Effectiveness of heterologous and booster Covid-19 vaccination in 5 European countries, using a cohort approach in children and adults with a full primary Covid-19 vaccination regimen (Covid Vaccines Effectiveness (CoVE))

First published: 17/06/2022

Last updated: 01/07/2024

Study   Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/50294

EU PAS number

EUPAS47725

Study ID

50294

DARWIN EU® study

No

Study countries

France
Italy
Netherlands
Spain
United Kingdom

Study description

Real-world effectiveness data demonstrated that Covid-19 vaccines' protection against severe SARS-CoV-2 infection is high in the short term but wanes over time, also depending on the virus variants. This study will deepen the real-world data effectiveness evidence of heterologous, homologous, and booster vaccination different regimes on a large population scale. The goal of this study is to assess the effectiveness and waning of immunity of primary Covid-19 vaccinations and the booster in preventing different covid-19 outcomes. The Primary objective is to estimate the effectiveness and waning of effectiveness in adults and adolescents (heterologous vs homologous primary vaccinations), children (vaccinations vs non-vaccination), homologous or heterologous booster vs no booster. Secondary objective: To estimate the effectiveness of booster against all-cause mortality in adults 60+. Retrospective multi-database cohort study. Cohort entry (time0) is the date of the 2nd dose for the primary vaccination regimens, or the booster. The same date for pairs who are matched on time0, birth year, sex and region. Outcomes: severe Covid-19, Covid-19-related death, all Covid-19 infections, and all-cause mortality. The study will include 8 data sources across from Spain, Italy, Netherlands, France, and United Kingdom. The population are estimated in around 67 millions patients with complete primary vaccination. Baseline characteristics, Incident rates differences and IPW Kaplan-Meier curves for covid outcomes by matched cohorts will be estimated. Vaccine effectiveness will be estimated as 1 minus the Hazard Ratio (estimated by Cox regression) for age groups, overall matched cohorts, and brands. Meta-analyses will be performed for small subpopulations. Different access to Covid-19 testing (restricting to patients with negative tests) and healthy vaccinee effect will be investigated in sensitivity analyses.

Study status
Finalised

Research institution and networks

Institutions

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)
Spain
First published: 01/02/2024
Last updated 01/07/2024

Institution

EU Institution/Body/Agency

Not-for-profit

Regulatory Authority

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

Servicio de Epidemiología, Prevención y Promoción de la Salud, Instituto de Salud Pública de Navarra (ISPN)

Spain
First published: 03/05/2012
Last updated 25/06/2014

Institution

Other

ENCePP partner

EpiChron Research Group on Chronic Diseases, Aragon Health Sciences Institute (IACS)

Spain
First published: 17/02/2017
Last updated 02/04/2024

Institution

Educational Institution

ENCePP partner

Pharmacoepidemiology and Pharmacovigilance department, Spanish Agency of medicines and medical devices (AEMPS)

Spain
First published: 31/07/2014

Last updated 01/07/2024

Institution

EU Institution/Body/Agency

Not-for-profit

Regulatory Authority

ENCePP partner

Innovative Solutions for Medical Prediction And Big Data Integration In Real World Setting Srl (INSPIRE Srl), University Of Messina

Italy
First published: 15/11/2021
Last updated 15/11/2021

Institution

Educational Institution

ENCePP partner

Drug Safety Research Unit (DSRU)

United Kingdom
First published: 10/11/2021
Last updated 16/02/2024

Institution

Not-for-profit

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

RTI Health Solutions (RTI-HS)

France
Spain
Sweden
United Kingdom
United Kingdom (Northern Ireland)
United States
First published: 21/04/2010
Last updated 19/02/2024

