Rapid Safety Assessment of SARS-CoV-2 vaccines in EU Member States using electronic health care datasources (CVM Covid19-Vaccine-Monitor-EHR)

First published: 16/08/2021

Last updated: 01/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/50433

EU PAS number

EUPAS42467

Study ID

50433

DARWIN EU® study

No

Study countries

- [ ] Belgium
- [ ] Italy
- [ ] Netherlands
- [ ] Norway
- [ ] Spain
- [ ] United Kingdom

Study description

Readiness The readiness phase will include the following objectives: • To provide an overview of the methods for identification of COVID-19 vaccine exposure in the data sources • To monitor the number of individuals exposed to any COVID-19 vaccine and to compare this to COVID-19 vaccine exposure data • To quantitatively evaluate different algorithms to identify adverse events by provenance in electronic health care data • To conduct time-to-onset analyses for the AESI with respect to time since vaccination • To assess the association between and the vaccines of interest and negative control events using the SCRI to estimate systematic bias (unmeasured confounding) • To test the impact of different comparators in the cohort design, using the negative control outcomes • To generate information for testing of methodological questions around misclassification of events/exposure Rapid assessment studies Primary objective The primary objective for this rapid assessment study is to assess the potential association between the occurrence of specific AESIs and vaccination with COVID-19 vaccines within disease-specific risk periods in individuals exposed to the COVID-19 vaccines compared to other COVID-19 vaccine exposed individuals or compared to a control window within the same individual. Secondary objectives The secondary objectives for the rapid assessments studies are: • To assess the potential association between the occurrence of specific AESIs and vaccination with COVID-19 vaccines in the following subgroups o immunocompromised persons o persons with the

presence of co-morbidities elevating the risk of serious COVID-19 o persons with a history of diagnosed COVID-19 disease o pregnant women o age groups o patients with a prior history (ever) of that event more than a year before. Study design: A retrospective, multi-database, self-controlled risk interval or cohort study

Study status

Finalised

Research institutions and networks

Institutions

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**

Electronic Health Records (EHR) Research Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010

Last updated: 30/10/2024

Institution | Educational Institution | ENCePP partner

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

First published: 01/03/2010

Last updated: 23/05/2024

Institution | Educational Institution | ENCePP partner

Department of Epidemiology of the Regional Health Service - Lazio

Italy

First published: 23/03/2010

Last updated: 22/06/2018

Institution | EU Institution/Body/Agency | 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

Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina

Italy

First published: 29/11/2021

Last updated: 20/08/2024

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

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 24/07/2024

Institution | Laboratory/Research/Testing facility | ENCePP partner

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom
- [ ] United Kingdom (Northern Ireland)
- [ ] United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | 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: 23/02/2024

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

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**

FISABIO Spain, University Oslo Norway

Networks

Vaccine monitoring Collaboration for Europe (VAC4EU)

Belgium
Denmark
Finland
France
Germany
Italy
Netherlands
Norway

Spain

United Kingdom

First published: 22/09/2020

Last updated: 22/09/2020

Network | ENCePP partner

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

Netherlands

First published: 01/02/2024

Last updated: 26/11/2024

Network

Contact details

Study institution contact

Miriam Sturkenboom

Study contact

m.c.j.sturkenboom@umcutrecht.nl

Primary lead investigator

Miriam Sturkenboom

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 06/04/2021

Actual: 06/04/2021

Study start date
Planned: 31/08/2021

Actual: 31/08/2021

Date of final study report
Planned: 08/05/2023

Actual: 08/05/2023

Sources of funding

- EMA

Study protocol

CVM_WP3_Protocol_v2.2_20210825.pdf(1.41 MB)

CVM_WP4_Protocol_v2.1_20210825.pdf(792.38 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 topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

The objective of the COVID-Vaccine Monitor study is to rapidly assess signals of potential safety concerns emerging from active surveillance and identified by PRAC.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Retrospective, multi-database, self-controlled risk interval study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(J07BX03) covid-19 vaccines

covid-19 vaccines

Medical condition to be studied

Guillain-Barre syndrome

Additional medical condition(s)

All COVID-19 AESI

Population studied

Short description of the study population

The study involved three cohorts: readiness, rapid assessment, and methodological assessment. Readiness cohort included subjects in the source population who were in follow-up for at least 365 days or were born during the study period. Rapid assessment cohort included subjects with the outcome of interest and a COVID-19 vaccination, while methodological assessment cohort included vaccinated subjects and different matched comparisons.

Inclusion Criteria:

Readiness study:

For the readiness study, the person will be included if there is at least one day of follow-up and the person has at least 12 months of data in the data source at the start of follow-up.

SCRI Design:

For analyses of outcomes assessed with the SCRI design, the following criteria must be met. Note that the study population for each outcome-specific analysis will thus be different.

• Received a dose of COVID-19 vaccine during the study period.

• Have experienced a specific event of interest during the predefined observation period.
• Have at least 12 months of data/registration in the data sources at study entry.
Cohort design:
Individuals must meet all the following inclusion criteria to be eligible for inclusion in the cohort study:
• At time zero, being in the underlying population of the data source for at least 12 months; or, being born in the previous 12 months in the underlying population.
• Study participants must be eligible (eg, lack of contra-indications) to receive the COVID-19 vaccines at time zero.
Exclusion Criteria:
For the readiness study, there will be no exclusion criteria.
Individuals will be excluded from the rapid assessment studies if:
• They have a recorded diagnosis for the specific event in the one year prior to cohort /SCRI entry. Persons with such acute diagnoses more than a year ago will be maintained to allow for subgroup analyses. Upon investigation of one event, we do not exclude any history or prevalence of other groups of events (AESIs).
• They have a contra-indicati

Age groups

Preterm newborn infants (0 – 27 days)
Term newborn infants (0 – 27 days)
Infants and toddlers (28 days – 23 months)
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)

Estimated number of subjects

59000000

Study design details

Data analysis plan

Risk estimation: IRR

Documents

Study results

D4.2_CVM_ExecutiveSummary_WP3-4_20230714.pdf(512.3 KB)

D4.2_CVM_FinalReport_WP3-4_14082023_ExSumm.pdf(589.48 KB)

Study, other information

FollowUp_version_CVM_WP3_Protocol_v2.1.pdf(1.3 MB)

Study publications

Bots SH, Riera-Arnau J, Belitser SV, Messina D, Aragón M, Alsina E, Douglas IJ,...

Durán, Carlos E., Messina, Davide, Gini, Rosa, Riefolo, Fabio, Aragón, María, B...

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink

The Information System for Research in Primary Care (SIDIAP)

Caserta claims database

ARS Toscana

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

PHARMO Data Network

Data source(s), other

ARS Toscana (Agenzia Regionale di Sanità della Toscana), Pedianet (Societa Servizi Informatici), Caserta local health database (INSPIRE srl), PHARMO Database Network (PHARMO Institute for Drug Outcomes Research), CPRD (Clinical Practice Research Datalink) & HES data (UK), SIDIAP (Sistema d'Informació per el Desenvolupament de la Investigació en Atenció Primària), BIFAP (Base de Datos para la Investigación Farmacoepidemiológica en Atención Primaria)

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

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