

# Nested case-control study evaluating effectiveness of immunization of girls and women of childbearing potential with GARDASIL(TM)/GARDASIL(TM) 9 against juvenile-onset recurrent respiratory papillomatosis (JoRRP) in Sweden, Denmark, and Norway (V503-095)

**First published:** 23/08/2024

**Last updated:** 26/11/2025

Study

Ongoing

## Administrative details

### EU PAS number

EUPAS1000000286

### Study ID

1000000286

### DARWIN EU® study

No

## **Study countries**

- Denmark
- Norway
- Sweden

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## **Study description**

Recurrent respiratory papillomatosis (RRP) is a medical condition where HPV types 6 and 11 cause wart-like growths in the larynx.

The condition is rarely fatal but associated with high morbidity. Current treatment only offers temporary symptomatic relief.

There is an expectation that HPV vaccination of mothers, targeting types 6 and 11, will reduce incidence of RRP in their children.

The primary objective of this study is to assess if the odds of JoRRP are lower among children whose biologic mothers were fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery versus unvaccinated mothers.

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## **Study status**

Ongoing

# Research institutions and networks

## Institutions

### [Merck Sharp & Dohme LLC](#)

- United States

**First published:** 01/02/2024

**Last updated:** 08/07/2025

Institution

Pharmaceutical company

## Karolinska Institutet

Sweden

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

Educational Institution

## Cancer Registry of Norway

## Danish Cancer Society

## Contact details

### **Study institution contact**

Clinical Trials Disclosure Merck Sharp & Dohme LLC

[ClinicalTrialsDisclosure@merck.com](mailto:ClinicalTrialsDisclosure@merck.com)

[Study contact](#)

[ClinicalTrialsDisclosure@merck.com](mailto:ClinicalTrialsDisclosure@merck.com)

### **Primary lead investigator**

Clinical Trials Disclosure Merck Sharp & Dohme LLC

[Primary lead investigator](#)

# Study timelines

## **Date when funding contract was signed**

Actual: 23/11/2021

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## **Study start date**

Actual: 03/03/2023

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## **Data analysis start date**

Planned: 21/12/2025

Actual: 31/10/2025

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## **Date of final study report**

Planned: 30/10/2026

# Sources of funding

- Pharmaceutical company and other private sector

# More details on funding

Merck Sharp & Dohme LLC

# Study protocol

[V503-095-00-v3-Protocol\\_final-redaction.pdf](#) (675.47 KB)

# Regulatory

## **Was the study required by a regulatory body?**

No

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### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

#### Study type list

##### **Study topic:**

Disease /health condition

Human medicinal product

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##### **Study type:**

Non-interventional study

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##### **Scope of the study:**

Effectiveness study (incl. comparative)

##### **Data collection methods:**

Secondary use of data

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##### **Study design:**

Population-based nested case-control study

##### **Main study objective:**

To assess if the odds of juvenile-onset recurrent respiratory papillomatosis (JoRRP) are lower among children whose biologic mothers were fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery versus unvaccinated mothers.

## Study Design

### **Non-interventional study design**

Case-control

Other

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### **Non-interventional study design, other**

Population-based nested case-control

## Study drug and medical condition

### **Medicinal product name**

GARDASIL

GARDASIL 9

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### **Medicinal product name, other**

Gardasil 4

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### **Anatomical Therapeutic Chemical (ATC) code**

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

papillomavirus (human types 6, 11, 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)

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## **Medical condition to be studied**

Respiratory papilloma

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## **Additional medical condition(s)**

juvenile-onset recurrent respiratory papillomatosis

## **Population studied**

### **Short description of the study population**

Inclusion Criteria:

- Birth cohorts 2008 to 2020
- The study subject (child) must be born and resident in Sweden, Denmark or Norway as defined through the Total Population Registry for their entire life.
- The study subject must be between 0 to 9 years of age
- The child's mother had the opportunity to be fully vaccinated with GARDASIL/GARDASIL 9 at least one year prior to delivery.

Exclusion Criteria:

- Children whose mother immigrated to Sweden, Denmark, or Norway both after 2006 and after age 9 years
- Adopted children, as the vaccination status of the actual, biological mother will be missing.
- Children whose mother received the bivalent vaccine Cervarix, since it provides no effectiveness against the causative HPV types (6 and 11) in RRP.
- Any child (case or control subject) who previously received any HPV vaccine

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## **Age groups**

- **Paediatric Population (< 18 years)**

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## **Estimated number of subjects**

## Study design details

### Setting

Nordic population, patient, and vaccine registries.

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### Comparators

Random selection of up to 100 controls per case from the underlying population at risk, using incidence density sampling procedures.

Matching criteria will be age of mother (+/- 1 year), sex of child, calendar year of case diagnosis, and region where case was diagnosed.

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### Outcomes

A subject will be defined as having JoRRP if he/she has > or =1 hospitalization or outpatient record with diagnosis registered as D14.1, with appropriate topography/morphology codes (where possible to obtain from pathology/cancer registry), between 0-9 years of age

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### Data analysis plan

Conditional logistic regression will be used for estimation of odds ratios (ORs) and corresponding 95% confidence intervals in the pooled analysis using 1-step approach, with adjustment for clustering and adjustment for relevant covariates; all measured with similar high accuracy in each country.

## 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)**

Landspatientregisteret (National Patient Register)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

The Cancer Registry of Norway

Norwegian Health Registers

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### **Data source(s), other**

Denmark Central Population Registry

Denmark Pregnancy/Birth Registry

Denmark Prescription Registry

Denmark- The National Health Insurance Service Registry

Denmark Family database

Statistics Denmark

Denmark Pathology Register

Sweden Total Population Registry

Sweden National Patient Registry

Sweden Medical Birth Registry

SVEVAC/National Vaccination Registry

Sweden Multi-generation registry

LISA (Swedish Longitudinal integrated database for health insurance and labour market studies)

The National Population Registry of Norway ("Folkeregisteret")

The National Patient Registry in Norway (NPR)  
The Medical Birth Registry of Norway (MBRN)  
Norwegian Prescribed Drug Registry  
The Norwegian Immunization Registry (SYSVAK)  
Statistics Norway (SSB)

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### **Data sources (types)**

[Disease registry](#)  
[Non-interventional study](#)  
[Population registry](#)  
[Pregnancy registry](#)

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Yes

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### **Check completeness**

Yes

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### **Check stability**

Unknown

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### **Check logical consistency**

Yes

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## Data characterisation

**Data characterisation conducted**

Yes