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

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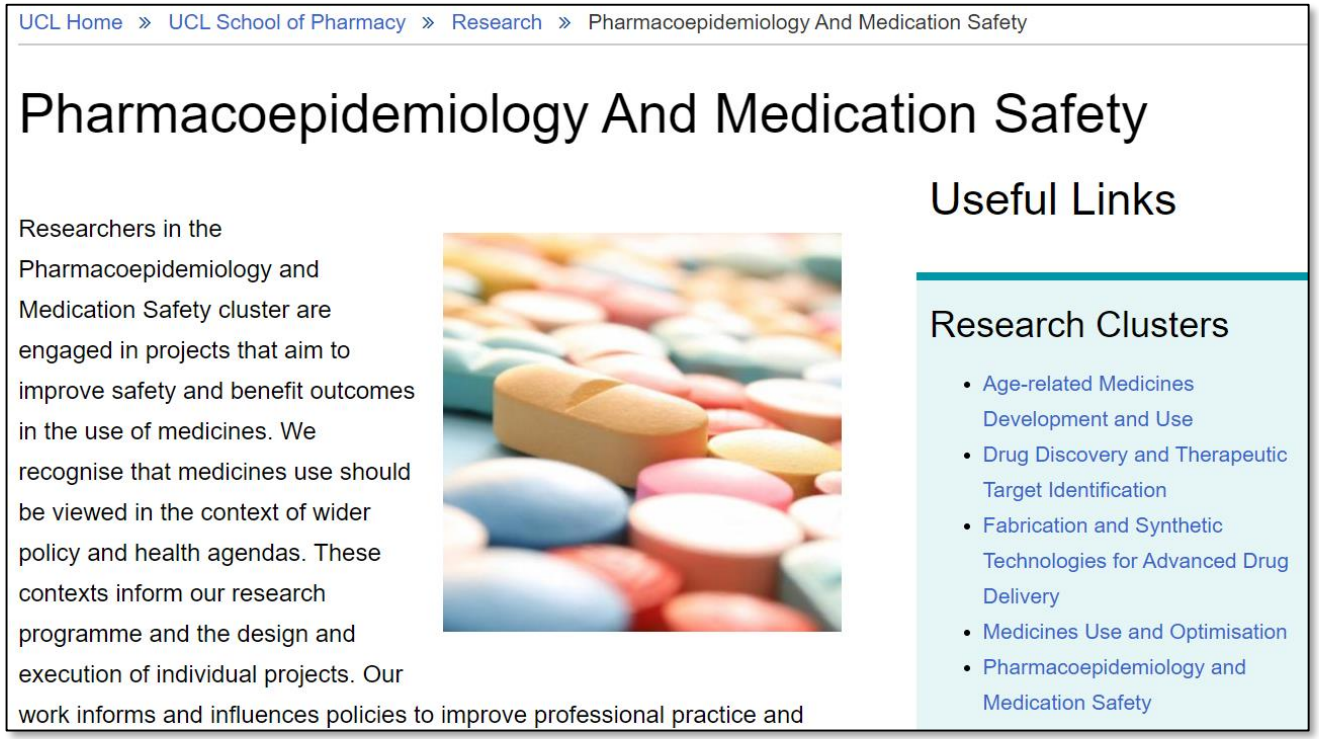
- A brief introduction to our research team
- Study background and objective
- Methods
- Study progress

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 …)



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

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

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 3, 2018

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

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

Gastroenterology

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

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

Comparative effectiveness and safety of direct ORal Anticoagulants in patients with atrial fibrillation: a standardiZed 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[1,2] 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
- Current guidelines[1,2] 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

