Estimation of background incidence rates of coagulation disorders and the association with COVID-19 vaccines in pregnant population: a multi-database study from 3 European countries

First published: 06/03/2026

Last updated: 06/03/2026

Study Planned

Administrative details

EU PAS number

EUPAS1000000918

Study ID

1000000918

DARWIN EU® study

No

Study countries

- [ ] Denmark
- [ ] Finland

- [ ] Italy
- [ ] Netherlands
- [ ] Spain

Study description

This study aims to estimate:
i)the background incidence rates of coagulation disorders—including thromboembolic and haemorrhagic events— during pregnancies and prior to vaccination with the EMA-approved COVID-19 vaccines
ii)evaluate the association between the exposure to each of the EMA-approved COVID-19 vaccines (BioNTech/Pfizer, Moderna, AstraZeneca, J&J) and the coagulation disorders* in pregnant women through a self-controlled case series (SCCS) design
This study will be conducted using routinely collected healthcare data including electronic health records and/or national register data from 4 data sources in 3 European countries (Spain, Denmark and Finland). A background incidence rate will be applied prior to vaccination with the four-EMA approved COVID-19 vaccines. A self-controlled case series (SCCS) analysis will be conducted with all pregnant women with at least one COVID-19 vaccine dose (BioNTech/Pfizer, Moderna, AstraZeneca, J&J) during pregnancy and coagulation disorders diagnosis during pregnancy

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Study status

Planned

Research institutions and networks

Institutions

Real-World Evidence Team, University of Eastern Finland (RWE team)

Finland

First published: 20/12/2017

Last updated: 27/08/2024

Institution | Educational Institution | ENCePP partner

Aarhus University & Aarhus University Hospital DEPARTMENT OF CLINICAL EPIDEMIOLOGY

Denmark

First published: 20/07/2021

Last updated: 02/04/2024

Institution | Educational Institution | ENCePP partner

University Medical Center Utrecht (UMCU)

Netherlands

First published: 24/11/2021

Last updated: 22/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility | ENCePP partner

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain

First published: 05/10/2012

Last updated: 23/05/2025

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Agenzia regionale di sanità della Toscana (ARS Toscana)

Italy

First published: 01/02/2024

Last updated: 23/03/2026

Institution | EU Institution/Body/Agency | ENCePP partner

The Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO)

Spain

First published: 01/02/2024

Last updated: 31/10/2025

Institution

Teamit Institute

Spain

First published: 12/03/2024

Last updated: 12/03/2024

Institution | Other | ENCePP partner

Contact details

Study institution contact

Leonardo R. Pereira L.RoquePereira@umcutrecht.nl

Study contact

L.RoquePereira@umcutrecht.nl

Primary lead investigator

Leonardo R. Pereira

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 28/05/2025

Actual: 28/05/2025

Study start date
Planned: 30/03/2026

Date of final study report
Planned: 30/06/2026

Study protocol

SafetyVac_BR_SCCS_Preg_Coagulation

D_Protocol_v2.0_19Jan26_FinalCleanVersion-3.pdf (1.52 MB)

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 topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Data collection methods:

Secondary use of data

Study design:

A background incidence rate will be applied before COVID-19 vaccination. Then, a self-controlled case series (SCCS) analysis will be conducted with all pregnant women with at least one COVID-19 vaccine dose (BioNTech/Pfizer, Moderna, AstraZeneca, J&J) during pregnancy.

Main study objective:

1. To estimate the background incidence rates of coagulation disorders—including thromboembolic and hemorrhagic events— during pregnancies and prior to vaccination with the four-EMA approved COVID-19 vaccines (BioNTech/Pfizer, Moderna, AstraZeneca, J&J).
2. To evaluate the association between the exposure to each of the four EMA-approved COVID-19 vaccines (BioNTech/Pfizer, Moderna, AstraZeneca, J&J) and the coagulation disorders* in pregnant women through a self-controlled case series (SCCS) design

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Self-controlled case series and background incidence rates

Study drug and medical condition

Medicinal product name, other

EMA-approved COVID-19 vaccines:

-BioNTech/Pfizer

-Moderna

-AstraZeneca

-J&J

Anatomical Therapeutic Chemical (ATC) code

(J07BN) Covid-19 vaccines

Covid-19 vaccines

Medical condition to be studied

Embolism venous

Cerebral venous sinus thrombosis

Arterial thrombosis

Thrombosis with thrombocytopenia syndrome

Deep vein thrombosis

Pulmonary embolism

Haemorrhagic stroke

Ischaemic stroke

Disseminated intravascular coagulation

Microangiopathy

Population studied

Short description of the study population

The source population comprises all persons entered in the data sources from 01-Jan-2019, through the most recent data availability. The study population consists of pregnant individuals, identified using the IMI-ConcePTION pregnancy algorithm which is used for background rate analysis. From this study population, we will define the study population for Self-controlled case series (SSCS) - Eligible for inclusion in the SCCS analysis are all pregnant women (which has one or more pregnancies) who received at least one dose of a COVID-19 vaccine and were diagnosed with a coagulation disorder during the follow-up period.

Special population of interest

Pregnant women

Study design details

Setting

This study will use data from secondary electronic health record databases that are population-based. The following data sources were included: SIDIAP (access provided by the Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAP JGol)), VID (access provided by the Foundation for the Promotion of Health and Biomedical Research of Valencia Region; (FISABIO)); Danish National Registries (DHR) (access provided by Aarhus University) and Finnish registers (access provided by University of Eastern Finland).

Each data source will produce a study-specific data instance. A data instance is a subset of the data source that has been ETL’ed into the CDM at a certain point in time. This instance does not necessarily contain data from all databanks in

the data source, but data required for one or more studies.
Pregnancies will be identified using the IMI-ConcePTION pregnancy algorithm.

Outcomes

Coagulation disorders are the main outcome of this study. We defined coagulation disorders as a composite outcome of any one of the following:

1. Venous thromboembolism (VTE)
2. Cerebral Venous Sinus Thrombosis (CVST)
3. Arterial Thrombosis
4. Thrombosis with thrombocytopenia syndrome (TTS)
5. Deep vein thrombosis (DVT)
6. Pulmonary Embolism (PE)
7. Hemorrhagic stroke
8. Ischemic stroke (IS)
9. Disseminated intravascular Coagulation (DIC)
10. Microangiopathy

These events will be captured from the EVENTS table using diagnosis code lists.
A separate table of algorithms linked to diagnostic code list that will be submitted with the publication
Code lists to identify events have been created using the VAC4EU Code Mapper tool29, which maps concepts across medical vocabularies based on the Unified Medical Language System. The output of the Code Mapper is a CSV list presented in Annex 1.
For the sub-analysis, thromboembolic outcome will be composed by the following events: VTE, DVT, PE, CVST, IS, Arterial thrombosis, and TTS.
For the sub-analysis of haemorrhagic disorders, we will combine the following events: DIC, Hemorrhagic stroke and Microangiopathy.

Data analysis plan

The background Incidence rates of outcomes among pregnant women with coagulation disorders will be calculated using total cases and person-time at risk. The incidence rates will be adjusted for the covariates (age, gestational age, prior Venous thromboembolism and anti-thrombotic agents) via Poisson regression. A 95% confidence intervals will be computed using exact methods. A modified SCCS analysis using conditional Poisson regression will be conducted to estimate the relative incidence, stratified by data source and gestational trimester. A 14-day risk window, pre-exposure transition window of 14 days and two-day post-exposure transition windows are proposed for this study. Sensitivity analyses using 7-day interval will be applied. Country specific estimates will be pooled via random-effects meta-analysis.

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)

The Information System for Research in Primary Care (SIDIAP)

The Valencia Health System Integrated Database

Danish Health Data Registries

Terveydenhuollon hoitoilmoitusrekisteri (Finland Care Register for Health Care)

Data sources (types)

Electronic healthcare records (EHR)

Population registry

Pregnancy registry

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after extract-transform-load to a common data model