DARWIN EU® - Association of venous thromboembolism with non-steroidal anti-inflammatory drug use in women 15-49 years using hormonal contraceptives

First published: 16/01/2025

Last updated: 13/02/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000443

Study ID

1000000443

DARWIN EU® study

Yes

Study countries

- [ ] Denmark
- [ ] Norway
- [ ] Spain

United Kingdom

Study description

Venous thromboembolism (VTE) refers to the formation of a blood clot in a deep vein and is a rare but potentially preventable cause of death in women of reproductive age. Multiple studies have showed that oral combined hormonal contraception is associated with an increased risk of VTE, especially high-dose combined oral contraception (>=50 µg ethinyl estradiol and progestins).[1]
Additionally, the use of non-steroidal anti-inflammatory drugs (NSAIDs) has also been linked to increased VTE risk. Meta-analyses and observational studies have suggested an increased risk of VTE among NSAIDs users.[2,3]
Recently, a nationwide study from Denmark found that NSAIDs use is associated with increased VTE risk in women 15-49 years old, especially among those with concomitant use of high/medium risk hormonal contraception. [4]
This study was fraught with limitations, particularly as the study design did not satisfactorily account for confounding.
More data on the association of venous thromboembolism with NSAIDs in women of reproductive age has been requested by medicines regulators to see if such associations are seen in other databases, including data on women using hormonal contraception.

Study status

Ongoing

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

☐ Netherlands

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Last updated: 02/05/2024

Institution | **Educational Institution** | **ENCePP partner**

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

☐ Belgium
☐ Croatia
☐ Denmark
☐ Estonia
☐ Finland
☐ France
☐ Germany
☐ Greece
☐ Hungary
☐ Italy
☐ Netherlands
☐ Norway
☐ Portugal

☐ Spain

☐ Sweden

☐ United Kingdom

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Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Xintong Li

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 26/06/2024

Actual: 26/06/2024

Study start date

Planned: 08/01/2025

Actual: 08/01/2025

Date of final study report
Planned: 20/06/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P3-C3-008_NSAIDS_V4.pdf(958.48 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Drug/Vaccine Safety Studies

Patient-level DUS

Main study objective:

1. To characterise the use of NSAIDs among women aged 15-49.
2. To measure the association of any NSAID use and the incidence of VTE among 15-49 years old women on high, medium, and low risk hormonal contraceptives.
3. To measure the association of ibuprofen, diclofenac and naproxen use on the incidence of VTE among 15-49 years old women on high, medium, and low risk hormonal contraceptives.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Anti-inflammatory and antirheumatic products, non-steroids (NSAIDS) Defined by all M01A group except M01AX05, M01AX12, M01AX25 and M01AX26

Medical condition to be studied

Venous thrombosis

Population studied

Short description of the study population

Objective 1: Drug utilisation of NSAIDs.

The study population will be women aged 15-49 who initiate oral NSAIDs of ibuprofen, diclofenac and naproxen on or after 2014 while using hormonal contraceptives, defined using a 90-day washout window. We will require at least 365 days of data availability before NSAIDs use.

Objective 2 and 3: Incidence of VTE

The source population will be women of reproductive age using hormonal contraceptives or therapies. We will not limited to medication with contraceptive as indication, but also medications as a combination of estrogen and progestin for other indications. For example, the DIANE®-35, which contains ethinylestradiol and cyproterone acetate, is a treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhoea) and/or hirsutism in women of reproductive age, will be included in this study.

The study population will include women aged 15-49, using hormonal contraceptives, and with no history of venous or arterial thromboembolism, cancer (except non-melanoma skin cancer), thrombophilia, hysterectomy, bilateral oophorectomy, sterilisation or infertility treatment.

Age groups

Adults (18 to < 46 years)

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink (CPRD) GOLD

Danish Health Data Registries

The Information System for Research in Primary Care (SIDIAP)

Norwegian Linked Health registry at University of Oslo

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown