

# Comparative effectiveness and safety of direct ORal Anticoagulants in patients with atrial fibrillation: a standardiZed Observational data Network study (CORAZON)

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# Contents

- A brief introduction to our research team
- Study background and objective
- Methods
- Study progress



British Medical Association (BMA) House,  
London

# Cluster of Pharmacoepidemiology And Medication Safety, UCL School of Pharmacy

- Observational studies using population databases in the UK (IMRD/CPRD)
- Asia Pharmacoepidemiology Network (AsPEN) (Hong Kong, Taiwan, Korea, Australia ...)

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## Pharmacoepidemiology And Medication Safety

Researchers in the Pharmacoepidemiology and Medication Safety cluster are engaged in projects that aim to improve safety and benefit outcomes in the use of medicines. We recognise that medicines use should be viewed in the context of wider policy and health agendas. These contexts inform our research programme and the design and execution of individual projects. Our work informs and influences policies to improve professional practice and



### Useful Links

#### Research Clusters

- [Age-related Medicines Development and Use](#)
- [Drug Discovery and Therapeutic Target Identification](#)
- [Fabrication and Synthetic Technologies for Advanced Drug Delivery](#)
- [Medicines Use and Optimisation](#)
- [Pharmacoepidemiology and Medication Safety](#)

# Research on direct oral anticoagulants

Research

JAMA | **Original Investigation**

## Association Between Dabigatran vs Warfarin and Risk of Osteoporotic Fractures Among Patients With Nonvalvular Atrial Fibrillation

Wallis C. Y. Lau, BSc; Esther W. Chan, PhD; Ching-Lung Cheung, PhD; Chor Wing Sing, BSc; Kenneth K. C. Man, MPH; Gregory Y. H. Lip, MD; Chung-Wah Siu, MD; Joanne K. Y. Lam, FHKAM; Alan C. H. Lee, FHKAM; Ian C. K. Wong, PhD

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## Sex-Based Differences in Outcomes of Oral Anticoagulation in Patients With Atrial Fibrillation

Sharon W.Y. Law, MPharm,<sup>a</sup> Wallis C.Y. Lau, PhD,<sup>a,b</sup> Ian C.K. Wong, PhD,<sup>a,b</sup> Gregory Y.H. Lip, MD,<sup>c,d</sup> Michael T. Mok, MBBS,<sup>e,f</sup> Chung-Wah Siu, MD,<sup>g</sup> Esther W. Chan, PhD<sup>a</sup>

Annals of Internal Medicine

ORIGINAL RESEARCH

## Association Between Treatment With Apixaban, Dabigatran, Rivaroxaban, or Warfarin and Risk for Osteoporotic Fractures Among Patients With Atrial Fibrillation

A Population-Based Cohort Study

Wallis C.Y. Lau, PhD; Ching-Lung Cheung, PhD; Kenneth K.C. Man, PhD; Esther W. Chan, PhD; Chor Wing Sing, PhD; Gregory Y.H. Lip, MD; Chung-Wah Siu, MD; Joanne K.Y. Lam, MBBS; Alan C.H. Lee, MBBS; and Ian C.K. Wong, PhD



Gastroenterology

## Prevention of Dabigatran-Related Gastrointestinal Bleeding With Gastroprotective Agents: A Population-Based Study



Esther W. Chan,<sup>1,\*</sup> Wallis C. Y. Lau,<sup>1,\*</sup> Wai K. Leung,<sup>2</sup> Michael T. C. Mok,<sup>3</sup> Ying He,<sup>1</sup> Teresa S. M. Tong,<sup>2</sup> and Ian C. K. Wong<sup>1</sup>

**Comparative effectiveness and safety of  
direct ORal Anticoagulants in patients with  
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Observational data Network study  
(CORAZON)**

# Study background

- Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting 33 million people worldwide and is a leading cause of stroke
- Current guidelines<sup>1,2</sup> recommend direct oral anticoagulants (DOACs) over warfarin for stroke prevention in AF
- No further guidance on how to choose between the DOACs, due to the absence of randomized controlled trials directly comparing the DOACs



1. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation  
2. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS.

