

# NESTED CASE-CONTROL STUDY TO ASSESS THE ASSOCIATION BETWEEN THE USE OF METHYLPHENIDATE AND THE RISK OF VALVULAR HEART DISEASE AND PULMONARY HYPERTENSION

**First published:** 15/01/2016

**Last updated:** 23/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS12083

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### Study ID

33437

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### DARWIN EU® study

No

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### Study countries

Spain

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## Study description

**OBJECTIVE:** To assess the association between the use of methylphenidate and the risk of valvular heart disease (VHD) and pulmonary hypertension (PH). **STUDY DESIGN:** We will perform a case-control study nested in the BIFAP cohort, a database maintained by the Spanish Medicines Agency. Cases will be defined as patients between 5 and 25 years of age and a first diagnosis of VHD or PH, recorded in the BIFAP database between 2002 and 2014. Information on exposures between 2002 and 2014 will be collected. We will select up to 10 controls matched with cases by age, gender and calendar year. We will evaluate the use of methylphenidate before the case index date or the corresponding date among controls. We will test the robustness of the results by repeating the analysis in patients diagnosed with Attention Deficit Hyperactivity Disorder (ADHD). **DATA ANALYSIS:** We will compute odds ratios of VHD and PH according to methylphenidate use using conditional logistic regression, adjusting for matching factors and potential confounders (smoking status, cardiovascular diseases, diabetes, COPD...).

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## Study status

Finalised

# Research institutions and networks

## Institutions

### Navarre Health Service

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

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Institution

## Contact details

### Study institution contact

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Study contact

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### Primary lead investigator

Luis Carlos Saiz

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Actual: 04/12/2015

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### Study start date

Planned: 01/03/2016

Actual: 01/03/2016

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### Date of final study report

Planned: 05/12/2016

Actual: 04/01/2017

## Sources of funding

- Other

## More details on funding

Navarre Health Department

## Study protocol

[Protocol\\_Spanish\\_v151127.pdf](#) (102.74 KB)

[Protocol\\_Spanish\\_v161018.pdf](#) (103.5 KB)

## 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:**

Secondary use of data

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**Main study objective:**

To study if use of methylphenidate, compared to 'no use', is associated to a greater incidence of heart valve disease and/or pulmonary hypertension.

## Study Design

**Non-interventional study design**

Case-control

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**

METHYLPHENIDATE

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**Medical condition to be studied**

Attention deficit hyperactivity disorder

Mitral valve prolapse

Mitral valve incompetence

Cardiac valve disease

Mitral valve disease

Tricuspid valve disease  
Mitral valve disease mixed  
Aortic valve disease  
Congenital aortic valve incompetence  
Pulmonary hypertension

## Population studied

### **Short description of the study population**

Cases were patients between 5 and 25 years of age and a first diagnosis of valvular heart disease (VHD) or pulmonary hypertension (PH), recorded in the BIFAP database between 2002 and 2014. Up to 10 controls matched with cases by age, gender and calendar year.

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### **Age groups**

- Adolescents (12 to < 18 years)
  - Children (2 to < 12 years)
  - Adults (18 to < 46 years)
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### **Special population of interest**

Other

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### **Special population of interest, other**

Patients with valvular heart disease (VHD) and pulmonary hypertension (PH)

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### **Estimated number of subjects**

16500

## Study design details

## Data analysis plan

In order to describe the variables considered for cases and controls, frequency distribution will be provided for categorical variables (sex, smoking, etc). Regarding quantitative variables (BMI), measures of central tendency and dispersion will be offered, as mean (SD) and median (Inter Quartile Range). In addition, categorical variables will be compared with X2 test or Fisher test, and continuous variables with t-Student test or Mann-Withney test. In order to estimate the pulmonary hypertension (PH) and heart valve disease (HVD) risk associated to methylphenidate use, we will use conditional logistic regression models, adjusting by other potential confounding factors. Odd ratios adjusted by age, sex and confounding factors will be calculated. In the main analysis, we will compare the PH and HVD risk for patients exposed and no exposed to methylphenidate and assess its increase depending on the duration of prescriptions. We will also explore effects in new, recent and past users

## Documents

### Study results

[Results\\_ENCePP.pdf](#) (21.1 KB)

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### Study publications

[Saiz LC, Gil M, Alonso A, Erviti J, Garjón J, Martínez M. Use of methylphenidat...](#)

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## 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.

### **Conflicts of interest of investigators**

[Col\\_AAAlonso.pdf](#) (19.62 KB)

[Col\\_CCalvo.pdf](#) (1.01 MB)

[Col\\_JBerjon.pdf](#) (147.76 KB)

[Col\\_JErviti.pdf](#) (20.39 KB)

[Col\\_JGarjon.pdf](#) (570.86 KB)

[Col\\_LCSaiz.pdf](#) (165.43 KB)

[Col\\_LMuruzabal.pdf](#) (131.73 KB)

[Col\\_MMartinez.pdf](#) (186.78 KB)

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## 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 \(EHR\)](#)

## 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**

No