for reproducibility?

- Any observational research with impact on human lives
- The question is not easily amenable to clinical trials
- Many patients involved



# Our approach

Identification of the reproducibility candidate

## Initial assessment

- Data
- Methodology
- Details

1. Call for collaboration
2. Protocol and phenotype development
3. Analytic package
4. Execution

## Other permutations

- Diagnostics
- Sensitivity analyses
- Different data
- Different population
- Different geography
- Different methods
- Meta-analysis

Dissemination



# OHDSI Center Reproducibility Services PoC:

## Original Investigation

December 21, 2021

# Association of Rivaroxaban vs Apixaban With Major Ischemic or Hemorrhagic Events in Patients With Atrial Fibrillation

Wayne A. Ray, PhD<sup>1</sup>; Cecilia P. Chung, MD, MPH<sup>2</sup>; C. Michael Stein, MB, ChB<sup>2,3</sup>; et al

» Author Affiliations

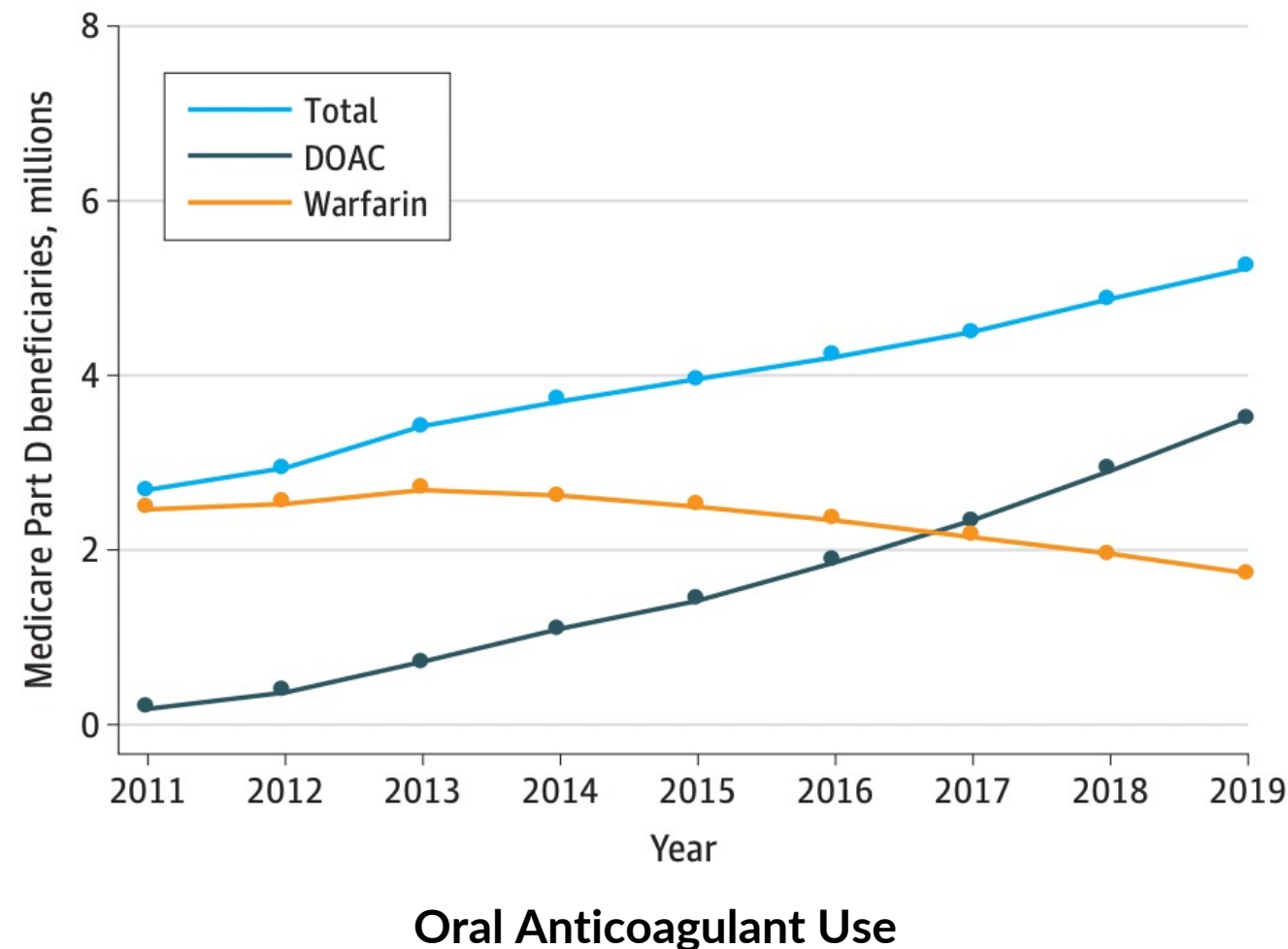
*JAMA*. 2021;326(23):2395-2404. doi:10.1001/jama.2021.21222





