Study Report

P4-C2-006

DARWIN EU® - Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) Medications

17/12/2025

Version 3.0

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Public

CONTENTS

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Study title[1]	DARWIN EU® - Trends in utilisation of Attention Deficit Hyperactivity Disorder (ADHD) Medications
Study report version	V3.0
Date	17/12/2025
EUPAS number	EUPAS1000000678
Active substance	Atomoxetine (N06BA09) Dexamphetamine (N06BA02) Guanfacine (C02AC02) Lisdexamfetamine (ATC code: N06BA12) Methylphenidate (N06BA04)
Medicinal product	n/a
Research question and objectives	The overall aim of this study was to characterise the use of ADHD medications in the period of 2010 to 2024. The specific objectives were: 1. To estimate the monthly and yearly period prevalence of use of each ADHD medicine, overall and stratified by age and sex in each data source. 2. To estimate the monthly and yearly incidence of use of each ADHD medicine, overall and stratified by age and sex in each data source. 3. Among incident users of each ADHD medicine, to identify the indication at the time of the initial prescribing/dispensing, overall and stratified by age and sex. 4. Among incident users of each ADHD medicine, to estimate the initial dose, cumulative dose, and time on treatment of the initial medication, overall and stratified by age, sex, and indication at index. 5. Among new users of any ADHD medicine, to estimate the total treatment duration, number of prescriptions overall and by medicine, stratified by initial medicine, age, and sex. 6. To identify the treatment pathway of each individual who initiated an ADHD medicine, including treatment add-on, switch, and concurrent medication/co-prescribing, stratify by calendar time of initiation, age, and sex.
Countries of study	Denmark, Germany, Norway, Spain, and Sweden.
Authors	Xintong Li x.li@darwin-eu.org Edward Burn e.burn@darwin-eu.org Kim Lopez-Guell k.lopezguell@darwin-eu.org

[1]This is a routinely repeated study from P3-C1-004 with EUPAS1000000219.

LIST OF ABBREVIATIONS

Acronyms/term	Description
ADHD	Attention deficit hyperactivity disorder
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
ATC	Anatomical Therapeutic Chemical
ATC-WHO	Anatomical Therapeutic Chemical classification (WHO version)
BIFAP	Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)
CC	Coordination Centre
CDM	Common Data Model
CIPA	Personal Identification Code for the Autonomous Community
DA	Disease Analyzer
DAC	Data Analytics Centre
DAR	Dødsårsagsregisteret
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DK-DHR	Danish Data Health Registries
DKMA	Danish Medicines Agency
DUS	Drug Utilization Study
EBM	Einheitlicher Bewertungsmaßstab
ED	Emergency Department
EHR	Electronic Health Records
EMA	European Medicines Agency
EU	European Union
EUPAS	EU Post-Authorisation Studies Register
GDPR	General Data Protection Regulation
GP	General Practitioner
HI-SPEED	Health Impact - Swedish Population Evidence Enabling Data-linkage
HMA-EMA	Heads of Medicines Agencies- European Medicines Agency
ICD	International Classification of Diseases
ICD-10-CM	International Classification of Diseases, Clinical Modification
ICD-10-GM	International Classification of Diseases, German Modification
ICPC-2	International Classification of Primary Care, 2nd Edition
ICU	Intensive Care Unit
IDIAPJGol	Institut Universitari d'Investigació en Atenció Primària Jordi Gol
InGef RDB	Institut für angewandte Gesundheitsforschung Berlin GmbH Research Database
IP	Inpatient
IPCI	Integrated Primary Care Information Project
IQR	Interquartile range

Acronyms/term	Description
KUHR	Norway Control and Payment of Health Reimbursement
LOINC	Logical Observation Identifiers Names and Codes
MBRN	Medical Birth Registry of Norway
MSIS	Norwegian Surveillance System for Communicable Diseases
NCMP	Norwegian Classification of Medical Procedures
NCRP	Norwegian Classification of Radiological Procedures
NCSP	Nordic Classification of Surgical Procedures
NLHR	Norwegian Linked Health Registries
NorPD	Norwegian Prescription Registry
NPR	Norwegian Patient Registry
NR	National Registry (Norway)
OHDSI	Observational Health Data Sciences and Informatics
OMOP	Observational Medical Outcomes Partnership
OP	Outpatient
OPS	Operationen- und Prozedurenschlüssel
PPC	Proportion of patients covered
PZN	Pharmazentralzummer
RxNorm	Medical prescription normalised
SDS	Sundhedsdatabanken
SHI	Statutory health insurances
SIDIAP	Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària
SMPA-GU	Swedish Medicines and Products Agency- University of Gothenburg
SNOMED	Systematized Nomenclature of Medicine
SNS	Spanish National Health Service
SPOC	Shortages Single Point of Contact
SYSVAK	Norwegian Immunisation Registry
WHO	World Health Organisation

1. TITLE

DARWIN EU® - Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) Medications

2. DESCRIPTION OF THE STUDY TEAM

Study team role	Names	Organisation
Principal Investigator	Xintong Li	University of Oxford
Data Scientist	Kim Lopez-Guell Edward Burn	University of Oxford University of Oxford
Clinical Domain Expert	Daniel Prieto Alhambra	University of Oxford/ Erasmus MC
Study Manager	Natasha Yefimenko	Erasmus MC
Data source	**Names**	**Data Partner Organisation***
Danish Data Health Registries (DK-DHR)	Elvira Bräuner Susanne Bruun Claus Møldrup	Danish Medicines Agency (DKMA)
InGef Research Database (InGef RDB)	Raeleesha Norris Annika Vivirito Alexander Harms Josephine Jacob	Institut für angewandte Gesundheitsforschung Berlin GmbH
Norwegian Linked Health Registry data (NLHR)	Hedvig Nordeng Nhung Trinh Saeed Hayati	Universitetet i Oslo
Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP)	Miguel-Ángel MACIÁ-MARTÍNEZ Martín Pérez, María del Mar Martínez-Alcalá García, Hermenegildo Carlos Llorente Garcia, Ana Redondo Álvarez, Emma Macia Martinez, Miguel Angel	Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)
The Information System for Research on Primary Care (SIDIAP)	Anna Palomar Cros Elena Roel Herranz Agustina Giuliodori Picco Irene López Sánchez	IDIAP JGol
Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)	Huiqi Li Fredrik Nyberg Marcel Ballin Mats Talbäck Rickard Ljung	Swedish Medicines and Products Agency- University of Gothenburg (SMPA-GU)

*Data partners do not have an investigator role. Data partners execute code at their data source, review, and approve their results.

3. ABSTRACT

Title

DARWIN EU® - Trends in utilisation of Attention-Deficit Hyperactivity Disorder (ADHD) Medications

Rationale and background

Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic neurodevelopmental disorder affecting both children and adults, with pharmacological therapy forming a central part of its management. In recent years, demand for ADHD medicines has risen markedly across Europe, accompanied by reports of constrained supply, new regulatory approvals, and market changes. In 2024, the SPOC Working party requested the initial study on ADHD medications to better anticipate and manage potential medicine shortages. Although the overall supply situation in the EU has since improved, future constraints remain possible. Monitoring real-world utilisation of ADHD medications is therefore essential to anticipate demand, support continuity of treatment, and inform public-health and regulatory planning.

The current study was requested by the Spanish Regulatory Authority (AEMPS) and the European Medicines Agency (EMA) as an update to the initial 2024 study, with the inclusion of additional data partners, particularly from Spain. The study provides an expanded, comparative overview of ADHD medication use across Europe and explores prescribing trends, treatment persistence, and switching behaviour over time.

Research question and objectives

Research questions

The overall aim of this study was to characterise the use of ADHD medications in the period of 2010 to 2023/2024.

Objectives

1. To estimate the monthly and yearly period prevalence of use of each ADHD medicine, overall and stratified by age and sex in each data source.
2. To estimate the monthly and yearly incidence of use of each ADHD medicine, overall and stratified by age and sex in each data source.
3. Among incident users of each ADHD medicine, to identify the indication at the time of the initial prescribing/dispensing, overall and stratified by age and sex.
4. Among incident users of each ADHD medicine, to estimate the initial dose, cumulative dose, and time on treatment of the initial medication, overall and stratified by age and sex.
5. Among new users of any ADHD medicine, to estimate the total treatment duration, number of prescriptions overall and by medicine, stratified by initial medicine, age, and sex.
6. To identify the treatment pathway of each individual who initiated an ADHD medicine, including treatment add-on, switch, and concurrent medication/co-prescribing, stratify by calendar time of initiation, age, and sex.

Methods

This population-based observational study used routinely collected electronic health record and claims data from six established data sources: DK-DHR (Denmark), InGef RDB (Germany), NLHR (Norway), BIFAP and SIDIAP (Spain), and HI-SPEED (Sweden).

Study design

Objectives 1 and 2 were population-level drug utilisation study that estimated prevalence and incidence of ADHD medication use.

Objectives 3 – 6 were patient-level utilisation studies with new user cohort design.

Population

All individuals aged ≥3 years with at least 365 days of prior data were eligible. Incident use was defined using a 365-day washout period. Discontinuation was defined as a 30-day gap between prescriptions; switching and restarting were measured thereafter.

Variables

ADHD medications of interest included methylphenidate, dexamphetamine, lisdexamfetamine, atomoxetine, and guanfacine. Covariates included age, sex, comorbidities (e.g., anxiety, depression, asthma, obesity), and comedications (e.g., antibacterials, antidepressants, psycholeptics).

Statistical analysis

Objectives 1 to 2 estimated monthly and yearly prevalence and incidence of ADHD medication use, overall and stratified by age and sex.

Objectives 3 to 6 described incident users' characteristics, initial dose, treatment duration, and recorded indication at initiation. Treatment persistence was assessed using proportion of patients covered. Treatment pathways, including add-on, switching, and concurrent use, were assessed among new users of any ADHD medication. A minimum cell count of 5 was used when reporting results, with any smaller count reported as "<5" and zero counts as "0>".

Results

A total of 973,816 individuals initiated at least one ADHD medication during the study period (DK-DHR: 193,612; InGef RDB: 94,057; NLHR: 123,611; BIFAP: 169,797; SIDIAP: 63,528; HI-SPEED: 329,211). Both prevalence and incidence of ADHD medication use increased across all data sources, although the magnitude of increase varied. Prevalence was generally higher in the Scandinavian countries compared to Spain and Germany. Since 2018, HI-SPEED showed the highest overall prevalence, while InGef RDB and SIDIAP reported lower but steadily rising rates.

Methylphenidate was consistently the most frequently used ADHD medication across all data sources. Atomoxetine was the second most common in earlier years but was gradually overtaken by lisdexamfetamine between 2015 and 2019. Guanfacine use, indicated only for children and adolescents aged 6–17 years, also showed a steady increase in use during the later study years.

Age- and sex-specific analyses showed higher use among boys than girls in all children and adolescent age groups, although the gap narrowed among older adolescents after 2020, as there was a steeper rise in medication use among girls. Among adults, ADHD medication use increased in both sexes, with a steeper rise observed among females since 2020. By the end of the study period, prevalence and incidence were higher among females than males in DK-DHR, InGef RDB, NLHR, and HI-SPEED.

Initiators in BIFAP, InGef RDB, and SIDIAP were younger compared with those in the Scandinavian data sources. Across all settings, a greater proportion of initiators were male. Common comorbidities included anxiety and depression, with asthma frequently recorded in DK-DHR, NLHR, and BIFAP, and obesity in SIDIAP. Antibacterials, antidepressants, psycholeptics, and anti-inflammatory drugs were the most commonly prescribed medications during the six months prior to ADHD medication initiation.

Persistence with treatment declined over time across all data sources. Six months after initiation, the proportion of patients continuing any ADHD medication ranged from 18.25% in InGef RDB to 60.15% in

SIDIAP, decreasing to between 3.67% and 31.76% at two years. Children aged 3–11 years showed higher persistence in BIFAP and SIDIAP, while adults aged 25 years or older had higher persistence in DK-DHR, NLHR, and HI-SPEED. After discontinuation, 18–54% of methylphenidate users restarted treatment within 90 days, while up to 14% switched to another ADHD medication; a substantial proportion remained untreated during follow-up.

Discussion

This multi-data source study described trends of ADHD medication use across five European countries from 2010 to 2023/2024. ADHD medication use increased consistently in all data sources, though to varying degrees. The overall increase in ADHD medication use aligns with previous European and international research, reflecting growing awareness, improved diagnostic recognition, and changes in clinical guidelines. Differences in observed trends likely reflect variations in healthcare organisation, access to specialist care, and national reimbursement and regulatory policies.

The results underscore the need for continued monitoring of ADHD treatment patterns, further investigation into factors influencing treatment persistence, and ongoing efforts in research and healthcare planning to optimise ADHD management across Europe.

4. AMENDMENTS AND UPDATES

None.

5. MILESTONES

Study deliverable	Timelines (planned)	Timelines (actual)
Final Study Protocol	July 2025	July 2025
Creation of Analytical code	August 2025	August 2025
Execution of Analytical Code on the data	September 2025	September 2025
Draft Study Report	October 2025	October 2025
Final Study Report	November 2025	17 December 2025

6. RATIONALE AND BACKGROUND

A first study (EUPAS1000000219) has been performed in 2024 at the request of the SPOC Working Party (responsible for monitoring and reporting events that could affect the supply of medicines in the EU). Monitoring possible shortages of different medicines to treat Attention-Deficit Hyperactivity Disorder (ADHD) is critical, mainly due to an increased demand in multiple markets, production constraints related to raw material availability, new regulatory approvals for some medicines, and changes in the competitive landscape. The main products under monitoring are lisdexamfetamine and methylphenidate, but three more have the indication in Europe (atomoxetine, dexamphetamine, and guanfacine). Currently, the situation has improved slightly in the EU and there are no critical shortages. However, it is anticipated that constraints in the supply may continue.

The initial study was conducted to better anticipate potential shortages and their impact on appropriate patient management, as it is important to assess the evolution of prescriptions over time and to get an overview of how these ADHD medicines are used across Europe.

The Spanish Regulatory Authority (AEMPS), after having seen the results of the initial study, had inquired with the EMA whether DARWIN EU® could repeat the study with additional data partners, especially the Spanish ones, as only one Spanish data partner was included in the first study (https://catalogues.ema.europa.eu/system/files/2025-03/DARWIN%20EU_Report_P3-C1-004_ADHD_V5.pdf). This study is now being repeated to include additional data sources with more recent data. In addition, as all ADHD medications are approved only for individuals aged six and older, their use in children under six years of age is considered off-label. Therefore, in the current study, a stratum of young child aged below five years old was added to assess potential off-label use of these medications.

7. RESEARCH QUESTION AND OBJECTIVES

Research question

The overall aim of this study was to characterise the use of ADHD medications in the period of 2010 to 2023/2024.

Objectives

The specific objectives were:

1. To estimate the monthly and yearly period prevalence of use of each ADHD medicine, overall and stratified by age and sex in each data source.
2. To estimate the monthly, and yearly incidence of use of each ADHD medicine, overall and stratified by age and sex in each data source.
3. Among incident users of each ADHD medicine, to identify the indication at the time of the initial prescribing/dispensing, overall and stratified by age and sex.
4. Among incident users of each ADHD medicine, to estimate the initial dose, cumulative dose, and time on treatment of the initial medication, overall and stratified by age and sex.
5. Among new users of any ADHD medicine, to estimate the total treatment duration, number of prescriptions overall and by medicine, stratified by initial medicine.
6. To identify the treatment pathway of each individual who initiated an ADHD medicine, including treatment add-on, switch, and concurrent medication/co-prescribing, stratified by calendar year of initiation, age group, and sex.

8. RESEARCH METHOD

8.1. Study design

Cohort studies were conducted using routinely collected health data from six data sources from five countries across Europe and in five EU member states.

The study comprised of:

1. Population-level cohort study was conducted to address objectives 1 and 2, in which prevalence and incidence of ADHD medications were estimated.
2. New drug user cohort design was used for objectives 3 to 6, in which new users of ADHD medications were identified and followed up.

8.2. Follow-up

In the analysis of population-level DUS (Objectives 1 and 2), a denominator population was constructed using all eligible individuals in the data source. Individuals contributed person time on the respective date of the latest of the following: 1) study start date, 2) date at which the 365 days data availability reached, and 3) aged 3 years old.

Subjects stopped contributing person time at the earliest date of the following: 1) end of available data in each of the data sources or 2) date at which the observation period of the specific person ended.

In the patient-level DUS analysis (Objective 3 to 6), new users of ADHD medications were followed from the date of the new incident prescription to the earliest date of the following: 1) the last medication record of ADHD medication, 2) end of available data in each of the data sources, or 3) date at which the observation period of the specific person ended.

8.3. Study population with inclusion and exclusion criteria

Population-level utilisation of ADHD medications: general population

All individuals aged 3 years and older [1], registered in the respective data sources since the 1st of January of 2010 to the latest available data, with at least 365 days of prior data availability, participated in the population-level analysis of period prevalence and incidence of ADHD medications of interest.

Patient-level utilisation of ADHD medications: new user cohort

In objectives 3 and 4, incident user cohorts of any ADHD medication, as well as each ADHD medication, were created, using a 365-day washout window.

Therefore, the "incident use of any ADHD medication" refers to a prescription/dispensation of any ADHD medication during the study period and without use of any ADHD medication in the previous year. An individual could enter the cohort multiple times if the inclusion/ exclusion criteria was met.

The "incident use of individual medication" refers to a prescription/dispensation of a specific ADHD medication during the study period and without use of respective medication in the previous year. For example, if an individual started methylphenidate, then switched to atomoxetine, the individual could contribute to the new user cohorts of both methylphenidate and atomoxetine.

In each data source, six incident user cohorts of the medications licensed for ADHD treatment were constructed separately: any ADHD medication, dexamphetamine, lisdexamfetamine, methylphenidate, atomoxetine, and guanfacine.

In objectives 5 and 6, new users were identified using the first record of any of the ADHD medications of interest within the study period, having no previous records for any study medication any time prior to entry (e.g., individual who received their first ever medication during study period). The index date was defined as the date of the first eligible medication record.

We excluded individuals with missing data on sex or age.

8.4. Study setting and data sources

Table 1. Data sources

Country	Name of Data source	Health Care setting	Type of Data	Number of active individuals	Calendar period covered by each data source	Contributing to
Denmark	DK-DHR	Primary and secondary	Registries	5.91M	1995-01-01 to 2024-11-07	Objectives 1–6
Germany	InGef RDB	Primary and secondary	Claims	7.64M	2015-01-01 to 2024-12-31	Objectives 1–6
Norway	NLHR	Primary and secondary	Registries	6.89M	2008-01-01 to 2023-12-31	Objectives 1–6
Spain	BIFAP	Primary Care, secondary care	EHR	24.0 M	1998-07-01 to 2024-12-31	Objectives 1–6
Spain	SIDIAP	Primary Care,	EHR	5.94 M	2006-01-01 to 2023-06-30	Objectives 1–6

Country	Name of Data source	Health Care setting	Type of Data	Number of active individuals	Calendar period covered by each data source	Contributing to
		secondary care				
Sweden	HI-SPEED	Primary and secondary	Registries	10.5M	2015-01-01* to 2024-08-30	Objectives 1–6

M=Millions; DK-DHR=Danish Data Health Registries; InGef RDB=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.
*In HI-SPEED, drug dispensation data is available from 2018-01-01.

This study was conducted using routinely collected data from six data sources in the DARWIN EU® network of data partners from five European countries, of which five EU member states. All data were a priori mapped to the OMOP CDM.

Data sources

1. Denmark: Danish Data Health Registries (DK-DHR)
2. Germany: InGef Research Database (InGef RDB)
3. Norway: Norwegian Linked Health Registry data (NLHR)
4. Spain: Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP)
5. Spain: The Information System for Research on Primary Care (SIDIAP)
6. Sweden: Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)

Data sources selection

The selection of data sources for this study was performed based on the relevance for the proposed research question among those data sources onboarded and available within DARWIN EU® at the time of the study feasibility assessment, as well as operational considerations knowing the timing of the study and the expansion of the initial study to additional fit-for-use data partners.

Medications for ADHD are primarily prescribed and managed in primary care settings in Europe. To estimate the population-level and patient-level drug utilisation study, population-based data sources are needed. The population-based data sources enabled us to properly define the denominator for the calculation of incidence and prevalence. All six selected data sources are population-level primary care records which include prescription information of medications, which allowed for the identification of new treatment episodes.

Data source justification and key characteristics

Two data sources from Spain (BIFAP and SIDIAP) were included in this study to increase the geographic coverage of the study population, as the two data sources do not cover the same regions.

The three linked national registries from Scandinavian countries included had relevant sample size and provided nationwide prevalence/ incidence data (DK-DHR, NLHR, HI-SPEED).

8.5. Study period

The study period started on 1st January 2010 to the latest data availability of each participated data source.

8.6. Variables

8.6.1. Exposure

- Dexamphetamine
- Lisdexamfetamine
- Methylphenidate
- Atomoxetine
- Guanfacine

Incident use of any ADHD medication was defined as having no use of any ADHD medication in the year before with a washout window of 365 days.

Incident use of individual ADHD medication was defined as having no use of the specific medication in the year before with a washout window of 365 days.

New use to any ADHD medication was defined as having no use of any ADHD medication any time before index.

8.6.2. Outcome

No outcome variable was included in this study.

8.6.3. Covariates, including confounders, effect modifiers, intercurrent events, and other variables

Population-level drug utilisation study (incidence and prevalence)

- Calendar time: Month, year
- Age groups:
    - Overall (3+ years old), children (aged 3–11 years), adolescents (12–17 years), young adults (18–24 years), and adults (≥25 years). [2]
    - Age wider group: children (aged 3–17 years) and adults (≥ 18 years).
    - Additional age group of young children to inspect off-label use (aged 3–5 years)
- Sex: Both, female, male

Patient-level drug utilisation study

Pre-specified conditions that are the potential indication of ADHD medications, including both authorised and non-authorised indications (Objective 3):

- Authorised indications:
    - ADHD
    - Narcolepsy (authorised for methylphenidate and dexamphetamine only)
    - Hypertension disorder (authorised for guanfacine only)
- Potential off-label conditions [3,4]:
    - Eating disorders
    - Fatigue
    - Major depressive disorder

- Apathy
- Mood disorders (excluding major depressive disorder)
- Cognitive dysfunction (excluding dementia)
- Dementia
- Treatment of addictions
- Behavioural disorders (excluding ADHD)
- Autism
- Intellectual disability
- Post-traumatic brain injury

The conditions were defined by concept set. Concept sets for these conditions are listed in the **ANNEX IV**.

8.7. Study size

No formal sample size was estimated for this study. However, based on the feasibility assessment performed before the initiation of the study, the expected total number of users of each ADHD medication of interest were the following across all data sources:

- Methylphenidate: DK-DHR: 208,500; InGef RDB: 23,500; NLHR: 109,100; BIFAP: 148,800; SIDIAP: 72,300; HI-SPEED: 260,700
- Lisdexamfetamine: DK-DHR: 62,800; InGef RDB: 28,600; NLHR: 58,400; BIFAP: 27,500; SIDIAP: 8,800; HI-SPEED: 188,600
- Dextroamphetamine: DK-DHR: 9,700; InGef RDB: 2,200; NLHR: 11,600; HI-SPEED: 34,500
- Atomoxetine: DK-DHR: 67,700; InGef RDB: 1,500; NLHR: 16,200; BIFAP: 20,200; SIDIAP: 9,500; HI-SPEED: 55,000
- Guanfacine: DK-DHR: 5,200; InGef RDB: 4,200; NLHR: 2,600; BIFAP: 7,900; SIDIAP: 3,300; HI-SPEED: 41,400

These numbers were estimated based on the number of unique individuals with a target medication recorded, without applying any inclusion or exclusion criteria, and were not limited to the study period. Dextroamphetamine was not available in BIFAP and SIDIAP.

8.8. Data transformation

Analyses were conducted separately for each data source. Before study initiation, test runs of the analyses were performed on a subset of the data sources and quality control checks were performed. Once all the tests passed (see **Annex III**), the final study codes package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP CDM in R Studio and reviewed and approved the, by default, aggregated results.

The study results of all data sources were checked, after which they were made available to the team, and the dissemination phase started. All results were locked and timestamped for reproducibility and transparency.

8.9. Statistical methods

8.9.1. Main summary measures

For objective 1, prevalence was reported. For objective 2, incidence rates were reported. For objectives 3-5, median and inter quarter ranges were reported for numeric variables, number and proportion were reported for categorical variables.

8.9.2. Main statistical methods

Objective 1: Prevalence

Prevalence was calculated as monthly and yearly period prevalence, which summarised the total number of users of the drug of interest during a given calendar month/year divided by the population under observation during that month/year. Therefore, period prevalence gave the proportion of users at any time during a specified interval. We did not require the denominator population to be under observation for the entire month/year. Binomial 95% confidence intervals were calculated.

The analysis was stratified by age group, sex, and age group by sex (e.g., group of “males aged 3–11 years old”).

Objective 2: Incidence

Monthly incidence rates of each ADHD medication of interest were calculated as the of number of new users per 100,000 person-years of the population at risk of getting exposed during the period for each calendar month (e.g., 1st January – 31st January). Incidence rates were also calculated yearly. Those study participants who enter the denominator population then contributed time at risk up to their first use (prescription or dispensation) of study medication during the study period. If they did not have a drug exposure, they contributed time at risk as described above in **Sections 8.3 Study period** and **8.4 Follow-up**. Incidence rates were given together with 95% Poisson exact confidence intervals.

The analysis was stratified by age group, sex, and age group by sex.

Objective 3: Indication and characteristics

For the new user cohorts of any ADHD medication or individual medication, we provided a patient-level characteristics index on cohort entry. Demographic information, common comorbidities (any time prior to index), and common medication use (one year prior to index) was reported. We further reported the percentage of individuals who used other ADHD medications (any time prior) to inspect potential off-label use. This is due to non-stimulants being recommended as second-line treatment for ADHD.

We assessed the potential indications of the study medication using four different windows: within 7 days before index, within 30 days, within 90 days, and any time before index. [5,6] Potential indications were presented as number and percentage of individuals with a record of the respective indication. We reported the potential indications as non-mutually exclusive groups, meaning that the percentages of all indications could add up to over one hundred.

We reported all listed potential indications using the 30 days prior window. We then grouped the off-label conditions together and finally assessed the following indication/indication groups for each medication within the three different time windows:

- Dexamphetamine: ADHD, narcolepsy, and potential off-label conditions as listed in **Section 8.6.3**.
- Lisdexamfetamine: ADHD, and potential off-label conditions as listed in **Section 8.6.3**.
- Methylphenidate: ADHD, narcolepsy, and potential off-label conditions as listed in **Section 8.6.3**.
- Atomoxetine: ADHD, and potential off-label conditions as listed in **Section 8.6.3**.

- Guanfacine: ADHD, hypertension, and potential off-label conditions as listed in **Section 8.6.3**.

The analysis was stratified by age group, sex, and age group by sex.

Guanfacine has been approved for treatment of ADHD in those aged 6–17 years old for whom stimulants are not suitable, not tolerated, or have been shown to be ineffective, as well as for hypertension. To contextualise the potential off-label use for the guanfacine initiator cohort, we reported the proportion of the following: a.) age 6–17 but with no approved condition of ADHD or hypertension, b.) any use in children under 6 years old and in adults without hypertension, or c.) age 6–17 but with no history of stimulant use.

Objective 4: Initial dose, cumulative dose, treatment duration, and number of prescriptions

Among the new user cohort of each individual ADHD medicine, initial dose and cumulative dose was assessed at ingredient level for the initial medication. Duration of the treatment episode was reported. As explained in the previous section, a grace period of 30 days was used to define the treatment episode. Treatment duration was summarized providing the minimum, p25, median, p75, and maximum treatment duration. Number of prescriptions within the treatment episode was reported.

We assessed the restart or switching to another medication after discontinuation of the original medication. We reported the number and percentage of individuals who restart or switch to another medication within 30 days, 90 days, and 180 days after their first discontinuation. The analysis was stratified by age group, sex, and age group by sex.

Objective 5: Total treatment duration

For this objective, new users of any ADHD medication were followed until the last drug record. Total treatment duration was calculated as the days between the first initiation of any ADHD medication until the last recorded ADHD medication. Number of prescriptions during this period was reported as total and at drug substance level.

We estimated the proportion of patients covered (PPC), which measured the proportion of live patients currently covered by treatment on a given day after treatment initiation. [7] This method has been used to study treatment persistence and is less sensitive to changes in grace periods.

Objective 6: treatment pathway

Individuals who started any ADHD medication were followed up from the date of first medication of interest to the last record of any study medication.

The minimum overlap of different treatments to be considered as combination treatment (combinationWindow) was 30 days in the purposed study. The target cohort referred to the new user cohort of any ADHD medication, whereas the event(s) refer to treatment(s) of interest.

We used a Sankey diagram to illustrate the treatment pathways. To avoid an overwhelming figure, we only included treatment pathways representing more than 5% individuals in the entire cohort. Pathways with less than 5% frequency were not reported.

8.9.3. Missing values

We excluded individuals with missing age or sex.

8.9.4. Sensitivity analysis

The ADHD population is known to take drug holidays and temporarily interrupt their treatment, which do not necessarily signify discontinuation of medication use. [9,10] Therefore, in the sensitivity analysis, instead of allowing a 30-days gap between drug exposure records, a 90-days gap was used in constructing treatment episode [11].

Table 2. Sensitivity analyses - rationale, strengths, and limitations.

	What is being varied? How?	Why? (What did you expect to learn?)	Strengths of the sensitivity analysis compared to the primary	Limitations of the sensitivity analysis compared to the primary
Gap between drug exposure	Allow 90 days gap between records of drug exposure.	Individuals especially kids may take drug holidays on purpose rather than discontinue	Capture longer treatment period	The treatment episode may not reflect the real drug utilisation

8.10. Deviations from the protocol

Not applicable.

9. RESULTS

The full set of results for this study is available through an interactive web-application (ShinyApp) at EUPAS1000000678.

The following tabs are included in the ShinyApp:

- Snapshot: “Snapshot” provides descriptive information on the data sources that participated, including total number of individuals in the data source, and time period the data source covered. “Code use” includes the codes that were used to identify ADHD medication, and their mapping from the source data.
- Objective 1: “Prevalence” presents the monthly and yearly prevalence of medication use, by medication type, age group, sex, and data source.
- Objective 2: “Incidence” presents the monthly and yearly incidence of medication use, by medication type, age group, sex, and data source.
- Objective 3: “Cohort Attrition” presents the process of constructing the incident ADHD medication user cohorts. “Cohort Characteristics” presents the baseline characteristics of the incident user cohorts, by medication type, age group, sex, and data source. “Indication” presents the recorded potential indication of medication use in pre-specified windows, by medication type, age group, sex, and data source.
- Objective 4: “Drug Utilisation” presents information on number and duration of prescription, as well dose of medications, by medication type, age group, sex, and data source.
- Objective 5: “Proportion of patient covered” includes the estimated proportion of patients covered among initiators.
- Objective 6: “Treatment pattern” includes the sanky plots for treatment sequence among initiators.

9.1. Participants

We identified a total of 973,816 individuals who initiated any of the studied ADHD medications during the study period from 2010 to 2023/2024 (DK-DHR: 193,612; InGef RDB: 94,057; NLHR: 123,611; BIFAP: 169,797; SIDIAP: 63,528; HI-SPEED: 329,211). Among the six data sources, data were available from the beginning of the study period (2010) in DK-DHR, BIFAP, and SIDIAP. In InGef RDB, data covered the period from 2016 to 2024. In NLHR, data were available from 2018 to 2023, and in HI-SPEED, from 2018 to 2024.

In DK-DHR data, the number of individuals who started atomoxetine, dextroamphetamine, guanfacine, lisdexamfetamine, and methylphenidate during the study period were 63,576; 9,209; 5,104; 62,073; and 180,889, respectively.

In InGef RDB, the number of individuals who started atomoxetine, dextroamphetamine, guanfacine, lisdexamfetamine, and methylphenidate during the study period were 9,781; 3,114; 4,646; 26,690; and 87,827, respectively.

In NLHR, the number of individuals who started atomoxetine, dextroamphetamine, guanfacine, lisdexamfetamine, and methylphenidate during the study period were 15,836; 11,340; 2,533; 56,233; and 107,262, respectively.

In SIDIAP, the number of individuals who started atomoxetine, guanfacine, lisdexamfetamine, and methylphenidate were 8,199; 3,228; 8,628; and 58,906, respectively. Dextroamphetamine was not found in this data source.

In BIFAP, the number of individuals who started atomoxetine, guanfacine, lisdexamfetamine, and methylphenidate were 21,796; 9,858; 34,747; and 155,537, respectively. Dextroamphetamine was not found in this data source.

In HI-SPEED, the number of individuals who started atomoxetine, dextroamphetamine, guanfacine, lisdexamfetamine, and methylphenidate during the study period were 54,687; 34,309; 41,243; 188,007; and 259,788, respectively.

9.2. Main results

9.2.1. Objective 1: Prevalence

In **Figure 1**, the overall prevalence (without age or sex stratification) of any ADHD medication use, as well as the prevalence of each study medication, is presented.

From 2010 to 2015, the prevalence of any ADHD medication use was highest in DK-DHR, followed by BIFAP and SIDIAP. Prevalence data were available in InGef RDB starting in 2016, and in NLHR and HI-SPEED starting in 2018. Since 2018, HI-SPEED has shown the highest prevalence of ADHD medication use among the six data sources, followed by DK-DHR and NLHR, where overall prevalence was similar. Prevalence in InGef RDB was lower than in the three Scandinavian countries but higher than in the two Spanish data sources.

An increasing trend in the prevalence of any ADHD medication use was observed in all six data sources, although the extent of increase varied. In DK-DHR, prevalence increased throughout the study period, particularly after 2020. The prevalence of any ADHD medication use was 0.60% in 2010, increased to 1.1% in 2020, and reached 2.1% in 2024. In InGef RDB, prevalence increased from 0.45% in 2016 to 0.88% in 2024, with a steeper rise after 2021. In NLHR, prevalence increased from 0.92% in 2018 to 1.77% in 2023. During the study period, prevalence in BIFAP increased steadily, from 0.19% in 2010 to 0.49% in 2024. In SIDIAP, prevalence increased from 0.26% in 2010 to 0.42% in 2015 and then stabilised thereafter. In HI-SPEED, prevalence of any ADHD medication use increased from 1.2% in 2018 to 2.2% in 2024.

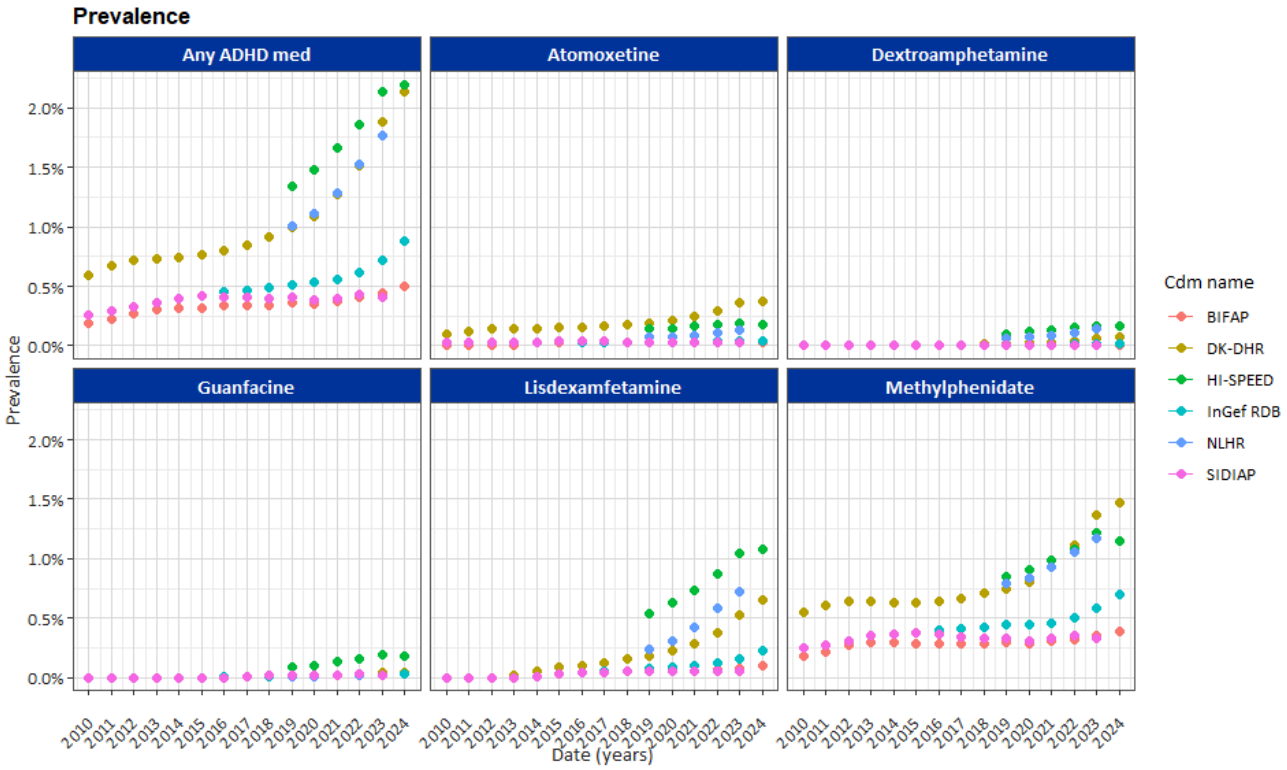

Figure 1. Yearly prevalence of ADHD medication use, by data source and medication.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; DK-DHR=Danish Data Health Registries; InGef RDB=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

In all six data sources, methylphenidate was consistently the most commonly used ADHD medication throughout the study period. In DK-DHR, atomoxetine had the second highest prevalence from 2010 to 2019, after which its use was surpassed by lisdexamfetamine. In InGef RDB, lisdexamfetamine was the second most frequently used medication between 2016 and 2024. In NLHR, atomoxetine was the second most common medication from 2018 to 2023, although lisdexamfetamine use also increased during this period. In BIFAP, atomoxetine initially ranked second between 2010 and 2015, but lisdexamfetamine later became more common. In SIDIAP, a similar trend was observed, with lisdexamfetamine overtaking atomoxetine from 2016 onwards. In HI-SPEED, lisdexamfetamine consistently held the second position since data became available in 2018.

