Real-world effectiveness of different COVID-19 vaccines in Spain: a cohort study based on public electronic health records (BIFAP) (effectiveness of COVID-19 vaccines in Spain)

First published: 27/08/2021

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS41134

Study ID

42710

DARWIN EU® study

No

Study countries

Spain

Study description

Background: The real-world effectiveness of COVID 19 vaccines must be evaluated in populations in Spain. Objectives: To evaluate the effectiveness of all COVID 19 vaccines administered in reducing the medically attended diagnosis of COVID 19 in any setting (confirmed through test and regardless the prognosis and clinical phenotype) Secondary objectives will split the effectiveness -by asymptomatic, symptomatic, Hospitalisations/Intensive care unit (ICU) admissions for COVID 19 and All-cause mortality -by clinical subgroups (old people, patients with cardiovascular disease, diabetes, chronic pulmonary disease, chronic renal impairment, treated cancer, patients with a history of transplantation, Down Syndrome, smoking, males and obesity) -along the time since complete vaccination (3 months, 6 months and ever after). Study design: Observational cohort study to compare the occurrence of covid-19 infection among unvaccinated and vaccinated individuals. Population: Individual with at least 1 year of record with their primary care physician from December 2020 till the last available date at study start. Data sources: Base de datos para la Investigación farmacoepidemiológica en Atención Primaria (BIFAP) and linked registries of 1) COVID positive test results, 2) hospital COVID diagnosis or 3) discharged COVID diagnosis. BIFAP database includes up-to-standard information for more than 9 million patients in Spain. Analysis: Characteristics of the vaccinated and unvaccinated groups at baseline will be described. Incidence rates of COVID 19 outcomes will compared between the two groups, and vaccine effectiveness measures will be estimated by 1 minus the hazard ratios (HR, 95%CI). Period effect estimates (e.g. at 3, 6, or >6 months after vaccination) will be estimated as well as stratified analysis by clinical subgroups and calendar periods. Sensitivity analyses will evaluate the robustness of the approach accross variations of the methodology.

Study status

Finalised

Research institutions 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: 04/09/2024

Institution | **EU Institution/Body/Agency** | **Not-for-profit** | **Regulatory Authority** | **ENCePP partner**

Contact details

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Primary lead investigator

Elisa Martín-Merino

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 04/01/2021

Actual: 04/01/2021

Study start date
Planned: 21/06/2021

Actual: 16/07/2021

Data analysis start date
Planned: 13/09/2021

Date of final study report
Planned: 04/04/2022

Actual: 15/02/2023

Sources of funding

- Other

More details on funding

AEMPS's own resources. No funding has been received.

Study protocol

BIFAP_COVID VacEffectiveness_20042021 approved SC.pdf (1.42 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

BIFAP Scientific Committee protocol number 02_2021 (Approved),Centre website:http://bifap.aemps.es/

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Main study objective:

This study addresses the research question of whether vaccinations with new licenced COVID 19 vaccines, (Comirnaty, Moderna, AstraZeneca’s and Janssen and subsequently approved vaccines in the EU during the data collection), are effective in reducing the burden of COVID 19 in Spain in comparison with no vaccination person-time.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

COMIRNATY

VAXZEVRIA

Medicinal product name, other

COVID-19 Vaccine Moderna dispersion for injection, COVID-19 Vaccine Janssen suspension for injection

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Anatomical Therapeutic Chemical (ATC) code

(J07BX03) covid-19 vaccines

covid-19 vaccines

Medical condition to be studied

SARS-CoV-2 test positive

Additional medical condition(s)

Symptomatic or Asymptomatic Diagnosis of COVID-19,Hospitalisations/Intensive care unit (ICU) admissions for COVID-19 All-Cause Mortality

Population studied

Age groups

- 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)

Special population of interest

Hepatic impaired

Immunocompromised

Pregnant women

Renal impaired

Estimated number of subjects

8

Study design details

Outcomes

Primary objective is to evaluate the effectiveness of each COVID-19 vaccine in reducing the covid-19 infections (confirmed through test and regardless the prognosis and clinical phenotype (i.e. whether symptomatic or asymptomatic, mild or severe). Effectiveness of each covid-19 vaccine in reducing asymptomatic or symptomatic COVID-19, Hospitalisations/Intensive care unit (ICU) admissions for COVID 19 and All-cause mortality. Effectiveness of each covid-19 vaccine in reducing the covid-19 infections among different clinical subgroups of patients, and along the time since complete vaccination.

Data analysis plan

Cox proportional hazards regression, yielding a hazard ratio (HR, 95%CI) will be estimated for 0-14 days after D1, 15 after D1 until D2, 0-14 days after D2 and 15-90d,91-180d,and ≥181d after D2 in comparison with similar followed periods from time zero in the unvaccinated group. This method will calculate a single vaccine effectiveness measure for each period of observation (assumed constant over those defined periods) in vaccinated versus unvaccinated groups.Flexible parametrical models will be run for comparison.Crude vaccine effectiveness (1-HR) will be calculated for all outcomes.Backward stepwise selection will be used to identify variables associated with outcome (p-exit≥0.1, p-entry<0.05), that could be confounders and thus adjust the final models. Confounders will be measured at baseline and updated before each vaccine dose or every 28 days. Adjusted time-specific risk differences (at 3, 6, 9, 12 months) will be calculated.Switching among vaccines will be analysed separately.

Documents

Study results

BIFAP_COVID VacEff_Report_ENCEPP.pdf (2.51 MB)

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.

Conflicts of interest of investigators

ENCePP DoIForm_v1.6_EMM.pdf (25.23 KB)

Signed checklist for study protocols

Study checklist.pdf (118.88 KB)

Data sources

Data source(s)

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

Data sources (types)

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