# Study background

- Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting 33 million people worldwide and is a leading cause of stroke
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Clinical trials of DOACs vs Warfarin in AF		
	Stroke or systemic embolism	Major bleeding
Dabigatran (Pradaxa)	↓	↔
Rivaroxaban (Xarelto)	↔	↔
Apixaban (Eliquis)	↓	↓
Edoxaban (Savaysa)	↔	↓

↓: reduced in comparison to warfarin;  
 ↔: comparable to warfarin  
 Adapted from Wadhera RK et al. 2014

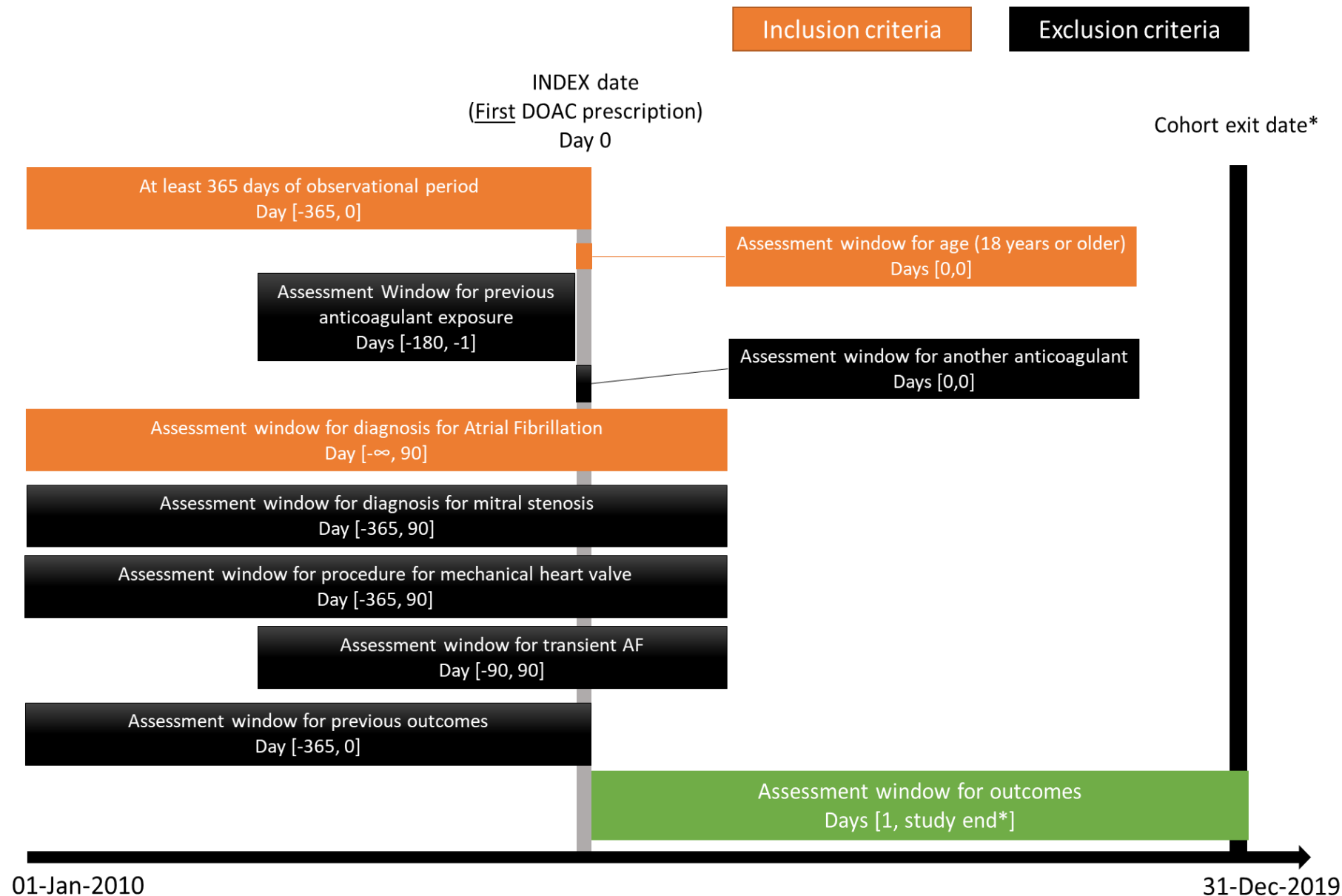


# Study objective

- To compare the effectiveness and safety outcomes between the four DOACs in patients with AF (dabigatran vs rivaroxaban vs apixaban vs edoxaban)
- Outcomes of interest:
  - Ischemic stroke/systemic embolism
  - Intracranial bleeding
  - Gastrointestinal bleeding
  - All-cause mortality

# Method

- A new user cohort  
