TARGET-EU: Effectiveness of BNT162b2 mRNA COVID-19 vaccine in healthy individuals or with stable pre-existing medical conditions against SARS-CoV-2 infection

First published: 12/05/2026

Last updated: 12/05/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000995

Study ID

1000000995

DARWIN EU® study

No

Study countries

Netherlands

Spain

United Kingdom

Study description

This case study is part of the broader TARGET EU project (EUPAS1000000539), which aims to advance the regulatory use of real-world data through the application of target trial emulation and estimand methodologies.

Objectives: To estimate the effectiveness of BNT162b2, an mRNA-based COVID-19 vaccine by Pfizer/BioNTech, in preventing SARS-CoV-2 infection among individuals ≥16 years, including those with stable pre-existing conditions, accounting for deviations from standard dosing schedules.
Methods: A matched cohort study using routinely collected healthcare data from the CPRD and VID databases (December 2020 – April 2022). Eligible participants were ≥16 years with ≥6 months of continuous registration. Individuals with prior non-BNT162b2 vaccines, prophylactic COVID-19 treatments, or immunocompromised status were excluded. Vaccinated individuals were matched 1:1 with unvaccinated comparators on age, sex, location, calendar time, and key risk factors. Follow-up began at first dose (or matched date) and continued up to 90 days or until SARS-CoV-2 infection, death, deregistration, or end of data availability. The primary outcome was laboratory-confirmed SARS-CoV-2 infection.
The study follows the target trial emulation and ICH E9(R1) estimand frameworks. Intercurrent events (IEs) include: missing or ineligibility for a second dose; early BNT162b2 booster receipt; non-BNT162b2 booster; non-COVID-19 vaccine post-completion; prophylactic COVID-19 treatment; and death. In the primary estimand, a treatment policy strategy applies to missing a second dose, early boosting, and non-COVID-19 vaccination; a hypothetical strategy applies to non-BNT162b2 boosters and preventive COVID-19 treatments; death is handled via a composite strategy. A supplementary estimand uses a principal stratum strategy for missing a second dose and a

while-alive strategy for death.

Study status

Ongoing

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: 27/05/2026

Institution | Educational Institution | ENCePP partner

Clinical Pharmacology, Vall d'Hebron Institut de Recerca (VHIR)

Spain

First published: 18/05/2021

Last updated: 20/05/2021

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

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 | Outdated | ENCePP partner

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

Netherlands

First published: 01/02/2024

Last updated: 24/09/2025

Network

Contact details

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Study timelines

Date when funding contract was signed
Planned: 19/09/2024

Study start date
Planned: 09/03/2026

Actual: 09/03/2026

Date of final study report
Planned: 10/06/2026

Sources of funding

- EMA

Study protocol

Emulation_Protocol_CS1_REV5_clean.pdf (1.27 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:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Matched cohort design to assess the real-world effectiveness of the BNT162b2 mRNA COVID-19 vaccine against SARS-CoV-2 infection involving two databases, that is CPRD and VID. We will estimate the incidence of SARS-CoV-2 infection after receipt of the Pfizer-BioNTech COVID-19 vaccine compared to not

Main study objective:

The overall aim is to assess whether BNT162b2 mRNA COVID-19 vaccine reduce the risk of SARS-CoV-2 infection compared to no COVID-19 vaccination in healthy individuals or with preexisting stable medical condition.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

COMIRNATY

Study drug International non-proprietary name (INN) or common name

TOZINAMERAN

Anatomical Therapeutic Chemical (ATC) code

(J07BN01) covid-19, RNA-based vaccine

covid-19, RNA-based vaccine

Medical condition to be studied

SARS-CoV-2 test positive

Population studied

Short description of the study population

The study population comprises individuals aged 16 years or older, drawn from the CPRD and VID linked population databases, who were continuously enrolled for at least six months prior to the index date. The cohort is designed to reflect a broadly healthy, immunocompetent population, including those with stable, well-managed chronic conditions, while excluding individuals with recent acute illness, defined as any hospitalisation within six weeks of the index date.
To ensure the cohort is appropriate for estimating the effectiveness of Comirnaty® (BNT162b2; tozinameran; ATC J07BN01) specifically, individuals with prior receipt of any other COVID-19 vaccine are excluded, preserving a vaccine-naïve unvaccinated comparator group. Additionally, individuals who received COVID-19 pre-exposure prophylaxis — including pemivibart or tixagevimab/cilgavimab (Evusheld) — are excluded, as these therapies may independently reduce infection risk and confound vaccine effectiveness

estimates.
Individuals with immunocompromised status, identified through diagnostic codes or use of immunosuppressive therapies (ATC codes L04A, L01X, L01B, H02AB, P01BA) in the six months prior to the index date, are also excluded. This ensures that the study population reflects typical immune function, supporting the internal validity and generalisability of the vaccine effectiveness estimates to the broader immunocompetent population.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Study design details

Setting

The exposure assessment window is defined from December 1, 2020, to January 31, 2022. Additionally, to ensure sufficient baseline and follow-up data, individuals must have at least 6 months of available data prior to time zero (to capture covariates and prior health status) thus covering the start of the COVID-19 vaccine rollout through to the end of mass testing for both symptomatic and asymptomatic individuals in the UK. Consequently, the study period will be from 01 June 2020 to 30 April 2022 (i.e. source data range), with the latter date

allowing for individuals enrolled on 31 January 2022 to enable 90 days of follow-up.

Outcomes

Laboratory-confirmed SARS-CoV-2 infection or death from any cause.

Data analysis plan

The BNT162b2 effectiveness in preventing the SARS-Cov-2 infection will be estimated as 1 - RR. Supplementary analyses including diagnostic and descriptive assessments to support the main analysis will be presented to contextualise data and results from the primary and sensitivity analyses. These will include number of infections per treatment group, crude incidence rates, covariate distributions of matched cohorts, number of individuals censored and censoring patterns (intercurrent events, loss to follow-up) as well as model diagnostics. An additional supplementary analysis will be produced whereby individuals in the control arm can contribute data multiple times to the control arm and also to the BNT162b2 arm after reception of the vaccine.
The results will be presented separately for each data source. In addition, we will explore the feasibility of combining the estimated Incidence Rate Ratios (IRR) from CPRD Aurum and VID using a random-effects meta-analysis of logarithmic transformation of the rate ratios. The combined IRRs and 95% CI will be calculated, and heterogeneity will be assessed using I2.

Summary results

Not yet available.

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)

Clinical Practice Research Datalink

The Valencia Health System Integrated Database

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

ConcepTION CDM

CDM website

https://www.imi-conception.eu/

CDM release frequency

6 months

CDM version

2.2

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation details

The feasibility assessment for this case study, detailed in the appendix of the study protocol, was conducted as part of the broader TARGET-EU feasibility assessment (EUPAS1000000791).

Data source suitability was evaluated using a structured framework based on the EMA data quality framework, assessing system characteristics, data quality, and fitness for the research question.

The Clinical Practice Research Datalink (CPRD) and The Valencia health system integrated database (VID) were selected as data sources for this study because they offer large, high-quality, population-based electronic health records with national coverage in the UK and Spain, respectively.

Both sources provide the required data elements to operationalize the study design, including demographics, diagnoses, prescriptions, laboratory test results, hospitalizations, and mortality data. In addition, both databases have previously been used in studies of vaccines effectiveness and safety.

Data characterisation details

CS1_Feasibility_Assessment.pdf

English (326.09 KB - PDF)

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