	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

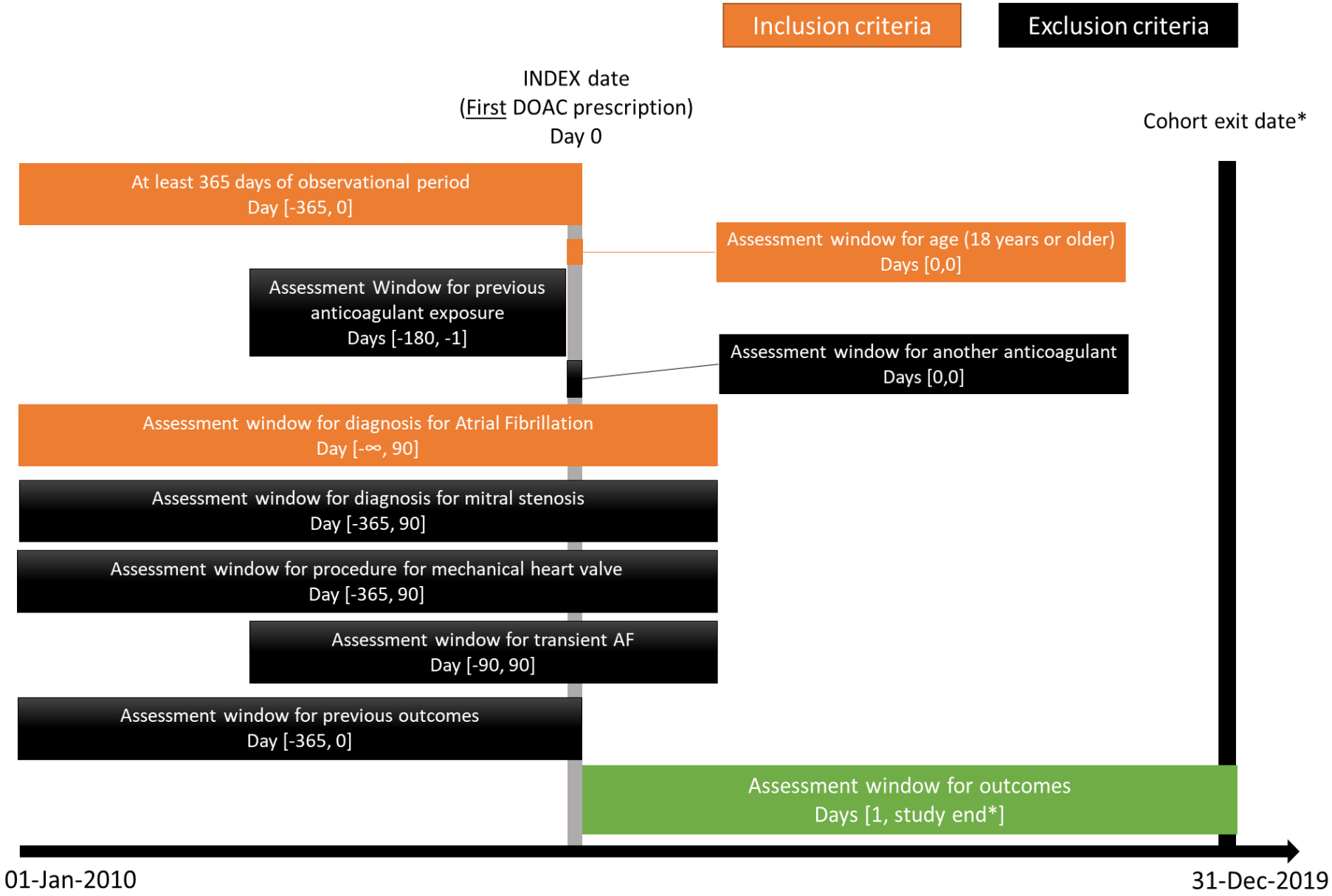
- To compare the effectiveness and safety outcomes between the four DOACs in patients with AF

(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>=80 years)

