DARWIN EU® - Incidence, period prevalence, and characterisation of individuals with paediatric pulmonary arterial hypertension

First published: 21/08/2025

Last updated: 12/03/2026

Study Finalised

Administrative details

EU PAS number

EUPAS1000000716

Study ID

1000000716

DARWIN EU® study

Yes

Study countries

- [ ] Denmark
- [ ] Finland
- [ ] France

- [ ] Germany
- [ ] Norway
- [ ] Sweden

Study description

The intention of the study is to investigate the occurrence of pulmonary arterial hypertension (PAH) in paediatric patients by age group and to understand the size of this population in various EU countries. Additionally, the study aims to characterise the disease and treatments use in the paediatric PAH population in a real-world setting. This study can therefore be used in any future paediatric PAH related regulatory procedures.

Study status

Finalised

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

- [ ] Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution | **Educational Institution** | **ENCePP partner**

Networks

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

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

First published: 01/02/2024

Last updated: 30/04/2025

Network

Contact details

Study institution contact

Natasha Yefimenko study@darwin-eu.org

Study contact

study@darwin-eu.org

Primary lead investigator

Nicholas Hunt

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 17/03/2025

Actual: 17/03/2025

Study start date

Planned: 11/08/2025

Actual: 11/08/2025

Date of final study report

Planned: 30/10/2026

Actual: 04/12/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P3-C3-011_PAH_V7.0.pdf (1.16 MB)

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:

Disease /health condition

Study topic, other:

paediatric pulmonary arterial hypertension

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Data collection methods:

Secondary use of data

Study design:

For the first objective, we will perform a disease epidemiology study

For the second objective, we will perform a characterisation study

Main study objective:

1. Estimate the yearly incidence and period prevalence of pulmonary arterial hypertension (PAH) in the paediatric population, stratified by age group (0 to 1 year, 1 to 2-years, 2 to 5-years, 5 to 12-years, and 12 to 17-years)

2. Characterise paediatric patients newly diagnosed with PAH:

a) Describe the number and proportions of individuals by sex and age at index date

b) Within 180-days prior to index date and then within the first five years after index date, within sequential 90-day periods, potential etiology (congenital heart disease, bronchopulmonary dysplasia, congenital diaphragmatic hernia, persistent pulmonary hypertension of the newborn) and comorbidities (right heart failure, ascites, arrythmia, hemoptysis, lung-heart transplant, atrial septostomy or Potts shunt, syncope)

c) Within the first five-years after index date, within sequential 90-day periods, describe the number and proportion of individuals treated with monotherapy of the following treatments, including endothelin receptor antagonists (ERAs, bosentan, ambrisentan, macitentan), phosphodiesterase type 5 inhibitors (PDE5-is, sildenafil, tadalafil), soluble guanylate cyclase stimulators (sGC, riociguat), prostacyclin receptor agonists (treprostinil, epoprostenol, iloprost, selexipag, ralinepag) or combination therapy of these classes, including ERAs + PDE5-I, ERAs + sGC, PDE5-i + prostacyclin receptor agonists, and ERA + PDE5-I + prostacyclin receptor agonists

d) Describe the number and proportion of individuals treated with monotherapy

of the following treatments, including endothelin receptor antagonists (ERAs, bosentan, ambrisentan, macitentan), phosphodiesterase type 5 inhibitors (PDE5-is, sildenafil, tadalafil), soluble guanylate cyclase stimulators (sGC, riociguat), prostacyclin receptor agonists (treprostinil, epoprostenol, iloprost, selexipag, ralinepag) or combination therapy of these classes, including ERAs + PDE5-I, ERAs + sGC, PDE5-i + Prostacyclin receptor agonists, and ERA + PDE5-I + prostacyclin receptor agonists by age group (0 to 1 year, 1 to 2-years, 2 to 5-years, 5 to 12-years, and 12 to 17-years) at time of prescription/dispensing
e) Within 180-days prior to index date and then within the first five-years after index date, within sequential 90-day periods, describe the number and proportion of individuals with at least one record for each of the following measures: 6-minute walk distance (6MWD) test, echocardiography, NT-proBNP, WHO functional class, right heart catheterisation, and cardiovascular MRI (Magnetic resonance imaging
f) Within the first five-years after index date in sequential 90-day periods, describe the number of and proportion of individuals who were admitted to hospital or died.

Study Design

Non-interventional study design

Cohort

Population studied

Short description of the study population

For objective 1 (incidence of individuals with PAH):

Inclusion criteria

• Aged <18 years at index date
• Observation in the data source of 365 days prior to the index date (except for those aged less than one year old and individuals in hospital settings, CDWBordeaux)
Exclusion criteria
• Prior occurrence of pulmonary arterial hypertension

For objective 1 (period prevalence of individuals with PAH):
Inclusion criteria
• Aged <18 years at index date
• Observation in the data source of 365 days prior to the index date (except for those aged less than one year old and individuals in hospital settings, CDWBordeaux)
For objective 2 (characterisation of individuals with PAH)
Inclusion criteria
• Recorded diagnosis of pulmonary arterial hypertension
• Aged <18 years at index date
• Observation in the data source of 365 days prior to the index date (except for those aged less than one year old and individuals in hospital settings, CDWBordeaux)
Exclusion criteria
• Occurrence of pulmonary arterial hypertension prior to index date
• Occurrence of right sided heart failure any time prior to index date (for characterisation of individuals in terms of right sided heart failure incidence)

Age groups

- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)

- Infants and toddlers (28 days – 23 months)
- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)

Study design details

Outcomes

The outcome for objective 1 is PAH diagnosis. For objective 2, covariates will be used to characterise the
included individuals with PAH: Demographic factors include sex, age and age group; conditions include right
heart failure, ascites, arrythmia, haemoptysis, and syncope, congenital heart disease, bronchopulmonary
dysplasia, congenital diaphragmatic hernia, persistent pulmonary hypertension of the newborn; procedures
or measurements include lung-heart transplant, atrial septostomy or Pott shunt, 6 minute walking test,
echocardiography, NT-proBNP test, WHO functional class, right heart catheterisation, cardiovascular MRI;
and drug treatments, including mono- and combination therapies of endothelin receptor antagonists,
phosphodiesterase type 5 inhibitors, soluble guanylate cyclase stimulators, and prostacyclin receptor
agonists.

Data analysis plan

The calculation of PAH incidence rates with 95% confidence intervals per data source will be stratified by
year and age group (0 to 1 year, 1 to 2-years, 2 to 5-years, 5 to 12-years, and

12 to 17-years). Period
prevalence will be reported as the percentage of patients with new or ongoing PAH of the total population
at risk in each data source, stratified by year and age group. We will characterise individuals with PAH in
terms of demographics at index date, as well as the number and proportion of records of comorbidities,
procedures, treatments, hospitalisation in sequential 90-day windows after index date, and at baseline [-
180,0] for procedures, measurements, and acute conditions. Chronic conditions will be measured at index
date and any time prior [-inf,0]. Characterisation by number and proportion of treatment records will also
be stratified by age group at time of prescribing/dispensing.

Documents

Study report

DARWIN EU_Report_P3_C3_011_PAH_V4.pdf (3.76 MB)

Shiny App

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)

Danish Health Data Registries

Clinical Data Warehouse of the Bordeaux University Hospital

Hospital District of Helsinki and Uusimaa patient cohort (FinOMOP)

InGef Research Database

Norwegian Linked Health registry at University of Oslo

Health Impact - Swedish Population Evidence Enabling Data-linkage

---

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

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

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No