Figures 2 to 7 show the yearly prevalence for each age group-sex stratification. The monthly prevalence is detailed in the online Shiny app.

Among children and adolescents, trends in the prevalence of any ADHD medication use varied across data sources. In all data sources, higher prevalence of medication use was observed among boys compared with girls within the same age groups. In DK-DHR, among children aged 3–11 years, medication use increased from 0.39% in 2014 to 0.83% in 2024 among girls, and from 1.31% in 2014 to 2.08% in 2024 among boys. Among adolescents aged 12–17 years, prevalence increased steadily since 2010, particularly among females after 2020. In InGef RDB, prevalence among children aged 3–11 years rose steadily from 2016 to 2024. Among those aged 12–17 years, prevalence increased in both males and females from 2016 onward, with a sharper rise after 2021. In NLHR, a similar pattern was observed, with increasing prevalence of medication use among individuals aged 3-17 years in both sexes. In BIFAP, prevalence among children aged 3–11 years remained stable between 2010 and 2020, then increased in both boys and girls from 2021

onward. Among adolescents aged 12–17 years, prevalence rose between 2010 and 2015, remained stable until 2020, and increased again toward 2024. In SIDIAP, prevalence increased between 2010 and 2015 but then declined gradually until the end of the study period for both males and females aged 3-17 years. In HI-SPEED, prevalence increased steadily from 2018 for both boys and girls.

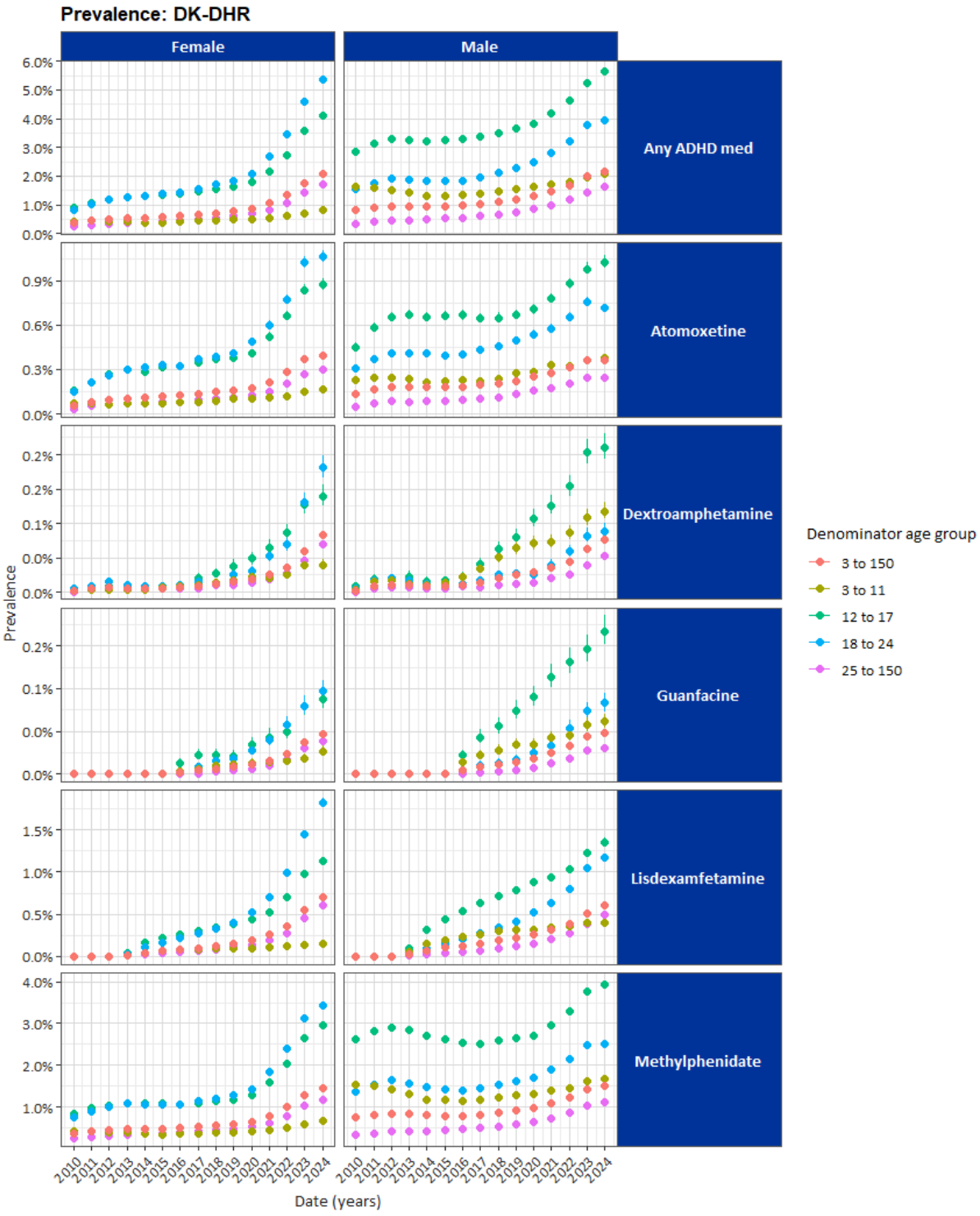

Figure 2. Yearly prevalence of ADHD medications by age groups and sex: DK-DHR.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; DK-DHR=Danish Data Health Registries.

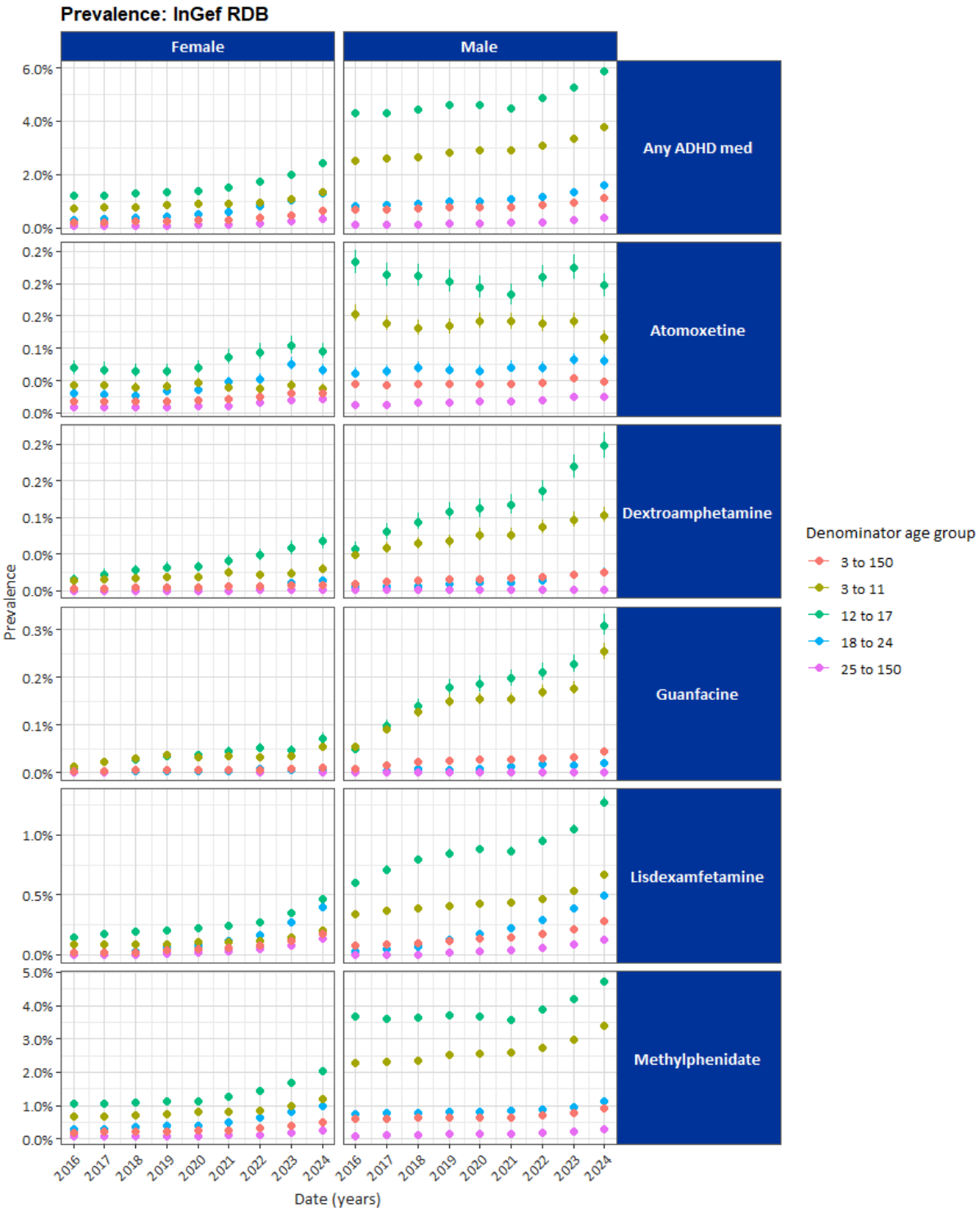

Figure 3. Yearly prevalence of ADHD medications by age groups and sex: InGef RDB.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; InGef RDB=InGef Research Database.

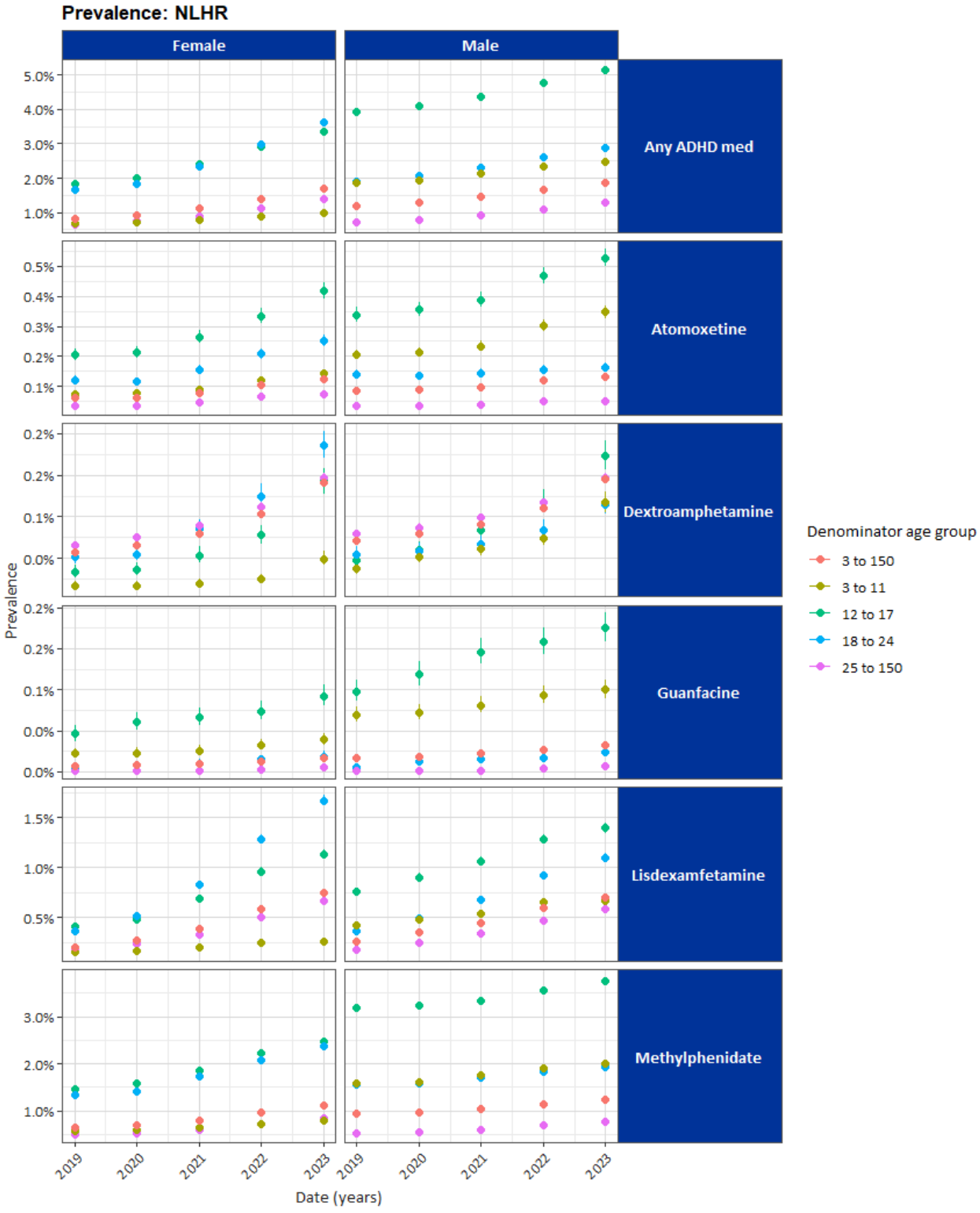

Figure 4. Yearly prevalence of ADHD medications by age groups and sex: NLHR.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; NLHR=Norwegian Linked Health Registry data.

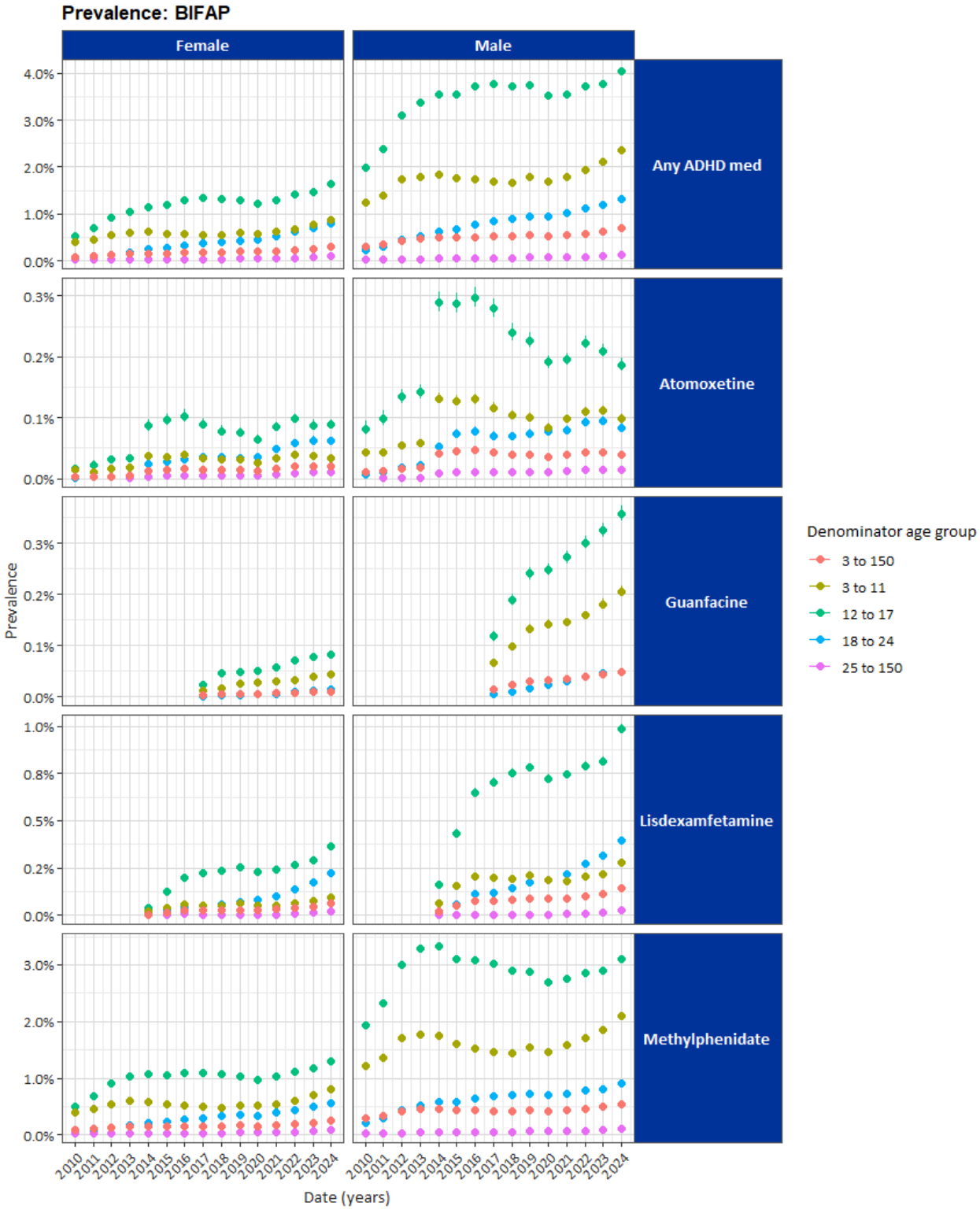

Figure 5. Yearly prevalence of ADHD medications by age groups and sex: BIFAP.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público.

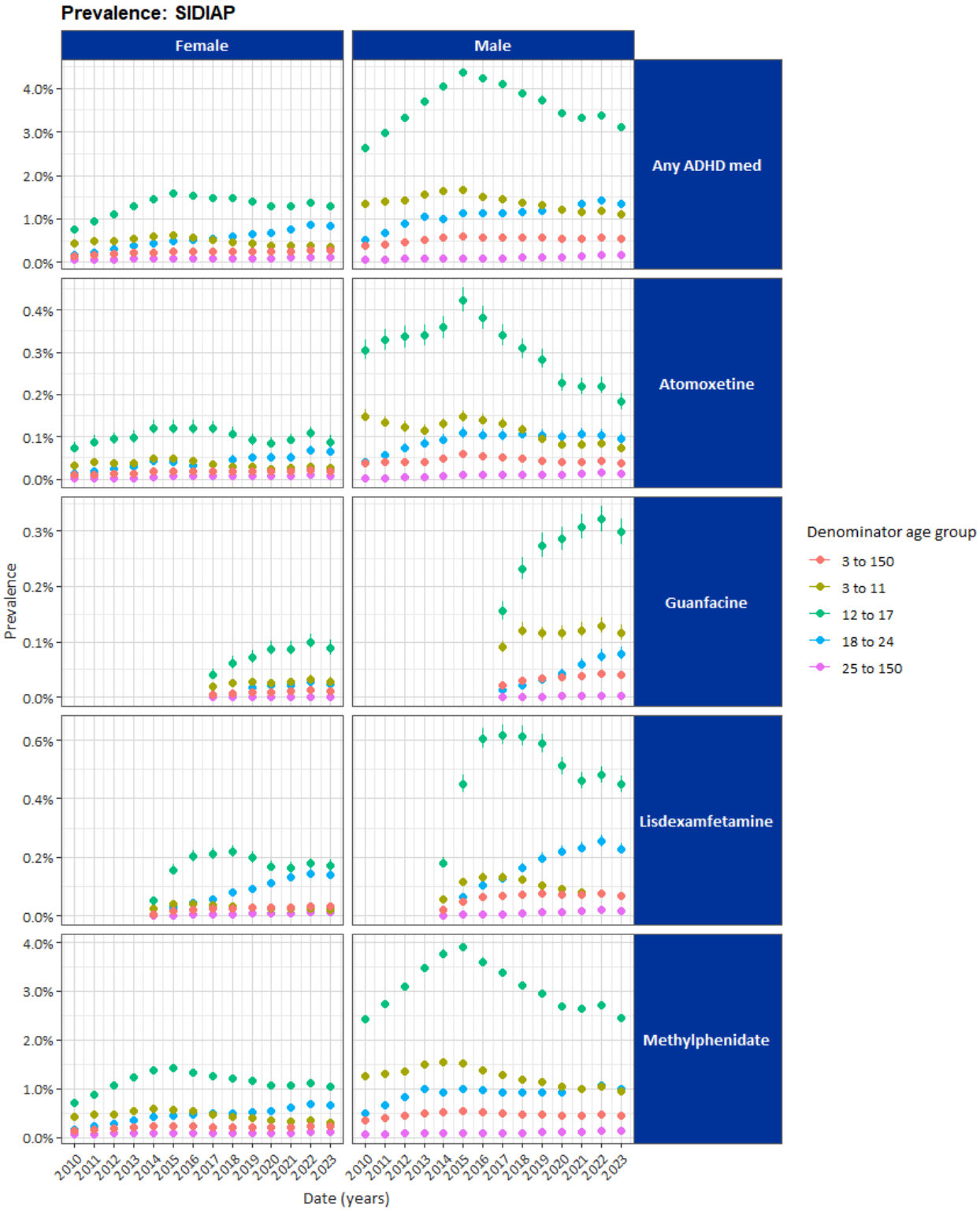

Figure 6. Yearly prevalence of ADHD medications by age groups and sex: SIDIAP.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; SIDIAP=The Information System for Research on Primary Care.

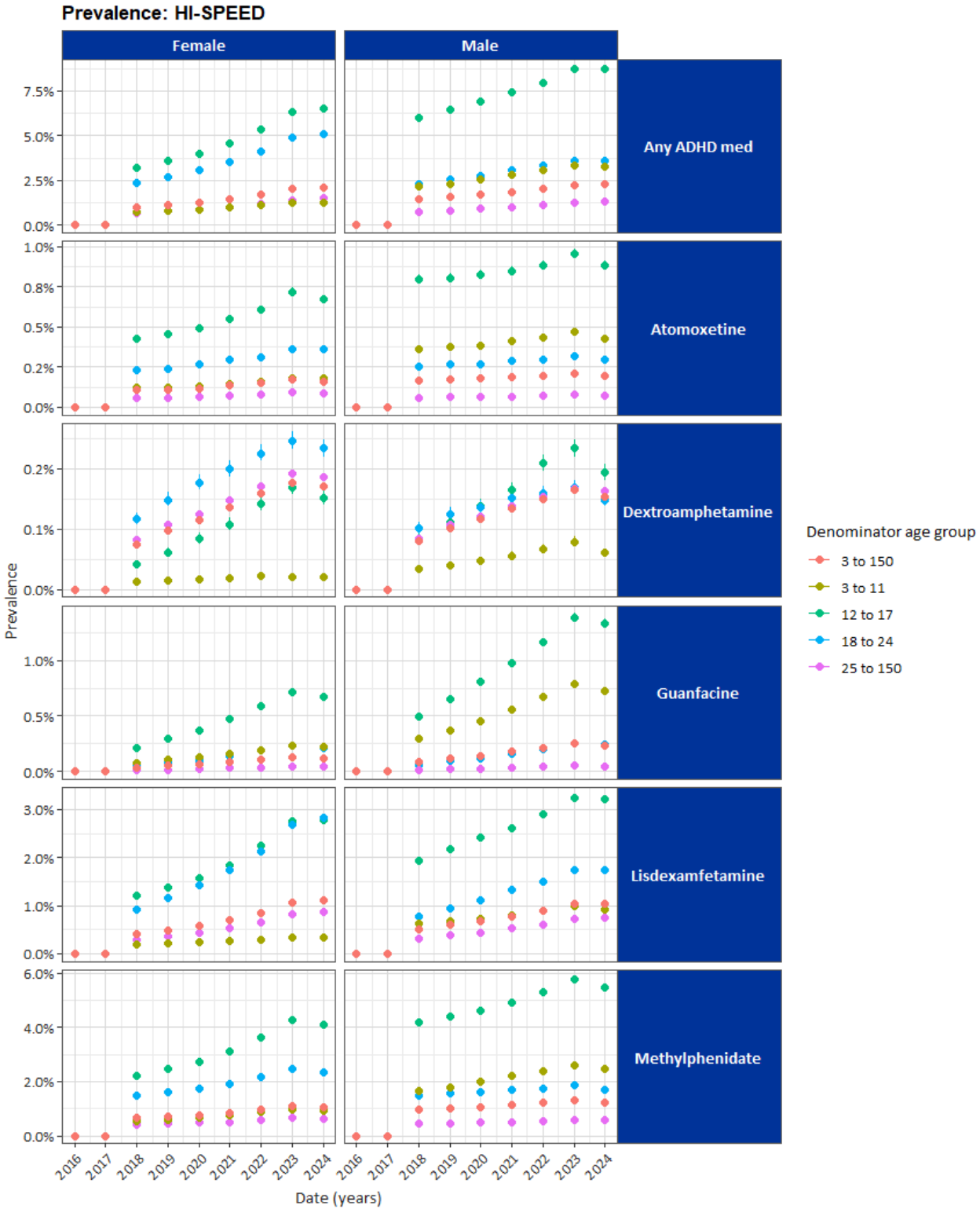

Figure 7. Yearly prevalence of ADHD medications by age groups and sex: HI-SPEED.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Among adults, the prevalence of any ADHD medication use increased across all data sources for both males and females. In DK-DHR, prevalence rose steadily throughout the study period, particularly among females. Among those aged 18-24 years, prevalence was higher in males than females between 2010 and 2021, but the pattern reversed thereafter. Among adults aged 25 years and older, prevalence was higher in females by 2024. In InGef RDB, prevalence increased continuously from 2016, when data became available. A sharp rise was observed among females aged 18-24 years after 2020. Although prevalence remained higher among males overall, the difference between sexes narrowed over time. In NLHR, prevalence increased from 2018 onward, with females showing higher rates than males from 2021 among those aged 18-24 years, and from 2022 among those aged 25 years and older. In BIFAP, prevalence among both males and females increased from 2010 to 2024. In SIDIAP, prevalence increased in both males and females, with consistently higher levels observed among males. In HI-SPEED, prevalence rose in both sexes since 2018. Among individuals aged 18-24 years, females had higher prevalence than males throughout the study period, and this pattern extended to older age groups from 2022 onward.

Trends in the use of individual study medications, particularly methylphenidate and lisdexamfetamine, were similar to those observed for overall ADHD medication use.

9.2.2. Objective 2: incidence

In NLHR and HI-SPEED, data were only available from 2018 onwards. Because a one-year washout period was applied to define incident use, incidence rates were calculated starting from 2019. **Figure 8** presents the incidence rates of ADHD medication use over the study period.

Among all data sources, the highest incidence rates of any ADHD medication use were observed in DK-DHR between 2010 and 2018. From 2019, when data became available for all six data sources, the highest incidence rates were seen in HI-SPEED from 2019 to 2022, and in DK-DHR from 2023 to 2024.

Trends in incidence rates of any ADHD medication use varied between data sources. In DK-DHR, rates decreased slightly from 2010 to 2016 and then increased, particularly after 2020. In InGef RDB, incidence rose modestly between 2016 and 2020, followed by a sharper increase from 2021 onwards. In NLHR, incidence increased steadily from 2019, when data became available. In BIFAP, rates remained stable between 2010 and 2021 and then increased thereafter. In SIDIAP, incidence increased from 2010 to 2014, declined until 2020, and rose again until 2023. In HI-SPEED, incidence increased steadily from 2019 to 2023.

Across all data sources, incidence rates of methylphenidate were the highest among the five study medications throughout the study period. In DK-DHR, lisdexamfetamine overtook atomoxetine between 2018 and 2019, becoming the second most commonly initiated medication. In InGef RDB, since data became available in 2016, lisdexamfetamine has been the second most frequently initiated medication. In NLHR, a similar pattern was observed, with lisdexamfetamine ranking second since 2019. In BIFAP, lisdexamfetamine surpassed atomoxetine in 2015 and has remained the second most commonly initiated medication thereafter. In SIDIAP, similar to BIFAP, lisdexamfetamine surpassed atomoxetine in 2015 and has remained the second most commonly initiated medication thereafter. In HI-SPEED, lisdexamfetamine has also been the second most initiated medication since data became available in 2019.

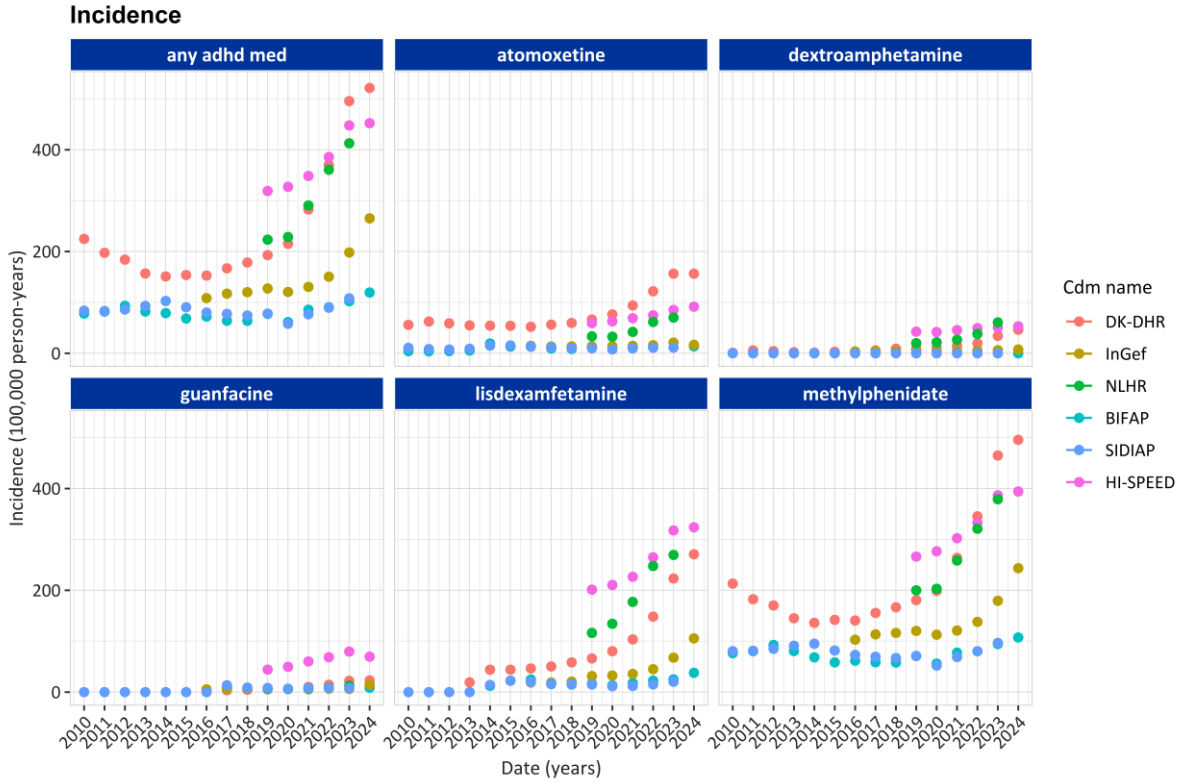

Figure 8. Yearly incidence rates of ADHD medication use by data source.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Figures 9 to 14 present the yearly incidence rates of ADHD medication use stratified by age group and sex. Monthly incidence rates are available in the accompanying online Shiny app.

Among children and adolescents aged 3-17 years, trends of incidence rates of any ADHD medication use varied across data sources before 2020, but incidence increased in all data sources from 2020 onwards.

In DK-DHR, incidence increased among both sexes aged 3–11 years, with higher rates in males. Among adolescents aged 12–17 years, incidence rose in both sexes from 2013, and rates became higher in females from 2021. In InGef RDB, incidence increased in both sexes, remaining higher in males than females. Boys aged 3–11 years had higher incidence rates compared with other child and adolescent groups. In NLHR, incidence increased across all age groups, with the sharpest rise observed among females aged 12–17 years, who showed the highest rates by 2023. In BIFAP, incidence declined between 2012 and 2020, followed by an increase thereafter. In SIDIAP, incidence increased among adolescents aged 12–17 years between 2010 and 2014, declined for all groups aged 3-17 years until 2020, and rose again after 2020. In HI-SPEED, incidence increased from 2019, particularly among females aged 12–17 years, who reached the highest rates by 2024.

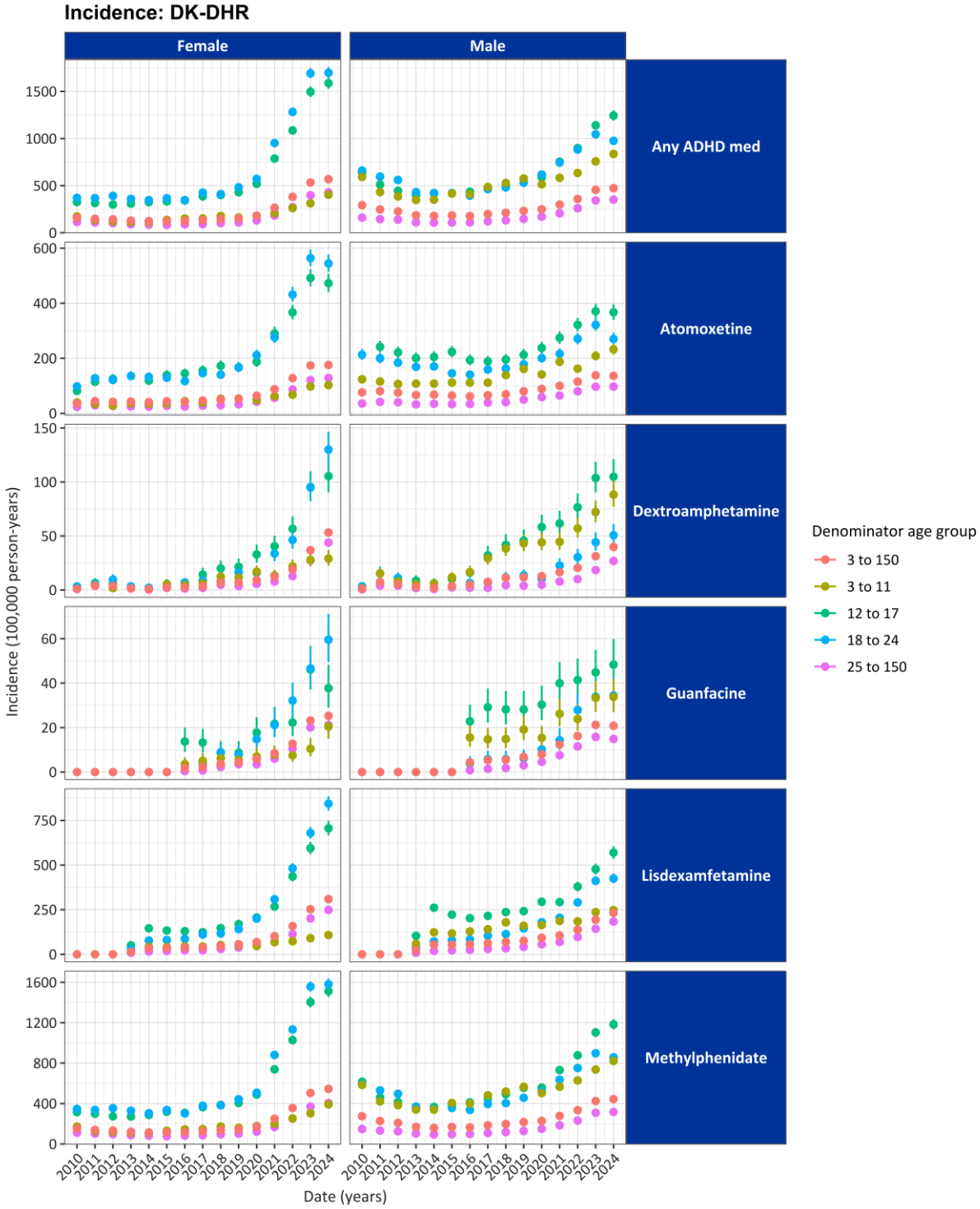

Figure 9. Yearly incidence rates of ADHD medication use by age groups and sex: DK-DHR.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; DK-DHR=Danish Data Health Registries.

