DARWIN EU® Effectiveness of Human Papillomavirus Vaccines (HPV) to prevent cervical cancer

First published: 22/03/2024

Last updated: 26/02/2025

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000080

EU PAS number

EUPAS1000000080

Study ID

1000000080

DARWIN EU® study

Yes

Study countries

☐ Germany

☐ Spain

☐ United Kingdom

Study description

Research question: What is the effectiveness of HPV vaccination in prevention of severe disease outcomes in women, including invasive cervical cancer and CIN2+ for the different licensed HPV vaccines in Europe.

More specifically, the study objectives are:
Main objectives:
- To assess the effectiveness of HPV vaccination in prevention of invasive cervical cancer stratified by licenced vaccine brand
- To assess the effectiveness of HPV vaccination in prevention of CIN2+, stratified by licenced vaccine brand
- To assess the effectiveness of HPV vaccination in prevention of, conization, stratified by licenced vaccine brand

Secondary objectives:
- To assess the effectiveness of HPV vaccination overall for the three outcomes (i.e. invasive cervical cancer, CIN2+ and conization)
- To assess the effectiveness of HPV vaccination in prevention of invasive cervical cancer, CIN2+ and conization in subgroups defined by number of doses, within each brand.

Results in both main and secondary analyses will be further stratified by age group.

Study status

Finalised

Research institutions and networks

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- [ ] Belgium
- [ ] Croatia
- [ ] Denmark
- [ ] Estonia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Hungary
- [ ] Netherlands
- [ ] Norway
- [ ] Portugal
- [ ] Spain
- [ ] United Kingdom

First published: 01/02/2024

Last updated: 11/06/2024

Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 10/02/2023

Actual: 10/02/2023

Study start date

Planned: 10/02/2023

Actual: 10/02/2023

Date of final study report

Planned: 15/05/2024

Actual: 19/11/2024

Sources of funding

- EMA

Study protocol

DARWIN EU_D2.2.3 Protocol P2-C3-004_HPV_Final_v3.6 Public.pdf(916.23 KB)

DARWIN EU_D2.2.3 Protocol P2-C3-004_HPV_Final_v3.6 Public (1).pdf(916.23 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 type list

Study topic:

Human medicinal product

Study type:

Not applicable

Study design:

New user matched cohort study

Study drug and medical condition

Name of medicine

CERVARIX

GARDASIL

GARDASIL 9

SILGARD

Name of medicine, other

- human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed)
- human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)
- human papillomavirus 9-valent vaccine (recombinant, adsorbed)

Anatomical Therapeutic Chemical (ATC) code

(J07BM01) papillomavirus (human types 6, 11, 16, 18)

papillomavirus (human types 6, 11, 16, 18)

(J07BM02) papillomavirus (human types 16, 18)

papillomavirus (human types 16, 18)

(J07BM03) papillomavirus (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)

papillomavirus (human types 6, 11, 16, 18, 31, 33, 45, 52, 58)

Additional medical condition(s)

Invasive cervical cancer and CIN2+

Population studied

Short description of the study population

All females aged 9 years or older on any date after the launch of the vaccination programme in any of the contributing datasets and with at least

365 days of prior data availability at the beginning of vaccination programme launch date in their country of residence will be eligible. The analysis will be further restricted to matched cohorts of vaccinated and unvaccinated participants with similar baseline characteristics.

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

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

Outcomes

The main outcome of interest is invasive cervical cancer. Two secondary outcomes are also considered: CIN2+ and Conization. These outcomes will be phenotyped and diagnostics will be carried out.

Data analysis plan

All analyses will be conducted separately for each database, and carried out in a federated manner, with effectiveness estimates meta-analysed and the I2 heterogeneity coefficient reported.

We will conduct a propensity score (PS) matched cohort design, where target

and comparator cohort participants will be matched 1:5.
Matching will be done based on PS, year of birth, year of first dose (for analyses not involving dose number) and geographic region using nearest neighbor matching, with caliper width 0.2 standard deviations as is standard for propensity score matching.
Large-scale PS will be estimated using lasso regression to estimate the probability of being in the target cohorts, potentially including any of the covariates mentioned above.

The following matched cohorts will be compared:
Main comparisons:
Vaccinated vs unvaccinated per brand:
- Vaccinated with Gardasil/Silgard (target) (1 or more dose) vs unvaccinated (comparator)
- Vaccinated with Cervarix (target) (1 or more dose) vs unvaccinated (comparator)
- Vaccinated with Gardasil-9 (target) (1 or more dose) vs unvaccinated (comparator)
Secondary comparisons:
- Vaccinated (target) (1 or more dose) (any brand) vs unvaccinated (comparator) overall.
Dose comparisons:
- Vaccinated with 2 or more doses (target) vs 1 dose (comparator) of the same brand.
- Vaccinated with 3 or more doses (target) vs 2 doses (comparator) of the same brand.

Documents

Study report

DARWIN EU_Report_P2-C3-004_HPVvaccine_effectiveness_V3.pdf(2.16 MB)

Data management

Data sources

Data source(s)

Clinical Practice Research Datalink (CPRD) GOLD

IQVIA Disease Analyzer Germany

The Information System for Research in Primary Care (SIDIAP)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No