

# Association of angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) on coronavirus disease (COVID-19) incidence and complications

**First published:** 14/05/2020

**Last updated:** 01/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS35296

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### Study ID

35854

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### DARWIN EU® study

No

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### Study countries

☐ Korea, Republic of

☐ Spain

☐ United Kingdom

☐ United States

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### Study description

This study will evaluate the effect of ACE inhibitor or ARB exposure on the risk of contracting COVID-19 infection and the risk of experiencing respiratory failure, pneumonia, acute kidney injury, and death in hypertensive patients following contracting COVID-19 infection. The analysis will be undertaken across a federated multi-national network of electronic health records and administrative claims from primary care and secondary care that have been mapped to the Observational Medical Outcomes Partnership Common Data Model in collaboration with the Observational Health Data Sciences and Informatics (OHDSI) and European Health Data and Evidence Network (EHDEN) initiatives.

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### Study status

Finalised

## Research institutions and networks

### Institutions

**UCL School of Pharmacy, University College London**

☐ United Kingdom

**First published:** 11/03/2010

**Last updated:** 21/04/2015

**Institution**

**Educational Institution**

**ENCePP partner**

# University of Dundee

☐ United Kingdom

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

**Educational Institution**

Ajou University South Korea, Columbia University  
US, Erasmus University Medical Centre The  
Netherlands, Janssen Research and Development  
US, UCLA US, University of Dundee UK, University  
of Oxford UK, University of South Australia  
Australia

## Contact details

### Study institution contact

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**Study contact**

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### Primary lead investigator

Marc Suchard

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Planned: 02/03/2020

Actual: 02/03/2020

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### **Study start date**

Planned: 26/03/2020

Actual: 26/03/2020

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### **Data analysis start date**

Planned: 07/04/2020

Actual: 07/04/2020

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### **Date of final study report**

Planned: 26/05/2020

Actual: 16/06/2020

## Sources of funding

- EU institutional research programme

## More details on funding

EHDEN

## Study protocol

## Regulatory

**Was the study required by a regulatory body?**

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

#### Study type list

**Study topic:**

Disease /health condition

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

**Main study objective:**

To measure the risk of COVID-19 susceptibility and severity in patients exposure to ACE inhibitors and ARBs compared to patient exposed to other antihypertensive agents.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(C09) AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM  
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

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**Medical condition to be studied**

COVID-19

## Population studied

**Short description of the study population**

Hypothesis 1, the cohort will consist of adult patients aged 18 years and over who receive at least one eligible prescription for an exposure drug between 1st November 2019 and 31st January 2020 (with index date set as the last

prescription in this window) and are observable in each database for at least one year prior to the index date. Patients are required to have a history of hypertension at any point prior to or including the index date and to be prescribed antihypertensive treatment recommended for first line or initial pharmacological treatment of hypertension at the index date as either monotherapy in one analysis or in combination with other hypertensive treatments that do overlap with the comparison cohort in a second analysis. Cohort exit will be the earliest of: the occurrence of an outcome event; the end of exposure; death; loss or deregistration from the database; or date of last data collection.

Hypothesis 2, We will identify adult patients aged 18 years or over who have an incident diagnosis of COVID19 occurring after 1st December 2019 and assign the date of diagnosis as the index date. Patients will be required to be registered or observable in each database for at least 180 days prior to index date, have a history of hypertension at any point prior to the index date and be a prevalent user of antihypertensive treatment recommended for first line treatment of hypertension as monotherapy at the index date. The end of follow-up will be the earliest occurrence of either: the outcome event, discharge, date of last data collection, end of follow-up (30 days) or death.

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### **Age groups**

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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### **Special population of interest**

Other

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## Special population of interest, other

COVID-19 patients

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## Estimated number of subjects

100000

# Study design details

## Outcomes

COVID-19 susceptibility and severity, Major acute cardiovascular events (MACE)

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## Data analysis plan

We will use a prevalent user cohort design to estimate the relative risk of each outcome associated with monotherapy only and monotherapy or combination therapy comparisons among patients prescribed ACE inhibitors and ARBs compared to patients with diuretics and calcium channel blockers. We will measure the risk of incident COVID-19 diagnosis and also outcomes following hospitalization with COVID-19. Data driven approaches will be used to identify potential covariates for inclusion in matched or stratified propensity score models identified using regularized logistic regression that allow balancing on a large number of baseline potential confounders. Cox regression analysis will be used to calculate hazard ratios. In addition negative control outcomes will allow for evaluating residual bias in the study design.

# Documents

## Study publications

[Morales DR, Conover MM, You SC, Pratt N, Kostka K, Duarte-Salles T, Fernández-B...](#)

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## Data management

## Data sources



**Data source(s), other**

South Korea: Health Insurance and Review Assessment (HIRA), Columbia University Irving Medical Center

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**Data sources (types)**

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

Unknown