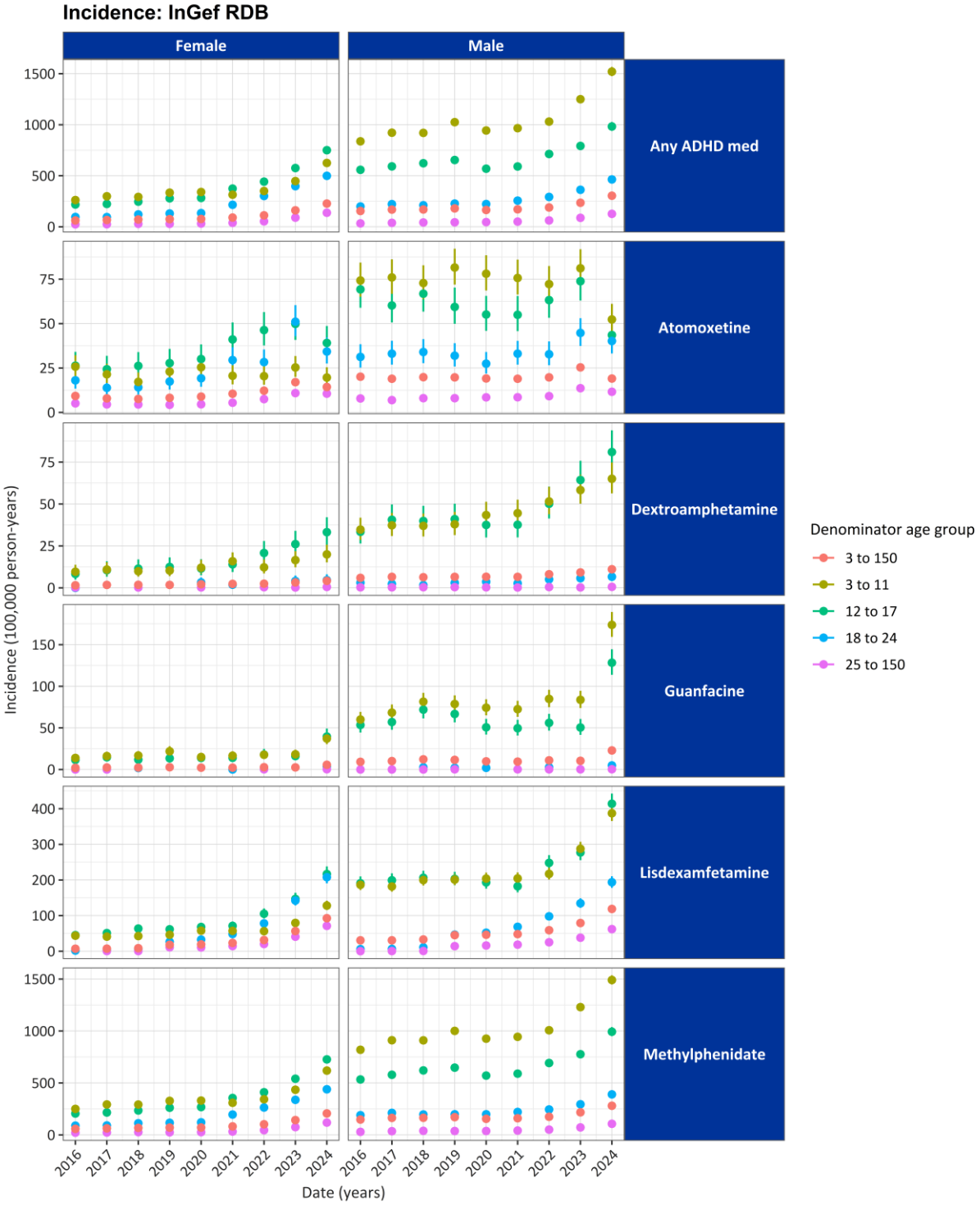

Figure 10. Yearly incidence rates of ADHD medication use by age groups and sex: InGef RDB.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; InGef=InGef Research Database.

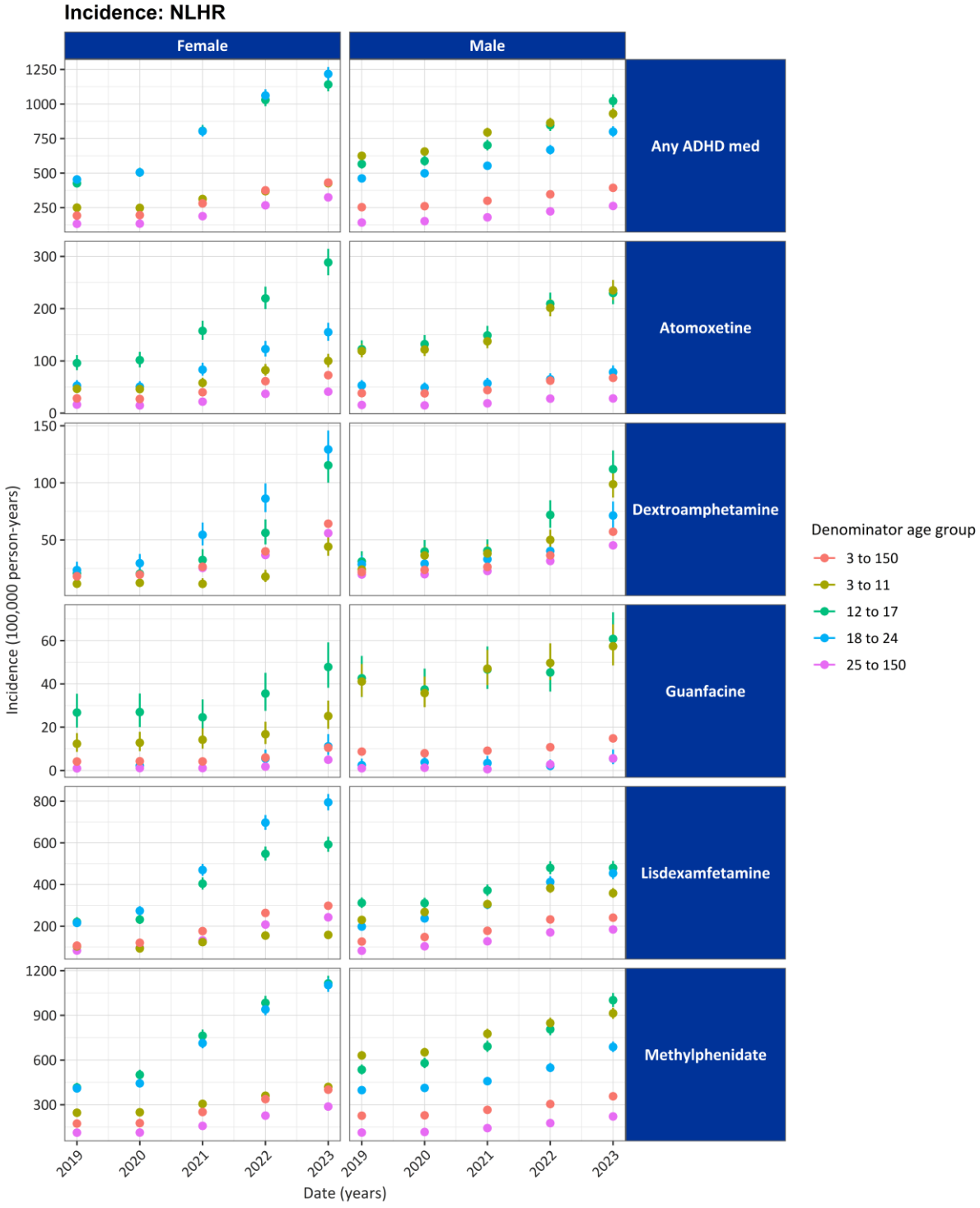

Figure 11. Yearly incidence rates of ADHD medication use by age groups and sex: NLHR.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; NLHR=Norwegian Linked Health Registry data.

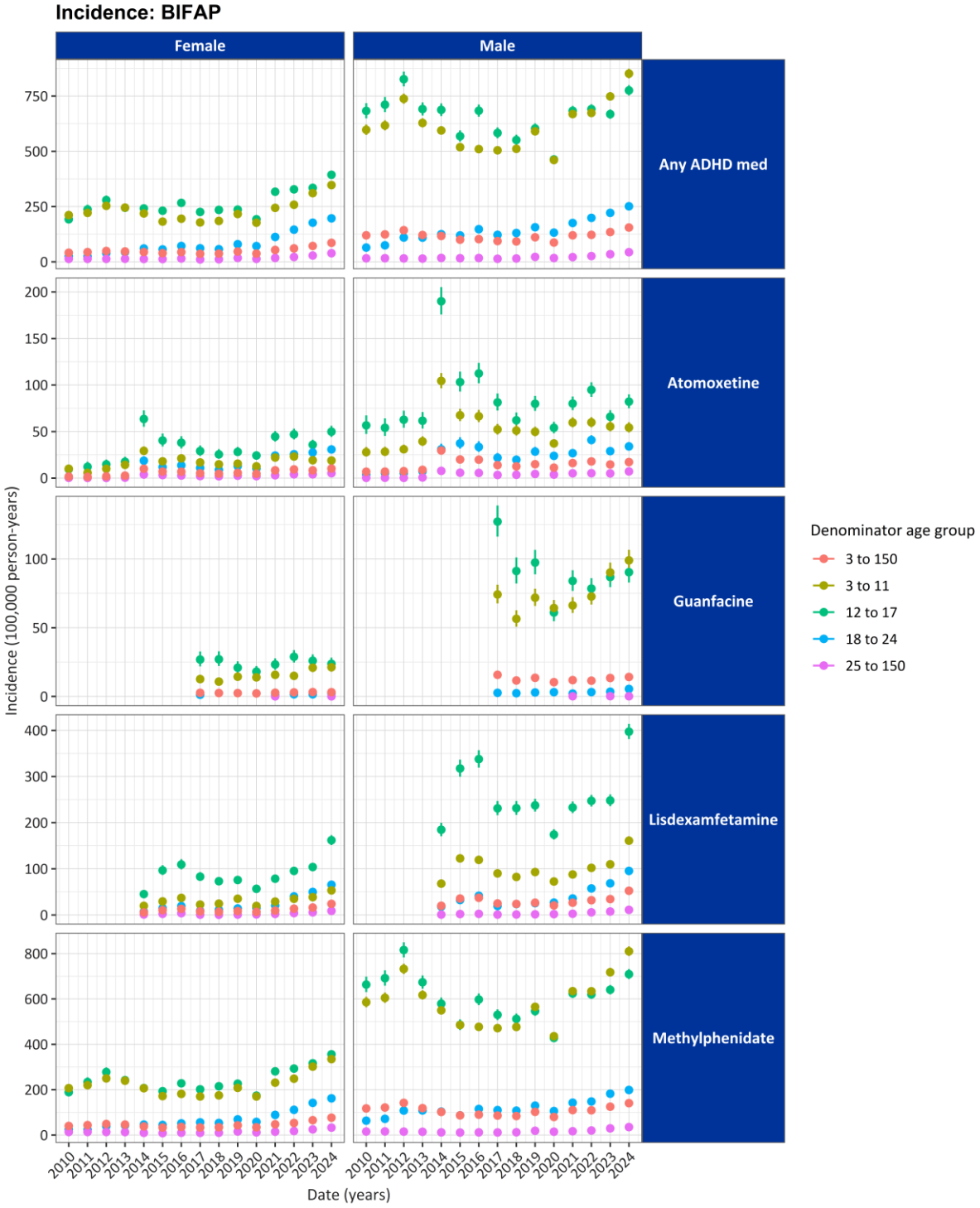

Figure 12. Yearly incidence rates of ADHD medication use by age groups and sex: BIFAP.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público.

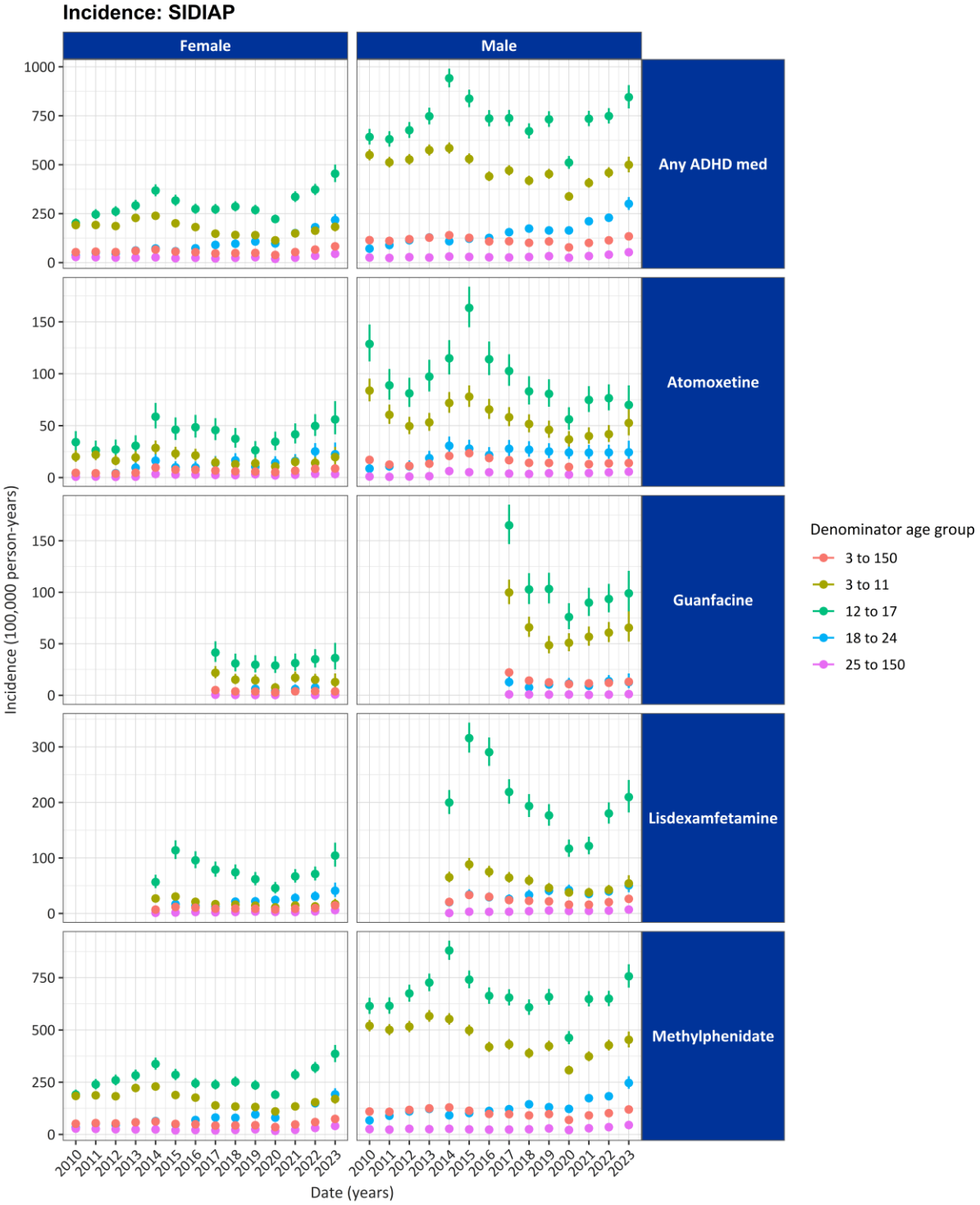

Figure 13. Yearly incidence rates of ADHD medication use by age groups and sex: SIDIAP.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; SIDIAP=The Information System for Research on Primary Care.

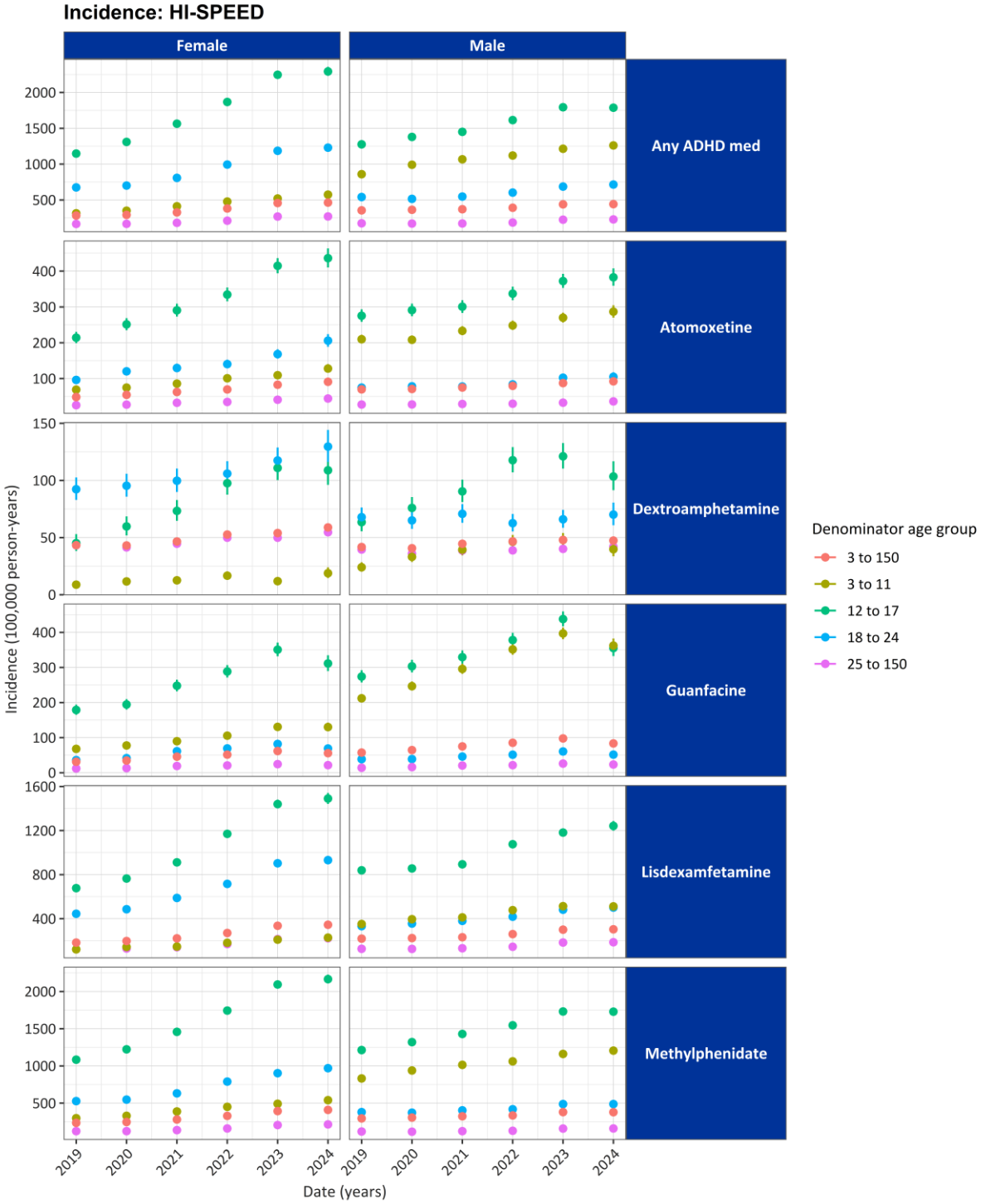

Figure 14. Yearly incidence rates of ADHD medication use by age groups and sex: HI-SPEED.

Any ADHD med= Any Attention-Deficit Hyperactivity Disorder medication; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Among adults, incidence rates of any ADHD medication use increased across all six data sources during the study period. By the end of the study period, rates were higher in females than in males in four data sources (DK-DHR, InGef RDB, NLHR, and HI-SPEED).

In DK-DHR, a sharp rise in incidence rates was observed among females aged 18–24 years after 2022. By 2024, incidence rates were higher in females than in males in both the 18–24 and 25+ age groups. In InGef RDB, rates became higher in females from 2022 among those aged 18–24 years, and from 2024 among adults aged 25 years and older. In NLHR, a marked increase occurred among females aged 18–24 years after 2020, with higher rates observed in females in both age groups by the end of data collection in 2023. In BIFAP, incidence increased in both sexes, particularly after 2020. In SIDIAP, similar increases were seen in both males and females, especially after 2020. In HI-SPEED, incidence rose in both sexes from 2019, with higher rates among females since 2019 in the 18–24-year group and since 2022 among those aged 25 years and older.

When examining individual study medications among adults, trends in incidence rates were broadly consistent with those observed for any ADHD medication use, showing increases across all data sources over time. This pattern suggests that the overall rise in ADHD medication use was not driven by a single product but reflected a general increase across multiple treatments. Notably, for guanfacine, which was approved only for individuals aged 6–17 years, incidence rates also increased among adults in all data sources during the study period.

9.2.3. Objective 3: characteristics and potential indications among initiators.

Tables 3 to 9 present the baseline characteristics of individuals who initiated any ADHD medication, as well as those who initiated one of the specific medications of interest during the study period.

Initiators were generally younger in BIFAP, InGef RDB, and SIDIAP compared with the Scandinavian data sources. The median (IQR) age at initiation was 24 [16–36] years in DK-DHR, 15 [9–27] in InGef RDB, 23 [14–34] in NLHR, 13 [9–19] in BIFAP, 14 [10–23] in SIDIAP, and 20 [13–32] in HI-SPEED. Across all data sources, a higher proportion of initiators were male compared with female. The proportion of males ranged from 53.96% in HI-SPEED to 67.97 in BIFAP. Specifically, the proportion of male initiators was 54.47% in DK-DHR, 64.31% in InGef RDB, 54.34% in NLHR, 67.97% in BIFAP, 67.29% in SIDIAP, and 53.96% in HI-SPEED.

The most common comorbidities among initiators were anxiety and depression, which were consistently observed across most data sources. Asthma was also frequent in DK-DHR, NLHR, and BIFAP, while obesity was more common in SIDIAP. The most commonly prescribed medications during the six months prior to ADHD medication initiation included antibacterials, antidepressants, psycholeptics, and anti-inflammatory drugs.

Among initiators of any ADHD medication, defined using a 365-day washout period, the proportion of individuals with previous ADHD medication use varied across data sources. The proportion was 21.79% in DK-DHR, 18.02% in InGef RDB, 10.69% in NLHR, 21.95% in BIFAP, 21.57% in SIDIAP, and 12.25% in HI-SPEED.

Among initiators of each specific study medication, the proportion of individuals with previous ADHD medication use varied across medications and data sources. In DK-DHR, over 95% of dextroamphetamine, guanfacine, and lisdexamfetamine initiators had used ADHD medications previously, compared with 75.18% of atomoxetine initiators and 23.89% of methylphenidate initiators. In InGef RDB, prior ADHD medication use was reported in 64.57% of atomoxetine initiators, 93.91% of dextroamphetamine initiators, 88.48% of guanfacine initiators, 83.04% of lisdexamfetamine initiators, and 21.36% of methylphenidate initiators. In NLHR, the corresponding proportions were 72.77% for atomoxetine, 78.39% for dextroamphetamine, 86.48% for guanfacine, 76.14% for lisdexamfetamine, and 13.82% for methylphenidate. In BIFAP, 57.27% of atomoxetine, 80.81% of guanfacine, 84.83% of lisdexamfetamine, and 23.69% of methylphenidate initiators had previously used ADHD medication. In SIDIAP, the proportions were 59.76% for atomoxetine, 77.50% for guanfacine, 81.37% for lisdexamfetamine, and 22.86% for

methylphenidate. In HI-SPEED, prior ADHD medication use was observed in 65.21% of atomoxetine initiators, 85.91% of dextroamphetamine initiators, 82.42% of guanfacine initiators, 67.97% of lisdexamfetamine initiators, and 19.37% of methylphenidate initiators.

We also examined the characteristics of children aged 3–5 years who initiated ADHD medication (**Table 10**). In all six data sources, incident user aged 3–5 represents a very small proportion of all incident users, ranging from 0.34% in NLHR to 2.06% in BIFAP. The median (IQR) age at initiation was 5 (5–5) years across all six data sources. The proportion of male initiators ranged from 77.31% in DK-DHR to 82.89% in BIFAP. Asthma was overall the most commonly observed comorbidity in this age group.

Table 3. Characteristics of incident user of any ADHD medication during study period, by data source.

Variable name	Variable level	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Number records	-	N	233,432	105,002	138,369	200,854	76,316	375,075
Number subjects	-	N	193,612	94,057	123,611	169,797	63,528	329,211
Age	-	Median [Q25 – Q75]	24 [16 – 36]	15 [9 – 27]	23 [14 – 34]	13 [9 – 19]	14 [10 – 23]	20 [13 – 32]
Sex	Female	N (%)	106,289 (45.53%)	37,479 (35.69%)	63,181 (45.66%)	64,328 (32.03%)	24,965 (32.71%)	172,687 (46.04%)
	Male	N (%)	127,143 (54.47%)	67,523 (64.31%)	75,188 (54.34%)	136,526 (67.97%)	51,351 (67.29%)	202,388 (53.96%)
Days in cohort	-	Median [Q25 – Q75]	138 [41 – 384]	66 [30 – 127]	180 [67 – 525]	80 [31 – 192]	233 [85 – 586]	159 [62 – 412]
Comorbidity	Anxiety disorder	N (%)	61,653 (26.41%)	10,335 (9.84%)	57,939 (41.87%)	20,194 (10.05%)	13,203 (17.30%)	134,871 (35.96%)
	Asthma	N (%)	68,509 (29.35%)	2,676 (2.55%)	32,704 (23.64%)	32,792 (16.33%)	6,535 (8.56%)	36,196 (9.65%)
	Chronic liver disease	N (%)	1,446 (0.62%)	208 (0.20%)	2,006 (1.45%)	310 (0.15%)	429 (0.56%)	6,924 (1.85%)
	Chronic obstructive pulmonary disease	N (%)	4,434 (1.90%)	429 (0.41%)	2,476 (1.79%)	839 (0.42%)	693 (0.91%)	1,159 (0.31%)
	Colitis	N (%)	2,011 (0.86%)	144 (0.14%)	758 (0.55%)	195 (0.10%)	94 (0.12%)	1,292 (0.34%)
	Crohn's disease	N (%)	1,333 (0.57%)	235 (0.22%)	708 (0.51%)	144 (0.07%)	100 (0.13%)	1,270 (0.34%)
	Depression	N (%)	77,820 (33.34%)	17,904 (17.05%)	29,774 (21.52%)	11,161 (5.56%)	7,281 (9.54%)	93,672 (24.97%)
	Diabetes mellitus	N (%)	7,011 (3.00%)	1,069 (1.02%)	3,817 (2.76%)	2,403 (1.20%)	1,508 (1.98%)	8,158 (2.18%)
	Gastro-esophageal reflux disease	N (%)	3,685 (1.58%)	438 (0.42%)	5,982 (4.32%)	4,862 (2.42%)	1,632 (2.14%)	4,877 (1.30%)
	Gastrointestinal hemorrhage	N (%)	4,633 (1.98%)	388 (0.37%)	7,926 (5.73%)	3,026 (1.51%)	1,238 (1.62%)	4,722 (1.26%)
	Hepatitis	N (%)	1,537 (0.66%)	185 (0.18%)	2,512 (1.82%)	721 (0.36%)	604 (0.79%)	6,935 (1.85%)
	Human immunodeficiency virus infection	N (%)	194 (0.08%)	45 (0.04%)	117 (0.08%)	216 (0.11%)	164 (0.21%)	262 (0.07%)

Variable name	Variable level	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
	Hyperlipidemia	N (%)	8,853 (3.79%)	863 (0.82%)	812 (0.59%)	6,722 (3.35%)	3,661 (4.80%)	2,561 (0.68%)
	Hypertension	N (%)	11,257 (4.82%)	2,725 (2.60%)	7,972 (5.76%)	3,933 (1.96%)	3,072 (4.03%)	10,651 (2.84%)
	Malignancy	N (%)	8,685 (3.72%)	792 (0.75%)	2,341 (1.69%)	2,594 (1.29%)	2,452 (3.21%)	3,345 (0.89%)
	Obesity	N (%)	20,198 (8.65%)	3,908 (3.72%)	12,081 (8.73%)	9,960 (4.96%)	8,102 (10.62%)	23,197 (6.18%)
	Osteoarthritis	N (%)	9,959 (4.27%)	1,036 (0.99%)	3,780 (2.73%)	3,547 (1.77%)	2,262 (2.96%)	7,601 (2.03%)
	Parkinson's disease	N (%)	494 (0.21%)	17 (0.02%)	109 (0.08%)	186 (0.09%)	218 (0.29%)	69 (0.02%)
	Pneumonia	N (%)	55,942 (23.97%)	1,331 (1.27%)	15,510 (11.21%)	15,382 (7.66%)	7,202 (9.44%)	8,781 (2.34%)
	Psoriasis	N (%)	9,315 (3.99%)	290 (0.28%)	5,001 (3.61%)	1,278 (0.64%)	679 (0.89%)	3,580 (0.95%)
	Renal impairment	N (%)	983 (0.42%)	418 (0.40%)	717 (0.52%)	5,895 (2.93%)	805 (1.05%)	1,505 (0.40%)
	Schizophrenia	N (%)	4,493 (1.92%)	542 (0.52%)	1,412 (1.02%)	319 (0.16%)	315 (0.41%)	917 (0.24%)
	Urinary tract infection	N (%)	39,314 (16.84%)	1,144 (1.09%)	5,103 (3.69%)	20,393 (10.15%)	6,423 (8.42%)	13,383 (3.57%)
Medications	Acid-related disorder drugs	N (%)	26,455 (11.33%)	7,836 (7.46%)	9,733 (7.03%)	17,293 (8.61%)	7,762 (10.17%)	21,430 (5.71%)
	Agents acting on the renin-angiotensin system	N (%)	8,159 (3.50%)	3,008 (2.86%)	2,737 (1.98%)	4,444 (2.21%)	2,555 (3.35%)	8,142 (2.17%)
	Anti-inflammatory and antirheumatic products	N (%)	37,255 (15.96%)	31,952 (30.43%)	19,372 (14.00%)	73,638 (36.66%)	25,502 (33.42%)	29,359 (7.83%)
	Antibacterials	N (%)	70,873 (30.36%)	30,385 (28.94%)	23,547 (17.02%)	59,779 (29.76%)	17,565 (23.02%)	50,514 (13.47%)
	Antidepressants	N (%)	57,549 (24.65%)	18,884 (17.98%)	18,432 (13.32%)	21,685 (10.80%)	13,271 (17.39%)	93,823 (25.01%)
	Antiepileptics	N (%)	19,116 (8.19%)	2,749 (2.62%)	5,706 (4.12%)	11,399 (5.68%)	7,531 (9.87%)	20,960 (5.59%)
	Antineoplastic agents	N (%)	4,455 (1.91%)	2,851 (2.72%)	848 (0.61%)	961 (0.48%)	372 (0.49%)	2,179 (0.58%)
	Antipsoriatics	N (%)	256 (0.11%)	246 (0.23%)	23 (0.02%)	356 (0.18%)	54 (0.07%)	59 (0.02%)
	Antithrombotic agents	N (%)	6,261 (2.68%)	1,826 (1.74%)	1,809 (1.31%)	4,308 (2.14%)	1,234 (1.62%)	3,348 (0.89%)
	Beta blocking agents	N (%)	5,419 (2.32%)	1,838 (1.75%)	2,117 (1.53%)	2,282 (1.14%)	1,308 (1.71%)	10,033 (2.67%)

Variable name	Variable level	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
	Calcium channel blockers	N (%)	4,766 (2.04%)	965 (0.92%)	864 (0.62%)	1,308 (0.65%)	838 (1.10%)	5,000 (1.33%)
	Diuretics	N (%)	5,492 (2.35%)	718 (0.68%)	688 (0.50%)	2,143 (1.07%)	1,317 (1.73%)	3,651 (0.97%)
	Drugs used in diabetes	N (%)	6,711 (2.87%)	1,164 (1.11%)	3,043 (2.20%)	2,913 (1.45%)	1,377 (1.80%)	6,906 (1.84%)
	Immunosuppressants	N (%)	2,352 (1.01%)	941 (0.90%)	1,051 (0.76%)	408 (0.20%)	265 (0.35%)	2,570 (0.69%)
	Lipid modifying agents	N (%)	6,984 (2.99%)	1,014 (0.97%)	2,077 (1.50%)	4,984 (2.48%)	2,655 (3.48%)	4,004 (1.07%)
	Obstetrical agents	N (%)	32,739 (14.03%)	17,331 (16.51%)	19,977 (14.44%)	20,421 (10.17%)	10,447 (13.69%)	46,359 (12.36%)
	Opioids	N (%)	20,220 (8.66%)	3,605 (3.43%)	14,439 (10.44%)	10,960 (5.46%)	4,196 (5.50%)	18,447 (4.92%)
	Psycholeptics	N (%)	62,330 (26.70%)	10,179 (9.69%)	34,140 (24.67%)	35,708 (17.78%)	17,073 (22.37%)	121,438 (32.38%)
	Psychostimulants	N (%)	1,804 (0.77%)	334 (0.32%)	608 (0.44%)	1,579 (0.79%)	560 (0.73%)	3,365 (0.90%)
Other ADHD medications	Any ADHD medications	N (%)	50,856 (21.79%)	18,919 (18.02%)	14,796 (10.69%)	44,082 (21.95%)	16,458 (21.57%)	45,938 (12.25%)
	Atomoxetine	N (%)	16,628 (7.12%)	2,035 (1.94%)	1,814 (1.31%)	4,733 (2.36%)	2,060 (2.70%)	7,174 (1.91%)
	Dextroamphetamine	N (%)	1,114 (0.48%)	437 (0.42%)	907 (0.66%)	0 (0.00%)	0 (0.00%)	3,943 (1.05%)
	Guanfacine	N (%)	377 (0.16%)	381 (0.36%)	212 (0.15%)	960 (0.48%)	395 (0.52%)	3,427 (0.91%)
	Lisdexamfetamine	N (%)	6,719 (2.88%)	2,691 (2.56%)	4,066 (2.94%)	4,666 (2.32%)	1,307 (1.71%)	22,673 (6.04%)
	Methylphenidate	N (%)	47,605 (20.39%)	17,569 (16.73%)	12,477 (9.02%)	41,192 (20.51%)	15,564 (20.39%)	32,428 (8.65%)
Stimulants	Any stimulant med	N (%)	48,003 (20.56%)	18,262 (17.39%)	14,188 (10.25%)	42,265 (21.04%)	15,748 (20.64%)	43,365 (11.56%)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 4. Characteristics of incident user of each ADHD medication during study period: DK-DHR.

Variable name	Variable level	Estimate name	CDM name DK-DHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	70,713	10,117	5,266	66,747	213,454
Number subjects	-	N	63,576	9,209	5,104	62,073	180,889
Age	-	Median [Q25 – Q75]	23 [16 – 33]	22 [13 – 35]	25 [15 – 37]	24 [16 – 35]	24 [16 – 36]
Sex	Female	N (%)	32,105 (45.40%)	4,815 (47.59%)	2,445 (46.43%)	33,298 (49.89%)	98,641 (46.21%)
	Male	N (%)	38,608 (54.60%)	5,302 (52.41%)	2,821 (53.57%)	33,449 (50.11%)	114,813 (53.79%)
Days in cohort	-	Median [Q25 – Q75]	69 [21 – 170]	20 [10 – 74]	72 [9 – 212]	149 [50 – 402]	99 [33 – 275]
Comorbidity	Anxiety disorder	N (%)	22,817 (32.27%)	2,807 (27.75%)	1,933 (36.71%)	19,816 (29.69%)	54,195 (25.39%)
	Asthma	N (%)	22,267 (31.49%)	3,578 (35.37%)	1,859 (35.30%)	21,617 (32.39%)	63,113 (29.57%)
	Chronic liver disease	N (%)	524 (0.74%)	34 (0.34%)	24 (0.46%)	255 (0.38%)	1,189 (0.56%)
	Chronic obstructive pulmonary disease	N (%)	1,207 (1.71%)	168 (1.66%)	101 (1.92%)	973 (1.46%)	4,006 (1.88%)
	Colitis	N (%)	577 (0.82%)	77 (0.76%)	58 (1.10%)	627 (0.94%)	1,825 (0.85%)
	Crohn's disease	N (%)	400 (0.57%)	65 (0.64%)	39 (0.74%)	398 (0.60%)	1,230 (0.58%)
	Depression	N (%)	26,608 (37.63%)	3,286 (32.48%)	2,186 (41.51%)	23,369 (35.01%)	69,224 (32.43%)
	Diabetes mellitus	N (%)	1,784 (2.52%)	270 (2.67%)	212 (4.03%)	1,928 (2.89%)	6,419 (3.01%)
	Gastro-esophageal reflux disease	N (%)	1,188 (1.68%)	217 (2.14%)	139 (2.64%)	1,221 (1.83%)	3,345 (1.57%)

Variable name	Variable level	Estimate name	CDM name DK-DHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Gastrointestinal hemorrhage	N (%)	1,477 (2.09%)	159 (1.57%)	132 (2.51%)	1,245 (1.87%)	4,077 (1.91%)
	Hepatitis	N (%)	572 (0.81%)	47 (0.46%)	30 (0.57%)	317 (0.47%)	1,266 (0.59%)
	Human immunodeficiency virus infection	N (%)	56 (0.08%)	5 (0.05%)	<5	52 (0.08%)	168 (0.08%)
	Hyperlipidemia	N (%)	2,005 (2.84%)	288 (2.85%)	228 (4.33%)	1,954 (2.93%)	8,137 (3.81%)
	Hypertension	N (%)	2,678 (3.79%)	481 (4.75%)	387 (7.35%)	3,002 (4.50%)	10,437 (4.89%)
	Malignancy	N (%)	751 (1.06%)	143 (1.41%)	67 (1.27%)	911 (1.36%)	8,412 (3.94%)
	Obesity	N (%)	5,983 (8.46%)	879 (8.69%)	521 (9.89%)	6,432 (9.64%)	18,640 (8.73%)
	Osteoarthritis	N (%)	2,744 (3.88%)	346 (3.42%)	242 (4.60%)	2,597 (3.89%)	9,059 (4.24%)
	Parkinson's disease	N (%)	155 (0.22%)	15 (0.15%)	18 (0.34%)	97 (0.15%)	452 (0.21%)
	Pneumonia	N (%)	16,815 (23.78%)	2,646 (26.15%)	1,474 (27.99%)	17,055 (25.55%)	51,368 (24.07%)
	Psoriasis	N (%)	2,833 (4.01%)	409 (4.04%)	261 (4.96%)	2,916 (4.37%)	8,411 (3.94%)
	Renal impairment	N (%)	224 (0.32%)	27 (0.27%)	31 (0.59%)	191 (0.29%)	865 (0.41%)
	Schizophrenia	N (%)	2,114 (2.99%)	120 (1.19%)	153 (2.91%)	1,149 (1.72%)	3,376 (1.58%)
	Urinary tract infection	N (%)	11,874 (16.79%)	1,791 (17.70%)	1,063 (20.19%)	13,069 (19.58%)	36,142 (16.93%)
Medications	Acid-related disorder drugs	N (%)	7,581 (10.72%)	939 (9.28%)	654 (12.42%)	6,595 (9.88%)	24,099 (11.29%)
	Agents acting on the renin-angiotensin system	N (%)	1,907 (2.70%)	352 (3.48%)	299 (5.68%)	2,172 (3.25%)	7,637 (3.58%)
	Anti-inflammatory and antirheumatic products	N (%)	11,786 (16.67%)	1,497 (14.80%)	910 (17.28%)	10,431 (15.63%)	33,729 (15.80%)

Variable name	Variable level	Estimate name	CDM name DK-DHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Antibacterials	N (%)	21,495 (30.40%)	2,742 (27.10%)	1,486 (28.22%)	18,816 (28.19%)	64,638 (30.28%)
	Antidepressants	N (%)	19,913 (28.16%)	2,534 (25.05%)	1,690 (32.09%)	17,241 (25.83%)	51,922 (24.32%)
	Antiepileptics	N (%)	6,878 (9.73%)	970 (9.59%)	727 (13.81%)	5,582 (8.36%)	17,096 (8.01%)
	Antineoplastic agents	N (%)	272 (0.38%)	54 (0.53%)	22 (0.42%)	294 (0.44%)	4,358 (2.04%)
	Antipsoriatics	N (%)	73 (0.10%)	17 (0.17%)	8 (0.15%)	99 (0.15%)	231 (0.11%)
	Antithrombotic agents	N (%)	1,088 (1.54%)	168 (1.66%)	89 (1.69%)	1,057 (1.58%)	5,860 (2.75%)
	Beta blocking agents	N (%)	1,494 (2.11%)	289 (2.86%)	205 (3.89%)	1,519 (2.28%)	5,069 (2.37%)
	Calcium channel blockers	N (%)	1,132 (1.60%)	205 (2.03%)	187 (3.55%)	1,205 (1.81%)	4,451 (2.09%)
	Diuretics	N (%)	915 (1.29%)	153 (1.51%)	100 (1.90%)	866 (1.30%)	5,192 (2.43%)
	Drugs used in diabetes	N (%)	1,598 (2.26%)	300 (2.97%)	208 (3.95%)	2,082 (3.12%)	6,161 (2.89%)
	Immunosuppressants	N (%)	586 (0.83%)	114 (1.13%)	60 (1.14%)	657 (0.98%)	2,171 (1.02%)
	Lipid modifying agents	N (%)	1,580 (2.23%)	232 (2.29%)	183 (3.48%)	1,574 (2.36%)	6,443 (3.02%)
	Obstetrical agents	N (%)	10,229 (14.47%)	1,722 (17.02%)	950 (18.04%)	10,710 (16.05%)	30,292 (14.19%)
	Opioids	N (%)	4,928 (6.97%)	549 (5.43%)	304 (5.77%)	3,902 (5.85%)	18,471 (8.65%)
	Psycholeptics	N (%)	29,079 (41.12%)	4,570 (45.17%)	3,022 (57.39%)	25,417 (38.08%)	56,396 (26.42%)
	Psychostimulants	N (%)	43,344 (61.30%)	9,364 (92.56%)	4,752 (90.24%)	58,138 (87.10%)	18,413 (8.63%)
Other ADHD medications	Any ADHD medications	N (%)	53,162 (75.18%)	9,951 (98.36%)	5,115 (97.13%)	64,413 (96.50%)	50,994 (23.89%)

Variable name	Variable level	Estimate name	CDM name DK-DHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Atomoxetine	N (%)	7,997 (11.31%)	3,572 (35.31%)	3,837 (72.86%)	17,837 (26.72%)	22,508 (10.54%)
	Dextroamphetamine	N (%)	1,886 (2.67%)	959 (9.48%)	779 (14.79%)	1,782 (2.67%)	1,454 (0.68%)
	Guanfacine	N (%)	549 (0.78%)	522 (5.16%)	165 (3.13%)	691 (1.04%)	960 (0.45%)
	Lisdexamfetamine	N (%)	13,824 (19.55%)	7,202 (71.19%)	3,891 (73.89%)	4,678 (7.01%)	9,479 (4.44%)
	Methylphenidate	N (%)	51,341 (72.60%)	9,658 (95.46%)	4,725 (89.73%)	63,063 (94.48%)	42,122 (19.73%)
Stimulants	Any stimulants	N (%)	51,778 (73.22%)	9,928 (98.13%)	4,899 (93.03%)	63,317 (94.86%)	43,156 (20.22%)

DK-DHR=Danish Data Health Registries.