Current progress

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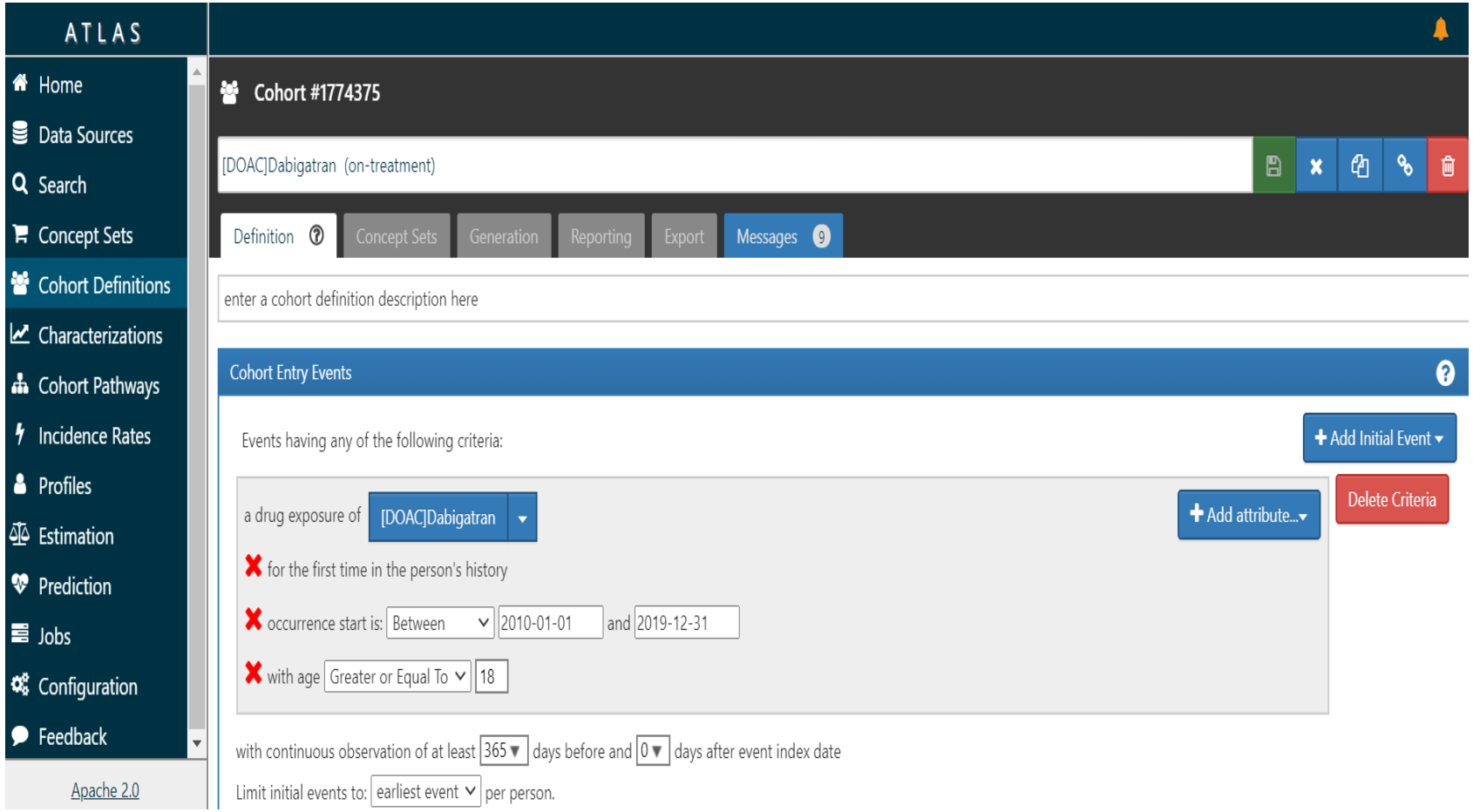
Kenneth KC Man, PhD, UCL School of Pharmacy, United Kingdom

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



Preliminary counts

Data Sources (IQVIA)	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
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!