Institution Not-for-profit ENCePP partner

Teamit Institute

Spain
First published: 12/03/2024
Last updated 12/03/2024

Institution Other ENCePP partner

l'Assistance Publique-Hôpitaux de Paris (APHP) France, Teamit Institute, S.L. Spain, PHARMO Institute for Drug Outcomes Research. Netherland, Società Servizi Telematici -Pedianet. Italy, Institute of Public Health, Riga Stradins University Latvia, Democritus University of Thrace Greece, National Public Health Agency (RIVM) Netherlands

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 22/07/2024

Network

Contact details

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Primary lead investigator

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Study timelines

Date when funding contract was signed
Planned:
20/04/2022
Actual:
20/04/2022

Study start date
Planned:
20/06/2022
Actual:
20/06/2022

Date of final study report
Planned:
20/01/2023
Actual:
23/04/2023

Sources of funding

- EMA

Study protocol

D2_StudyProtocol_v0.4_ROC12_FINAL_20220615.pdf(1.12 MB)

Regulatory

Was the study required by a regulatory body?
No

Is the study required by a Risk Management Plan (RMP)?
Not applicable

Other study registration identification numbers and links

The project has received support from the European Medicines Agency under the Framework service contract nr EMA/2020/46/TDA/L5.06

Methodological aspects

Study type

Study type list

Study topic:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Effectiveness study (incl. comparative)

Data collection methods:
Secondary data collection

Main study objective:
The goal of this study is to assess the effectiveness and waning of immunity of primary Covid-19 vaccinations and the booster in preventing different covid-19 outcomes.

Study Design

Non-interventional study design
Cohort
Other

Non-interventional study design, other
Retrospective multi-database study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(J07BX03) covid-19 vaccines

Medical condition to be studied
SARS-CoV-2 test positive

Additional medical condition(s)
Severe Covid-19 (i.e. admitted to hospital or intensive care units) Covid-19-related death, all Covid-19 infections, all-cause mortality (secondary objective)

Population studied

Short description of the study population
The study population comprised of all children, adolescents, and adults, had at least 2 years of available healthcare data registered in the 6 electronic health care databases for the study period of December 2020 to February 2022.
The study also included vaccinated individuals with at least two recorded vaccinations since the start of the study period.

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)

Special population of interest
Other

Special population of interest, other
COVID-19 patients

Estimated number of subjects
67271319

Study design details

Outcomes
covid-19 (positive test and/or diagnosis) severe covid-19 covid-19 related death, all-cause mortality

Data analysis plan
Distributions of baseline and Covid-19 vaccination characteristics at time0 will be assessed in all-Covid-19 vaccinated population and matched populations. Incident rates differences (95% confidence intervals) of each Covid-19 outcome for both primary vaccination matched and booster/non-booster matched cohorts estimated by overall, age groups, brands, and time since (booster-)time0 will be estimated. IPW-weight Kaplan-Meier curves will be generated to depict the cumulative incidence of the outcomes by matched cohorts over time after (booster-)time0. Cox proportional hazards regression (95% confidence intervals) to derive the average hazard ratio (HR) of Covid-19 related outcomes will be produced. The adjusted vaccine effectiveness for all the outcomes and all-cause death will be estimated as 1 minus the adjusted HR (and 1-95% confidence intervals) for age groups, overall matched cohorts, and brands.Random-effects meta-analyses will be performed in subpopulations reduced in number.

Documents

Study, other information
ROC12_CoVE_Abstract.pdf(816.91 KB)

Data management

Data sources

Data source(s)
Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público
(Pharmacoepidemiological Research Database for Public Health Systems)
Pedianet network
ARS Toscana
PHARMO Data Network
The Information System for Research in Primary Care (SIDIAP)
Caserta claims database
Clinical Practice Research Datalink

Data source(s), other
SNDS (Système National des Données de Santé) France

Data sources (types)
Administrative data (e.g. claims)
Disease registry
Drug dispensing/prescription data
Drug registry
Electronic healthcare records (EHR)
Other

Data sources (types), other
Secondary care electronic patients registry, Hospital registry

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