Table 5. Characteristics of incident user of each ADHD medication during study period: InGef RDB.

Variable name	Variable level	Estimate name	CDM name InGef RDB Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	10,190	3,333	4,878	28,373	97,986
Number subjects	-	N	9,781	3,114	4,646	26,690	87,827
Age	-	Median [Q25 – Q75]	19 [11 – 33]	11 [9 – 14]	10 [8 – 13]	16 [11 – 31]	14 [9 – 26]
Sex	Female	N (%)	3,563 (34.97%)	812 (24.36%)	914 (18.74%)	9,948 (35.06%)	34,278 (34.98%)
	Male	N (%)	6,627 (65.03%)	2,521 (75.64%)	3,964 (81.26%)	18,425 (64.94%)	63,708 (65.02%)
Days in cohort	-	Median [Q25 – Q75]	62 [30 – 119]	30 [30 – 87]	100 [43 – 213]	71 [30 – 150]	61 [30 – 115]
Comorbidity	Anxiety disorder	N (%)	1,401 (13.75%)	214 (6.42%)	432 (8.86%)	3,494 (12.31%)	9,091 (9.28%)
	Asthma	N (%)	354 (3.47%)	97 (2.91%)	145 (2.97%)	871 (3.07%)	2,429 (2.48%)
	Chronic liver disease	N (%)	32 (0.31%)	<5	0 (0.00%)	64 (0.23%)	166 (0.17%)
	Chronic obstructive pulmonary disease	N (%)	68 (0.67%)	11 (0.33%)	14 (0.29%)	105 (0.37%)	359 (0.37%)
	Colitis	N (%)	17 (0.17%)	0 (0.00%)	5 (0.10%)	53 (0.19%)	121 (0.12%)
	Crohn's disease	N (%)	27 (0.26%)	5 (0.15%)	<5	69 (0.24%)	209 (0.21%)
	Depression	N (%)	2,763 (27.11%)	246 (7.38%)	408 (8.36%)	6,077 (21.42%)	15,360 (15.68%)
	Diabetes mellitus	N (%)	131 (1.29%)	14 (0.42%)	26 (0.53%)	354 (1.25%)	928 (0.95%)
	Gastro-esophageal reflux disease	N (%)	48 (0.47%)	10 (0.30%)	18 (0.37%)	143 (0.50%)	392 (0.40%)
	Gastrointestinal hemorrhage	N (%)	60 (0.59%)	<5	8 (0.16%)	129 (0.45%)	322 (0.33%)

Variable name	Variable level	Estimate name	CDM name InGef RDB Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Hepatitis	N (%)	24 (0.24%)	<5	0 (0.00%)	50 (0.18%)	150 (0.15%)
	Human immunodeficiency virus infection	N (%)	11 (0.11%)	0 (0.00%)	0 (0.00%)	19 (0.07%)	36 (0.04%)
	Hyperlipidemia	N (%)	138 (1.35%)	<5	11 (0.23%)	259 (0.91%)	729 (0.74%)
	Hypertension	N (%)	434 (4.26%)	21 (0.63%)	51 (1.05%)	913 (3.22%)	2,289 (2.34%)
	Malignancy	N (%)	90 (0.88%)	12 (0.36%)	22 (0.45%)	236 (0.83%)	709 (0.72%)
	Obesity	N (%)	483 (4.74%)	64 (1.92%)	150 (3.08%)	1,271 (4.48%)	3,394 (3.46%)
	Osteoarthritis	N (%)	143 (1.40%)	<5	5 (0.10%)	362 (1.28%)	884 (0.90%)
	Parkinson's disease	N (%)	<5	0 (0.00%)	0 (0.00%)	5 (0.02%)	15 (0.02%)
	Pneumonia	N (%)	128 (1.26%)	44 (1.32%)	87 (1.78%)	339 (1.19%)	1,245 (1.27%)
	Psoriasis	N (%)	45 (0.44%)	9 (0.27%)	<5	100 (0.35%)	243 (0.25%)
	Renal impairment	N (%)	53 (0.52%)	<5	6 (0.12%)	106 (0.37%)	354 (0.36%)
	Schizophrenia	N (%)	159 (1.56%)	12 (0.36%)	12 (0.25%)	144 (0.51%)	416 (0.42%)
	Urinary tract infection	N (%)	141 (1.38%)	19 (0.57%)	36 (0.74%)	357 (1.26%)	1,006 (1.03%)
Medications	Acid-related disorder drugs	N (%)	1,096 (10.76%)	107 (3.21%)	101 (2.07%)	2,306 (8.13%)	6,778 (6.92%)
	Agents acting on the renin-angiotensin system	N (%)	434 (4.26%)	21 (0.63%)	35 (0.72%)	1,062 (3.74%)	2,554 (2.61%)
	Anti-inflammatory and antirheumatic products	N (%)	3,138 (30.79%)	962 (28.86%)	1,529 (31.34%)	8,043 (28.35%)	30,011 (30.63%)
	Antibacterials	N (%)	3,090 (30.32%)	837 (25.11%)	1,164 (23.86%)	7,983 (28.14%)	28,083 (28.66%)
	Antidepressants	N (%)	2,773 (27.21%)	221 (6.63%)	202 (4.14%)	6,110 (21.53%)	16,357 (16.69%)

Variable name	Variable level	Estimate name	CDM name				
			InGef RDB				
			Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Antiepileptics	N (%)	444 (4.36%)	54 (1.62%)	118 (2.42%)	885 (3.12%)	2,337 (2.39%)
	Antineoplastic agents	N (%)	245 (2.40%)	110 (3.30%)	158 (3.24%)	754 (2.66%)	2,738 (2.79%)
	Antipsoriatics	N (%)	27 (0.26%)	6 (0.18%)	<5	72 (0.25%)	225 (0.23%)
	Antithrombotic agents	N (%)	232 (2.28%)	30 (0.90%)	33 (0.68%)	524 (1.85%)	1,610 (1.64%)
	Beta blocking agents	N (%)	286 (2.81%)	20 (0.60%)	35 (0.72%)	587 (2.07%)	1,604 (1.64%)
	Calcium channel blockers	N (%)	146 (1.43%)	9 (0.27%)	8 (0.16%)	341 (1.20%)	804 (0.82%)
	Diuretics	N (%)	90 (0.88%)	5 (0.15%)	6 (0.12%)	210 (0.74%)	622 (0.63%)
	Drugs used in diabetes	N (%)	145 (1.42%)	15 (0.45%)	30 (0.62%)	361 (1.27%)	1,002 (1.02%)
	Immunosuppressants	N (%)	95 (0.93%)	13 (0.39%)	15 (0.31%)	277 (0.98%)	844 (0.86%)
	Lipid modifying agents	N (%)	148 (1.45%)	6 (0.18%)	6 (0.12%)	329 (1.16%)	845 (0.86%)
	Obstetrical agents	N (%)	1,799 (17.65%)	543 (16.29%)	813 (16.67%)	4,758 (16.77%)	16,097 (16.43%)
	Opioids	N (%)	456 (4.47%)	73 (2.19%)	41 (0.84%)	1,069 (3.77%)	3,123 (3.19%)
	Psycholeptics	N (%)	2,038 (20.00%)	452 (13.56%)	1,211 (24.83%)	4,072 (14.35%)	8,987 (9.17%)
	Psychostimulants	N (%)	5,443 (53.42%)	2,872 (86.17%)	4,066 (83.35%)	20,511 (72.29%)	6,443 (6.58%)
Other ADHD medications	Any ADHD medications	N (%)	6,580 (64.57%)	3,130 (93.91%)	4,316 (88.48%)	23,562 (83.04%)	20,926 (21.36%)
	Atomoxetine	N (%)	645 (6.33%)	396 (11.88%)	869 (17.81%)	2,734 (9.64%)	3,858 (3.94%)
	Dextroamphetamine	N (%)	267 (2.62%)	270 (8.10%)	397 (8.14%)	846 (2.98%)	790 (0.81%)
	Guanfacine	N (%)	402 (3.95%)	316 (9.48%)	244 (5.00%)	956 (3.37%)	1,036 (1.06%)

Variable name	Variable level	Estimate name	CDM name InGef RDB Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Lisdexamfetamine	N (%)	1,933 (18.97%)	1,609 (48.27%)	2,059 (42.21%)	2,244 (7.91%)	5,506 (5.62%)
	Methylphenidate	N (%)	6,085 (59.72%)	2,850 (85.51%)	3,962 (81.22%)	22,670 (79.90%)	17,321 (17.68%)
Stimulants	Any stimulants	N (%)	6,342 (62.24%)	3,104 (93.13%)	4,213 (86.37%)	23,188 (81.73%)	19,067 (19.46%)

InGef RDB=InGef Research Database.

Table 6. Characteristics of incident user of each ADHD medication during study period: NLHR.

Variable name	Variable level	Estimate name	CDM name NLHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	16,459	12,284	2,589	59,688	118,925
Number subjects	-	N	15,836	11,340	2,533	56,233	107,262
Age	-	Median [Q25 – Q75]	17 [12 – 30]	31 [22 – 41]	12 [10 – 16]	26 [16 – 36]	22 [13 – 33]
Sex	Female	N (%)	7,574 (46.02%)	5,931 (48.28%)	881 (34.03%)	29,444 (49.33%)	54,667 (45.97%)
	Male	N (%)	8,885 (53.98%)	6,353 (51.72%)	1,708 (65.97%)	30,244 (50.67%)	64,258 (54.03%)
Days in cohort	-	Median [Q25 – Q75]	48 [15 – 118]	57 [21 – 241]	79 [26 – 236]	156 [60 – 418]	107 [43 – 319]
Comorbidity	Anxiety disorder	N (%)	6,647 (40.39%)	6,911 (56.26%)	650 (25.11%)	29,638 (49.65%)	47,274 (39.75%)
	Asthma	N (%)	4,316 (26.22%)	3,114 (25.35%)	779 (30.09%)	14,956 (25.06%)	28,448 (23.92%)
	Chronic liver disease	N (%)	153 (0.93%)	410 (3.34%)	13 (0.50%)	1,203 (2.02%)	1,072 (0.90%)
	Chronic obstructive pulmonary disease	N (%)	263 (1.60%)	339 (2.76%)	37 (1.43%)	1,210 (2.03%)	2,015 (1.69%)
	Colitis	N (%)	95 (0.58%)	105 (0.85%)	12 (0.46%)	371 (0.62%)	631 (0.53%)
	Crohn's disease	N (%)	95 (0.58%)	76 (0.62%)	5 (0.19%)	365 (0.61%)	581 (0.49%)
	Depression	N (%)	3,539 (21.50%)	3,674 (29.91%)	278 (10.74%)	15,982 (26.78%)	24,306 (20.44%)
	Diabetes mellitus	N (%)	403 (2.45%)	455 (3.70%)	37 (1.43%)	1,764 (2.96%)	3,161 (2.66%)
	Gastro-esophageal reflux disease	N (%)	910 (5.53%)	706 (5.75%)	153 (5.91%)	3,136 (5.25%)	5,116 (4.30%)
	Gastrointestinal hemorrhage	N (%)	920 (5.59%)	886 (7.21%)	98 (3.79%)	3,936 (6.59%)	6,591 (5.54%)
	Hepatitis	N (%)	187 (1.14%)	511 (4.16%)	21 (0.81%)	1,459 (2.44%)	1,400 (1.18%)

Variable name	Variable level	Estimate name	CDM name / NLHR / Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Human immunodeficiency virus infection	N (%)	7 (0.04%)	13 (0.11%)	<5	56 (0.09%)	81 (0.07%)
	Hyperlipidemia	N (%)	94 (0.57%)	124 (1.01%)	5 (0.19%)	411 (0.69%)	670 (0.56%)
	Hypertension	N (%)	777 (4.72%)	1,169 (9.52%)	119 (4.60%)	4,014 (6.72%)	6,409 (5.39%)
	Malignancy	N (%)	246 (1.49%)	338 (2.75%)	23 (0.89%)	1,094 (1.83%)	1,897 (1.60%)
	Obesity	N (%)	1,190 (7.23%)	1,220 (9.93%)	97 (3.75%)	5,832 (9.77%)	10,285 (8.65%)
	Osteoarthritis	N (%)	338 (2.05%)	566 (4.61%)	29 (1.12%)	1,930 (3.23%)	3,032 (2.55%)
	Parkinson's disease	N (%)	12 (0.07%)	23 (0.19%)	0 (0.00%)	60 (0.10%)	84 (0.07%)
	Pneumonia	N (%)	1,861 (11.31%)	1,624 (13.22%)	311 (12.01%)	7,178 (12.03%)	13,081 (11.00%)
	Psoriasis	N (%)	511 (3.10%)	626 (5.10%)	42 (1.62%)	2,488 (4.17%)	4,205 (3.54%)
	Renal impairment	N (%)	75 (0.46%)	129 (1.05%)	12 (0.46%)	421 (0.71%)	537 (0.45%)
	Schizophrenia	N (%)	253 (1.54%)	220 (1.79%)	12 (0.46%)	673 (1.13%)	912 (0.77%)
	Urinary tract infection	N (%)	529 (3.21%)	692 (5.63%)	66 (2.55%)	2,692 (4.51%)	4,177 (3.51%)
Medications	Acid-related disorder drugs	N (%)	1,262 (7.67%)	1,320 (10.75%)	151 (5.83%)	5,849 (9.80%)	8,174 (6.87%)
	Agents acting on the renin-angiotensin system	N (%)	338 (2.05%)	442 (3.60%)	55 (2.12%)	1,669 (2.80%)	2,259 (1.90%)
	Anti-inflammatory and antirheumatic products	N (%)	2,230 (13.55%)	2,563 (20.86%)	230 (8.88%)	11,795 (19.76%)	16,463 (13.84%)
	Antibacterials	N (%)	2,899 (17.61%)	2,722 (22.16%)	347 (13.40%)	13,432 (22.50%)	20,270 (17.04%)
	Antidepressants	N (%)	2,617 (15.90%)	2,524 (20.55%)	316 (12.21%)	11,607 (19.45%)	15,465 (13.00%)
	Antiepileptics	N (%)	842 (5.12%)	972 (7.91%)	132 (5.10%)	3,557 (5.96%)	4,537 (3.82%)
	Antineoplastic agents	N (%)	76 (0.46%)	115 (0.94%)	<5	479 (0.80%)	741 (0.62%)

Variable name	Variable level	Estimate name	CDM name NLHR Cohort name Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Antipsoriatics	N (%)	6 (0.04%)	6 (0.05%)	0 (0.00%)	10 (0.02%)	19 (0.02%)
	Antithrombotic agents	N (%)	185 (1.12%)	277 (2.25%)	25 (0.97%)	944 (1.58%)	1,441 (1.21%)
	Beta blocking agents	N (%)	327 (1.99%)	432 (3.52%)	64 (2.47%)	1,439 (2.41%)	1,731 (1.46%)
	Calcium channel blockers	N (%)	122 (0.74%)	160 (1.30%)	24 (0.93%)	519 (0.87%)	696 (0.59%)
	Diuretics	N (%)	79 (0.48%)	149 (1.21%)	9 (0.35%)	432 (0.72%)	547 (0.46%)
	Drugs used in diabetes	N (%)	345 (2.10%)	371 (3.02%)	33 (1.27%)	1,780 (2.98%)	2,547 (2.14%)
	Immunosuppressants	N (%)	108 (0.66%)	141 (1.15%)	11 (0.42%)	587 (0.98%)	900 (0.76%)
	Lipid modifying agents	N (%)	231 (1.40%)	296 (2.41%)	25 (0.97%)	1,183 (1.98%)	1,662 (1.40%)
	Obstetrical agents	N (%)	2,710 (16.47%)	2,509 (20.42%)	397 (15.33%)	11,694 (19.59%)	17,561 (14.77%)
	Opioids	N (%)	1,509 (9.17%)	2,244 (18.27%)	121 (4.67%)	8,885 (14.89%)	11,803 (9.92%)
	Psycholeptics	N (%)	7,207 (43.79%)	5,575 (45.38%)	1,508 (58.25%)	23,419 (39.24%)	29,296 (24.63%)
	Psychostimulants	N (%)	10,955 (66.56%)	9,065 (73.80%)	2,152 (83.12%)	41,192 (69.01%)	7,802 (6.56%)
Other ADHD medications	Any ADHD medications	N (%)	11,978 (72.77%)	9,629 (78.39%)	2,239 (86.48%)	45,447 (76.14%)	16,441 (13.82%)
	Atomoxetine	N (%)	626 (3.80%)	1,111 (9.04%)	897 (34.65%)	3,316 (5.56%)	3,191 (2.68%)
	Dextroamphetamine	N (%)	891 (5.41%)	947 (7.71%)	306 (11.82%)	1,741 (2.92%)	1,090 (0.92%)
	Guanfacine	N (%)	323 (1.96%)	265 (2.16%)	56 (2.16%)	382 (0.64%)	560 (0.47%)
	Lisdexamfetamine	N (%)	6,895 (41.89%)	7,631 (62.12%)	1,685 (65.08%)	3,464 (5.80%)	7,273 (6.12%)
	Methylphenidate	N (%)	10,788 (65.54%)	7,597 (61.84%)	1,931 (74.58%)	42,959 (71.97%)	11,687 (9.83%)

Variable name	Variable level	Estimate name	CDM name NLHR Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Stimulants	Any stimulants	N (%)	11,742 (71.34%)	9,566 (77.87%)	2,181 (84.24%)	44,731 (74.94%)	15,119 (12.71%)

NLHR=Norwegian Linked Health Registry data.

Table 7. Characteristics of incident user of each ADHD medication during study period: BIFAP.

Variable name	Variable level	Estimate name	CDM name BIFAP Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	23,477	0	10,397	37,891	182,389
Number subjects	-	N	21,796	0	9,858	34,747	155,537
Age	-	Median [Q25 – Q75]	15 [11 – 25]	–	11 [9 – 14]	14 [11 – 17]	12 [9 – 17]
Sex	Female	N (%)	7,330 (31.22%)	–	1,951 (18.77%)	10,853 (28.64%)	57,961 (31.78%)
	Male	N (%)	16,147 (68.78%)	–	8,446 (81.23%)	27,038 (71.36%)	124,428 (68.22%)
Days in cohort	-	Median [Q25 – Q75]	76 [29 – 192]	–	130 [47 – 359]	92 [31 – 218]	77 [31 – 181]
Comorbidity	Anxiety disorder	N (%)	3,807 (16.22%)	-	566 (5.44%)	3,768 (9.94%)	16,499 (9.05%)
	Asthma	N (%)	3,890 (16.57%)	-	1,937 (18.63%)	7,168 (18.92%)	30,097 (16.50%)
	Chronic liver disease	N (%)	37 (0.16%)	-	<5	34 (0.09%)	261 (0.14%)
	Chronic obstructive pulmonary disease	N (%)	86 (0.37%)	-	26 (0.25%)	111 (0.29%)	750 (0.41%)
	Colitis	N (%)	29 (0.12%)	-	6 (0.06%)	38 (0.10%)	173 (0.09%)
	Crohn's disease	N (%)	25 (0.11%)	-	8 (0.08%)	24 (0.06%)	114 (0.06%)
	Depression	N (%)	1,842 (7.85%)	-	106 (1.02%)	1,689 (4.46%)	9,298 (5.10%)
	Diabetes mellitus	N (%)	270 (1.15%)	-	42 (0.40%)	279 (0.74%)	2,124 (1.16%)
	Gastro-esophageal reflux disease	N (%)	670 (2.85%)	-	392 (3.77%)	952 (2.51%)	4,334 (2.38%)
	Gastrointestinal hemorrhage	N (%)	495 (2.11%)	-	117 (1.13%)	531 (1.40%)	2,636 (1.45%)
	Hepatitis	N (%)	126 (0.54%)	-	10 (0.10%)	86 (0.23%)	606 (0.33%)
	Human immunodeficiency virus infection	N (%)	35 (0.15%)	-	6 (0.06%)	35 (0.09%)	180 (0.10%)

Variable name	Variable level	Estimate name	CDM name BIFAP Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Hyperlipidemia	N (%)	960 (4.09%)	-	223 (2.14%)	1,106 (2.92%)	5,900 (3.23%)
	Hypertension	N (%)	406 (1.73%)	-	47 (0.45%)	415 (1.10%)	3,498 (1.92%)
	Malignancy	N (%)	128 (0.55%)	-	33 (0.32%)	149 (0.39%)	2,441 (1.34%)
	Obesity	N (%)	1,205 (5.13%)	-	516 (4.96%)	2,318 (6.12%)	8,714 (4.78%)
	Osteoarthritis	N (%)	461 (1.96%)	-	50 (0.48%)	464 (1.22%)	3,116 (1.71%)
	Parkinson's disease	N (%)	6 (0.03%)	-	0 (0.00%)	<5	179 (0.10%)
	Pneumonia	N (%)	1,535 (6.54%)	-	1,017 (9.78%)	3,203 (8.45%)	14,111 (7.74%)
	Psoriasis	N (%)	209 (0.89%)	-	32 (0.31%)	240 (0.63%)	1,094 (0.60%)
	Renal impairment	N (%)	928 (3.95%)	-	185 (1.78%)	955 (2.52%)	5,100 (2.80%)
	Schizophrenia	N (%)	100 (0.43%)	-	6 (0.06%)	32 (0.08%)	238 (0.13%)
	Urinary tract infection	N (%)	2,731 (11.63%)	-	892 (8.58%)	3,782 (9.98%)	18,031 (9.89%)
Medications	Acid-related disorder drugs	N (%)	2,621 (11.16%)	-	369 (3.55%)	2,491 (6.57%)	14,979 (8.21%)
	Agents acting on the renin-angiotensin system	N (%)	473 (2.01%)	-	26 (0.25%)	373 (0.98%)	3,940 (2.16%)
	Anti-inflammatory and antirheumatic products	N (%)	9,121 (38.85%)	-	4,096 (39.40%)	13,883 (36.64%)	67,282 (36.89%)
	Antibacterials	N (%)	7,159 (30.49%)	-	2,998 (28.84%)	10,402 (27.45%)	54,413 (29.83%)
	Antidepressants	N (%)	4,155 (17.70%)	-	675 (6.49%)	3,815 (10.07%)	17,578 (9.64%)
	Antiepileptics	N (%)	2,379 (10.13%)	-	936 (9.00%)	2,023 (5.34%)	9,060 (4.97%)
	Antineoplastic agents	N (%)	131 (0.56%)	-	12 (0.12%)	125 (0.33%)	823 (0.45%)
	Antipsoriatics	N (%)	69 (0.29%)	-	12 (0.12%)	70 (0.18%)	286 (0.16%)
	Antithrombotic agents	N (%)	426 (1.81%)	-	43 (0.41%)	403 (1.06%)	3,872 (2.12%)
	Beta blocking agents	N (%)	267 (1.14%)	-	34 (0.33%)	266 (0.70%)	2,031 (1.11%)
	Calcium channel blockers	N (%)	127 (0.54%)	-	22 (0.21%)	77 (0.20%)	1,176 (0.64%)

Variable name	Variable level	Estimate name	CDM name				
			BIFAP				
			Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Diuretics	N (%)	137 (0.58%)	-	10 (0.10%)	91 (0.24%)	1,995 (1.09%)
	Drugs used in diabetes	N (%)	323 (1.38%)	-	50 (0.48%)	374 (0.99%)	2,561 (1.40%)
	Immunosuppressants	N (%)	44 (0.19%)	-	17 (0.16%)	64 (0.17%)	381 (0.21%)
	Lipid modifying agents	N (%)	637 (2.71%)	-	25 (0.24%)	436 (1.15%)	4,338 (2.38%)
	Obstetrical agents	N (%)	2,570 (10.95%)	-	1,145 (11.01%)	4,005 (10.57%)	18,486 (10.14%)
	Opioids	N (%)	1,488 (6.34%)	-	137 (1.32%)	1,546 (4.08%)	9,588 (5.26%)
	Psycholeptics	N (%)	7,442 (31.70%)	-	4,174 (40.15%)	7,055 (18.62%)	29,292 (16.06%)
	Psychostimulants	N (%)	9,571 (40.77%)	-	7,226 (69.50%)	26,416 (69.72%)	9,948 (5.45%)
Other ADHD medications	Any ADHD medications	N (%)	13,446 (57.27%)	-	8,402 (80.81%)	32,142 (84.83%)	43,211 (23.69%)
	Atomoxetine	N (%)	1,992 (8.48%)	-	1,912 (18.39%)	3,952 (10.43%)	6,729 (3.69%)
	Dextroamphetamine	N (%)	0 (0.00%)	-	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Guanfacine	N (%)	790 (3.36%)	-	610 (5.87%)	1,728 (4.56%)	1,992 (1.09%)
	Lisdexamfetamine	N (%)	2,488 (10.60%)	-	3,306 (31.80%)	3,572 (9.43%)	6,984 (3.83%)
	Methylphenidate	N (%)	12,234 (52.11%)	-	7,604 (73.14%)	30,657 (80.91%)	38,423 (21.07%)
Stimulants	Any stimulants	N (%)	12,570 (53.54%)	-	7,952 (76.48%)	31,402 (82.87%)	39,916 (21.89%)

BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público.

Table 8. Characteristics of incident user of each ADHD medication during study period: SIDIAP.

Variable name	Variable level	Estimate name	CDM name SIDIAP Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	8,841	0	3,502	9,487	69,903
Number subjects	-	N	8,199	0	3,228	8,628	58,906
Age	-	Median [Q25 – Q75]	14 [11 – 20]	–	12 [10 – 15]	15 [12 – 18]	14 [10 – 23]
Sex	Female	N (%)	2,618 (29.61%)	–	764 (21.82%)	2,785 (29.36%)	22,929 (32.80%)
	Male	N (%)	6,223 (70.39%)	–	2,738 (78.18%)	6,702 (70.64%)	46,974 (67.20%)
Days in cohort	-	Median [Q25 – Q75]	186 [72 – 429]	–	226 [91 – 472]	241 [93 – 528]	222 [81 – 554]
Comorbidity	Anxiety disorder	N (%)	1,918 (21.69%)	-	493 (14.08%)	1,585 (16.71%)	11,580 (16.57%)
	Asthma	N (%)	852 (9.64%)	-	437 (12.48%)	1,063 (11.20%)	5,989 (8.57%)
	Chronic liver disease	N (%)	51 (0.58%)	-	10 (0.29%)	31 (0.33%)	382 (0.55%)
	Chronic obstructive pulmonary disease	N (%)	47 (0.53%)	-	6 (0.17%)	33 (0.35%)	650 (0.93%)
	Colitis	N (%)	7 (0.08%)	-	<5	<5	90 (0.13%)
	Crohn's disease	N (%)	17 (0.19%)	-	<5	8 (0.08%)	91 (0.13%)
	Depression	N (%)	731 (8.27%)	-	126 (3.60%)	717 (7.56%)	6,537 (9.35%)
	Diabetes mellitus	N (%)	104 (1.18%)	-	17 (0.49%)	80 (0.84%)	1,410 (2.02%)
	Gastro-esophageal reflux disease	N (%)	179 (2.02%)	-	93 (2.66%)	212 (2.23%)	1,482 (2.12%)
	Gastrointestinal hemorrhage	N (%)	162 (1.83%)	-	60 (1.71%)	142 (1.50%)	1,104 (1.58%)
	Hepatitis	N (%)	73 (0.83%)	-	16 (0.46%)	41 (0.43%)	538 (0.77%)
	Human immunodeficiency virus infection	N (%)	17 (0.19%)	-	<5	12 (0.13%)	144 (0.21%)
	Hyperlipidemia	N (%)	345 (3.90%)	-	93 (2.66%)	334 (3.52%)	3,381 (4.84%)

Variable name	Variable level	Estimate name	CDM name				
			SIDIAP				
			Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Hypertension	N (%)	174 (1.97%)	-	36 (1.03%)	171 (1.80%)	2,899 (4.15%)
	Malignancy	N (%)	57 (0.64%)	-	28 (0.80%)	69 (0.73%)	2,384 (3.41%)
	Obesity	N (%)	814 (9.21%)	-	512 (14.62%)	1,250 (13.18%)	7,334 (10.49%)
	Osteoarthritis	N (%)	172 (1.95%)	-	19 (0.54%)	115 (1.21%)	2,129 (3.05%)
	Parkinson's disease	N (%)	18 (0.20%)	-	0 (0.00%)	<5	204 (0.29%)
	Pneumonia	N (%)	833 (9.42%)	-	511 (14.59%)	1,028 (10.84%)	6,590 (9.43%)
	Psoriasis	N (%)	84 (0.95%)	-	28 (0.80%)	77 (0.81%)	614 (0.88%)
	Renal impairment	N (%)	35 (0.40%)	-	21 (0.60%)	44 (0.46%)	763 (1.09%)
	Schizophrenia	N (%)	48 (0.54%)	-	12 (0.34%)	26 (0.27%)	267 (0.38%)
	Urinary tract infection	N (%)	717 (8.11%)	-	326 (9.31%)	827 (8.72%)	5,836 (8.35%)
Medications	Acid-related disorder drugs	N (%)	671 (7.59%)	-	149 (4.25%)	598 (6.30%)	7,223 (10.33%)
	Agents acting on the renin-angiotensin system	N (%)	135 (1.53%)	-	25 (0.71%)	117 (1.23%)	2,421 (3.46%)
	Anti-inflammatory and antirheumatic products	N (%)	3,142 (35.54%)	-	1,215 (34.69%)	3,074 (32.40%)	23,757 (33.99%)
	Antibacterials	N (%)	2,072 (23.44%)	-	799 (22.82%)	2,071 (21.83%)	16,307 (23.33%)
	Antidepressants	N (%)	1,684 (19.05%)	-	509 (14.53%)	1,523 (16.05%)	11,877 (16.99%)
	Antiepileptics	N (%)	1,098 (12.42%)	-	482 (13.76%)	876 (9.23%)	6,577 (9.41%)
	Antineoplastic agents	N (%)	22 (0.25%)	-	8 (0.23%)	23 (0.24%)	348 (0.50%)
	Antipsoriatics	N (%)	<5	-	<5	<5	52 (0.07%)
	Antithrombotic agents	N (%)	83 (0.94%)	-	18 (0.51%)	74 (0.78%)	1,156 (1.65%)
	Beta blocking agents	N (%)	106 (1.20%)	-	26 (0.74%)	78 (0.82%)	1,208 (1.73%)

Variable name	Variable level	Estimate name	CDM name SIDIAP Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Calcium channel blockers	N (%)	34 (0.38%)	-	8 (0.23%)	36 (0.38%)	801 (1.15%)
	Diuretics	N (%)	49 (0.55%)	-	<5	39 (0.41%)	1,270 (1.82%)
	Drugs used in diabetes	N (%)	100 (1.13%)	-	16 (0.46%)	89 (0.94%)	1,278 (1.83%)
	Immunosuppressants	N (%)	29 (0.33%)	-	15 (0.43%)	31 (0.33%)	237 (0.34%)
	Lipid modifying agents	N (%)	157 (1.78%)	-	21 (0.60%)	123 (1.30%)	2,491 (3.56%)
	Obstetrical agents	N (%)	1,301 (14.72%)	-	505 (14.42%)	1,344 (14.17%)	9,752 (13.95%)
	Opioids	N (%)	320 (3.62%)	-	38 (1.09%)	262 (2.76%)	3,958 (5.66%)
	Psycholeptics	N (%)	2,721 (30.78%)	-	1,819 (51.94%)	2,356 (24.83%)	15,229 (21.79%)
	Psychostimulants	N (%)	3,891 (44.01%)	-	2,066 (58.99%)	6,083 (64.12%)	3,137 (4.49%)
Other ADHD medications	Any ADHD medications	N (%)	5,283 (59.76%)	-	2,714 (77.50%)	7,720 (81.37%)	15,978 (22.86%)
	Atomoxetine	N (%)	790 (8.94%)	-	743 (21.22%)	1,102 (11.62%)	2,788 (3.99%)
	Dextroamphetamine	N (%)	0 (0.00%)	-	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Guanfacine	N (%)	167 (1.89%)	-	277 (7.91%)	321 (3.38%)	588 (0.84%)
	Lisdexamfetamine	N (%)	607 (6.87%)	-	794 (22.67%)	868 (9.15%)	1,756 (2.51%)
	Methylphenidate	N (%)	4,892 (55.33%)	-	2,469 (70.50%)	7,443 (78.45%)	14,358 (20.54%)
Stimulants	Any stimulants	N (%)	4,963 (56.14%)	-	2,534 (72.36%)	7,561 (79.70%)	14,717 (21.05%)

SIDIAP=The Information System for Research on Primary Care.

Table 9. Characteristics of incident user of each ADHD medication during study period: HI-SPEED.

