DARWIN EU® - Antipsychotic prescribing in children in Europe: a descriptive analysis of trends and patient characteristics

First published: 22/05/2025

Last updated: 07/08/2026

Study Finalised

Administrative details

EU PAS number

EUPAS1000000592

Study ID

1000000592

DARWIN EU® study

Yes

Study countries

- Croatia
- Denmark
- Germany
- Netherlands

Norway

Spain

Study description

Antipsychotic drugs are indicated for the management of schizophrenia and bipolar disorder.

They are also used in adults to manage behavioral and psychological symptoms of dementia (BPSD) with the recommendation to be discontinued after BPSD symptoms resolve.

Antipsychotic drugs can be classified into typical and atypical antipsychotics with different recommendations for their use.

For example, guidelines recommend the preferential use of atypical antipsychotic in adults when required for the management of BPSD.

Safety concerns have previously led to regulatory warnings and risk communications over their use.

Antipsychotic drugs have been associated with several adverse drug reactions, particularly in the elderly. Somnolence, hypotension, extrapyramidal side effects and gait abnormalities are well-recognized side effects that may in turn contribute to the risk of falls and fracture in elderly persons.[1] Similarly, cardiovascular adverse effects, falls and injuries may increase mortality.

Antipsychotics are sometimes used in children and adolescents; however, not all antipsychotics have been approved for use in children and adolescents and if prescribed their use would be considered off-label.

A prior study reported an increased use of antipsychotics between 2008 and 2017 in the paediatric populations of Catalonia (35.7%), Norway (45.1%) and Sweeden (57.6%).

Likewise, in England, the use of antipsychotics in patients between 3 and 18 years doubled between 2000 and 2019.

This study aims to provide an overview of antipsychotic prescribing in children from databases in Europe, and to describe the characteristics of children

initiating antipsychotics.

This will provide a benchmark to understand current clinical practice over their use in children and adolescents and help to understand whether off-label use may occur.

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

Marta Pineda Moncusi

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 17/03/2025

Actual: 17/03/2025

Study start date
Planned: 12/05/2025

Actual: 12/05/2025

Date of final study report
Planned: 30/08/2025

Actual: 29/09/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P4-C2-003_Antipsychotic in Children_V3.pdf (900.14 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:

Non-interventional study

Scope of the study:

Drug utilisation

Data collection methods:

Secondary use of data

Study design:

Retrospective cohort studies will be conducted using routinely collected health data from 7 databases.

Main study objective:

1. To characterise children with a first prescription of an antipsychotic in each database in terms of age, sex, comorbidities and indication of use.
2. To measure trends in the incidence/prevalence of antipsychotic prescribing in

children overall, by typical/atypical grouping and separately for 11 drug substances in each database. Results would be stratified by calendar year, age and sex.
3. To characterise first use of antipsychotic initiation in children (overall, by typical/atypical use, and by the 11 prespecified drug substances) in terms of dose and duration in each database. Results will be stratified by age and sex.

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Medicinal product name, other
All antipsychotics under the ATC code N05A (all, and by grouped by typical/atypical);
and eleven prespecified drug substances: risperidone, aripiprazole, olanzapine, quetiapine, paliperidone, chlorprothixene, clozapine, methotrimeprazine (levomepromazine), pipamperone, sulpiride, and promazine.

Anatomical Therapeutic Chemical (ATC) code
(N05A) ANTIPSYCHOTICS
ANTIPSYCHOTICS

Population studied

Short description of the study population

The study cohort will comprise all paediatric individuals between 1- and 18-years old present in the database during the study period (i.e., 2013-2023). Additional eligibility criteria for patient-level antipsychotic characterisation and drug utilisation, and for the calculation of incidence rates will be applied, where a minimum follow-up of 365 days of data availability will be required to exclude individuals with a prior use of the respective drug of interest:
- When overall, no prior use of any of the common antipsychotics will be required.
In other words, users with prior use of any of the antipsychotics of interest will be excluded from the analysis.
- When stratified by specific antipsychotic drug, no prior use of the specific antipsychotic will be required.
In other words, users with prior use of the same antipsychotic will be excluded from the analysis.

Study design details

Data analysis plan

Statistical analysis

1. Patient-level new user characterisation: characterisation of patient-level features for new users of antipsychotics was calculated for all (all antipsychotic drugs), by typical/atypical, and separately for the 11 pre-specified drug substances for each database. Analyses included the description of age at index date (date of first prescription of the antipsychotic of interest), pre-defined comorbidities of interest recorded within 30 days or any time before index date, and potential indications based on the record of pre-defined conditions of interest recorded within 7 days, 30 days, or any time before index date.
2. Population-level drug utilisation: annual incidence and annual period prevalence estimates were

calculated for antipsychotic treatment for all, by typical/atypical and for the 11 pre-specified drug substances for each database.
3. Patient-level drug utilisation: prescribed initial and cumulative dose of antipsychotics, and median treatment duration were described for all antipsychotic use, for typical/atypical antipsychotics, and for the 11 pre-specified drug substances for each database.
For all analyses, a minimum cell counts of 5 was used when reporting results, with any smaller counts noted
as <5.

Summary results

Trends in antipsychotic use in children increased in Spain, the Netherlands, Germany, and Croatia. These increases were driven by atypical antipsychotic prescribing, with the highest incidence and prevalence use observed in Spain. All antipsychotic use in Denmark was stable, driven by an increase in atypical use and a decrease in typical use. Typical antipsychotic prescribing also decreased in Croatia, the Netherlands, and Norway over the study period; but increased in Germany and increased or remained stable in Spain depending on database. Antipsychotic prescribing was more common in children aged 12–18 years but occurred in all age groups. Quetiapine, risperidone, and aripiprazole tended to be the most frequently prescribed antipsychotics. Between 38.3% of children in BIFAP (Spain) to 78.2% of children in DK-DHR (Denmark) had recorded at least one condition linked to a potential clinical indication for antipsychotic use in children. Most frequently recorded conditions linked to potential clinical indications were depression in Croatia and Germany, anxiety in Spain, autism in the Netherlands, and sleep disorders in Denmark and Norway. Whilst a limited number of the 11-pre-selected substances have been formally centrally licensed in Europe for use in children to treat the most commonly observed conditions in this population, some products might have been authorised nationally. Further work may be required to better characterise the

clinical indications for antipsychotic use in children and to establish the proportion of exposure that is on- versus off-label. Future studies could focus on comparing new diagnoses of conditions linked to potential clinical indications for antipsychotic use with the number of children receiving pharmaceutical interventions. This could help distinguish between over treatment with medication instead of first trying lifestyle interventions, and an increase in prescriptions that simply reflects more new diagnoses

Documents

Study report

DARWIN EU_Report_P4-C2-003_Antipsychotics in children_V4.0.pdf (7.2 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

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

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

Norwegian Linked Health registry at University of Oslo

Croatia National Public Health Information System (Nacionalni javnozdravstveni informacijski sustav)

InGef Research Database

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

Unknown