# Direct Oral Anticoagulant Therapy in Patients with Atrial Fibrillation

- Widespread use
- Increasing rate of DOACs use since approval



- What about the choice of DOACs for patients with atrial fibrillation?
- DOACs have not been compared directly in randomized trials
- Evidence on the comparative benefit and/or risk of DOACs comes from
  - indirect comparison of trial data
  - observational data using US claims
- Choice of DOACs is driven by clinical preference, local practices and insurance coverage
- A randomized trial with head-to-head comparison of all DOACs would be lengthy and expensive
  - ~85,000 patients should be followed up for at least 5 years to observe a 10% difference in major bleeding events





## Editorial

December 21, 2021

# Informing the Choice of Direct Oral Anticoagulant Therapy in Patients With Atrial Fibrillation

Enrico G. Ferro, MD<sup>1,2,3</sup>; Dhruv S. Kazi, MD, MSc, MS<sup>1,2,3</sup>; Peter J. Zimetbaum, MD<sup>1,2,3,4</sup>

Another approach could reexamine the observational data using more sophisticated methods for causal inference that are less susceptible to bias from residual confounding or immortal time (like the target trial emulation approach, which uses observational data to emulate pragmatic comparative effectiveness trials).<sup>17</sup>



# Ray et al. JAMA 2021

**Design:** Active comparator, new-user cohort design

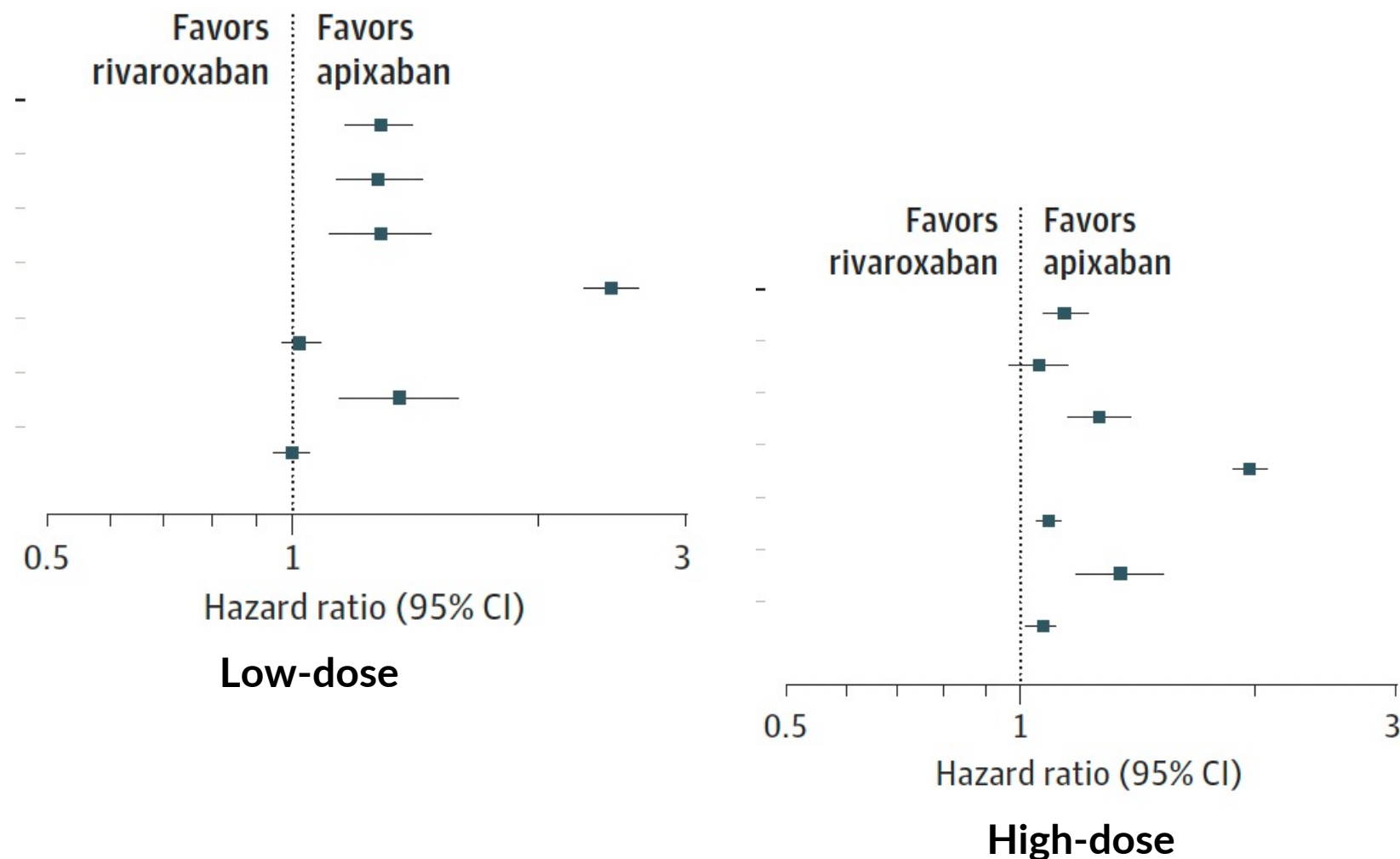
**Data source:** Medicare beneficiaries

**Study population (T& C):** atrial fibrillation/flutter patients who initiated treatment between 2013 & 2018

**Outcomes (O):** Major ischemic and hemorrhagic events

**Analysis:**

- Inverse probability of treatment weighting using propensity scores to balance the characteristics between the groups
- Cox-Proportional hazard & Poisson models

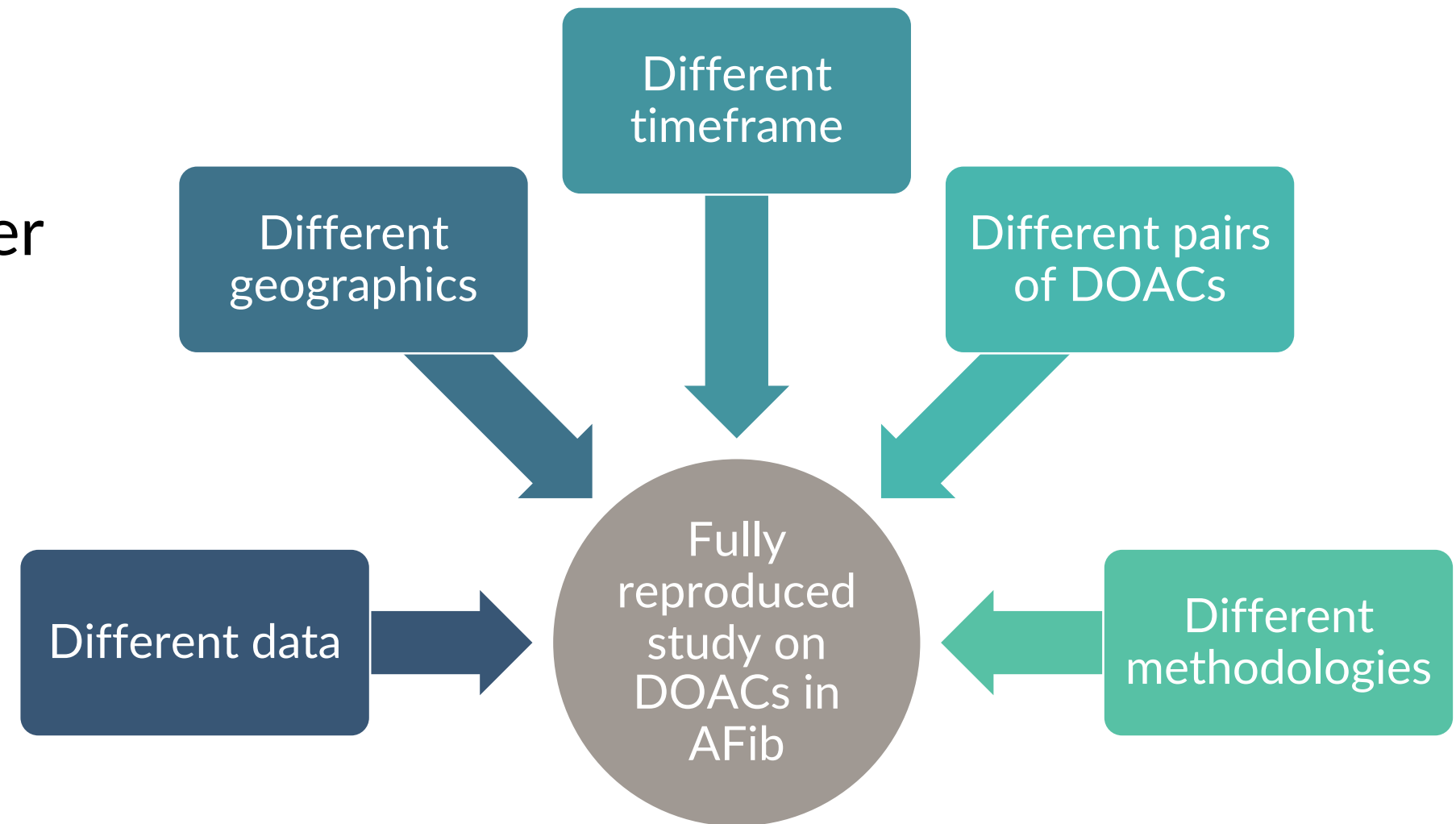


**Finding:** treatment with rivaroxaban compared with apixaban was associated with a significantly increased risk of major ischemic or hemorrhagic events