Variable name	Variable level	Estimate name	CDM name HI-SPEED Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
Number records	-	N	57,086	38,462	43,157	208,859	289,196
Number subjects	-	N	54,687	34,309	41,243	188,007	259,788
Age	-	Median [Q25 – Q75]	16 [12 – 29]	31 [22 – 40]	14 [10 – 21]	23 [15 – 34]	17 [12 – 30]
Sex	Female	N (%)	25,151 (44.06%)	19,848 (51.60%)	15,494 (35.90%)	101,433 (48.57%)	133,021 (46.00%)
	Male	N (%)	31,935 (55.94%)	18,614 (48.40%)	27,663 (64.10%)	107,426 (51.43%)	156,175 (54.00%)
Days in cohort	-	Median [Q25 – Q75]	87 [31 – 216]	69 [37 – 186]	103 [29 – 288]	130 [49 – 334]	99 [43 – 242]
Comorbidity	Anxiety disorder	N (%)	20,815 (36.46%)	19,247 (50.04%)	14,027 (32.50%)	87,771 (42.02%)	96,535 (33.38%)
	Asthma	N (%)	6,513 (11.41%)	3,742 (9.73%)	5,874 (13.61%)	20,764 (9.94%)	29,837 (10.32%)
	Chronic liver disease	N (%)	708 (1.24%)	905 (2.35%)	597 (1.38%)	4,716 (2.26%)	3,470 (1.20%)
	Chronic obstructive pulmonary disease	N (%)	168 (0.29%)	177 (0.46%)	112 (0.26%)	641 (0.31%)	786 (0.27%)
	Colitis	N (%)	176 (0.31%)	218 (0.57%)	110 (0.25%)	838 (0.40%)	907 (0.31%)
	Crohn's disease	N (%)	193 (0.34%)	207 (0.54%)	129 (0.30%)	793 (0.38%)	905 (0.31%)
	Depression	N (%)	13,948 (24.43%)	14,380 (37.39%)	8,465 (19.61%)	61,577 (29.48%)	65,904 (22.79%)
	Diabetes mellitus	N (%)	1,196 (2.10%)	998 (2.59%)	747 (1.73%)	4,734 (2.27%)	5,777 (2.00%)
	Gastro-esophageal reflux disease	N (%)	889 (1.56%)	719 (1.87%)	668 (1.55%)	3,084 (1.48%)	3,690 (1.28%)
	Gastrointestinal hemorrhage	N (%)	696 (1.22%)	750 (1.95%)	539 (1.25%)	3,142 (1.50%)	3,242 (1.12%)

Variable name	Variable level	Estimate name	CDM name HI-SPEED Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Hepatitis	N (%)	700 (1.23%)	910 (2.37%)	599 (1.39%)	4,749 (2.27%)	3,455 (1.19%)
	Human immunodeficiency virus infection	N (%)	25 (0.04%)	48 (0.12%)	18 (0.04%)	165 (0.08%)	173 (0.06%)
	Hyperlipidemia	N (%)	342 (0.60%)	399 (1.04%)	274 (0.63%)	1,565 (0.75%)	1,742 (0.60%)
	Hypertension	N (%)	1,359 (2.38%)	1,965 (5.11%)	1,284 (2.98%)	6,800 (3.26%)	7,120 (2.46%)
	Malignancy	N (%)	453 (0.79%)	532 (1.38%)	263 (0.61%)	1,933 (0.93%)	2,385 (0.82%)
	Obesity	N (%)	3,552 (6.22%)	2,372 (6.17%)	2,564 (5.94%)	14,236 (6.82%)	17,983 (6.22%)
	Osteoarthritis	N (%)	1,004 (1.76%)	1,516 (3.94%)	715 (1.66%)	5,049 (2.42%)	5,296 (1.83%)
	Parkinson's disease	N (%)	10 (0.02%)	12 (0.03%)	<5	26 (0.01%)	40 (0.01%)
	Pneumonia	N (%)	1,369 (2.40%)	1,162 (3.02%)	1,137 (2.63%)	5,237 (2.51%)	6,474 (2.24%)
	Psoriasis	N (%)	455 (0.80%)	620 (1.61%)	324 (0.75%)	2,301 (1.10%)	2,514 (0.87%)
	Renal impairment	N (%)	211 (0.37%)	182 (0.47%)	148 (0.34%)	922 (0.44%)	1,005 (0.35%)
	Schizophrenia	N (%)	269 (0.47%)	85 (0.22%)	123 (0.29%)	438 (0.21%)	449 (0.16%)
	Urinary tract infection	N (%)	1,996 (3.50%)	1,986 (5.16%)	1,379 (3.20%)	8,865 (4.24%)	9,758 (3.37%)
Medications	Acid-related disorder drugs	N (%)	3,905 (6.84%)	4,325 (11.24%)	2,873 (6.66%)	15,330 (7.34%)	15,987 (5.53%)
	Agents acting on the renin-angiotensin system	N (%)	1,207 (2.11%)	1,821 (4.73%)	1,123 (2.60%)	5,904 (2.83%)	5,728 (1.98%)
	Anti-inflammatory and antirheumatic products	N (%)	4,795 (8.40%)	5,847 (15.20%)	3,186 (7.38%)	21,323 (10.21%)	21,877 (7.56%)
	Antibacterials	N (%)	8,255 (14.46%)	7,256 (18.87%)	6,204 (14.38%)	33,784 (16.18%)	39,350 (13.61%)
	Antidepressants	N (%)	15,808 (27.69%)	15,934 (41.43%)	11,482 (26.61%)	65,330 (31.28%)	71,029 (24.56%)

Variable name	Variable level	Estimate name	CDM name HI-SPEED Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Antiepileptics	N (%)	3,841 (6.73%)	4,365 (11.35%)	2,982 (6.91%)	14,972 (7.17%)	14,203 (4.91%)
	Antineoplastic agents	N (%)	333 (0.58%)	430 (1.12%)	229 (0.53%)	1,554 (0.74%)	1,620 (0.56%)
	Antipsoriatics	N (%)	13 (0.02%)	12 (0.03%)	7 (0.02%)	44 (0.02%)	50 (0.02%)
	Antithrombotic agents	N (%)	405 (0.71%)	650 (1.69%)	313 (0.73%)	2,289 (1.10%)	2,313 (0.80%)
	Beta blocking agents	N (%)	1,968 (3.45%)	3,300 (8.58%)	1,767 (4.09%)	8,145 (3.90%)	7,206 (2.49%)
	Calcium channel blockers	N (%)	762 (1.33%)	1,151 (2.99%)	729 (1.69%)	3,735 (1.79%)	3,529 (1.22%)
	Diuretics	N (%)	556 (0.97%)	828 (2.15%)	451 (1.05%)	2,701 (1.29%)	2,537 (0.88%)
	Drugs used in diabetes	N (%)	1,150 (2.01%)	998 (2.59%)	808 (1.87%)	4,503 (2.16%)	5,048 (1.75%)
	Immunosuppressants	N (%)	378 (0.66%)	460 (1.20%)	296 (0.69%)	1,756 (0.84%)	1,945 (0.67%)
	Lipid modifying agents	N (%)	630 (1.10%)	755 (1.96%)	521 (1.21%)	2,669 (1.28%)	2,730 (0.94%)
	Obstetrical agents	N (%)	8,408 (14.73%)	6,962 (18.10%)	6,934 (16.07%)	30,320 (14.52%)	38,315 (13.25%)
	Opioids	N (%)	2,578 (4.52%)	3,928 (10.21%)	1,706 (3.95%)	13,469 (6.45%)	12,692 (4.39%)
	Psycholeptics	N (%)	29,591 (51.84%)	22,109 (57.48%)	27,666 (64.11%)	97,757 (46.81%)	98,975 (34.22%)
	Psychostimulants	N (%)	33,083 (57.95%)	30,959 (80.49%)	33,926 (78.61%)	121,114 (57.99%)	35,533 (12.29%)
Other ADHD medications	Any ADHD medications	N (%)	37,224 (65.21%)	33,044 (85.91%)	35,569 (82.42%)	141,963 (67.97%)	56,031 (19.37%)
	Atomoxetine	N (%)	2,407 (4.22%)	4,016 (10.44%)	8,924 (20.68%)	16,907 (8.09%)	16,013 (5.54%)
	Dextroamphetamine	N (%)	2,883 (5.05%)	4,159 (10.81%)	2,987 (6.92%)	6,546 (3.13%)	4,997 (1.73%)
	Guanfacine	N (%)	5,657 (9.91%)	3,166 (8.23%)	1,915 (4.44%)	11,039 (5.29%)	9,358 (3.24%)

Variable name	Variable level	Estimate name	CDM name HI-SPEED Cohort name				
			Atomoxetine	Dextroamphetamine	Guanfacine	Lisdexamfetamine	Methylphenidate
	Lisdexamfetamine	N (%)	22,639 (39.66%)	29,323 (76.24%)	21,350 (49.47%)	20,869 (9.99%)	32,195 (11.13%)
	Methylphenidate	N (%)	31,198 (54.65%)	20,472 (53.23%)	28,730 (66.57%)	127,597 (61.09%)	29,458 (10.19%)
Stimulants	Any stimulants	N (%)	36,099 (63.24%)	32,759 (85.17%)	34,331 (79.55%)	137,553 (65.86%)	46,381 (16.04%)

HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 10. Characteristics of incident user of any ADHD medication age 3–5 years old, by data sources.

Variable name	Variable level	Estimate name	Age group 3 to 5 CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Number records	-	N	1,146	898	425	3,530	763	1,801
Number subjects	-	N	1,143	891	424	3,498	761	1,792
Age	-	Median [Q25 – Q75]	5 [5 – 5]	5 [5 – 5]	5 [5 – 5]	5 [5 – 5]	5 [5 – 5]	5 [5 – 5]
Sex	Female	N (%)	260 (22.69%)	158 (17.59%)	95 (22.35%)	604 (17.11%)	153 (20.05%)	360 (19.99%)
	Male	N (%)	886 (77.31%)	740 (82.41%)	330 (77.65%)	2,926 (82.89%)	610 (79.95%)	1,441 (80.01%)
Days in cohort	-	Median [Q25 – Q75]	126 [42 – 321]	101 [30 – 249]	172 [48 – 468]	87 [31 – 270]	248 [76 – 902]	238 [67 – 694]
Comorbidity	Anxiety disorder	N (%)	10 (0.87%)	27 (3.01%)	7 (1.65%)	35 (0.99%)	12 (1.57%)	20 (1.11%)
	Asthma	N (%)	475 (41.45%)	18 (2.00%)	127 (29.88%)	470 (13.31%)	92 (12.06%)	470 (26.10%)
	Chronic liver disease	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)
	Chronic obstructive pulmonary disease	N (%)	16 (1.40%)	5 (0.56%)	7 (1.65%)	14 (0.40%)	<5	6 (0.33%)
	Colitis	N (%)	<5	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)
	Crohn's disease	N (%)	<5	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)
	Depression	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)
	Diabetes mellitus	N (%)	<5	0 (0.00%)	<5	7 (0.20%)	<5	7 (0.39%)
	Gastro-esophageal reflux disease	N (%)	33 (2.88%)	7 (0.78%)	33 (7.76%)	163 (4.62%)	27 (3.54%)	55 (3.05%)
	Gastrointestinal hemorrhage	N (%)	<5	<5	18 (4.24%)	34 (0.96%)	9 (1.18%)	6 (0.33%)
	Hepatitis	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)
	Human immunodeficiency virus infection	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5

Variable name	Variable level	Estimate name	Age group 3 to 5 CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
	Hyperlipidemia	N (%)	0 (0.00%)	<5	0 (0.00%)	27 (0.76%)	<5	<5
	Hypertension	N (%)	<5	<5	<5	7 (0.20%)	<5	6 (0.33%)
	Malignancy	N (%)	<5	6 (0.67%)	<5	12 (0.34%)	<5	<5
	Obesity	N (%)	20 (1.75%)	23 (2.56%)	10 (2.35%)	54 (1.53%)	53 (6.95%)	73 (4.05%)
	Osteoarthritis	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	13 (0.37%)	0 (0.00%)	0 (0.00%)
	Parkinson's disease	N (%)	<5	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Pneumonia	N (%)	322 (28.10%)	32 (3.56%)	37 (8.71%)	344 (9.75%)	98 (12.84%)	100 (5.55%)
	Psoriasis	N (%)	9 (0.79%)	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	<5
	Renal impairment	N (%)	<5	<5	0 (0.00%)	44 (1.25%)	<5	<5
	Schizophrenia	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Urinary tract infection	N (%)	49 (4.28%)	<5	<5	260 (7.37%)	56 (7.34%)	51 (2.83%)
Medications	Acid-related disorder drugs	N (%)	16 (1.40%)	5 (0.56%)	11 (2.59%)	36 (1.02%)	5 (0.66%)	28 (1.55%)
	Agents acting on the renin-angiotensin system	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	0 (0.00%)	<5
	Anti-inflammatory and antirheumatic products	N (%)	22 (1.92%)	477 (53.12%)	12 (2.82%)	1,572 (44.53%)	352 (46.13%)	26 (1.44%)
	Antibacterials	N (%)	354 (30.89%)	372 (41.43%)	63 (14.82%)	1,718 (48.67%)	330 (43.25%)	312 (17.32%)
	Antidepressants	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	11 (0.31%)	5 (0.66%)	12 (0.67%)
	Antiepileptics	N (%)	33 (2.88%)	28 (3.12%)	11 (2.59%)	153 (4.33%)	38 (4.98%)	54 (3.00%)
	Antineoplastic agents	N (%)	0 (0.00%)	10 (1.11%)	0 (0.00%)	<5	<5	<5
	Antipsoriatics	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Antithrombotic agents	N (%)	<5	<5	0 (0.00%)	<5	0 (0.00%)	<5
	Beta blocking agents	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	<5	<5
	Calcium channel blockers	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)

Variable name	Variable level	Estimate name	Age group 3 to 5 CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
	Diuretics	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	0 (0.00%)	<5
	Drugs used in diabetes	N (%)	<5	0 (0.00%)	0 (0.00%)	5 (0.14%)	0 (0.00%)	6 (0.33%)
	Immunosuppressants	N (%)	<5	0 (0.00%)	<5	0 (0.00%)	<5	<5
	Lipid modifying agents	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)
	Obstetrical agents	N (%)	186 (16.23%)	245 (27.28%)	70 (16.47%)	569 (16.12%)	214 (28.05%)	425 (23.60%)
	Opioids	N (%)	<5	<5	0 (0.00%)	27 (0.76%)	9 (1.18%)	<5
	Psycholeptics	N (%)	175 (15.27%)	147 (16.37%)	137 (32.24%)	795 (22.52%)	187 (24.51%)	760 (42.20%)
	Psychostimulants	N (%)	<5	0 (0.00%)	0 (0.00%)	22 (0.62%)	<5	<5
Other ADHD medications	Any ADHD medications	N (%)	<5	8 (0.89%)	<5	51 (1.44%)	<5	9 (0.50%)
	Atomoxetine	N (%)	<5	<5	0 (0.00%)	<5	0 (0.00%)	<5
	Dextroamphetamine	N (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5
	Guanfacine	N (%)	0 (0.00%)	<5	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)
	Lisdexamfetamine	N (%)	0 (0.00%)	<5	0 (0.00%)	5 (0.14%)	0 (0.00%)	0 (0.00%)
	Methylphenidate	N (%)	<5	7 (0.78%)	<5	45 (1.27%)	<5	7 (0.39%)
Stimulants	Any stimulants	N (%)	<5	7 (0.78%)	<5	48 (1.36%)	<5	7 (0.39%)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Potential indications

We assessed the potential indication for individuals who initiated an ADHD medication using different time windows, on or before the initial prescription date (index date) (**Table 11**). The groups are not mutually exclusive; therefore, the percentages of individuals with each potential indication may add up to more than 100%. "Unknown" refers to cases where, during the predefined period on or before the index date, one or more diagnoses other than ADHD, narcolepsy, or any of the specified off-label conditions were recorded.

The percentages of individuals with an ADHD diagnosis code recorded (with or without narcolepsy or off-label conditions) within seven days prior to the index date of any ADHD medication were as follows: 65.61% in DK-DHR, 9.57% in InGef, 93.69% in NLHR, 10.58% in BIFAP, 19.09% in SIDIAP, and 38.37% in HI-SPEED. Proportion of individuals with a recorded ADHD diagnosis increased when longer look back periods were used.

Table 11. Potential indications of any ADHD medication use from 7, 30, 90 days, and any time before or on the index date, by data source.

Indication	Estimate name	Cohort name: Any ADHD medication; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Indication from 7 days before to the index date							
Addiction	N (%)	-	-	-	140 (0.07 %)	-	-
ADHD	N (%)	153,149 (65.61 %)	10,050 (9.57 %)	129,644 (93.69 %)	21,260 (10.58 %)	14,570 (19.09 %)	143,922 (38.37 %)
Apathy	N (%)	-	-	-	-	-	-
Autism	N (%)	8,313 (3.56 %)	635 (0.60 %)	856 (0.62 %)	451 (0.22 %)	508 (0.67 %)	22,332 (5.95 %)
Behavioural disorder	N (%)	4,085 (1.75 %)	2,864 (2.73 %)	1,673 (1.21 %)	2,666 (1.33 %)	914 (1.20 %)	3,657 (0.98 %)
Cognitive dysfunction	N (%)	50 (0.02 %)	116 (0.11 %)	14 (0.01 %)	2,436 (1.21 %)	139 (0.18 %)	84 (0.02 %)
Dementia	N (%)	24 (0.01 %)	<5	5 (0.00 %)	52 (0.03 %)	35 (0.05 %)	8 (0.00 %)
Eating disorder	N (%)	1,736 (0.74 %)	224 (0.21 %)	790 (0.57 %)	205 (0.10 %)	174 (0.23 %)	1,385 (0.37 %)
Fatigue	N (%)	2,733 (1.17 %)	29 (0.03 %)	772 (0.56 %)	202 (0.10 %)	1,493 (1.96 %)	73 (0.02 %)
Hypertension	N (%)	841 (0.36 %)	248 (0.24 %)	1,196 (0.86 %)	280 (0.14 %)	223 (0.29 %)	544 (0.15 %)
Intellectual disability	N (%)	1,991 (0.85 %)	469 (0.45 %)	354 (0.26 %)	60 (0.03 %)	104 (0.14 %)	2,869 (0.76 %)
Major depressive disorder	N (%)	3,787 (1.62 %)	3,327 (3.17 %)	3,960 (2.86 %)	134 (0.07 %)	1,207 (1.58 %)	12,075 (3.22 %)
Mood disorders	N (%)	11,739 (5.03 %)	342 (0.33 %)	8,524 (6.16 %)	1,102 (0.55 %)	367 (0.48 %)	4,463 (1.19 %)
Narcolepsy	N (%)	3,009 (1.29 %)	42 (0.04 %)	590 (0.43 %)	90 (0.04 %)	47 (0.06 %)	234 (0.06 %)

Indication	Estimate name	Cohort name: Any ADHD medication; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Post traumatic brain injury	N (%)	81 (0.03 %)	27 (0.03 %)	88 (0.06 %)	19 (0.01 %)	29 (0.04 %)	53 (0.01 %)
Unknown	N (%)	54,031 (23.15 %)	1,631 (1.55 %)	3,191 (2.31 %)	14,643 (7.29 %)	15,280 (20.02 %)	13,235 (3.53 %)
None	N (%)	14,043 (6.02 %)	91,798 (87.43 %)	4,191 (3.03 %)	162,238 (80.77 %)	42,456 (55.63 %)	210,743 (56.19 %)
Indication from 30 days before to the index date							
Addiction	N (%)	-	-	-	178 (0.09 %)	-	-
ADHD	N (%)	156,614 (67.09 %)	14,066 (13.40 %)	130,891 (94.60 %)	26,199 (13.04 %)	15,660 (20.52 %)	179,775 (47.93 %)
Apathy	N (%)	-	-	-	<5	-	-
Autism	N (%)	9,810 (4.20 %)	981 (0.93 %)	1,252 (0.90 %)	596 (0.30 %)	587 (0.77 %)	29,215 (7.79 %)
Behavioural disorder	N (%)	5,012 (2.15 %)	3,839 (3.66 %)	2,662 (1.92 %)	3,115 (1.55 %)	1,030 (1.35 %)	4,569 (1.22 %)
Cognitive dysfunction	N (%)	72 (0.03 %)	154 (0.15 %)	28 (0.02 %)	2,999 (1.49 %)	162 (0.21 %)	134 (0.04 %)
Dementia	N (%)	39 (0.02 %)	7 (0.01 %)	8 (0.01 %)	66 (0.03 %)	48 (0.06 %)	14 (0.00 %)
Eating disorder	N (%)	2,177 (0.93 %)	327 (0.31 %)	975 (0.70 %)	246 (0.12 %)	195 (0.26 %)	2,023 (0.54 %)
Fatigue	N (%)	3,136 (1.34 %)	55 (0.05 %)	1,759 (1.27 %)	384 (0.19 %)	1,558 (2.04 %)	143 (0.04 %)
Hypertension	N (%)	1,823 (0.78 %)	325 (0.31 %)	1,964 (1.42 %)	375 (0.19 %)	333 (0.44 %)	1,369 (0.36 %)
Intellectual disability	N (%)	2,512 (1.08 %)	711 (0.68 %)	587 (0.42 %)	89 (0.04 %)	139 (0.18 %)	3,978 (1.06 %)
Major depressive disorder	N (%)	4,802 (2.06 %)	4,558 (4.34 %)	4,952 (3.58 %)	166 (0.08 %)	1,342 (1.76 %)	17,848 (4.76 %)
Mood disorders	N (%)	20,830 (8.92 %)	522 (0.50 %)	10,476 (7.57 %)	1,400 (0.70 %)	424 (0.56 %)	6,445 (1.72 %)
Narcolepsy	N (%)	3,097 (1.33 %)	67 (0.06 %)	620 (0.45 %)	111 (0.06 %)	53 (0.07 %)	345 (0.09 %)
Post traumatic brain injury	N (%)	204 (0.09 %)	61 (0.06 %)	212 (0.15 %)	24 (0.01 %)	34 (0.04 %)	178 (0.05 %)
Unknown	N (%)	50,461 (21.62 %)	3,480 (3.31 %)	3,667 (2.65 %)	30,085 (14.98 %)	19,558 (25.63 %)	21,577 (5.75 %)
None	N (%)	10,153 (4.35 %)	84,883 (80.84 %)	2,265 (1.64 %)	141,066 (70.23 %)	36,712 (48.11 %)	164,096 (43.75 %)

Indication	Estimate name	Cohort name: Any ADHD medication; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Indication from 90 days before to the index date							
Addiction	N (%)	-	-	-	299 (0.15 %)	-	-
ADHD	N (%)	158,582 (67.93 %)	19,981 (19.03 %)	131,911 (95.33 %)	33,985 (16.92 %)	17,731 (23.23 %)	218,534 (58.26 %)
Apathy	N (%)	-	-	-	<5	-	-
Autism	N (%)	11,074 (4.74 %)	1,560 (1.49 %)	1,787 (1.29 %)	822 (0.41 %)	769 (1.01 %)	37,271 (9.94 %)
Behavioural disorder	N (%)	5,666 (2.43 %)	5,487 (5.23 %)	4,188 (3.03 %)	3,967 (1.98 %)	1,304 (1.71 %)	5,773 (1.54 %)
Cognitive dysfunction	N (%)	95 (0.04 %)	239 (0.23 %)	57 (0.04 %)	4,066 (2.02 %)	211 (0.28 %)	221 (0.06 %)
Dementia	N (%)	65 (0.03 %)	10 (0.01 %)	15 (0.01 %)	90 (0.04 %)	72 (0.09 %)	19 (0.01 %)
Eating disorder	N (%)	2,506 (1.07 %)	510 (0.49 %)	1,164 (0.84 %)	314 (0.16 %)	241 (0.32 %)	2,913 (0.78 %)
Fatigue	N (%)	3,385 (1.45 %)	106 (0.10 %)	3,524 (2.55 %)	785 (0.39 %)	1,714 (2.25 %)	256 (0.07 %)
Hypertension	N (%)	3,440 (1.47 %)	520 (0.50 %)	3,072 (2.22 %)	562 (0.28 %)	537 (0.70 %)	2,849 (0.76 %)
Intellectual disability	N (%)	2,924 (1.25 %)	1,135 (1.08 %)	933 (0.67 %)	117 (0.06 %)	209 (0.27 %)	5,500 (1.47 %)
Major depressive disorder	N (%)	5,891 (2.52 %)	6,857 (6.53 %)	5,855 (4.23 %)	203 (0.10 %)	1,662 (2.18 %)	26,749 (7.13 %)
Mood disorders	N (%)	33,018 (14.14 %)	978 (0.93 %)	12,107 (8.75 %)	1,912 (0.95 %)	557 (0.73 %)	9,264 (2.47 %)
Narcolepsy	N (%)	3,229 (1.38 %)	95 (0.09 %)	656 (0.47 %)	143 (0.07 %)	74 (0.10 %)	543 (0.14 %)
Post traumatic brain injury	N (%)	428 (0.18 %)	157 (0.15 %)	498 (0.36 %)	39 (0.02 %)	53 (0.07 %)	456 (0.12 %)
Unknown	N (%)	47,385 (20.30 %)	6,671 (6.35 %)	3,690 (2.67 %)	57,469 (28.61 %)	26,193 (34.32 %)	29,532 (7.87 %)
None	N (%)	6,782 (2.91 %)	73,654 (70.15 %)	1,040 (0.75 %)	104,466 (52.01 %)	27,130 (35.55 %)	114,717 (30.59 %)
Indication any time before or on index date							
Addiction	N (%)	-	-	-	1,952 (0.97 %)	-	-
ADHD	N (%)	171,034 (73.27 %)	32,066 (30.54 %)	135,115 (97.65 %)	90,161 (44.89 %)	39,650 (51.96 %)	298,067 (79.47 %)
Apathy	N (%)	-	-	-	36 (0.02 %)	-	-

Indication	Estimate name	Cohort name: Any ADHD medication; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Autism	N (%)	18,497 (7.92 %)	3,667 (3.49 %)	4,882 (3.53 %)	5,204 (2.59 %)	4,362 (5.72 %)	57,157 (15.24 %)
Behavioural disorder	N (%)	13,797 (5.91 %)	11,158 (10.63 %)	29,517 (21.33 %)	16,400 (8.17 %)	8,124 (10.65 %)	15,185 (4.05 %)
Cognitive dysfunction	N (%)	568 (0.24 %)	1,278 (1.22 %)	423 (0.31 %)	11,696 (5.82 %)	976 (1.28 %)	1,205 (0.32 %)
Dementia	N (%)	229 (0.10 %)	46 (0.04 %)	93 (0.07 %)	395 (0.20 %)	264 (0.35 %)	87 (0.02 %)
Eating disorder	N (%)	7,200 (3.08 %)	1,925 (1.83 %)	5,593 (4.04 %)	1,618 (0.81 %)	1,391 (1.82 %)	10,951 (2.92 %)
Fatigue	N (%)	5,710 (2.45 %)	1,064 (1.01 %)	46,648 (33.71 %)	14,314 (7.13 %)	4,234 (5.55 %)	1,207 (0.32 %)
Hypertension	N (%)	11,359 (4.87 %)	2,761 (2.63 %)	8,074 (5.84 %)	3,954 (1.97 %)	3,104 (4.07 %)	10,675 (2.85 %)
Intellectual disability	N (%)	5,823 (2.49 %)	2,946 (2.81 %)	2,593 (1.87 %)	483 (0.24 %)	1,342 (1.76 %)	10,766 (2.87 %)
Major depressive disorder	N (%)	24,965 (10.69 %)	16,423 (15.64 %)	21,962 (15.87 %)	713 (0.35 %)	6,912 (9.06 %)	90,056 (24.01 %)
Mood disorders	N (%)	80,459 (34.47 %)	3,847 (3.66 %)	25,807 (18.65 %)	12,654 (6.30 %)	3,096 (4.06 %)	24,745 (6.60 %)
Narcolepsy	N (%)	6,387 (2.74 %)	219 (0.21 %)	990 (0.72 %)	632 (0.31 %)	225 (0.29 %)	1,129 (0.30 %)
Post traumatic brain injury	N (%)	21,891 (9.38 %)	3,061 (2.92 %)	16,243 (11.74 %)	584 (0.29 %)	588 (0.77 %)	10,321 (2.75 %)
Unknown	N (%)	27,826 (11.92 %)	26,255 (25.00 %)	736 (0.53 %)	80,459 (40.06 %)	19,958 (26.15 %)	44,148 (11.77 %)
None	N (%)	66 (0.03 %)	31,894 (30.37 %)	20 (0.01 %)	3,191 (1.59 %)	669 (0.88 %)	6,697 (1.79 %)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Guanfacine is an antihypertensive medication, which is approved for the treatment of ADHD in children and adolescents aged 6–17 years.

Among individuals in this age group who initiated guanfacine, the proportion with an ADHD diagnosis recorded at any time prior to the index date was 99.54% in DK-DHR, 58.95% in InGef RDB, 99.46% in NLHR, 48.82% in BIFAP, 81.60% in SIDIAP, and 87.28% in HI-SPEED. (**Table 12**)

Among adults aged 18 years and older who initiated guanfacine, the proportion with a recorded diagnosis of hypertension any time prior to initiation was 10.58% in DK-DHR, 10.39% in InGef RDB, 17.42% in NLHR, 3.25% in BIFAP, 4.61% in SIDIAP, and 9.49% in HI-SPEED. The proportion with a recorded ADHD diagnosis prior to initiation was 99.40% in DK-DHR, 51.95% in InGef RDB, 96.73% in NLHR, 41.88% in BIFAP, 81.03% in SIDIAP, and 82.80% in HI-SPEED.

The number of children who initiated ADHD medication before the age of 5 was very small across all data sources. In the table below we reported each potential indication separately for the 30 days before index assessment window. For the windows of 7 days before index, 90 days before index, and any time before index, off label use was grouped together, including any of addictions, apathy, autism, behavioural disorders (exclude ADHD), dysfunction (exclude dementia), dementia, eating disorders, fatigue, intellectual disability, major depression disorder, mood disorders (exclude major depressive disorder), or post-traumatic brain injury.

Table 12. Potential indication of guanfacine use, by age groups and data sources.

Indication	Estimate name	Cohort name: guanfacine; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
3 to 5; Indication from 30 days before to the index date							
ADHD	N (%)	8 (100.00 %)	13 (22.81 %)	5 (83.33 %)	7 (4.67 %)	18 (62.07 %)	154 (46.39 %)
Autism	N (%)	<5	9 (15.79 %)	-	5 (3.33 %)	<5	60 (18.07 %)
Intellectual disability	N (%)	<5	5 (8.77 %)	-	-	<5	8 (2.41 %)
Behavioural disorder	N (%)	-	5 (8.77 %)	-	-	-	18 (5.42 %)
Cognitive dysfunction	N (%)	-	<5	-	<5	-	-
Hypertension	N (%)	-	-	-	-	<5	-
Unknown	N (%)	-	<5	<5	31 (20.67 %)	<5	20 (6.02 %)
None	N (%)	-	34 (59.65 %)	-	107 (71.33 %)	7 (24.14 %)	133 (40.06 %)
6 to 17; Indication from 30 days before to the index date							
Addiction	N (%)	-	-	-	<5	-	-
ADHD	N (%)	1,719 (98.62 %)	1,083 (23.21 %)	1,821 (89.62 %)	557 (5.59 %)	880 (28.35 %)	14,597 (47.89 %)
Autism	N (%)	267 (15.32 %)	173 (3.71 %)	27 (1.33 %)	94 (0.94 %)	63 (2.03 %)	3,752 (12.31 %)
Behavioural disorder	N (%)	141 (8.09 %)	646 (13.84 %)	51 (2.51 %)	148 (1.48 %)	61 (1.97 %)	1,138 (3.73 %)
Cognitive dysfunction	N (%)	-	<5	-	42 (0.42 %)	<5	-
Eating disorder	N (%)	12 (0.69 %)	16 (0.34 %)	15 (0.74 %)	25 (0.25 %)	5 (0.16 %)	193 (0.63 %)
Fatigue	N (%)	-	<5	10 (0.49 %)	8 (0.08 %)	43 (1.39 %)	-
Hypertension	N (%)	<5	9 (0.19 %)	9 (0.44 %)	6 (0.06 %)	<5	31 (0.10 %)
Intellectual disability	N (%)	50 (2.87 %)	96 (2.06 %)	12 (0.59 %)	29 (0.29 %)	20 (0.64 %)	732 (2.40 %)
Major depressive disorder	N (%)	16 (0.92 %)	67 (1.44 %)	<5	<5	6 (0.19 %)	777 (2.55 %)
Mood disorders	N (%)	44 (2.52 %)	8 (0.17 %)	50 (2.46 %)	13 (0.13 %)	5 (0.16 %)	95 (0.31 %)
Narcolepsy	N (%)	<5	-	-	-	-	-

Indication	Estimate name	Cohort name guanfacine CDM name					
		DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Post traumatic brain injury	N (%)	-	6 (0.13 %)	<5	<5	-	7 (0.02 %)
Unknown	N (%)	13 (0.75 %)	124 (2.66 %)	88 (4.33 %)	1,392 (13.96 %)	748 (24.10 %)	1,353 (4.44 %)
None	N (%)	10 (0.57 %)	3,322 (71.18 %)	105 (5.17 %)	7,831 (78.55 %)	1,368 (44.07 %)	13,426 (44.04 %)
Over 18; Indication from 30 days before to the index date							
ADHD	N (%)	3,469 (98.69 %)	35 (22.73 %)	510 (92.56 %)	20 (7.22 %)	158 (42.82 %)	5,918 (47.95 %)
Autism	N (%)	156 (4.44 %)	<5	6 (1.09 %)	7 (2.53 %)	7 (1.90 %)	1,042 (8.44 %)
Behavioural disorder	N (%)	12 (0.34 %)	<5	15 (2.72 %)	7 (2.53 %)	<5	15 (0.12 %)
Cognitive dysfunction	N (%)	<5	5 (3.25 %)	-	-	<5	13 (0.11 %)
Dementia	N (%)	<5	-	-	-	<5	<5
Eating disorder	N (%)	27 (0.77 %)	<5	5 (0.91 %)	<5	<5	91 (0.74 %)
Fatigue	N (%)	-	<5	20 (3.63 %)	-	8 (2.17 %)	8 (0.06 %)
Hypertension	N (%)	81 (2.30 %)	5 (3.25 %)	31 (5.63 %)	-	<5	178 (1.44 %)
Intellectual disability	N (%)	31 (0.88 %)	5 (3.25 %)	<5	5 (1.81 %)	<5	200 (1.62 %)
Major depressive disorder	N (%)	123 (3.50 %)	25 (16.23 %)	39 (7.08 %)	<5	8 (2.17 %)	976 (7.91 %)
Mood disorders	N (%)	558 (15.87 %)	<5	85 (15.43 %)	<5	6 (1.63 %)	489 (3.96 %)
Narcolepsy	N (%)	10 (0.28 %)	-	-	-	-	-
Post traumatic brain injury	N (%)	<5	-	<5	-	-	<5
Unknown	N (%)	21 (0.60 %)	<5	14 (2.54 %)	33 (11.91 %)	52 (14.09 %)	899 (7.28 %)
None	N (%)	8 (0.23 %)	102 (66.23 %)	12 (2.18 %)	215 (77.62 %)	141 (38.21 %)	5,134 (41.60 %)
Over 18; Indication from 90 days before to the index date							
ADHD	N (%)	3,475 (98.86 %)	46 (29.87 %)	521 (94.56 %)	25 (9.03 %)	161 (43.63 %)	7,145 (57.89 %)
Hypertension	N (%)	155 (4.41 %)	5 (3.25 %)	50 (9.07 %)	<5	<5	331 (2.68 %)
Off-label	N (%)	1,117 (31.78 %)	43 (27.92 %)	149 (27.04 %)	23 (8.30 %)	38 (10.30 %)	3,250 (26.33 %)
Unknown	N (%)	21 (0.60 %)	11 (7.14 %)	13 (2.36 %)	63 (22.74 %)	76 (20.60 %)	1,139 (9.23 %)
None	N (%)	<5	82 (53.25 %)	<5	173 (62.45 %)	109 (29.54 %)	3,587 (29.06 %)

Indication	Estimate name	Cohort name: guanfacine; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Over 18; Indication from 7 days before to the index date							
ADHD	N (%)	3,462 (98.49 %)	27 (17.53 %)	484 (87.84 %)	16 (5.78 %)	154 (41.73 %)	4,535 (36.74 %)
Hypertension	N (%)	41 (1.17 %)	<5	12 (2.18 %)	-	<5	88 (0.71 %)
Off-label	N (%)	524 (14.91 %)	26 (16.88 %)	94 (17.06 %)	11 (3.97 %)	24 (6.50 %)	1,770 (14.34 %)
Unknown	N (%)	16 (0.46 %)	<5	21 (3.81 %)	12 (4.33 %)	34 (9.21 %)	595 (4.82 %)
None	N (%)	23 (0.65 %)	116 (75.32 %)	33 (5.99 %)	241 (87.00 %)	165 (44.72 %)	6,912 (56.00 %)
Over 18; Indication any time before or on index date							
ADHD	N (%)	3,494 (99.40 %)	80 (51.95 %)	533 (96.73 %)	116 (41.88 %)	299 (81.03 %)	10,219 (82.80 %)
Hypertension	N (%)	372 (10.58 %)	16 (10.39 %)	96 (17.42 %)	9 (3.25 %)	17 (4.61 %)	1,171 (9.49 %)
Off-label	N (%)	2,569 (73.09 %)	93 (60.39 %)	440 (79.85 %)	116 (41.88 %)	216 (58.54 %)	7,777 (63.01 %)
Unknown	N (%)	6 (0.17 %)	15 (9.74 %)	<5	92 (33.21 %)	22 (5.96 %)	1,039 (8.42 %)
None	N (%)	-	28 (18.18 %)	-	<5	<5	140 (1.13 %)
3 to 5; Indication from 90 days before to the index date							
ADHD	N (%)	8 (100.00 %)	16 (28.07 %)	5 (83.33 %)	11 (7.33 %)	19 (65.52 %)	198 (59.64 %)
Hypertension	N (%)	-	-	-	-	<5	-
Off-label	N (%)	<5	17 (29.82 %)	-	11 (7.33 %)	<5	96 (28.92 %)
Unknown	N (%)	-	7 (12.28 %)	<5	67 (44.67 %)	5 (17.24 %)	26 (7.83 %)
None	N (%)	-	27 (47.37 %)	-	63 (42.00 %)	<5	81 (24.40 %)
3 to 5; Indication from 7 days before to the index date							
ADHD	N (%)	8 (100.00 %)	11 (19.30 %)	5 (83.33 %)	6 (4.00 %)	18 (62.07 %)	124 (37.35 %)
Hypertension	N (%)	-	-	-	-	<5	-
Off-label	N (%)	<5	11 (19.30 %)	-	<5	<5	58 (17.47 %)
Unknown	N (%)	-	<5	-	8 (5.33 %)	<5	12 (3.61 %)
None	N (%)	-	42 (73.68 %)	<5	135 (90.00 %)	8 (27.59 %)	177 (53.31 %)
3 to 5; Indication any time before or on index date							

Indication	Estimate name	Cohort name: guanfacine; CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
ADHD	N (%)	8 (100.00 %)	27 (47.37 %)	5 (83.33 %)	27 (18.00 %)	20 (68.97 %)	251 (75.60 %)
Hypertension	N (%)	-	-	-	-	<5	<5
Off-label	N (%)	<5	32 (56.14 %)	<5	64 (42.67 %)	21 (72.41 %)	140 (42.17 %)
Unknown	N (%)	-	15 (26.32 %)	-	71 (47.33 %)	<5	49 (14.76 %)
None	N (%)	-	6 (10.53 %)	-	<5	-	-
6 to 17; Indication from 90 days before to the index date							
ADHD	N (%)	1,723 (98.85 %)	1,540 (33.00 %)	1,962 (96.56 %)	724 (7.26 %)	932 (30.03 %)	17,926 (58.81 %)
Hypertension	N (%)	6 (0.34 %)	12 (0.26 %)	12 (0.59 %)	8 (0.08 %)	<5	49 (0.16 %)
Off-label	N (%)	551 (31.61 %)	1,227 (26.29 %)	255 (12.55 %)	458 (4.59 %)	250 (8.05 %)	7,336 (24.07 %)
Unknown	N (%)	13 (0.75 %)	236 (5.06 %)	43 (2.12 %)	2,949 (29.58 %)	1,034 (33.31 %)	1,800 (5.90 %)
None	N (%)	<5	2,686 (57.55 %)	21 (1.03 %)	6,006 (60.24 %)	1,000 (32.22 %)	9,582 (31.43 %)
6 to 17; Indication from 7 days before to the index date							
ADHD	N (%)	1,712 (98.22 %)	794 (17.01 %)	1,665 (81.94 %)	432 (4.33 %)	854 (27.51 %)	11,547 (37.88 %)
Hypertension	N (%)	<5	6 (0.13 %)	<5	<5	<5	17 (0.06 %)
Off-label	N (%)	340 (19.51 %)	654 (14.01 %)	91 (4.48 %)	232 (2.33 %)	159 (5.12 %)	4,350 (14.27 %)
Unknown	N (%)	11 (0.63 %)	58 (1.24 %)	87 (4.28 %)	498 (4.99 %)	554 (17.85 %)	940 (3.08 %)
None	N (%)	20 (1.15 %)	3,719 (79.69 %)	261 (12.84 %)	8,907 (89.34 %)	1,601 (51.58 %)	17,052 (55.94 %)
6 to 17; Indication any time before or on index date							
ADHD	N (%)	1,735 (99.54 %)	2,751 (58.95 %)	2,021 (99.46 %)	4,867 (48.82 %)	2,533 (81.60 %)	26,605 (87.28 %)
Hypertension	N (%)	17 (0.98 %)	35 (0.75 %)	24 (1.18 %)	38 (0.38 %)	18 (0.58 %)	118 (0.39 %)
Off-label	N (%)	832 (47.73 %)	2,433 (52.13 %)	1,308 (64.37 %)	3,220 (32.30 %)	1,747 (56.28 %)	13,692 (44.92 %)
Unknown	N (%)	6 (0.34 %)	712 (15.26 %)	<5	3,537 (35.48 %)	172 (5.54 %)	2,269 (7.44 %)
None	N (%)	-	849 (18.19 %)	-	203 (2.04 %)	-	259 (0.85 %)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

9.2.4. Objective 4: drug utilisation

Tables 13–17 present the treatment dose and quantity of all study medications in each data source.