Population-Level Estimation (PLE) study
- Propensity score matching
- Pair-wise hazard ratios



\*The earliest of 31-Dec-2019 (study end), date of death, discontinuation of index DOAC (90 days gap), prescription of another anticoagulant

# Method

- Subgroup analyses for clinically important patient groups who are unlikely to be included in future RCTs:
  - Renal impairment
  - Older age (aged  $\geq 80$  years)

# Current progress



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OHDSI Comparative effectiveness and  
safety of direct ORal Anticoagulants in  
patients with atrial fibrillation: a  
standardized Observational data Network  
study (CORAZON)

**Version: 1.2**

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Wallis CY Lau, PhD, UCL School of Pharmacy, United Kingdom

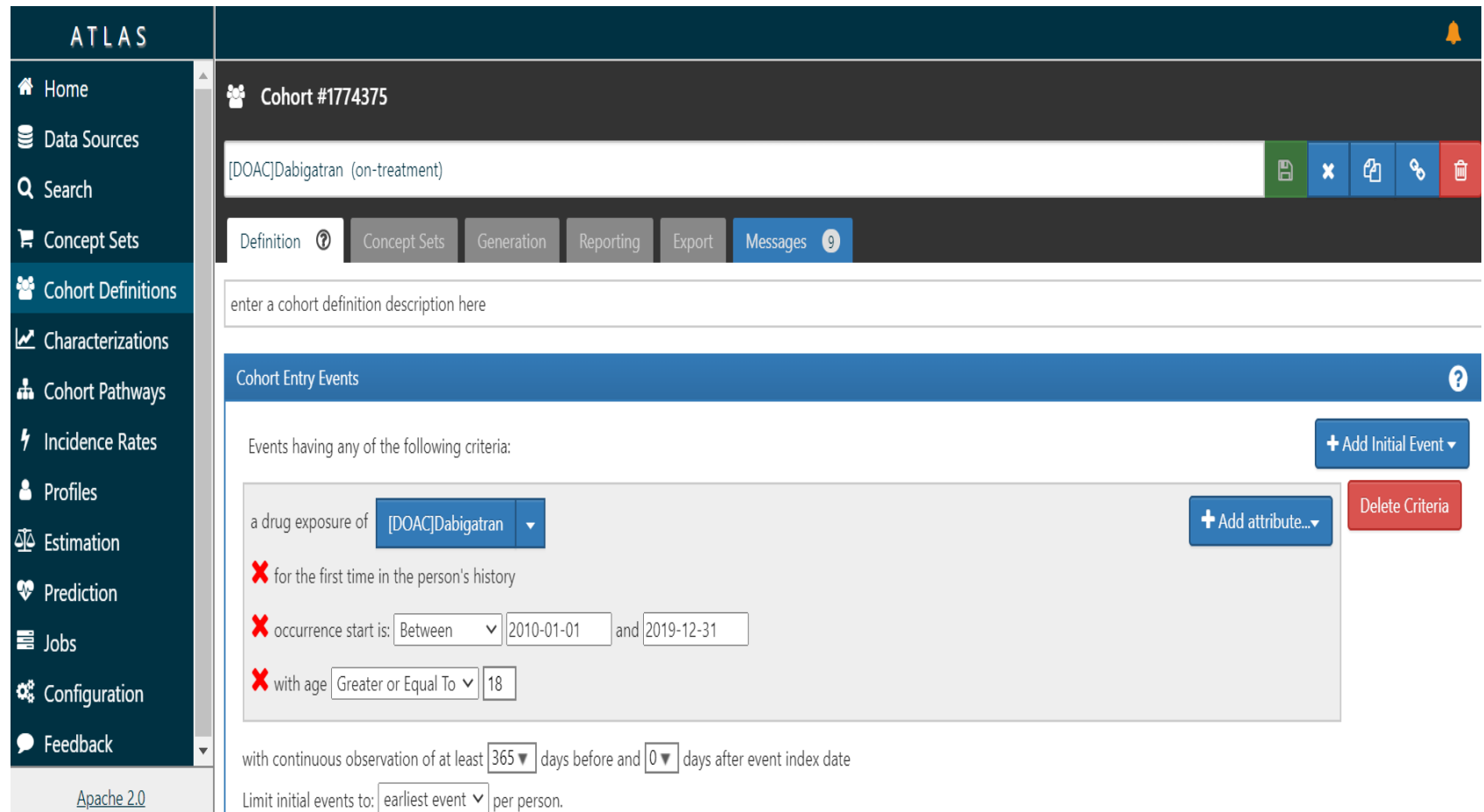
Kenneth KC Man, PhD, UCL School of Pharmacy, United Kingdom