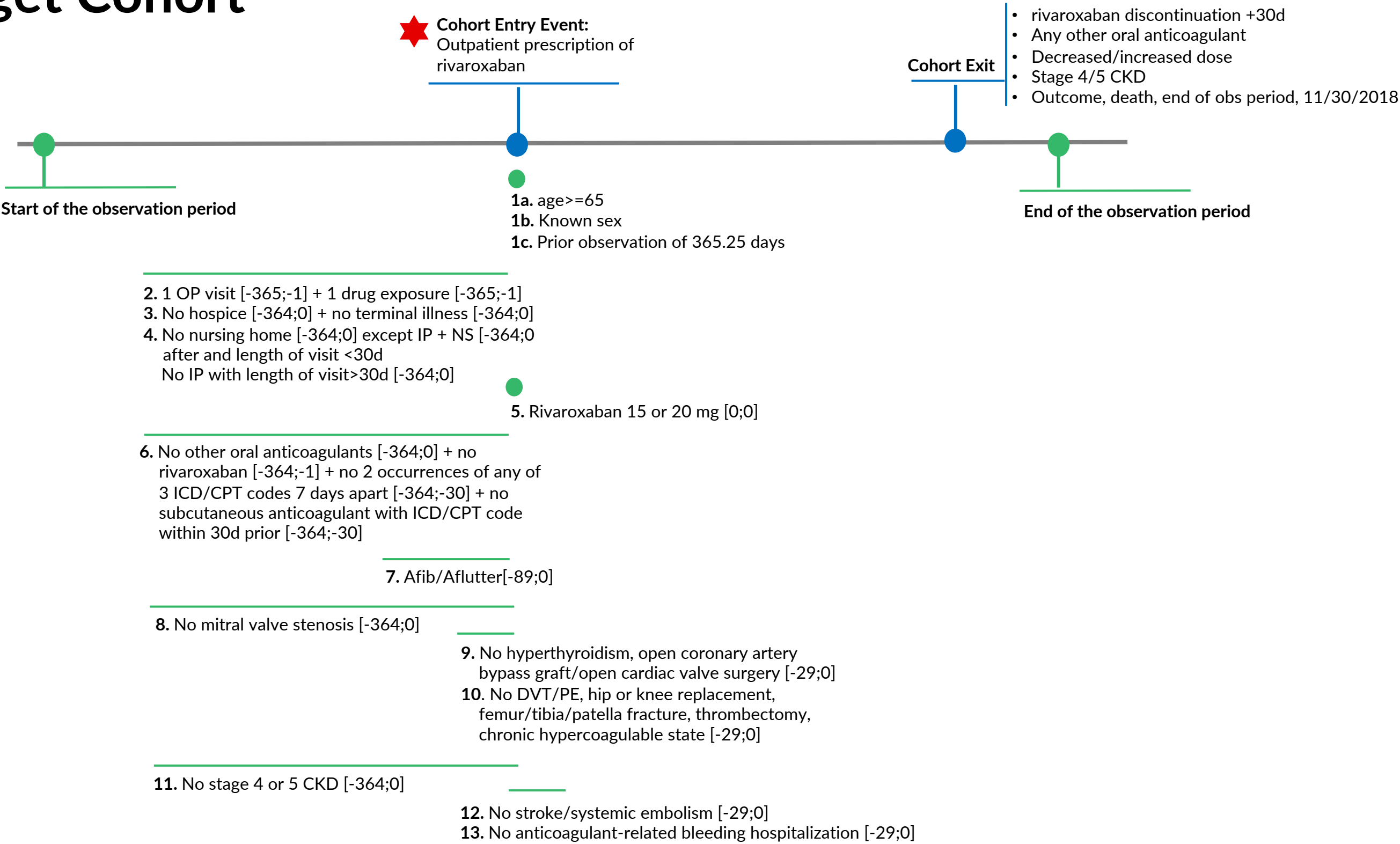
# Ray et al. JAMA 2021

- A single measure for clinical impact
  - benefits and harms of anticoagulation for patients with atrial fibrillation assessed together
- Evaluation of multiple doses
  - Standard and reduced
- Large sample size
- One data
- One method
- One anticoagulant pair





# Target Cohort







# So far

- ~800k patients on Apixaban or Rivaroxaban in Open Claims
- Similar demographics and baseline characteristics to Ray's cohorts
- **Full protocol development and execution**
- **Call for collaboration**