Among individuals who initiated atomoxetine, the median starting dose ranged from 26.13mg in InGef RDB to 39.78mg in SIDIAP, with a higher median dose of 96.13mg observed in DK-DHR. Initiators typically received two to four prescriptions before discontinuation (defined as a 30-day gap) or switching. The median duration of prescribed treatment episodes ranged from 38 days in NLHR to 91 days in HI-SPEED. A longer treatment duration was observed in SIDIAP, with a median of 205 days. (**Table 13**)

Among individuals who initiated guanfacine, the median starting dose ranged from 0.93mg in NLHR to 1.94 mg in SIDIAP, while a notably higher median dose of 3.03mg was observed in DK-DHR. Initiators typically received 2–5 prescriptions before discontinuation or switching. The median duration of prescribed treatment episodes ranged from 55 days in DK-DHR to 120 days in InGef RDB. A particularly long treatment duration was observed in SIDIAP, with a median of 262 days. (**Table 14**)

Among individuals who initiated lisdexamfetamine, the median starting dose was 29.03–30.00mg in all data sources. Initiators typically received 2 to 5 prescriptions before discontinuation or switching. The median duration of prescribed treatment episodes ranged from 60 days in InGef RDB to 252 days in SIDIAP. (**Table 15**)

Among individuals who initiated methylphenidate, the median starting dose ranged from 16.67mg in InGef RDB to 30.00mg in DK-DHR. Initiators typically received 2 to 4 prescriptions before discontinuation or switching. The median duration of prescribed treatment episodes ranged from 60 days in InGef RDB to 123 days in NLHR. A longer treatment duration was observed in SIDIAP, with a median of 255 days. (**Table 16**)

Among individuals who initiated dextroamphetamine in four data sources, the median starting dose ranged from 4.90mg in NLHR to 15.00mg in DK-DHR. Initiators typically received 1–2 prescriptions before discontinuation or switching. The median duration of prescribed treatment episodes ranged from 20 days in DK-DHR to 67 in HI-SPEED. (**Table 17**)

Table 18 summarises methylphenidate utilisation in each data source, stratified by age group. Results for other stratifications are available in the accompanying Shiny app. In DK-DHR, the median starting dose was similar across all age groups, at approximately 30.00mg, with a higher number of prescriptions observed among children and adolescents. In InGef RDB, the median starting daily dose was 16.67mg among children aged 3–11 years and 18.67–20.00mg among those aged 12 years and older. Longer treatment durations were observed in the youngest age group. In NLHR, the median starting dose was 9.52mg among children aged 3–11 years and 19.05mg among those aged 12 years and older. The number of prescribed days was similar across most age groups (3–11, 12–17, and ≥25 years), while adults aged 18–24 years had shorter treatment durations. In BIFAP, the median starting dose was 9.68mg among children aged 3–11 years and 18.00–27.00 mg among individuals aged 13 years and older, with longer treatment durations again observed in the youngest group. In SIDIAP, the initial dose ranged from 17.97–19.84mg in children aged 3–11 years and adults aged ≥25 years, and around 36mg among adolescents aged 13-18 years and young adults aged 18–24 years. In HI-SPEED, the starting dose was similar across all age groups (17.42–19.67mg), with total prescribed days longest in the youngest group, followed by adults aged ≥25 years.

Table 13. Dosage and quantity of incident user by data source: atomoxetine.

Ingredient	Variable name	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Atomoxetine	Number records	N	70,713	10,190	16,459	23,477	8,841	57,086
	Number subjects	N	63,576	9,781	15,836	21,796	8,199	54,687
	Number exposures	Median (Q25 – Q75)	4 (2 – 8)	3 (2 – 5)	3 (1 – 6)	3 (1 – 7)	2 (1 – 4)	3 (2 – 8)
	Cumulative quantity	Median (Q25 – Q75)	84.00 (28.00 – 196.00)	91.00 (56.00 – 168.00)	35.88 (14.00 – 85.75)	84.00 (35.00 – 252.00)	240.00 (86.00 – 598.00)	140.00 (56.00 – 336.00)
	Initial quantity	Median (Q25 – Q75)	28.00 (0.00 – 30.00)	28.00 (28.00 – 56.00)	10.50 (5.00 – 16.19)	28.00 (28.00 – 28.00)	90.00 (33.00 – 216.00)	28.00 (28.00 – 56.00)
	Initial exposure duration	Median (Q25 – Q75)	8 (3 – 14)	30 (30 – 30)	9 (6 – 15)	29 (16 – 29)	75 (29 – 181)	29 (16 – 31)
	Number eras	Median (Q25 – Q75)	3 (1 – 5)	1 (1 – 2)	2 (1 – 4)	2 (1 – 4)	1 (1 – 1)	2 (1 – 3)
	Days prescribed	Median (Q25 – Q75)	49 (16 – 138)	90 (31 – 150)	38 (15 – 89)	76 (29 – 190)	205 (80 – 477)	91 (31 – 254)
	Cumulative dose milligram	Median (Q25 – Q75)	2,559.20 (800.80 – 8,430.00)	2,744.00 (1,120.00 – 5,971.52)	1,144.85 (437.50 – 3,718.75)	2,415.00 (1,120.00 – 7,222.07)	7,960.00 (2,375.00 – 21,616.00)	3,560.24 (1,200.00 – 10,638.82)
	Initial daily dose milligram	Median (Q25 – Q75)	96.13 (91.40 – 103.00)	26.13 (10.03 – 49.47)	33.06 (16.20 – 38.62)	38.62 (21.88 – 57.93)	39.78 (24.72 – 61.09)	37.62 (17.42 – 63.64)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 14. Dosage and quantity of incident user by data source: guanfacine.

Ingredient	Variable name	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Guanfacine	Number records	N	5,266	4,878	2,589	10,397	3,502	43,157
	Number subjects	N	5,104	4,646	2,533	9,858	3,228	41,243
	Number exposures	Median (Q25 – Q75)	4 (1 – 8)	4 (2 – 8)	4 (2 – 9)	5 (2 – 14)	2 (1 – 5)	4 (1 – 9)
	Cumulative quantity	Median (Q25 – Q75)	28.00 (0.00 – 84.00)	140.00 (56.00 – 252.00)	65.33 (18.67 – 242.67)	140.00 (56.00 – 392.00)	312.50 (118.00 – 727.00)	140.00 (56.00 – 364.00)
	Initial quantity	Median (Q25 – Q75)	0.00 (0.00 – 28.00)	28.00 (28.00 – 28.00)	9.33 (9.33 – 9.33)	28.00 (28.00 – 28.00)	89.00 (30.00 – 207.75)	28.00 (28.00 – 28.00)
	Initial exposure duration	Median (Q25 – Q75)	9 (9 – 9)	30 (30 – 30)	10 (10 – 10)	29 (28 – 29)	75 (29 – 180)	29 (29 – 29)
	Number eras	Median (Q25 – Q75)	2 (1 – 5)	2 (1 – 3)	2 (1 – 4)	2 (1 – 6)	1 (1 – 1)	2 (1 – 4)
	Days prescribed	Median (Q25 – Q75)	55 (18 – 193)	120 (60 – 240)	68 (20 – 240)	143 (58 – 380)	262 (103 – 604)	115 (29 – 329)
	Cumulative dose milligram	Median (Q25 – Q75)	28.00 (0.00 – 196.00)	140.00 (0.00 – 448.00)	112.00 (18.67 – 563.51)	235.00 (73.00 – 842.00)	512.00 (170.00 – 1,463.77)	168.00 (56.00 – 644.00)
	Initial daily dose milligram	Median (Q25 – Q75)	3.03 (0.00 – 3.11)	1.87 (0.00 – 1.87)	0.93 (0.93 – 0.93)	1.00 (1.00 – 2.00)	1.94 (0.98 – 2.98)	0.97 (0.97 – 1.87)

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Table 15. Dosage and quantity of incident user by data source: lisdexamfetamine.

Ingredient	Variable name	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Lisdexamfetamine	Number records	N	66,747	28,373	59,688	37,891	9,487	208,859
	Number subjects	N	62,073	26,690	56,233	34,747	8,628	188,007
	Number exposures	Median (Q25 – Q75)	4 (2 – 11)	2 (1 – 5)	5 (2 – 12)	3 (1 – 7)	2 (1 – 3)	4 (2 – 11)
	Cumulative quantity	Median (Q25 – Q75)	90.00 (30.00 – 270.00)	90.00 (30.00 – 180.00)	220.00 (70.00 – 730.00)	90.00 (30.00 – 210.00)	284.00 (106.00 – 627.50)	150.00 (60.00 – 420.00)
	Initial quantity	Median (Q25 – Q75)	0.00 (0.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 50.00)	30.00 (30.00 – 30.00)	117.00 (46.00 – 255.50)	30.00 (30.00 – 30.00)
	Initial exposure duration	Median (Q25 – Q75)	20 (20 – 30)	30 (30 – 30)	31 (31 – 41)	31 (31 – 31)	117 (48 – 251)	31 (31 – 31)
	Number eras	Median (Q25 – Q75)	1 (1 – 2)	2 (1 – 3)	1 (1 – 2)	2 (1 – 4)	1 (1 – 1)	2 (1 – 4)
	Days prescribed	Median (Q25 – Q75)	180 (50 – 604)	60 (30 – 150)	209 (71 – 700)	93 (31 – 217)	252 (98 – 586)	153 (62 – 401)
	Cumulative dose milligram	Median (Q25 – Q75)	2,400.00 (600.00 – 10,800.00)	2,700.00 (1,200.00 – 6,570.00)	8,300.00 (2,100.00 – 32,400.00)	3,029.03 (1,500.00 – 8,400.00)	9,703.34 (3,475.54 – 25,300.00)	5,400.00 (1,800.00 – 16,800.00)
	Initial daily dose milligram	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	30.00 (20.00 – 30.00)	29.03 (29.03 – 29.51)	29.03 (29.03 – 48.39)	29.87 (29.52 – 49.71)	29.03 (19.35 – 39.34)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 16. Dosage and quantity of incident users by data source: methylphenidate.

Ingredient	Variable name	Estimate name	CDM name					
			DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
Methylphenidate	Number records	N	213,454	97,986	118,925	182,389	69,903	289,196
	Number subjects	N	180,889	87,827	107,262	155,537	58,906	259,788
	Number exposures	Median (Q25 – Q75)	4 (2 – 9)	2 (1 – 4)	4 (2 – 10)	3 (1 – 6)	2 (1 – 4)	4 (2 – 8)
	Cumulative quantity	Median (Q25 – Q75)	150.00 (60.00 – 420.00)	120.00 (60.00 – 224.00)	120.00 (50.00 – 436.67)	90.00 (30.00 – 180.00)	321.00 (90.00 – 825.00)	150.00 (60.00 – 360.00)
	Initial quantity	Median (Q25 – Q75)	30.00 (30.00 – 60.00)	50.00 (50.00 – 70.00)	20.00 (18.00 – 54.00)	30.00 (30.00 – 30.00)	113.00 (34.00 – 300.00)	30.00 (30.00 – 60.00)
	Initial exposure duration	Median (Q25 – Q75)	18 (10 – 30)	30 (30 – 30)	21 (16 – 41)	31 (30 – 31)	91 (31 – 227)	31 (31 – 31)
	Number eras	Median (Q25 – Q75)	2 (1 – 3)	1 (1 – 2)	1 (1 – 3)	2 (1 – 3)	1 (1 – 1)	2 (1 – 3)
	Days prescribed	Median (Q25 – Q75)	108 (33 – 376)	60 (30 – 120)	123 (49 – 437)	78 (31 – 186)	255 (90 – 693)	122 (48 – 304)
	Cumulative dose milligram	Median (Q25 – Q75)	2,400.00 (690.00 – 9,000.00)	1,680.00 (774.21 – 3,430.00)	1,053.00 (324.00 – 4,600.00)	837.00 (0.00 – 2,904.00)	6,180.00 (1,620.00 – 19,413.00)	3,240.00 (1,080.00 – 9,300.00)
	Initial daily dose milligram	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	16.67 (10.00 – 33.33)	19.05 (9.09 – 19.67)	18.00 (0.00 – 29.03)	26.68 (17.10 – 39.83)	19.35 (17.42 – 38.57)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 17. Dosage and quantity of incident user by data source: dextroamphetamine.

Ingredient	Variable name	Estimate name	CDM name			
			DK-DHR	InGef RDB	NLHR	HI-SPEED
Dextroamphetamine	Number records	N	10,117	3,333	12,284	38,462
	Number subjects	N	9,209	3,114	11,340	34,309
	Number exposures	Median (Q25 – Q75)	1 (1 – 3)	1 (1 – 3)	2 (1 – 8)	2 (1 – 5)
	Cumulative quantity	Median (Q25 – Q75)	30.00 (0.00 – 60.00)	50.00 (30.00 – 120.00)	53.33 (20.00 – 320.00)	100.00 (60.00 – 350.00)
	Initial quantity	Median (Q25 – Q75)	30.00 (0.00 – 30.00)	30.00 (20.00 – 50.00)	20.00 (10.00 – 33.33)	50.00 (30.00 – 100.00)
	Initial exposure duration	Median (Q25 – Q75)	10 (10 – 20)	30 (30 – 30)	21 (11 – 34)	34 (19 – 51)
	Number eras	Median (Q25 – Q75)	1 (1 – 2)	1 (1 – 2)	1 (1 – 2)	1 (1 – 2)
	Days prescribed	Median (Q25 – Q75)	20 (10 – 60)	30 (30 – 90)	51 (21 – 316)	67 (34 – 202)
	Cumulative dose milligram	Median (Q25 – Q75)	150.00 (0.00 – 450.00)	400.00 (250.00 – 1,000.00)	333.33 (112.74 – 2,460.51)	500.00 (450.00 – 2,150.00)
	Initial daily dose milligram	Median (Q25 – Q75)	15.00 (0.00 – 15.00)	8.33 (3.33 – 10.00)	4.90 (4.55 – 4.99)	11.54 (6.02 – 12.20)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

Table 18. Dosage and quantity of incident methylphenidate user by age group and data source.

Variable name	Estimate name	Cohort name: Methylphenidate; Age group: 3 to 11	12 to 17	18 to 24	25 to 150
DK-DHR					
Number records	N	30,365	35,061	43,683	104,345
Number subjects	N	29,023	33,521	39,996	90,068
Number exposures	Median (Q25 – Q75)	6 (3 – 12)	4 (2 – 9)	3 (1 – 7)	3 (1 – 10)
Cumulative quantity	Median (Q25 – Q75)	210.00 (90.00 – 540.00)	150.00 (60.00 – 360.00)	120.00 (30.00 – 300.00)	130.00 (60.00 – 460.00)
Initial quantity	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 56.00)	30.00 (30.00 – 60.00)
Initial exposure duration	Median (Q25 – Q75)	10 (5 – 20)	18 (10 – 20)	18 (10 – 30)	18 (10 – 30)
Number eras	Median (Q25 – Q75)	3 (2 – 5)	2 (1 – 3)	2 (1 – 2)	1 (1 – 2)
Days prescribed	Median (Q25 – Q75)	130 (40 – 380)	140 (50 – 395)	90 (30 – 282)	99 (30 – 414)
Cumulative dose milligram	Median (Q25 – Q75)	3,000.00 (900.00 – 9,000.00)	3,240.00 (1,050.00 – 10,020.00)	2,100.00 (600.00 – 6,960.00)	2,160.00 (600.00 – 9,720.00)
Initial daily dose milligram	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)
InGef RDB					
Number records	N	39,305	20,794	11,942	25,945
Number subjects	N	37,692	19,644	10,992	23,158
Number exposures	Median (Q25 – Q75)	3 (2 – 5)	2 (1 – 4)	2 (1 – 3)	2 (1 – 4)
Cumulative quantity	Median (Q25 – Q75)	150.00 (84.00 – 250.00)	102.00 (56.00 – 180.00)	100.00 (52.00 – 180.00)	130.00 (56.00 – 258.00)
Initial quantity	Median (Q25 – Q75)	50.00 (40.00 – 60.00)	50.00 (40.00 – 60.00)	52.00 (50.00 – 78.00)	52.00 (50.00 – 78.00)
Initial exposure duration	Median (Q25 – Q75)	30 (30 – 30)	30 (30 – 30)	30 (30 – 30)	30 (30 – 30)
Number eras	Median (Q25 – Q75)	2 (1 – 3)	1 (1 – 2)	1 (1 – 2)	1 (1 – 2)

Variable name	Estimate name	Cohort name: Methylphenidate; Age group: 3 to 11	12 to 17	18 to 24	25 to 150
Days prescribed	Median (Q25 – Q75)	90 (60 – 150)	60 (30 – 120)	60 (30 – 90)	60 (30 – 120)
Cumulative dose milligram	Median (Q25 – Q75)	1,700.00 (810.00 – 3,500.00)	1,740.00 (980.00 – 3,360.00)	1,500.00 (600.00 – 2,860.00)	1,670.00 (598.00 – 3,640.00)
Initial daily dose milligram	Median (Q25 – Q75)	16.67 (9.00 – 25.00)	20.00 (16.67 – 36.67)	19.50 (13.00 – 37.33)	18.67 (13.00 – 33.33)
NLHR					
Number records	N	21,845	23,396	21,256	52,428
Number subjects	N	21,097	22,188	19,665	47,943
Number exposures	Median (Q25 – Q75)	5 (2 – 11)	4 (2 – 8)	3 (1 – 7)	4 (2 – 13)
Cumulative quantity	Median (Q25 – Q75)	127.00 (50.00 – 380.00)	130.00 (54.00 – 352.00)	90.00 (40.00 – 300.00)	133.33 (50.00 – 620.00)
Initial quantity	Median (Q25 – Q75)	20.00 (10.00 – 35.00)	30.00 (18.00 – 60.00)	20.00 (20.00 – 50.00)	20.00 (20.00 – 60.00)
Initial exposure duration	Median (Q25 – Q75)	21 (11 – 31)	31 (19 – 55)	21 (21 – 41)	21 (21 – 55)
Number eras	Median (Q25 – Q75)	2 (1 – 5)	1 (1 – 3)	1 (1 – 2)	1 (1 – 2)
Days prescribed	Median (Q25 – Q75)	129 (52 – 384)	128 (55 – 356)	93 (41 – 296)	134 (47 – 619)
Cumulative dose milligram	Median (Q25 – Q75)	972.00 (50.00 – 4,600.00)	1,200.00 (100.00 – 5,488.50)	800.00 (400.00 – 2,916.00)	1,200.00 (400.00 – 5,149.37)
Initial daily dose milligram	Median (Q25 – Q75)	9.52 (4.17 – 19.05)	19.05 (9.09 – 29.67)	19.05 (9.09 – 19.51)	19.05 (9.09 – 19.51)
BIFAP					
Number records	N	81,003	55,857	15,593	29,936
Number subjects	N	75,891	51,860	14,152	26,852
Number exposures	Median (Q25 – Q75)	3 (2 – 8)	2 (1 – 5)	2 (1 – 4)	2 (1 – 6)
Cumulative quantity	Median (Q25 – Q75)	90.00 (60.00 – 240.00)	60.00 (30.00 – 150.00)	60.00 (30.00 – 120.00)	60.00 (30.00 – 180.00)
Initial quantity	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 30.00)
Initial exposure duration	Median (Q25 – Q75)	31 (30 – 31)	31 (31 – 31)	31 (31 – 31)	31 (20 – 31)

Variable name	Estimate name	Cohort name: Methylphenidate; Age group: 3 to 11	12 to 17	18 to 24	25 to 150
Number eras	Median (Q25 – Q75)	2 (1 – 4)	1 (1 – 3)	1 (1 – 2)	1 (1 – 3)
Days prescribed	Median (Q25 – Q75)	93 (32 – 233)	69 (31 – 163)	61 (31 – 124)	62 (31 – 163)
Cumulative dose milligram	Median (Q25 – Q75)	450.00 (0.00 – 2,088.00)	1,200.00 (300.00 – 3,906.00)	1,116.00 (300.00 – 3,000.00)	900.00 (300.00 – 3,300.00)
Initial daily dose milligram	Median (Q25 – Q75)	9.68 (0.00 – 18.75)	27.00 (9.38 – 36.00)	19.35 (9.68 – 37.50)	18.00 (9.38 – 36.00)
SIDIAP					
Number records	N	24,345	22,923	5,881	16,754
Number subjects	N	22,638	21,156	5,543	15,131
Number exposures	Median (Q25 – Q75)	2 (1 – 5)	2 (1 – 3)	2 (1 – 3)	2 (1 – 3)
Cumulative quantity	Median (Q25 – Q75)	360.00 (100.00 – 1,032.00)	317.00 (104.00 – 744.50)	348.00 (102.00 – 748.00)	240.00 (61.00 – 730.00)
Initial quantity	Median (Q25 – Q75)	113.00 (33.00 – 294.00)	126.00 (45.00 – 318.00)	146.00 (45.00 – 364.00)	85.25 (30.00 – 240.00)
Initial exposure duration	Median (Q25 – Q75)	91 (31 – 214)	111 (37 – 250)	121 (38 – 308)	70 (31 – 181)
Number eras	Median (Q25 – Q75)	1 (1 – 1)	1 (1 – 1)	1 (1 – 1)	1 (1 – 1)
Days prescribed	Median (Q25 – Q75)	302 (93 – 846)	272 (101 – 663)	254 (91 – 621)	181 (61 – 539)
Cumulative dose milligram	Median (Q25 – Q75)	5,970.00 (1,540.00 – 20,043.00)	8,046.00 (2,474.10 – 21,559.00)	7,263.00 (2,160.00 – 20,130.00)	3,500.00 (810.00 – 13,696.46)
Initial daily dose milligram	Median (Q25 – Q75)	19.84 (14.17 – 29.91)	35.85 (19.93 – 53.41)	35.60 (17.95 – 53.38)	17.97 (9.84 – 35.60)
HI-SPEED					
Number records	N	60,490	88,087	39,486	101,133
Number subjects	N	58,068	82,876	36,803	91,533
Number exposures	Median (Q25 – Q75)	5 (2 – 10)	3 (2 – 6)	3 (1 – 6)	4 (2 – 11)
Cumulative quantity	Median (Q25 – Q75)	180.00 (90.00 – 420.00)	120.00 (60.00 – 270.00)	90.00 (30.00 – 240.00)	150.00 (60.00 – 510.00)

Variable name	Estimate name	Cohort name: Methylphenidate; Age group: 3 to 11	12 to 17	18 to 24	25 to 150
Initial quantity	Median (Q25 – Q75)	30.00 (30.00 – 30.00)	30.00 (30.00 – 60.00)	30.00 (30.00 – 30.00)	30.00 (30.00 – 60.00)
Initial exposure duration	Median (Q25 – Q75)	31 (28 – 31)	31 (31 – 31)	31 (31 – 31)	31 (31 – 31)
Number eras	Median (Q25 – Q75)	2 (1 – 4)	2 (1 – 3)	1 (1 – 3)	2 (1 – 4)
Days prescribed	Median (Q25 – Q75)	155 (62 – 372)	109 (55 – 229)	91 (31 – 214)	124 (44 – 390)
Cumulative dose milligram	Median (Q25 – Q75)	3,300.00 (1,200.00 – 9,180.00)	3,179.03 (1,200.00 – 7,290.00)	2,280.00 (900.00 – 7,020.00)	3,600.00 (1,080.00 – 14,002.00)
Initial daily dose milligram	Median (Q25 – Q75)	17.42 (9.68 – 30.00)	19.35 (17.42 – 38.57)	19.35 (17.42 – 42.86)	19.67 (17.42 – 45.00)

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DRUG RESTART

We assessed the patterns of restarting and switching medications after initiation of one of the study drugs. (**Table 19**) Among individuals who initiated methylphenidate, during the first 90 days following discontinuation (defined as a 30-day prescription gap), 18% in SIDIAP to 54% in InGef RDB restarted methylphenidate; 2.6% in BIFAP to 14% in HI-SPEED switched to another study medication; and 40% in InGef RDB to 77% in SIDIAP did not use any ADHD medication during this period.

From the first methylphenidate discontinuation to the end of the observation period, 29% in HI-SPEED to 56% in InGef RDB restarted the same medication, while 10% in SIDIAP to 26% in HI-SPEED both restarted the same medication and switched to another ADHD treatment. Between 21% in InGef RDB and 50% in SIDIAP had no record of further ADHD medication use and remained untreated for the remainder of the observation period.

Table 19. Medication restarts or switch within different time windows after first discontinuation of methylphenidate use, by data source.

Sex	Treatment	Estimate name	CDM name: DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
			Cohort name: methylphenidate					
Drug restart in 90 days								
Overall	Restart	N (%)	64,458 (30.92 %)	65,319 (54.13 %)	30,924 (28.70 %)	95,818 (42.31 %)	12,995 (18.01 %)	86,434 (33.19 %)
	Switch	N (%)	22,391 (10.74 %)	5,379 (4.46 %)	11,934 (11.07 %)	5,893 (2.60 %)	3,142 (4.35 %)	36,594 (14.05 %)
	Restart and switch	N (%)	3,048 (1.46 %)	1,670 (1.38 %)	1,872 (1.74 %)	1,297 (0.57 %)	350 (0.49 %)	6,971 (2.68 %)
	Untreated	N (%)	118,581 (56.88 %)	48,295 (40.02 %)	63,031 (58.49 %)	123,434 (54.51 %)	55,671 (77.15 %)	130,423 (50.08 %)
Drug restart in 180 days								
Overall	Restart	N (%)	73,663 (35.33 %)	74,863 (62.04 %)	36,766 (34.12 %)	124,392 (54.93 %)	19,182 (26.58 %)	98,157 (37.69 %)
	Switch	N (%)	26,082 (12.51 %)	6,340 (5.25 %)	14,002 (12.99 %)	7,623 (3.37 %)	3,303 (4.58 %)	44,339 (17.03 %)
	Restart and switch	N (%)	7,466 (3.58 %)	4,108 (3.40 %)	4,408 (4.09 %)	3,796 (1.68 %)	775 (1.07 %)	17,610 (6.76 %)
	Untreated	N (%)	101,267 (48.57 %)	35,352 (29.30 %)	52,585 (48.80 %)	90,631 (40.02 %)	48,898 (67.77 %)	100,316 (38.52 %)
Drug restart till end of observation								
Overall	Restart	N (%)	65,117 (31.23 %)	67,648 (56.06 %)	34,959 (32.44 %)	118,537 (52.35 %)	25,449 (35.27 %)	74,908 (28.76 %)
	Switch	N (%)	29,788 (14.29 %)	6,745 (5.59 %)	17,282 (16.04 %)	9,958 (4.40 %)	3,639 (5.04 %)	52,448 (20.14 %)
	Restart and switch	N (%)	40,181 (19.27 %)	20,624 (17.09 %)	16,775 (15.57 %)	35,352 (15.61 %)	7,088 (9.82 %)	67,868 (26.06 %)
	Untreated	N (%)	73,392 (35.20 %)	25,646 (21.25 %)	38,745 (35.95 %)	62,595 (27.64 %)	35,982 (49.87 %)	65,198 (25.04 %)

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

9.2.5. Objective 5: proportion of patient covered

Table 20 summarises the proportion of patients who continued treatment (PPC) among individuals who initiated each of the study medications during the first four years after initiation. After six months of treatment initiation, the PPC for any ADHD medication was 50.37% in DK-DHR, 18.25% in InGef RDB, 57.66% in NLHR, 30.02% in BIFAP, 60.15% in SIDIAP, and 52.26% in HI-SPEED.

As expected, PPC declined at both one and two years after initiation. Two years after treatment initiation, the PPC for any ADHD medication was 22.36% in DK-DHR, 3.67% in InGef RDB, 31.76% in NLHR, 7.88% in BIFAP, 29.76% in SIDIAP, and 22.25% in HI-SPEED.

We also estimated PPC by age and sex. **Figure 15** presents the PPC of any ADHD medication across different age groups in each data source. After initiation, individuals aged 3–11 years showed better treatment persistence compared with the other three age groups in BIFAP and SIDIAP. In contrast, in DK-DHR, NLHR, and HI-SPEED, higher persistence was observed among adults aged over 25 years. Results for individual medications within each data source are available in the online Shiny app.

Table 20. Proportion of patients covered since initiation of any ADHD medication, by data source.

Time	Estimate name	CDM name					
		DK-DHR	InGef RDB	NLHR	BIFAP	SIDIAP	HI-SPEED
6 months	PPC (95%CI)	50.37% [50.13% – 50.60%]	18.25% [17.99% – 18.52%]	57.66% [57.37% – 57.94%]	30.02% [29.79% – 30.24%]	60.15% [59.76% – 60.54%]	52.26% [52.09% – 52.44%]
1 year	PPC (95%CI)	34.25% [34.02% – 34.49%]	6.97% [6.79% – 7.16%]	42.31% [42.01% – 42.62%]	14.86% [14.68% – 15.05%]	43.86% [43.45% – 44.27%]	34.76% [34.59% – 34.94%]
2 years	PPC (95%CI)	22.36% [22.14% – 22.59%]	3.67% [3.52% – 3.83%]	31.76% [31.45% – 32.08%]	7.88% [7.74% – 8.03%]	29.76% [29.37% – 30.16%]	22.25% [22.09% – 22.42%]
3 years	PPC (95%CI)	17.20% [16.98% – 17.42%]	2.56% [2.42% – 2.71%]	27.34% [27.01% – 27.68%]	5.35% [5.22% – 5.49%]	23.13% [22.75% – 23.51%]	17.07% [16.90% – 17.23%]
4 years	PPC (95%CI)	14.40% [14.18% – 14.62%]	1.98% [1.84% – 2.12%]	25.28% [24.93% – 25.64%]	3.90% [3.78% – 4.03%]	18.68% [18.31% – 19.05%]	14.24% [14.07% – 14.41%]
5 years	PPC (95%CI)	12.56% [12.34% – 12.79%]	1.66% [1.52% – 1.82%]	24.45% [24.06% – 24.85%]	3.03% [2.92% – 3.15%]	15.45% [15.09% – 15.81%]	12.85% [12.68% – 13.03%]

PPC=Proportion of patients covered; DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

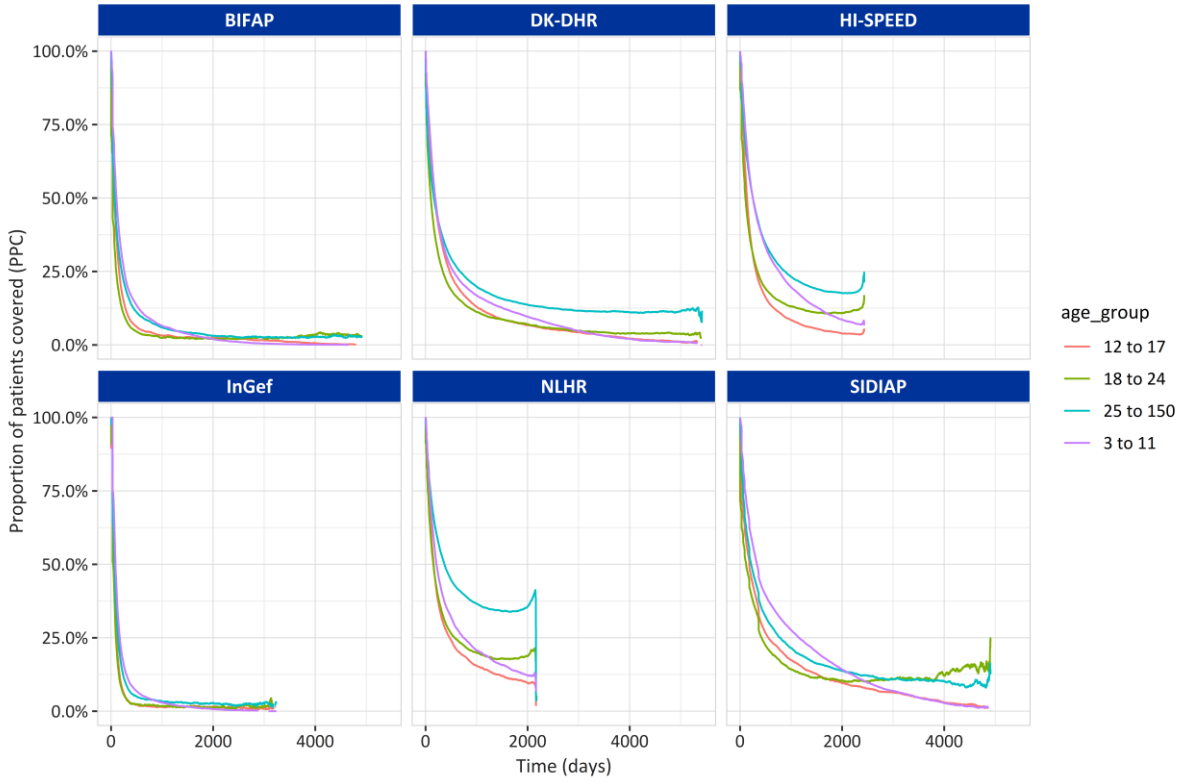

Figure 15. Proportion of patients covered of using any ADHD medication by age groups and data sources.

DK-DHR=Danish Data Health Registries; InGef=InGef Research Database; NLHR=Norwegian Linked Health Registry data; BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público; SIDIAP=The Information System for Research on Primary Care; HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage.

9.2.6. Objective 6: treatment patterns

Among individuals who started any of the study medication during the study period, we illustrated the treatment pathways using Sankey diagrams.

In all data sources, the most common first line treatment was methylphenidate, followed by lisdexamfetamine and atomoxetine. Most individuals stopped the treatment after initiation, while a small proportion of individuals switch to another medication. **Figures 16 – 21** shows the overall treatment pathway in each data source.

Further stratification by age groups, sex, and calendar period can be visualised in the shiny app.