Ian CK Wong, PhD, University of Hong Kong, Hong Kong; UCL School of Pharmacy, United Kingdom

# Current progress – ATLAS

- We are working with IQVIA OHDSI team for the data analyses

- Exposure cohorts:
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban
- Outcome cohorts:
  - Ischemic stroke/systemic embolism
  - Intracranial bleeding
  - Gastrointestinal bleeding
  - All-cause mortality



The screenshot displays the ATLAS web interface for defining a cohort. The left sidebar contains navigation options: Home, Data Sources, Search, Concept Sets, Cohort Definitions (selected), Characterizations, Cohort Pathways, Incidence Rates, Profiles, Estimation, Prediction, Jobs, Configuration, and Feedback. The main content area shows the configuration for Cohort #1774375, titled "[DOAC]Dabigatran (on-treatment)". The "Definition" tab is active, showing a text input field for a description. Below this, the "Cohort Entry Events" section is configured with the following criteria:

- Events having any of the following criteria:
  - a drug exposure of [DOAC]Dabigatran
    - for the first time in the person's history
    - occurrence start is: Between 2010-01-01 and 2019-12-31
    - with age Greater or Equal To 18

Additional settings include: "with continuous observation of at least 365 days before and 0 days after event index date" and "Limit initial events to: earliest event per person".

# Preliminary counts

<b>Data Sources (IQVIA)</b>	<b>Apixaban</b>	<b>Dabigatran</b>	<b>Edoxaban</b>	<b>Rivaroxaban</b>
France. LPD 2019/04	3,300	1,932	0	4,767
Germany. DA 2019Q3	13,302	3,721	5,788	14,807
UK. IMRD 2019/03	15,092	2,564	1,554	12,883
US AmbEMR. 2019/11	121,904	32,863	1,043	78,935
US Hospital. Full 2020/01	65,045	18,178	70	44,585
US Open Claims. Full 2019/07	951,389	269,867	6,438	706,820

**More preliminary results...**

# Summary

- There has been no RCTs directly comparing DOACs to guide the choice of DOACs
- The objective of this study is to generate comprehensive evidence on the comparative outcomes of dabigatran, rivaroxaban, apixaban, and edoxaban in patients with AF, using data from a range of data sources





# Join us!

