

# Comparative cardiovascular side effects of medications for attention-deficit/hyperactivity disorder: protocol of a case non-case study based on the WHO international pharmacovigilance database

**First published:** 07/06/2022

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

Study

Planned

## Administrative details

### EU PAS number

EUPAS47582

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### Study ID

47583

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### DARWIN EU® study

No

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### Study countries

 France

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## Study description

Treatment for individuals with ADHD includes both non-pharmacological and pharmacological strategies. Medications approved by the U.S. Food and Drug Administration (FDA) include stimulants (amphetamines and methylphenidate) and non-stimulants (atomoxetine, clonidine, guanfacine extended release, and viloxazine). In the past few decades, prescriptions for ADHD drugs have increased significantly across many countries. Overall, these medications are effective and generally well tolerated, although their use may be associated with adverse effects, in particular decreased appetite, decreased height and weight gain, sleep disturbances, tics, seizures, psychotic symptoms, and increased blood pressure and heart rate. To our knowledge, no study has been carried out using VigiBase® to compare ADHD drugs in terms of the risk of reporting cardiovascular adverse effects. Here, we present the protocol of a study aimed at comparing the risk of reporting cardiovascular events among 12 medications used to treat ADHD, individually and grouped according to their major pharmacological classes.

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## Study status

Planned

## Research institutions and networks

### Institutions

[Toulouse University Hospital](#)

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

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

## Pharmacologie En Population cohorteS et biobanqueS

### Contact details

#### Study institution contact

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Study contact

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#### Primary lead investigator

Pierjan Fourniols

Primary lead investigator

### Study timelines

#### Date when funding contract was signed

Planned: 02/05/2022

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#### Study start date

Planned: 30/05/2022

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#### Data analysis start date

Planned: 02/06/2022

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

Planned: 21/06/2022

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Toulouse University Hospital

## 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 type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

**Main study objective:**

The main objective : comparing the risk of reporting cardiovascular events among 12 medications used to treat ADHD, individually and grouped according to their major pharmacological classes.

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Case non-case study

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(N06BA07) modafinil

modafinil

(N06BA03) metamfetamine

metamfetamine

(N06BA09) atomoxetine

atomoxetine

(N06BA02) dexamfetamine

dexamfetamine

(N06BA01) amfetamine

amfetamine

(A08AA62) bupropion and naltrexone

bupropion and naltrexone

(N06BA04) methylphenidate

methylphenidate

(C02AC02) guanfacine

guanfacine

(C02AC01) clonidine

clonidine

(N06BA11) dexmethylphenidate

dexmethylphenidate

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### **Medical condition to be studied**

Cardiac disorder

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### **Additional medical condition(s)**

Hypertension Cardiac Arrhythmias, Torsade de pointes/QT prolongation, Heart failure, Ischemic heart disease, Central nervous system haemorrhages and cerebrovascular conditions, Cardiac valve disorders, Myocardial disorders

## **Population studied**

### **Age groups**

- Children (2 to < 12 years)

- Adolescents (12 to < 18 years)
  - 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**

10000

## Study design details

### **Outcomes**

Risk of reporting cardiovascular events among : 1. Hypertension 2. Cardiac Arrhythmias 3. Torsade de pointes/QT prolongation 4. Heart failure 5. Ischemic heart disease 6. Central nervous system haemorrhages and cerebrovascular conditions 7. Central nervous system haemorrhages and cerebrovascular conditions 8. Myocardial disorders

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### **Data analysis plan**

This is a disproportionality analyses using Vigibase®, the World Health Organization's global database of Individual Case Safety Reports (ICSRs), which has included more than 30 million reports since 1967 (as of May 2022) from over 130 countries. The WHO Uppsala Monitoring Center stores these ICSRs, which are spontaneous reports of adverse drug reactions from a suspected causative agent, as reported by health professionals, consumers, or drug manufacturers. Vigibase® includes information on the patient's age, gender, medical history, and country, as well as on the medications taken, with their start and end dates. Reports are categorized according to the seriousness of

the adverse drug reaction. The Medical Dictionary for Regulatory Activities (MedDRA) is used to code adverse effects

## 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), other**

WHO international pharmacovigilance database France

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### **Data sources (types)**

[Spontaneous reports of suspected adverse drug reactions](#)

## 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