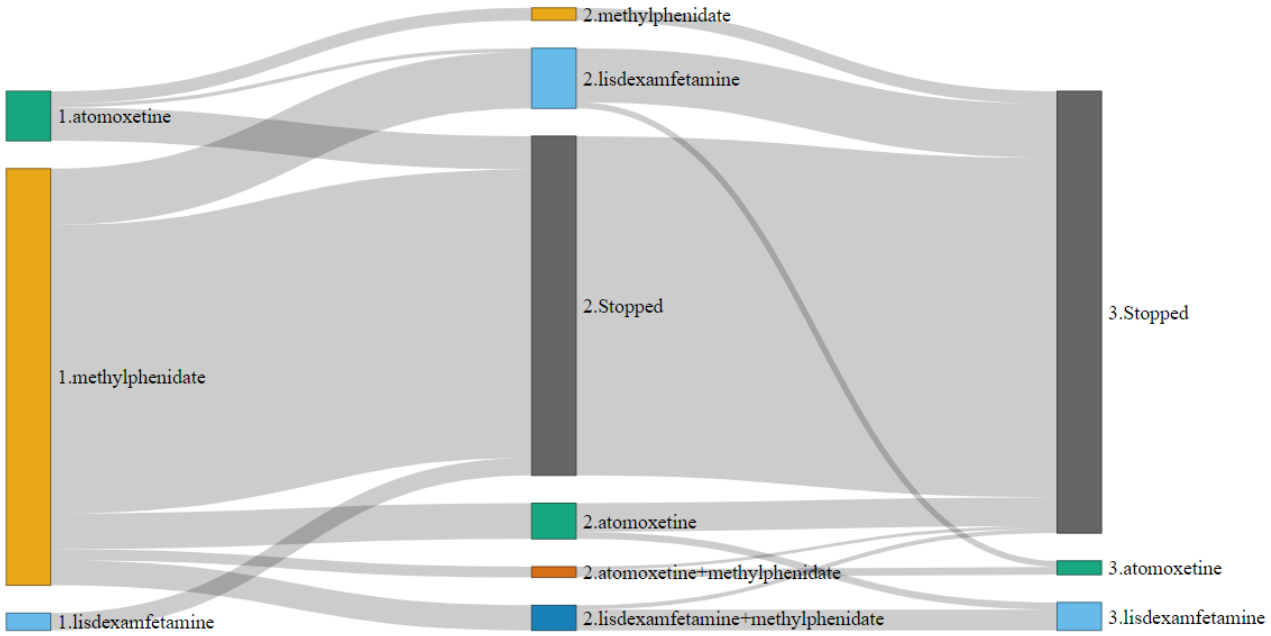

Figure 16. Sankey diagram of ADHD medication treatment pathway: DK-DHR.

DK-DHR=Danish Data Health Registries

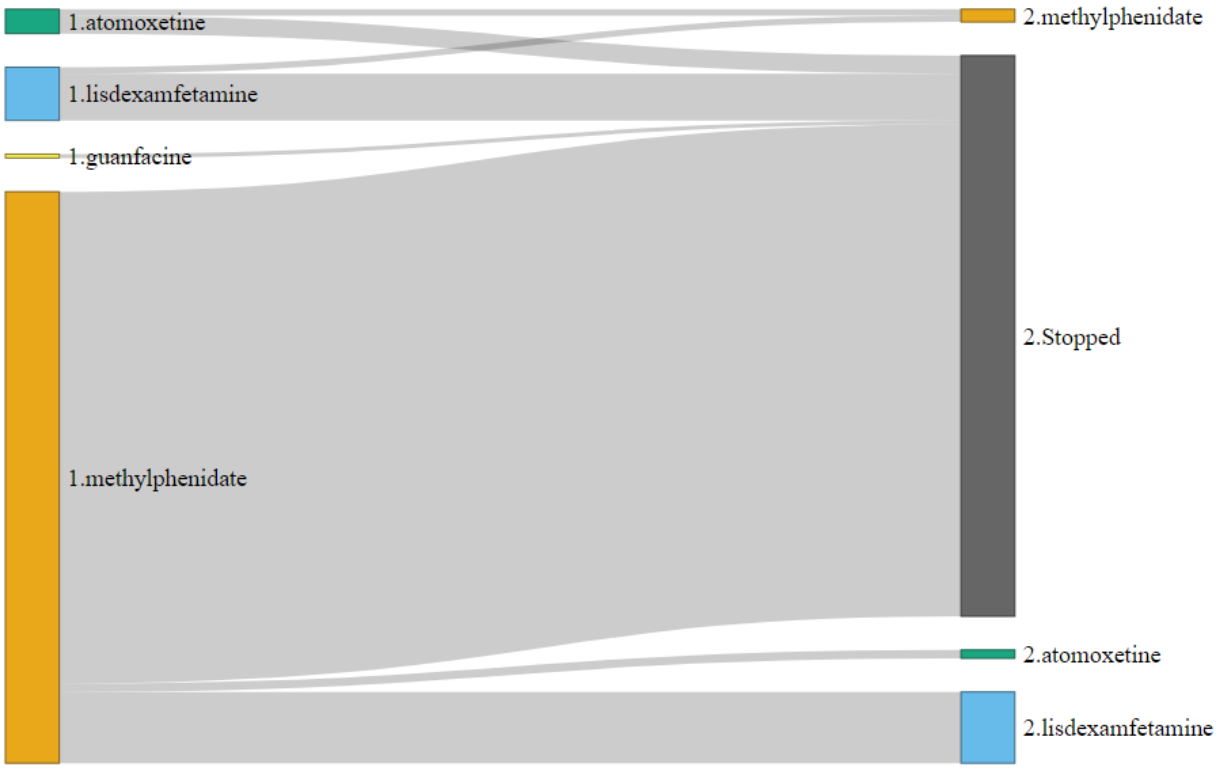

Figure 17. Sankey diagram of ADHD medication treatment pathway: InGef RDB.

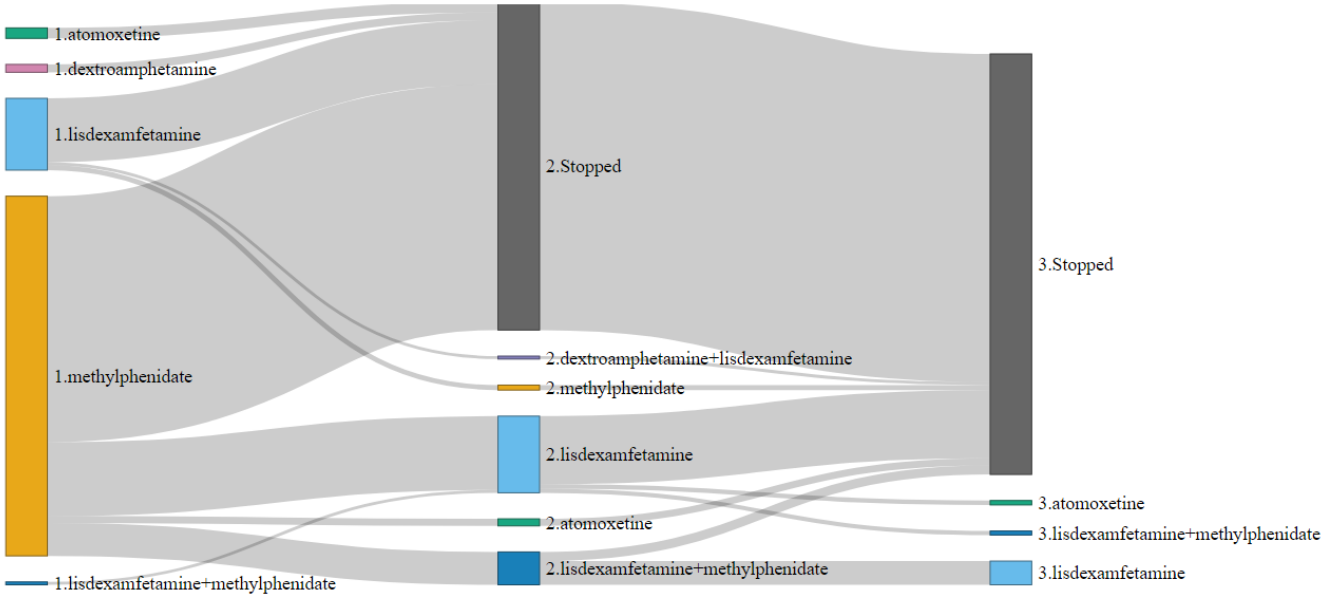

Figure 18. Sankey diagram of ADHD medication treatment pathway: NLHR.

InGef RDB=InGef Research Database

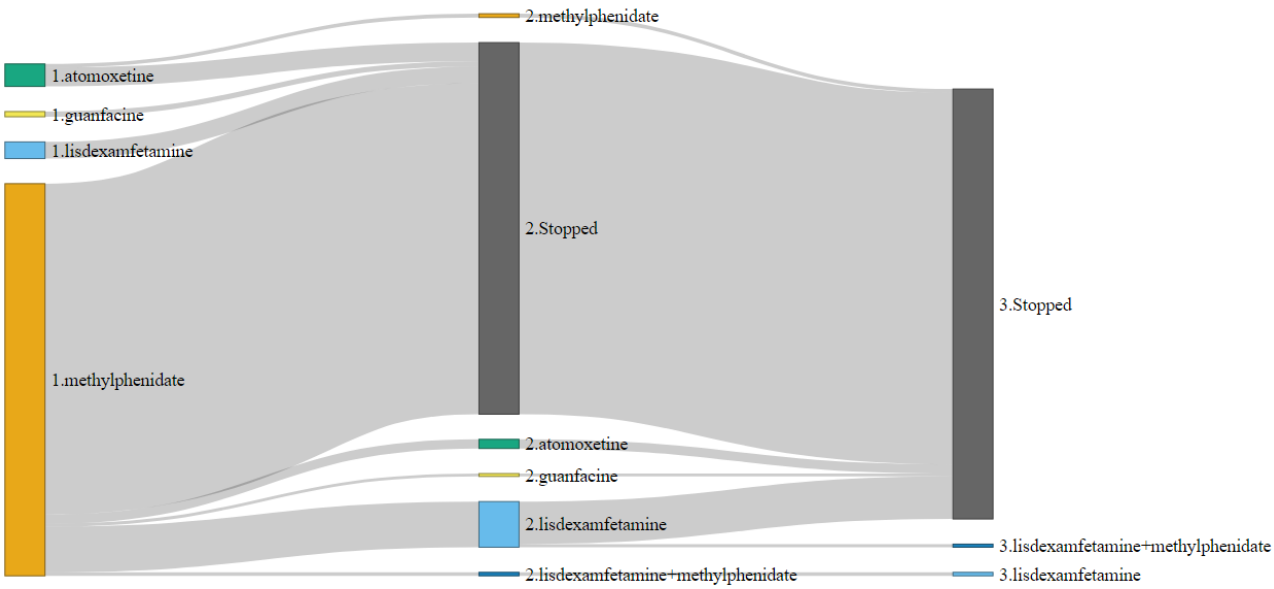

Figure 19. Sankey diagram of ADHD medication treatment pathway: BIFAP.

BIFAP=Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público

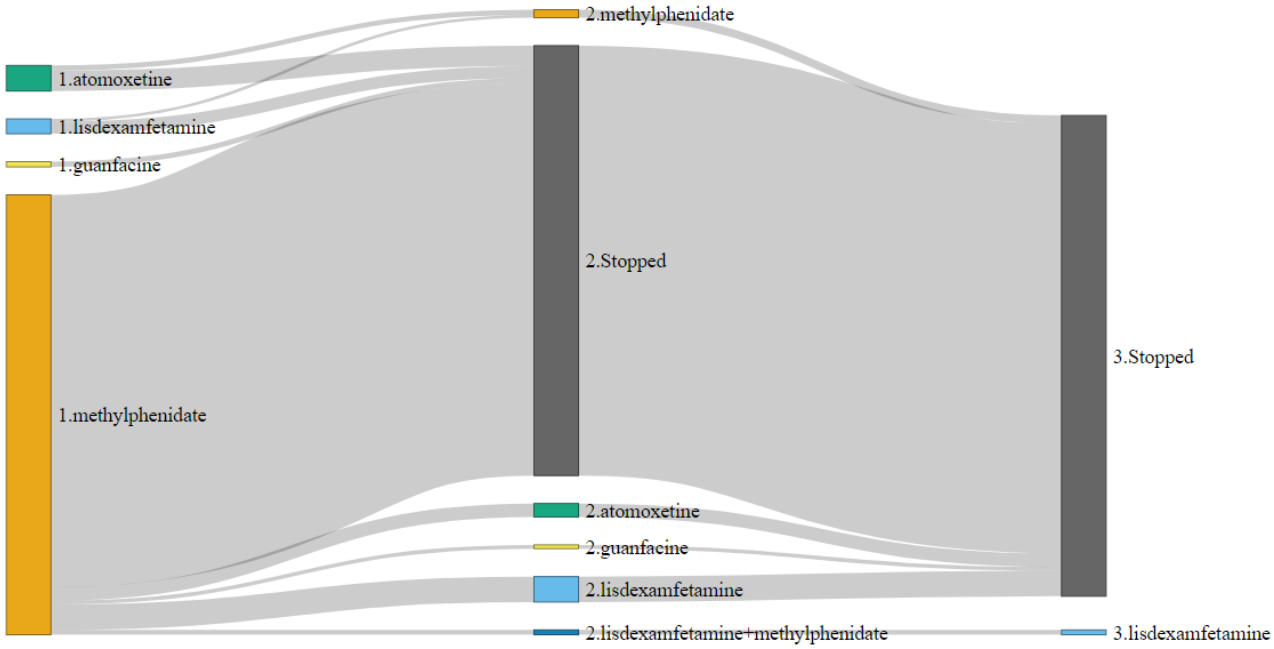

Figure 20. Sankey diagram of ADHD medication treatment pathway: SIDIAP.

SIDIAP=The Information System for Research on Primary Care

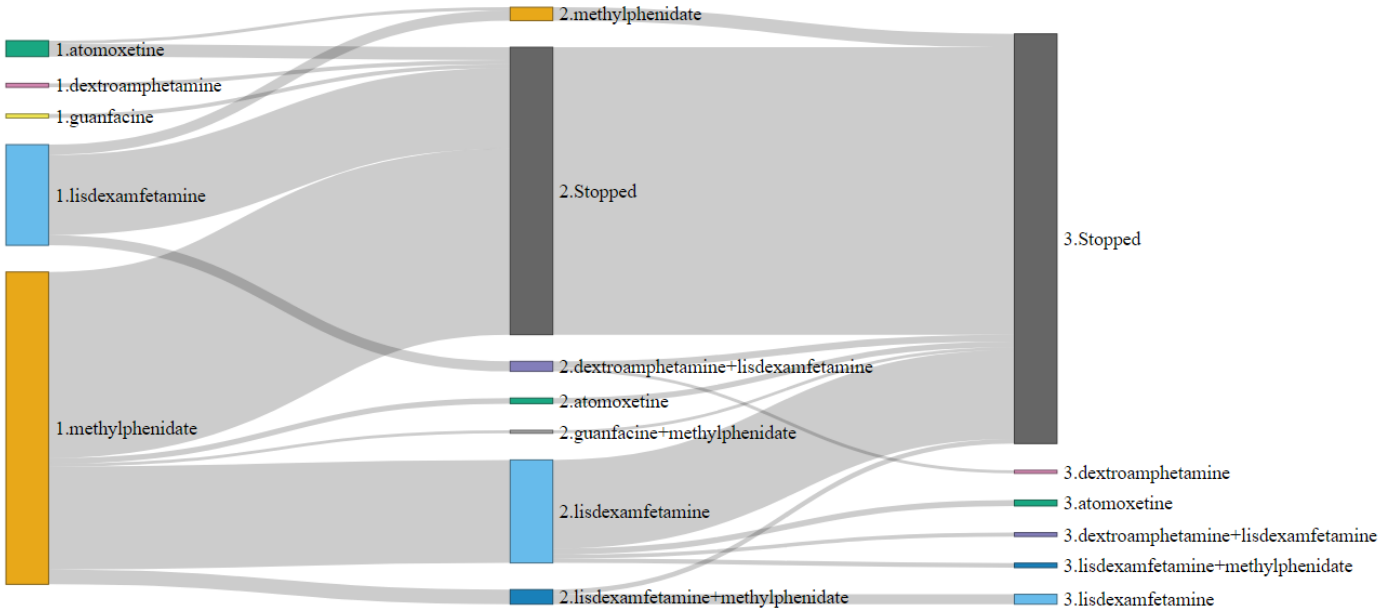

Figure 21. Sankey diagram of ADHD medication treatment pathway: HI-SPEED.

HI-SPEED=Health Impact - Swedish Population Evidence Enabling Data-linkage

9.3. Other analysis

Results from the sensitivity analysis where we allowed 90-day gap between records of drug exposure are available in the Shiny app online.

10. DISCUSSION

10.1. Key results

Between 2010 and 2023/2024, a total of 973,816 individuals initiated at least one ADHD medication across six European data sources (DK-DHR, InGef, NLHR, BIFAP, SIDIAP, and HI-SPEED) from five countries. Overall, both the prevalence and incidence of ADHD medication use increased across all data sources, although the extent of the increase varied. DK-DHR and HI-SPEED showed the highest rates in recent years, while the Spanish data sources (BIFAP and SIDIAP) recorded lower but steadily rising use. ADHD medication use in Spain has risen by a 2.5 factor from 2010 to 2024 in both databases, with a faster increase since 2021, though still slower than in Denmark, Norway, Sweden, and Germany. Overall, usage in Spain remains less than half that of these countries, especially compared to the Nordic countries.

Methylphenidate was consistently the most commonly used medication throughout the study period. Atomoxetine initially ranked second in most data sources but was gradually overtaken by lisdexamfetamine between 2015 and 2019. Similar upward trends were observed for individual medications, including guanfacine, which is approved for children and adolescents aged 6–17 years and showed increasing use in all data sources.

Patterns of use differed by age and sex. Among children and adolescents, medication use was higher in boys than in girls across all data sources, although the difference narrowed in older adolescents. Among adults, use increased in both sexes over time, with a steeper rise among females after 2020. Within BIFAP, a significant decrease in overall usage was observed in 2020 among individuals under 18 years old, likely attributable to the pandemic and associated lockdown measures; this trend was not reflected among adults. Methylphenidate usage has increased since 2021, following a period of relative stability over several years. Additionally, lisdexamfetamine use has shown a notable rise since 2021, particularly among

individuals aged 12–17 and above. In Catalonia (SIDIAP), the utilisation pattern of methylphenidate is distinct, as its use has continued to decline since 2014–2015. This differs from trends in the other countries examined, where the use of most medications has increased across most age groups and both sexes since 2021. By the end of the study period, females had higher rates of use in DK-DHR, InGef RDB, NLHR, and HI-SPEED.

Treatment persistence declined over time in all data sources. Six months after initiation, the proportion of individuals continuing any ADHD medication ranged from 18% in InGef RDB to 60% in SIDIAP, dropping further to between 3.7% in InGef RDB and 31.8% in NLHR after two years. Younger children (3–11 years) demonstrated better persistence in BIFAP and SIDIAP, while adults aged 25 years and older had higher persistence in DK-DHR, NLHR, and HI-SPEED. Patterns of restarting or switching medications after discontinuation were heterogeneous. Within 90 days after discontinuing methylphenidate, between 18% (SIDIAP) and 54% (InGef RDB) restarted the same medication, while 2.6% (BIFAP) to 14% (HI-SPEED) switched to another ADHD medication. Over longer follow-up, up to 56% in InGef RDB restarted methylphenidate, whereas around half of individuals in SIDIAP had no further ADHD medication use.

10.2. Strengths and limitations of the research methods

Strengths

This study draws on large, population-based healthcare data sources from five European countries, providing comprehensive coverage of ADHD medication use across diverse healthcare settings. The inclusion of multiple data sources with differing healthcare structures and prescribing practices enhances the generalisability of the findings to real-world clinical practice in Europe. The use of longitudinal data allowed for the assessment of temporal trends in medication use, treatment persistence, and switching behaviour over more than a decade. The application of a distributed analysis through common data model helped protect patient confidentiality while ensuring analytic uniformity. Furthermore, by including both primary and secondary care data, where available, the study provides a detailed picture of medication use patterns in different healthcare contexts.

Limitations

However, the use of routinely collected data also introduces several limitations. These data were not collected for research purposes, and the recording of a prescription or dispensation does not necessarily confirm that the medication was actually taken. Differences in coding practices, data completeness, and healthcare coverage between data sources may have introduced heterogeneity in the study results.

Diagnostic coding for ADHD and off-label indications may be incomplete, particularly in data sources with limited access to specialist data, which may lead to underestimation of diagnosed cases or misclassification of treatment indications. The reliance on diagnosis codes alone, without validation of phenotypes, further limits certainty about the clinical indication for prescribing.

Specific analytic limitations should also be noted. For the estimation of incidence rates (Objective 2), a 365-day washout period was applied to define incident use of each ADHD medication. Consequently, an individual classified as an incident user of one medication may have used another ADHD medication before initiation, for example, as part of a treatment switch. For incidence rates of any ADHD medication use, individuals were required to have no record of any ADHD medication during the 365-day washout window. In Objectives 3 and 4, where analyses focus on incident use of specific study medications at the drug-substance level, the same washout period was applied. Therefore, the identified initiations may represent true new use, add-on therapy, or a switch from another ADHD medication, rather than strictly new treatment episodes.

Variability in data capture across data sources may have influenced estimates of comorbidities and treatment indications. Some relevant conditions are typically diagnosed by specialists, whose records may

not be available in all data sources. Incomplete or inconsistent recording of clinical events could affect patient characterisation and identification of treatment indications. Reduced access to healthcare during the COVID-19 pandemic may also have delayed diagnosis and prescribing of ADHD medications. Additionally, some individuals may have obtained ADHD medications through private prescriptions or other channels not captured in these data sources, leading to potential underestimation of use.

Information on socioeconomic status, education, or ADHD symptom severity was not available, which are important factors that may impact the use of ADHD medications. Nevertheless, the use of harmonised definitions, a common data model, and standardised analytical methods across all data sources likely improved the internal validity and comparability of findings.

10.3. Interpretation

This study provides a comprehensive, cross-national overview of ADHD medication use across six large European data sources, highlighting both common patterns and regional differences in prescribing and treatment dynamics. The increasing prevalence and incidence of ADHD medication use observed across all data sources suggest greater recognition and management of ADHD in clinical practice, consistent with trends reported in recent European and North American studies. These findings likely reflect a combination of improved diagnosis, expanded treatment guidelines, and increased awareness among healthcare professionals and individuals.

Comparing to existing evidence

The observed patterns of ADHD medication use across the included countries are generally consistent with existing evidence and prior pharmacoepidemiological studies. We previously conducted the original study of this routinely repeated study (EUPAS1000000219) with data sources from five countries: Belgium, Germany, the Netherlands, Spain, and the UK. The SIDIAP data source from Spain was included in both the previous study and the current study. For Germany, the IQVIA DA Germany data source was included in the previous study, and the InGef RDB was included in the current study. In the previous study, we observed that the overall prevalence was high in IPCI compared to other data sources from 2010 onward.

Among the five countries examined, a higher prevalence of ADHD medication use was observed in the three Scandinavian countries. This finding is consistent with previous research reporting greater consumption of ADHD medications in Northern European countries compared to other parts of Europe.[12] When compared with the five data sources included in the previous DARWIN EU® study, prevalence of ADHD medication use observed from Denmark, Norway, and Sweden in the current study remained higher. Within the Scandinavian region, our results indicate that Sweden had the highest prevalence, while Norway and Denmark exhibited similar levels of use. Among children and adolescents aged 5–19 years, studies utilizing aggregated prescription data from Denmark, Norway, and Sweden have shown that the use of ADHD medications increased steadily between 2010 and 2020 across all three countries, with the most pronounced rise observed in Sweden.[13] The same study also documented increased use of guanfacine in Sweden since 2015, while its use remained limited in Denmark and Norway. These findings are consistent with the trends observed in our analysis.

Several studies have also examined ADHD medication use within individual countries and data sources. In Denmark, a national register-based open cohort study reported a rising prevalence of ADHD medication use between 2010 and 2022. The study found that stimulant use increased over the 2010s, with methylphenidate being the most commonly used medication.[14] Another Danish study, based on national healthcare registries and focusing specifically on children and adolescents, reported that the incidence rates of ADHD medication use followed a U-shaped pattern between 2010 and 2022. Rates decreased from 2010 to 2013 and then increased steadily until 2020.[15]

In Norway, previous studies with data from the Norwegian Prescription Database indicate that the overall prevalence of ADHD medication use has increased over time, with a more pronounced rise observed from 2020 onwards. The highest use was reported among older children and adolescents aged 6–17 years, alongside an increase in both prevalence and incidence among adults.[16] Similarly, Swedish registry studies have documented increasing use among both children and adults.[17]

In Germany, one study using data from the IMS® Disease Analyzer showed that the number of ADHD medication users aged ≤16 years increased between 2008 and 2012, followed by a gradual decline until 2018.[18] Another study using nationwide drug prescription data from outpatient care between 2009 and 2016 similarly reported that the proportion of children and adolescents receiving ADHD medication prescriptions decreased over this period.[19] The authors suggested that this decline may be partly explained by prescription restrictions introduced by the Federal Joint Committee in recent years.

Compared to the previous DARWIN EU® study, prevalence of ADHD medication use from the two German data sources showed a similar trend but in different magnitude. For example, in the previous study, the overall prevalence of any ADHD medication use was 0.14% in 2016 and increased to 0.23% in 2022. In the current study, we observed a prevalence of 0.45% in 2016, which increased to 0.62 in 2022 and continued to increase to 0.88% in 2024. However, since InGef RDB data is only available from 2016 onward, we were not able to compare the estimated prevalence between the two data sources before 2016.

In Spain, an upward trend in overall ADHD medication consumption and treated prevalence was observed across many regions during the 2010s, with consistently higher use among children compared with adults. Analyses based on IQVIA data (2013–2018) and several regional studies confirmed rising methylphenidate consumption over this period.[20,21] Regional variability was noted, with higher use in Navarre and Catalonia and lower levels in Asturias and Murcia, likely reflecting local healthcare policies and diagnostic practices.[21] Unlike other data sources, where an increase in ADHD medication use was observed among children and adolescents during the study period, we observed a decrease in prevalence from 2010 to 2020 in BIFAP, and from 2015 to 2020 in SIDIAP among individuals aged 3–17 years. Similar findings were reported in a previous study using SIDIAP data, which described psychotropic medication use, including psychostimulants, and observed a decline in psychostimulant prevalence among both boys and girls in Catalonia from 2014 to 2017.[22] However, the authors did not provide potential explanations for this decrease. Another study examining ADHD incidence among children aged 4–17 years in Catalonia between 2009 and 2017 found that incidence rates declined from 2013 to 2016, particularly among those aged 7–12 years. Changes in ADHD diagnosis patterns may partly explain these downward trends in medication use. Additionally, modifications to drug reimbursement policies in Spain could have influenced treatment uptake. For example, evidence from Catalan administrative data indicates that increases in parental co-payments introduced through Spain's 2012 pharmaceutical co-payment reform reduced children's consumption of ADHD medications.[23] The observed decreased use among children in BIFAP further supported this explanation. Further research is warranted to better understand the factors contributing to the observed reduction in ADHD medication use in this population.

We assessed the off-label use of ADHD medication in children under 6 years of age and found that users in this age group only represented a very small proportion of all incident users. Among children aged 3–5 years old, most initiated ADHD medication at the age of 5. Overall, our results suggest that off-label use of ADHD medication was not common. As an example, within BIFAP, this group represents a very small proportion: only 3,500 patients under 6 years old out of a total of 170,000 incident users.

We assessed the potential indication of ADHD medication use (and possible off-label use) on and before drug initiation and found that recorded indications varied between data sources and the assessment windows. Even when looking at any time prior to medication initiation, lower percentages of ADHD diagnosis were recorded in InGef RDB, BIFAP, and SIDIAP. For example, in BIFAP, only between 10% and 13% of patients using these medications are recorded with a diagnosis of ADHD in the 30 days prior to the

index date; 2% have other diagnoses and the remaining 85% correspond to cases that are either unknown or have no diagnosis registered. If the time window is extended to any point prior, the percentage of ADHD diagnoses increases to 45%. These findings are similar to those from SIDIAP, the other primary care-based data source, and are generally lower than results from data sources in the study that use specialist records.

Apart from the limitation of lack of specialist data in some of the data sources, another possible explanation is that ADHD diagnosis codes may be recorded after medication initiation. In primary care electronic health records data sources, such as BIFAP and SIDIAP, dispensations made by specialists are recorded, but not the diagnoses they assign. When the primary care physician clinically suspects a case, they would refer the patient to a specialist, whose indications we are unable to capture. Subsequently, once treatment has been initiated, if the patient returns to the primary care physician for follow-up, the primary care physician records the diagnosis in the primary care medical record, using the date of the consultation. In Spain, the indication to initiate pharmacological treatment for ADHD is determined by specialists, such as neurologists or psychiatrists. It is possible that we observed more ADHD diagnoses after the index date among initiators. Further studies should also consider including a post-index window for assessing potential indications.

10.4. Generalisability

The findings of this study are expected to be broadly generalisable to European populations with healthcare systems and prescribing practices similar to those represented in the included data sources. The six population-based data sources cover diverse regions, age groups, and healthcare settings, supporting external validity across different contexts. However, variation in data capture, diagnostic recording, and healthcare access, particularly in private care or specialist settings, may limit generalisability to populations not fully represented in the data sources.

11. CONCLUSION

This multi-data source study provides a comprehensive overview of ADHD medication use across six European data sources in five countries. Overall, ADHD medication use increased over time in all data sources, reflecting growing recognition and management of ADHD in both children and adults. While the extent of use varied across countries, consistent trends were observed in treatment initiation, switching, and persistence. Methylphenidate remained the most widely used medication, with rising use of lisdexamfetamine in recent years. Treatment persistence was generally low, particularly among adolescents and young adults, although longer durations were observed among younger children and older adults. The results underscore the need for continued monitoring of ADHD treatment patterns, further investigation into factors influencing treatment persistence, and ongoing efforts in research and healthcare planning to optimise ADHD management across Europe.

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13. ANNEXES

ANNEX I. Description of data sources

Danish Data Health Registries (DK-DHR)

#	Section	Description
1	Database Identification and country	DK-DHR (Danish Data Health Registries) Denmark
2	Data partner information section	Danish Medicines Agency (DKMA) Data Analytics Centre (DAC)
3	Coverage and timespan	Data collection since: 1995 Extent: Nation-wide. The data is representative of the entire Danish population.
4	Healthcare setting / type of data	Community pharmacists, and secondary care - specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following data elements are collected: diagnosis (including rare diseases and pregnancy data), hospital admissions, discharge and ICU data, Cause of death, Drug prescriptions, dispensing, vaccination and contraception, Procedures, Devices, and Sociodemographic information.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries, and Other. All causes of deaths, all retrieved drug prescriptions, all records of vaccinations, all hospital inpatient and outpatients contacts including disease diagnoses and hospital surgical and non-surgical procedures, cancers, laboratory test results for the entire Danish population from 1/1/1995 onwards.
6	General representativeness	The data is representative of the entire Danish population. Healthcare is free in Denmark, so we do not expect any bias in data collection based on socio-economic status.
7	Data content /source coding	Diagnoses and causes of death are collected using the ICD-10 vocabulary. ATC and RxNorm are used for Drugs. SNOMED codes are used for Procedures.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No.
9	Quality control (database specific)	The data we have received relating to nationwide Danish Health Data registries offer an opportunity for large-scale, population-based studies with several advantages 1) Their large size improves the precision of estimates and enables the study of rare exposures and outcomes with long-term latency, 2) Inclusion of nearly all individuals in the target population ensures that the data reflect routine clinical care and all clinical segments of the source population, 3) Data are collected independently of each research study, thus minimising certain types of bias, e.g., non-response, and the influence from attention to the research question on the diagnostic process. Before the source data is sent to us, the Danish Health Data Authority runs and does comprehensive checks of the registry table data validity of the variables, breaks in data, changes in variable coding, missingness, etc. We perform checks of missingness/completeness in relation to requested variables. In essence, we are receiving a dump of a mirror of the data that is controlled by the SDS. The documentation performed by SDS is available online, in Danish primarily https://www.esundhed.dk/Dokumentation (all variables), but also in English https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/national_health_registers
10	Linkage	There is no linkage in this data source.
11	Vital status	The Cause of Death registry (DAR) is used, the cause of death is collected using ICD-10 codes.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.

#	Section	Description
13	Main references	Schmidt M, Schmidt SAJ,Adelborg K,Sundbøll J,Laugesen K,Ehrenstein V,Sørensen HT "The Danish health care system and epidemiological research: from health care contacts to database records." Clinical epidemiology (2019): 31372058
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111217 Website: https://sundhedsdatastyrelsen.dk/da/english/health_data_and_registers/healthdatadenmark

InGef Research Database (InGef RDB)

#	Section	Description
1	Database Identification and country	InGef RDB (InGef Research Database) Germany
2	Data partner information section	Institut für angewandte Gesundheitsforschung Berlin GmbH
3	Coverage and timespan	Data collection since: 2015 Extent: Nation-wide. The data source contains information from the statutory health insurances (SHI), which insure a total of about 89% (~73 million individuals) of the German population. Since the InGef RDC currently includes about ten million individuals, it covers about 13% of the total population insured in one of the German SHIs. The data in the database depicts all health care use which has been reimbursed by the SHI.
4	Healthcare setting / type of data	Primary care - gps, and community pharmacists, and primary care specialists (e.g. paediatricians), and secondary care - specialists (ambulatory or hospital outpatient care), and hospital inpatient care, and claims data. The following data elements are collected: pregnancy data, hospital admission and/or discharge also with ICU admission. Prescription, dispensing drugs and Advanced therapy medicinal products. Contraception, medical devices, vaccinations, procedures, diagnoses and demographic information.
5	Data collection process	Insurance/administrative claims. The data in the database depicts all health care use which has been reimbursed by the SHI (statutory health insurances).
6	General representativeness	The data source contains information from the statutory health insurances (SHI), which insure a total of about 89% (~73 million individuals) of the German population. Since the InGef RDC currently includes about ten million individuals, it covers about 13% of the total population insured in one of the German SHIs.
7	Data content /source coding	The ATC and OPS (Operationen- und Prozedurenschlüssel) are used for prescription and dispensing drugs. For Procedures the EBM (Einheitlicher Bewertungsmaßstab - doctor's fee scale) and for ambulatory procedures; OPS (Operationen- und Prozedurenschlüssel) for operations conducted at the hospital are used. Medical events are coded in ICD-10-GM and another vocabulary used is PZN (Pharmazentralzummer -pharmaceutical reference number).
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No. In the German statutory health system, a person can only be enrolled in one health insurance at a time. However, if a person changes from one contributing insurer to another, a new ID number will be generated.
9	Quality control (database specific)	Before entering the InGef database, the data elements are checked with respect to data format, completeness, and plausibility. After each data update, data are compared with the previous data update in regard to number of records, number of data providers, etc. Due to the anonymized nature of the database, no direct validation of the data (e.g. using medical

#	Section	Description
		charts as the gold standard) is possible. Data delivery by health care providers is generally based upon standardized data requirements and formats provided by the National Association of Statutory Health Insurance Funds (compare: https://www.gkv-datenaustausch.de/leistungserbringer/leistungserbringer.jsp)
10	Linkage	No
11	Vital status	The Cause of Death is not captured, the date of death is captured.
12	Limitations	Ambulatory diagnosis are received from the source on a quarterly basis. These diagnoses are mapped to the observation table with the concept_id History of event within 3 months (1340222), with the actual diagnosis concept_id recorded in the field value_as_concept_id, and the date as the last day of the respective quarter (i.e. 30/31st of Mar/Jun/Sept/Dec). Ambulatory prescriptions are available with exact dates. The cause of death is not captured and there is no linkage with other data sources. Approx. 10.5 Million insurees are included in the database, 7.8 Million of these actively insured in 2024. This corresponds to 7% of the total German population. Data are longitudinally linked over a period of currently ten years.
13	Main references	Andersohn F, Walker J "Characteristics and external validity of the German Health Risk Institute (HRI) Database." Pharmacoepidemiology and drug safety (2016): 26530279
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1111207 Website: https://www.ingef.de/en/

Norwegian Linked Health Registry data (NLHR)

#	Section	Description
1	Database Identification and country	NLHR (Norwegian Linked Health Registry data) Norway
2	Data partner information section	University of Oslo Faculty of Mathematics and Natural Science - Department of Pharmacy
3	Coverage and timespan	Data collection since: 2008 Extent: Nation-wide. Norway has a universal public health care system, consisting of primary and specialist health care services covering a population of approximately 5.4 million inhabitants.
4	Healthcare setting / type of data	Primary care - gps, and primary care specialists (e.g. paediatricians), and secondary care - specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following registries are included: the Medical Birth Registry of Norway (MBRN), the Norwegian Prescription Registry (NorPD), the Norwegian Patient Registry (NPR), Norway Control and Payment of Health Reimbursement (KUHR), the Norwegian Surveillance System for Communicable Diseases (MSIS), the Norwegian Immunisation Registry (SYSVAK), the National Death Registry, and the National Registry (NR).
5	Data collection process	Registries. Many population-based health registries were established in the 1960s, with use of unique personal identifiers facilitating linkage between registries. Data in these health registries are used for health analysis, health statistics, improving the quality of healthcare, research, administration, and emergency preparedness.
6	General representativeness	The NLHR data covers the full Norwegian population.
7	Data content /source coding	NPR: ICD-10 for diagnosis, ATC and some special codes for drug use, Norwegian codes for clinical procedures (surgery (NCSP), medicine (NCMP) and diagnostic imaging, image-guided intervention, and nuclear medicine (NCRP)). KUHR: ICD-10 and ICPC-2 and ICPC-2B for diagnosis/procedure.

