# USE OF DRUGS ACTING ON RENIN-ANGIOTENSIN SYSTEM (RAS) AND RISK OF COVID-19: A CASE-POPULATION STUDY (SRAA-COVID19)

**First published:** 31/03/2020

**Last updated:** 01/07/2024

Study Ongoing

## Administrative details

**EU PAS number**

EUPAS34437

**Study ID**

34501

**DARWIN EU® study**

No

**Study countries**

☐ Spain

**Study description**

The coronavirus SARS-CoV-2 uses the protein ACE2 (angiotensin converting enzyme 2) as the receptor binding domain for its protein S (spike) to gain entry into cells and replicate. Blockers of the renin-angiotensin system (RAS) have been reported to upregulate the expression of ACE2 and this observation has raised the hypothesis that the use of these drugs could facilitate COVID-19 infection and/or make it more serious. Yet, the epidemiological evidence is lacking. The aim of this project is to carry out a quick case-population study using patients admitted to hospital with a diagnosis of COVID-19 as cases and a random sample of patients from a primary care database as the control series matched with cases for exact age, sex, and month-day (10 controls per case). Information on comorbidities and drugs used in the last month (current use) will be extracted from the clinical records in both cases and controls. We will examine the association of COVID-19 with the current use of RAS blockers as compared to non-use and as compared to current use of other antihypertensive drugs by computing the adjusted Odds Ratio through a conditional logistic regression model. The feasibility of selecting a secondary series of COVID-19+ cases who were not admitted to hospital (milder cases) will be assessed.

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**Study status**

Ongoing

# Research institutions and networks

## Institutions

### Hospital Universitario Príncipe de Asturias

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

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

Institution

## Puerta de Hierro-Majadahonda University Hospital

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

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

Institution

## Hospital Clinico San Carlos

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

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

Institution

## Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain

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

**Last updated:** 04/09/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority | ENCePP partner

Hospital Universitario Ramón y Cajal Madrid, Hospital Central de la Defensa Madrid, Hospital Clínico San Carlos Madrid, Hospital Universitario de la Princesa Madrid, Hospital Universitario Puerta de Hierro-Majadahonda Madrid, Hospital Universitario de Getafe Madrid

## Contact details


**Study institution contact**

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**Primary lead investigator**

Francisco José de Abajo Iglesias

**Primary lead investigator**


## Study timelines

**Date when funding contract was signed**

Planned: 18/03/2020

Actual: 18/03/2020

**Study start date**
Planned: 18/03/2020

Actual: 18/03/2020

**Data analysis start date**
Planned: 13/04/2020

**Date of interim report, if expected**
Planned: 06/04/2020

**Date of final study report**
Planned: 30/04/2020

## Sources of funding

- Other

## More details on funding

Instituto de Salud Carlos III

## Study protocol

ACE2_COVID-19_V5_2.pdf (440.28 KB)

## Regulatory

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

No

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

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Main study objective:**

To assess the association of renin-angiotensin system (RAS) blockers and non-steroidal anti-inflammatory drugs (NSAIDs) with hospital admission due to COVID-19 infection adjusted for age, sex, and cardiovascular risk factors.

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Case-population study

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(C03DA) Aldosterone antagonists

Aldosterone antagonists

(C09) AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

(M01AA) Butylpyrazolidines

Butylpyrazolidines

(M01AB) Acetic acid derivatives and related substances

Acetic acid derivatives and related substances

(M01AC56) meloxicam, combinations

meloxicam, combinations

(M01AE01) ibuprofen

ibuprofen

(M01AE02) naproxen

naproxen

(M01AG) Fenamates

Fenamates

(M01AH) Coxibs

Coxibs

(M01AX) Other antiinflammatory and antirheumatic agents, non-steroids

Other antiinflammatory and antirheumatic agents, non-steroids

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**Medical condition to be studied**

Coronavirus infection

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**Additional medical condition(s)**

COVID-19

# Population studied

**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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**Estimated number of subjects**

11000

## Study design details

**Outcomes**

- Hospital admission due to COVID-19- Hospital admission to the intensive care unit (ICU) due to COVID-19- In-hospital death after admission due to COVID-19- Admission to ICU or in-hospital death (combined)

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**Data analysis plan**

Main analysis:Crude odds ratios (ORs) and their 95% confidence intervals (CIs) will be computed through univariate conditional logistic regression to assess the association of current use of RAS blockers with the outcome of interest as compared to non-use and as compared to other antihypertensive drugs. After that, we built a multivariate model including the potential confounders (other comorbidities and comedications) all at once. Intermediate analyses: Intermediate analyses will be performed at different points along the study when the number of cases included are: 100, 500 and 750.Sensitivity analysis: Two sources of information from different years will be used (2020 for cases and 2018 for controls). To correct for a secular trend in the prevalence of antihypertensive drugs, we will estimate the prevalence for 2020 and we will

obtain a correction factor to adjust the odds ratios for.

# Data management

## ENCePP Seal

> The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

**Data source(s)**

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)

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**Data sources (types)**

Electronic healthcare records (EHR)

Other

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**Data sources (types), other**

Electronic medical records from the participating Hospitals

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No