#	Section	Description
		NorPD: ATC. SYSVAK and MSIS: national classifications. MBRN: custom classifications by questionnaires (incl. check box variables in Maternity health care card)
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Linkage between the registries was facilitated using project-specific person IDs generated from unique personal identification assigned at birth or immigration for all legal residents in Norway.
9	Quality control (database specific)	In-house data quality checks of rates of common conditions, drug exposures, and outcomes. We compare obtained rates with official national statistics (e.g., birth statistics, yearly rates of drug dispensing, and diagnosis by age and gender). We also review missing data and outliers and inform registry holders of any unusual patterns.
10	Linkage	The NLHR is, by definition, a linkage of datasets. Helsedata.no is one central portal to apply for 11 national health registries, including all the registries that have been mapped to the OMOP CDM.
11	Vital status	The national death registry is linked.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.
13	Main references	Mitter VR, Lupattelli A,Bjørk MH,Nordeng HME "Identification and characterization of migraine in pregnancy: A Norwegian registry-based cohort study." Cephalalgia : an international journal of headache (2024): 38663979
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/1000000409 Website: https://www.mn.uio.no/farmasi/english/research/groups/pharma-safe/

Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (BIFAP)

#	Section	Description
1	Database Identification and country	BIFAP (Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)) Spain
2	Data partner information section	AEMPS Pharmacoepidemiology and Pharmacovigilance Division - Medicines for human use Department
3	Coverage and timespan	Data collection since: 2001 Extent: Regional. Spanish National Health Service (SNS) from 9 of the 17 regions in Spain. The population currently included represents 36% of the total Spanish population.
4	Healthcare setting / type of data	Primary care - gps, and community pharmacists, and primary care specialists (e.g. paediatricians), and hospital inpatient care. BIFAP includes a collection of databases linked at individual patient level. The main one is the Primary care Database, given the central role of PCPs in the SNS. Linked, there are additional important structural databases, like the medicines dispensed at community pharmacies and the patients' hospital diagnosis at discharge. 7 out of the 9 regions have linkage to hospital data. However, hospital data is available for different time periods for each region. From 2014 onwards, linkage to hospital data is available for >68% of patients.
5	Data collection process	Insurance/administrative claims, and Outpatient electronic health records, and Inpatient hospital electronic health records, and Registries. Data in BIFAP is collected from Primary Care and Hospital EHR.
6	General representativeness	Spain has a SNS that provides universal access to health services through the Regional Healthcare Services. Primary care physicians (PCPs), both general practitioners and paediatricians, have a central role. They act as gatekeepers of the system and exchange information with other levels of care to ensure the continuity of care. Most of the population

#	Section	Description
		(98.9%) is registered with a PCP and, in addition, most drug prescriptions are written at the primary care level.
7	Data content /source coding	The BIFAP source data is coded in SNOMED, ICD, ICPC-2 (diagnoses), AEMPS (drugs), and local lab codes.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. Pseudonymized ID numbers are generated at regional level. The Personal Identification Code for the Autonomous Community (CIPA) is used to perform the pseudonymisation procedure. Therefore, upon changing practice or de- and re-registration within the same region, (Autonomous Community) the patient in BIFAP is correctly identified as the same person with the same ID number. However, the same patient would obtain different ID numbers if the patient moves to a different region and is registered in a primary care practice in the new region. The percentage of people who are de-registered due to moving to other region in relation to the BIFAP population is, for example, 5% in Madrid and 4% Castilla y Leon. This situation would have a very limited impact on the data analysis due to the following: - The proportion is low (less than 5%) in relation to the overall population in BIFAP. - In BIFAP, only stable residents are included. This means that patients living in another region for a foreseen short time period and are provisionally assigned to a primary care practice are not included in BIFAP. - Medical events of those patients who have more than one ID do not overlap in time, since dates of events correspond to different periods. This means that counts of these events are never duplicated. - A number of study designs allows the same patient to be part of different cohorts or to be selected both as case and as control, provided that their person-time experience correspond to a different period of time. In all these cases, the impact in study analysis of duplicated IDs would be negligible.
9	Quality control (database specific)	Patients who meet any of the following disability criteria are discarded: - Non-owners of the individual health card - Date of birth before 01/01/1801 - Active patients over 115 years of age - Patients without clinical records (only contains administrative information) - Patients marked as “fictitious” in the clinical history - Badly coded sex - Inactive without termination date - Start date = End date - Clinical records prior to date of birth
10	Linkage	The following data are also linked at individual patient level and available. For a subset of the BIFAP population (regions and/or periods of time): • Information on dispensation of medicines at hospital pharmacies from outpatients and inpatients. • Registration of Causes of Death by the National Institute for Statistics. From the start of the COVID-19 pandemic: • Vaccines COVID-19 Administration Registry linked to patients included in BIFAP. • Diagnosis Tests of COVID-19 linked to patients included in BIFAP, for some regions.
11	Vital status	Source for vital status unknown.
12	Limitations	Primary care is available from 2001, but is considered complete since 2005. Hospital discharge has different coverage periods per region Spain, with most starting between 2014-2016. This means that for different regions and different time periods there is a different coverage of healthcare events. In the release of July 2025, the laboratory results are not covered. These will be added again at the next release, expected at the end of 2025.
13	Main references	Maciá-Martínez MA, Gil M,Huerta C,Martín-Merino E,Álvarez A,Bryant V,Montero D "Base de Datos para la Investigación Farmacoepidemiológica en Atención Primaria (BIFAP): A data

#	Section	Description
		resource for pharmacoepidemiology in Spain." Pharmacoepidemiology and drug safety (2020): 32337840
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/21501 Website: http://www.bifap.org/index_EN.html

The Information System for Research on Primary Care (SIDIAP)

#	Section	Description
1	Database Identification and country	SIDIAP (The Information System for the Development of Research in Primary Care) Catalunya, Spain
2	Data partner information section	IDIAPJGol
3	Coverage and timespan	Data collection since: 2006 Extent: Regional. The SIDIAP database contains records of around 6 million people residing in Catalonia, estimated to be representing around 76% of the Catalan population.
4	Healthcare setting / type of data	Primary care - gps, and hospital inpatient care. SIDIAP captured data includes routine visits, demographics, diagnoses, laboratory tests, drugs (prescribed and dispensed), referrals, and lifestyle information.
5	Data collection process	Outpatient electronic health records, and Inpatient hospital electronic health records, and Other. Data is entered by primary care physicians upon healthcare contact, supplemented with hospital discharge records. The Institut Catala de la Salut is the owner of the data and acts as the data controller.
6	General representativeness	It was previously shown that the captured SIDIAP population is highly representative of the entire Catalan region in terms of geographic, age, and sex distributions.
7	Data content /source coding	SIDIAP data covers all services that occur at the Primary Care Centres, as well as support services, such as sexual and reproductive health or home end-of-life care. Drugs are coded in ATC-WHO terminology in the source data. Health outcomes are captured in ICD-10CM codes. The SIDIAP contains all laboratory tests and results performed in primary health centres. Demographics, geographical, as well as socio-economic factors are recorded for each patient.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No.
9	Quality control (database specific)	Internal and external validation processes are carried out to determine the data quality of the SIDIAP information at each data update. These include stratifying the data by geographical regions and year in order to identify differences in data collection that need to be harmonized (e.g. recording of specific information under different codes). The measurement units of variables measuring one characteristic are also homogenized (e.g. transformation of the data from every laboratory that measures haemoglobin to grams per decilitre). Visual inspection of all data included in the database by week is also conducted, allowing one to see temporal patterns in the registry of a certain variable. With this information, the SIDIAP team can issue recommendations to researchers about the most common variable(s) where certain information is recorded (e.g., there are several variables with information concerning the women's menopausal status and with these visual inspection tools the SIDIAP team can inform the researchers about which related variables have the largest number of records and could be more helpful to capture menopause). Data availability (longitudinally and reliability), plausibility (range checks and unusual values), and consistency are inspected through visualisation tools. In

#	Section	Description
		addition, before accessing the data for a requested project, research teams have access to a quality-control report. This document contains counts, years, percentiles, maximums and minimums, incidences, and prevalence of the data requested for the project, allowing detection of inconsistencies in the data extraction prior to data delivery. External validation processes of the SIDIAP database mainly include assessing the data recorded in SIDIAP through linkage to external gold standard data sources, by analysing free text, or by sending questionnaires to health professionals.
10	Linkage	SIDIAP is linked to a hospital discharge database, pharmacy dispensation, and primary care laboratories. It can also be linked to other registries in Catalonia on a project by project basis.
11	Vital status	Mortality is fully captured in SIDIAP. The cause of death is not available, but can be linked to the Spanish death registry on a project by project basis.
12	Limitations	The SIDIAP data is not representative of individuals not using public primary care, and conditions that are usually followed by specialist care might not be properly captured. In addition, there is limited information on lifestyle variables. Patients are followed until Death or when transferring to another primary health care centre that does not contribute to SIDIAP.
13	Main references	Recalde M, Rodríguez C,Burn E,Far M,García D,Carrere-Molina J,Benítez M,Moleras A,Pistillo A,Bolíbar B,Aragón M,Duarte-Salles T "Data Resource Profile: The Information System for Research in Primary Care (SIDIAP)." International journal of epidemiology (2022): 35415748
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: https://catalogues.ema.europa.eu/data-source/50190 Website: https://www.sidiap.org/index.php/en

Health Impact - Swedish Population Evidence Enabling Data-linkage (HI-SPEED)

#	Section	Description
1	Database Identification and country	HI-SPEED (Health Impact - Swedish Population Evidence Enabling Data-linkage) Sweden
2	Data partner information section	SMPA-GU, Läkemedelsverket, Box 26 Pharmacoepidemiology and Analysis Department (FeA)
3	Coverage and timespan	Data collection since: 2020 Extent: Nation-wide. The catchment area includes the whole of Sweden, covering the full population of approximately 10 million.
4	Healthcare setting / type of data	Primary care - gps, and secondary care - specialists (ambulatory or hospital outpatient care), and hospital inpatient care. The following data elements are collected: Socio-demographics, drug use and prescriptions, diagnoses, cause of death, primary care procedures and visits, as well as secondary care and inpatient visits or clinical events.
5	Data collection process	Registries. The data is acquired from the Swedish nation and regional registries, only once all legislative, GDPR and ethical approvals have been granted. Therefore only relevant data is passed on, which will then be entered and processed by the
6	General representativeness	The coverage includes all patients of all sociodemographic characteristics. Therefore it should mirror the source population to a very good extent.
7	Data content /source coding	Medicines are coded with ATC, ICD10 is used for diagnoses and the Swedish procedure coding system (KVA) is used for clincal procedures.
8	Data Harmonization	The data has been mapped to the OMOP CDM v5.4 and the OMOP standard vocabularies (SNOMED, RxNorm, LOINC). The format, structural and semantic conformance has been verified upon onboarding into the DARWIN EU® data network. No.

#	Section	Description
9	Quality control (database specific)	The source data is obtained from the Swedish National and Regional Registers. The registers perform some regular quality controls on their data. After receiving the data, we perform additional checks and cleaning. We also run regular quality checks on the data we manage.
10	Linkage	Data on specialist care is acquired from the National Patient Register, mortality information is provided by the Cause-Of-Death Registry. Drug data is provided by the Patient Drug Register.
11	Vital status	Data on death and cause-of-death are extracted from the Cause-of-Death registry.
12	Limitations	No database-specific limitations documented. General limitations for the data type applicable.
13	Main references	No main reference provided.
14	Link to HMA-EMA catalogue and database webpage	HMA-EMA Catalogue entry: Website:

ANNEX II. Fitness for use assessment

Data source justification for inclusion and key characteristics

Two data sources from Spain (BIFAP and SIDIAP) were included in this study to increase the geographic coverage of the study population, as the two data sources do not cover the same regions.

The three linked national registries from Scandinavian countries included had sufficient sample size and provided nationwide prevalence/ incidence data (DK-DHR, NLHR, HI-SPEED).

DK-DHR was included in this study because it is a registry data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in DK-DHR was 208,500. Moreover, data availability and follow-up in DK-DHR is sufficient, as data availability starts in 1995, and the date of most recent data extraction is 2024-08-30, which aligns with the study period.

InGef RDB was included in this study because it is a claims data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in InGef RDB was 23,500. Moreover, data availability and follow-up in InGef RDB is sufficient, as data availability starts in 2015, and the date of most recent data extraction is 2024-12-31, which aligns with the study period. Due to the data availability the study period for InGef RDB started at 2015-01-01.

NLHR was included in this study because it is a claims data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in NLHR was 109,100. Moreover, data availability and follow-up in InGef RDB is sufficient, as data availability starts in 2008, and the date of most recent data extraction is 2025-01-28, which aligns with the study period. Due to the data availability of the linked hospital data, the study period for NLHR started at 2018.

BIFAP was included in this study because it is an electronic health records data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in BIFAP was 148,800. Moreover, data availability and follow-up in BIFAP is sufficient, as data availability starts in 1998, and the date of most recent data extraction is 2025-02-17, which aligns with the study period.

SIDIAP was included in this study because it is a claims data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in SIDIAP was 72,300. Moreover, data availability and follow-up in SIDIAP is sufficient, as data availability starts in 2015, and the date of most recent data extraction is 2023-08-30, which aligns with the study period.

HI-SPEED was included in this study because it is a claims data source that provides relevant information on the exposure of interest in the general population. Based on a preliminary feasibility assessment, the expected number of person counts for methylphenidate exposure in HI-SPEED was 260,700. Moreover, data availability and follow-up in HI-SPEED is sufficient, as data availability starts in 2015, and the date of most recent data extraction is 2024-12-31, which aligns with the study period.

EMA Data Quality Framework for EU medicines regulation: application to Real-World Data for more information (https://www.ema.europa.eu/system/files/documents/other/data-quality-framework-eu-medicines-regulation-application-real-world-data_en.pdf)

ANNEX III. Operational and reporting considerations

DATA MANAGEMENT

Data management

All data sources have previously mapped their data to the OMOP common data model. This enabled the use of standardised analytics and using DARWIN EU® tools across the network since the structure of the data and the terminology system was harmonised. The OMOP CDM was developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org

The analytic code for this study was written in R and used standardized analytics wherever possible. Each data partner executed the study code against their data source containing individual data and then returned the results (csv files) which only contained aggregated data. The results from each of the contributing data sites were then combined in tables and figures for the study report.

Data storage and protection

For this study, personal data from individuals in various EU member states were processed, using information collected from national/regional electronic health record data sources. Due to the sensitive nature of this personal medical data, it is important to be fully aware of ethical and regulatory aspects and to strive to take all reasonable measures to ensure compliance with ethical and regulatory issues on privacy.

All data sources used in this study were already used for pharmaco-epidemiological research and have a well-developed mechanism to ensure that European and local regulations dealing with ethical use of the data and adequate privacy control were adhered to. In agreement with these regulations, rather than combining person level data and performing only a central analysis, local analyses were run, which generate non-identifiable aggregate summary results.

QUALITY CONTROL

Data source quality control

When defining drug cohorts, non-systemic products was excluded from the list of included codes summarised on the ingredient level.

When defining cohorts for indications, a systematic search of possible codes for inclusion was identified using the *CodelistGenerator* R package (https://github.com/darwin-eu/CodelistGenerator). This package allows the user to define a search strategy and used this to query the vocabulary tables of the OMOP common data model so as to find potentially relevant codes. In addition, the *DrugExposureDiagnostics* (https://cran.r-project.org/web/packages/DrugExposureDiagnostics/index.html) R packages was ran, if needed, to assess the use of different codes across the data sources contributing to the study and identify any codes potentially omitted in error. The *DrugExposureDiagnostics* package evaluates ingredient-specific attributes and patterns in drug exposure records.

The study code will be based on DARWIN EU® R packages: *IncidencePrevalence* to estimate Incidence and Prevalence, *DrugUtilisation* to characterise the drug use, *CohortCharacteristics* to characterise the medication users, and *TreatmentPatterns* to characterise the treatment pathways. These packages included numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The R packages are publicly available via GitHub.

ANNEX IV: List of stand-alone documents

Table S1. List of medicines definitions.

Substance Name	Concept name	Class	ATC code	Ingredient Concept ID	Include descendants
Methylphenidate	Methylphenidate	Stimulants	N06BA04	705944	Yes
Dexamphetamine	Dexamphetamine	Stimulants	N06BA02	719311	Yes
Lisdexamfetamine	Lisdexamfetamine	Stimulants	N06BA12	709567	Yes
Atomoxetine	Atomoxetine	Non-stimulants	N06BA09	742185	Yes
Guanfacine	Guanfacine	Non-stimulants	C02AC02	1344965	Yes

Table S2. List of conditions definitions.

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
ADHD	Adult attention deficit hyperactivity disorder	40480225		SNOMED
ADHD	Attention deficit hyperactivity disorder	438409		SNOMED
ADHD	Attention deficit hyperactivity disorder, combined type	4149904		SNOMED
ADHD	Attention deficit hyperactivity disorder, inattentive presentation (restrictive)	45765796		SNOMED
ADHD	Attention deficit hyperactivity disorder, predominantly hyperactive impulsive type	4253962		SNOMED
ADHD	Attention deficit hyperactivity disorder, predominantly hyperactive impulsive type in remission	44784525		SNOMED
ADHD	Attention deficit hyperactivity disorder, predominantly inattentive type	4149353		SNOMED
ADHD	Attention deficit hyperactivity disorder, predominantly inattentive type in remission	44782517		SNOMED
ADHD	Child attention deficit disorder	440086		SNOMED
ADHD	Deficits in attention motor control and perception	4041692		SNOMED
ADHD	Disorders of attention and motor control	4047120		SNOMED
ADHD	Exacerbation of attention deficit hyperactivity disorder	1340259		OMOP Extension
ADHD	Hyperkinesis with developmental delay	437261		SNOMED
ADHD	Hyperkinetic conduct disorder	438132		SNOMED
ADHD	Hyperkinetic syndrome with developmental delay	4262921		SNOMED
ADHD	Reduced concentration span	4085043		SNOMED
ADHD	Undifferentiated attention deficit disorder	4049391		SNOMED
ADHD	Stimulant drug therapy for attention deficit hyperactivity disorder	45765568		SNOMED
ADHD	Drug therapy for attention deficit hyperactivity disorder	45765570		SNOMED
Narcolepsy	Cataplexy and narcolepsy	437854		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Narcolepsy	Narcolepsy	436100		SNOMED
Narcolepsy	Exacerbation of narcolepsy	1340405		OMOP Extension
Narcolepsy	Narcolepsy type 1	42536721		SNOMED
Narcolepsy	Autosomal dominant cerebellar ataxia, deafness and narcolepsy syndrome	36716323		SNOMED
Narcolepsy	Narcolepsy without cataplexy	43531721		SNOMED
Narcolepsy	Secondary narcolepsy	762958		SNOMED
Hypertension	Hypertension disorder	316866		SNOMED
Autism	Active infantile autism	439703		SNOMED
Autism	Residual infantile autism	439702		SNOMED
Autism	Atypical autism	4338037		SNOMED
Autism	Autism spectrum disorder	439776		SNOMED
Autism	Infantile autism	4254211		SNOMED
Autism	Active but odd autism	40482738		SNOMED
Autism	High-functioning autism	45765723		SNOMED
Autism	Autism and facial port-wine stain syndrome	36716319		SNOMED
Autism	Autism spectrum disorder, epilepsy, arthrogryposis syndrome	37116742		SNOMED
Autism	ADNP-related multiple congenital anomalies, intellectual disability, autism spectrum disorder	35624210		SNOMED
Autism	Developmental delay with autism spectrum disorder and gait instability	36674903		SNOMED
Autism	Autism epilepsy syndrome due to branched chain ketoacid dehydrogenase kinase deficiency	36675122		SNOMED
Autism	Autism spectrum disorder due to AUTS2 deficiency	36675177		SNOMED
Autism	Macrocephaly, intellectual disability, autism syndrome	37204430		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development without loss of previously acquired skills	3655811		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and absence of functional language with loss of previously acquired skills	3661684		SNOMED
Autism	Pervasive developmental disorder with complete impairment of functional language with loss of previously acquired skills	3661689		SNOMED
Autism	Autistic disorder	439780		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and complete impairment of functional language with loss of previously acquired skills	3661686		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Autism	Pervasive developmental disorder with cognitive developmental delay and marked impairment of functional language	3661691		SNOMED
Autism	Pervasive developmental disorder with cognitive developmental delay and complete impairment of functional language	3661694		SNOMED
Autism	Adenylosuccinate lyase deficiency	4034867		SNOMED
Autism	Autistic disorder of childhood onset	434902		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development with loss of previously acquired skills	3655812		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and pervasive impairment of functional language without loss of previously acquired skills	3661680		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and marked impairment of functional language without loss of previously acquired skills	3661682		SNOMED
Autism	Pervasive developmental disorder with severe impairment of functional language with loss of previously acquired skills	3661687		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and marked impairment of functional language with loss of previously acquired skills	3661681		SNOMED
Autism	Pervasive developmental disorder with severe impairment of functional language without loss of previously acquired skills	3661688		SNOMED
Autism	Pervasive developmental disorder with marked impairment of functional language without loss of previously acquired skills	3661678		SNOMED
Autism	Pervasive developmental disorder with disorder of intellectual development and complete impairment of functional language without loss of previously acquired skills	3661683		SNOMED
Autism	Pervasive developmental disorder with absence of functional language	3661693		SNOMED
Autism	Akinetic mutism	4203306		SNOMED
Autism	Pervasive developmental disorder with impairment of functional language	3661679		SNOMED
Autism	Pervasive developmental disorder with marked impairment of functional language with loss of previously acquired skills	3661677		SNOMED
Autism	Pervasive developmental disorder with complete impairment of functional language without loss of previously acquired skills	3661690		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Autism	Pervasive developmental disorder with complete impairment of functional language	3661692		SNOMED
Autism	Active disintegrative psychoses	439705		SNOMED
Autism	Pervasive developmental disorder of residual state	43020503		SNOMED
Autism	FOXG1 syndrome	45765499		SNOMED
Autism	Pathological demand avoidance	37016769		SNOMED
Autism	Autistic spectrum disorder with isolated skills	4189466		SNOMED
Autism	Savant syndrome	4332239		SNOMED
Autism	1p21.3 microdeletion syndrome	36717734		SNOMED
Autism	Residual Asperger's disorder	45769394		SNOMED
Autism	Isodicentric chromosome 15 syndrome	37109594		SNOMED
Autism	Residual disintegrative psychoses	439704		SNOMED
Autism	Asperger's disorder	4053178		SNOMED
Fatigue	Exacerbation of fatigue	1340332		OMOP Extension
Fatigue	Reduced level of fatigue	607123		SNOMED
Fatigue	Transient heat fatigue	442024		SNOMED
Fatigue	Peripheral muscle fatigue	4063119		SNOMED
Fatigue	Fatigue during pregnancy - delivered	4062571		SNOMED
Fatigue	Fatigue during pregnancy - not delivered	4060299		SNOMED
Fatigue	Fatigue during pregnancy with postnatal complication	4062925		SNOMED
Fatigue	Severe systemic illness respiratory muscle fatigue	4347293		SNOMED
Fatigue	Rapid fatigue of gait	4092860		SNOMED
Fatigue	Malaise and fatigue	439926		SNOMED
Fatigue	Accommodative fatigue	4209103		SNOMED
Fatigue	Severe chronic fatigue syndrome	44793521		SNOMED
Fatigue	Moderate chronic fatigue syndrome	44793522		SNOMED
Fatigue	Mild chronic fatigue syndrome	44793523		SNOMED
Fatigue	Fatigue associated with AIDS	4221911		SNOMED
Fatigue	Psychogenic fatigue	40481844		SNOMED
Fatigue	Postexertional fatigue	40484614		SNOMED
Fatigue	Postviral fatigue syndrome	4202045		SNOMED
Fatigue	Chronic fatigue syndrome	432738		SNOMED
Fatigue	Combat fatigue	4247433		SNOMED
Fatigue	Low frequency muscle fatigue	4279937		SNOMED
Fatigue	Fatigue due to treatment	45772721		SNOMED
Fatigue	Cancer-related fatigue	37396808		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Fatigue	Fatigue due to chemotherapy	37205051		SNOMED
Fatigue	Fatigue due to radiation therapy	37205052		SNOMED
Fatigue	Central muscle fatigue	4193374		SNOMED
Fatigue	High frequency muscle fatigue	4193763		SNOMED
Fatigue	Muscle fatigue	4214612		SNOMED
Fatigue	Fatigue	4223659		SNOMED
Fatigue	Fatigue during pregnancy	4230221		SNOMED
Fatigue	Bilateral weakness of upper limbs	36686942		SNOMED
Fatigue	Heavy feeling	4060217		SNOMED
Fatigue	Tired all the time	4149857		SNOMED
Fatigue	Senile asthenia	4090207		SNOMED
Fatigue	Asthenia	437113		SNOMED
Fatigue	Tired	4074624		SNOMED
Fatigue	Asthenia due to disease	765190		SNOMED
Fatigue	Attacks of weakness	4093848		SNOMED
Fatigue	Tired on least exertion	4086973		SNOMED
Fatigue	Occasionally tired	37017316		SNOMED
Fatigue	Weakness as a late effect of stroke	44782753		SNOMED
Fatigue	Heavy legs	4059010		SNOMED
Fatigue	Sensation of heaviness in limbs	4161600		SNOMED
Eating disorder	Eating disorder co-occurrent with diabetes mellitus type 1	42689695		SNOMED
Eating disorder	Nocturnal sleep-related eating disorder	4253315		SNOMED
Eating disorder	Eating disorder in remission	4144892		SNOMED
Eating disorder	Eating disorder	439002		SNOMED
Eating disorder	Bulimia nervosa in full remission	609050		SNOMED
Eating disorder	Bulimia nervosa in partial remission	609049		SNOMED
Eating disorder	Anorexia nervosa in remission	44784528		SNOMED
Eating disorder	Bulimia nervosa in remission	44784532		SNOMED
Eating disorder	Rumination disorder of infancy	4262968		SNOMED
Eating disorder	Self-induced purging to lose weight	4085361		SNOMED
Eating disorder	Non-organic infant feeding disturbance	4103560		SNOMED
Eating disorder	Overeating associated with other psychological disturbances	4152972		SNOMED
Eating disorder	Anorexia nervosa, binge-eating purging type	4269485		SNOMED
Eating disorder	Dangerously low body weight co-occurrent and due to anorexia nervosa of restricting type	37109945		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Eating disorder	Self-induced vomiting to lose weight	45767550		SNOMED
Eating disorder	Dangerously low body weight co-occurrent and due to anorexia nervosa of binge-eating purging type	37109946		SNOMED
Eating disorder	Bulimia nervosa, nonpurging type	4245170		SNOMED
Eating disorder	Anorexia nervosa	436675		SNOMED
Eating disorder	Avoidant restrictive food intake disorder	45763720		SNOMED
Eating disorder	Orthorexia nervosa	3655965		SNOMED
Eating disorder	Adult rumination syndrome of ingested food	36716719		SNOMED
Eating disorder	Atypical bulimia nervosa	4333684		SNOMED
Eating disorder	Developmental delay in feeding	4143677		SNOMED
Eating disorder	Anorexia nervosa co-occurrent with significantly low body weight	36717597		SNOMED
Eating disorder	Binge eating disorder	4208913		SNOMED
Eating disorder	Rumination disorder	4242221		SNOMED
Eating disorder	Bulimia nervosa, purging type	4139256		SNOMED
Eating disorder	Pica	437839		SNOMED
Eating disorder	Significantly low body weight co-occurrent and due to anorexia nervosa of restricting type	37109947		SNOMED
Eating disorder	Feeding disorder of infancy OR early childhood	4250314		SNOMED
Eating disorder	Psychogenic overeating	4173812		SNOMED
Eating disorder	Weight fixation	4333682		SNOMED
Eating disorder	Atypical anorexia nervosa	4333683		SNOMED
Eating disorder	Anorexia nervosa co-occurrent with dangerously low body weight	36716779		SNOMED
Eating disorder	Anorexia nervosa, restricting type	4300305		SNOMED
Eating disorder	Self-induced purging	4091520		SNOMED
Eating disorder	Non-organic loss of appetite	4102962		SNOMED
Eating disorder	Pica of infancy and childhood	4100683		SNOMED
Eating disorder	Bulimia nervosa	438407		SNOMED
Eating disorder	Acquired delay in feeding	46285098		SNOMED
Eating disorder	Significantly low body weight co-occurrent and due to anorexia nervosa of binge-eating purging type	37118987		SNOMED
Eating disorder	Emergency hospital admission to eating disorders service	35609103		SNOMED
Eating disorder	Binge eating disorder	4208913		SNOMED
Eating disorder	Eating disorders service	44808062		SNOMED
Cognitive dysfunction	Cognitive dysfunction with epilepsy	3188590		Nebraska Lexicon

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Cognitive dysfunction	Cognitive dysfunction accompanying multiple sclerosis	3174547		Nebraska Lexicon
Cognitive dysfunction	Postoperative cognitive dysfunction	36675110		SNOMED
Cognitive dysfunction	Cognitive changes due to organic disorder	44782725		SNOMED
Cognitive dysfunction	Language-related cognitive disorder	4047110		SNOMED
Cognitive dysfunction	Mild cognitive disorder	4297400		SNOMED
Cognitive dysfunction	Cognitive disorder	40480615		SNOMED
Cognitive dysfunction	Cognitive disorder in remission	44784524		SNOMED
Cognitive dysfunction	Neurocognitive disorder	46271045		SNOMED
Cognitive dysfunction	Cognitive communication disorder	37396726		SNOMED
Cognitive dysfunction	Cognitive impairment co-occurrent and due to primary psychotic disorder	37110498		SNOMED
Cognitive dysfunction	Dissociative neurological symptom disorder co-occurrent with cognitive symptoms	42537139		SNOMED
Cognitive dysfunction	Amnestic mild cognitive disorder	3654469		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with cognitive developmental delay and marked impairment of functional language	3661691		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with cognitive developmental delay and complete impairment of functional language	3661694		SNOMED
Cognitive dysfunction	Impaired cognition	443432		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following embolic cerebrovascular accident	42535706		SNOMED
Cognitive dysfunction	Human immunodeficiency virus infection with cognitive impairment	36687122		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following nontraumatic subarachnoid hemorrhage	42539270		SNOMED
Cognitive dysfunction	Cognitive impairment caused by ingestible alcohol	3654907		SNOMED
Cognitive dysfunction	Cognitive developmental delay	4137543		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following nontraumatic intracerebral hemorrhage	42539271		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Cognitive dysfunction	Borderline cognitive developmental delay	43020439		SNOMED
Cognitive dysfunction	Indication for modification of patient cognitive status	4003688		SNOMED
Cognitive dysfunction	Cognitive impairment, coarse facies, heart defects, obesity, pulmonary involvement, short stature, skeletal dysplasia syndrome	35607999		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following cerebrovascular disease	42539256		SNOMED
Cognitive dysfunction	Infantile-onset mesial temporal lobe epilepsy with severe cognitive regression	36676518		SNOMED
Cognitive dysfunction	Residual cognitive deficit as late effect of cerebrovascular accident	40482301		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following ischemic cerebrovascular accident	42535681		SNOMED
Cognitive dysfunction	Hypotonia, speech impairment, severe cognitive delay syndrome	35622315		SNOMED
Cognitive dysfunction	Cognitive deficit due to and following hemorrhagic cerebrovascular accident	42535682		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development without loss of previously acquired skills	3655811		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and absence of functional language with loss of previously acquired skills	3661684		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and complete impairment of functional language with loss of previously acquired skills	3661686		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and pervasive impairment of functional language without loss of previously acquired skills	3661680		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and marked impairment of functional language without loss of previously acquired skills	3661682		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development with loss of previously acquired skills	3655812		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and marked impairment of functional language with loss of previously acquired skills	3661681		SNOMED
Cognitive dysfunction	Pervasive developmental disorder with disorder of intellectual development and complete impairment of	3661683		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
	functional language without loss of previously acquired skills			
Cognitive dysfunction	Organic amnesia of language	4162498		SNOMED
Cognitive dysfunction	Anterograde amnesia	4229448		SNOMED
Cognitive dysfunction	Transient memory loss	4145069		SNOMED
Cognitive dysfunction	Minimal cognitive impairment	439795		SNOMED
Cognitive dysfunction	Memory deficit due to and following hemorrhagic cerebrovascular accident	37309660		SNOMED
Cognitive dysfunction	Cognitive impairment due to toxicity of substance	42538566		SNOMED
Cognitive dysfunction	Impaired environmental interpretation syndrome	4036509		SNOMED
Cognitive dysfunction	Amnesia	439147		SNOMED
Cognitive dysfunction	Transient global amnesia	437306		SNOMED
Cognitive dysfunction	Post-traumatic dementia with behavioral change	44784521		SNOMED
Cognitive dysfunction	Memory deficit due to and following ischemic cerebrovascular accident	37309661		SNOMED
Cognitive dysfunction	Memory lapses	4076654		SNOMED
Cognitive dysfunction	Exacerbation of amnesia	1340245		OMOP Extension
Cognitive dysfunction	Memory deficit due to and following cerebrovascular disease	37309663		SNOMED
Cognitive dysfunction	Amnesia for remote events	4264146		SNOMED
Cognitive dysfunction	Disturbance of memory for order of events	4166262		SNOMED
Cognitive dysfunction	Forgetful	4206332		SNOMED
Cognitive dysfunction	Memory impairment	4304008		SNOMED
Cognitive dysfunction	Severe cognitive impairment	45765900		SNOMED
Cognitive dysfunction	Disturbance of cognitive learning	4022572		SNOMED
Cognitive dysfunction	Mixes past with present	4076655		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Cognitive dysfunction	Impairment of registration	4152488		SNOMED
Cognitive dysfunction	Mild memory disturbance	4099961		SNOMED
Cognitive dysfunction	Memory deficit due to and following spontaneous subarachnoid hemorrhage	609091		SNOMED
Cognitive dysfunction	Memory deficit due to and following spontaneous intracerebral hemorrhage	609090		SNOMED
Cognitive dysfunction	Lack of thinking ability	4005009		SNOMED
Cognitive dysfunction	Amnesia for important personal information	4083456		SNOMED
Cognitive dysfunction	Memory deficit due to and following cerebrovascular accident	37309662		SNOMED
Cognitive dysfunction	Age-related cognitive decline	4009705		SNOMED
Cognitive dysfunction	Depressed mood in Alzheimer's disease	44782727		SNOMED
Cognitive dysfunction	Temporary loss of memory	4012209		SNOMED
Cognitive dysfunction	Moderate cognitive impairment	45765899		SNOMED
Cognitive dysfunction	Cognitive deficit in attention	37016192		SNOMED
Cognitive dysfunction	Information conversion problem	4296610		SNOMED
Cognitive dysfunction	Cognitive deficit complicating stroke	3179559		Nebraska Lexicon
Cognitive dysfunction	Memory deficit due to and following embolic cerebrovascular accident	609092		SNOMED
Cognitive dysfunction	Minor memory lapses	4074319		SNOMED
Cognitive dysfunction	Altered behavior in Alzheimer's disease	44784643		SNOMED
Cognitive dysfunction	Paramnesia	4138824		SNOMED
Cognitive dysfunction	Retrospective falsification	4132117		SNOMED
Cognitive dysfunction	Impaired executive functioning	42537141		SNOMED
Cognitive dysfunction	Transient epileptic amnesia	4193675		SNOMED
Cognitive dysfunction	Amnesia for day to day facts	4092086		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Cognitive dysfunction	Post-traumatic amnesia	4173661		SNOMED
Cognitive dysfunction	Retrograde amnesia	4198081		SNOMED
Cognitive dysfunction	Amnesia for recent events	4171718		SNOMED
Cognitive dysfunction	Early onset Alzheimer's disease with behavioral disturbance	44782432		SNOMED
Addiction	Absinthe addiction	4338024		SNOMED
Addiction	Addiction	4139144		SNOMED
Addiction	Physical addiction	4215081		SNOMED
Addiction	Psychological addiction	4312088		SNOMED
Addiction	Glue sniffing dependence	4102814		SNOMED
Addiction	Heroin dependence	4333676		SNOMED
Addiction	Dependent drug abuse	4275756		SNOMED
Addiction	Glue sniffing dependence, continuous	4102815		SNOMED
Addiction	Glue sniffing dependence in remission	4103410		SNOMED
Addiction	Glue sniffing dependence, episodic	4100517		SNOMED
Behavioural disorder	Oppositional defiant disorder	441547		SNOMED
Behavioural disorder	Oppositional defiant disorder co-occurrent with chronic irritability-anger	37110475		SNOMED
Behavioural disorder	Oppositional defiant disorder co-occurrent with chronic irritability-anger with normal prosocial emotions	37110476		SNOMED
Behavioural disorder	Oppositional defiant disorder without chronic irritability-anger	37110477		SNOMED
Behavioural disorder	Oppositional defiant disorder without chronic irritability-anger with limited prosocial emotions	37110478		SNOMED
Behavioural disorder	Oppositional defiant disorder without chronic irritability-anger with normal prosocial emotions	37110479		SNOMED
Behavioural disorder	Conduct disorder, childhood-onset type	437843		SNOMED
Behavioural disorder	Aggressive unsocial conduct disorder	433451		SNOMED
Behavioural disorder	Childhood disorder of conduct and emotion	4105183		SNOMED
Behavioural disorder	Hyperkinetic conduct disorder	438132		SNOMED
Behavioural disorder	Conduct disorder - in family context	4338038		SNOMED
Behavioural disorder	Conduct disorder - unsocialized	4335176		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Behavioural disorder	Depressive conduct disorder	4333687		SNOMED
Behavioural disorder	Nonaggressive unsocial conduct disorder	440697		SNOMED
Behavioural disorder	Conduct disorder	443617		SNOMED
Behavioural disorder	Conduct disorder, adolescent-onset type	439800		SNOMED
Behavioural disorder	Conduct disorder, undifferentiated type	4268025		SNOMED
Behavioural disorder	Conduct disorder, group type	4279455		SNOMED
Behavioural disorder	Adjustment disorder with mixed disturbance of emotions AND conduct	436076		SNOMED
Behavioural disorder	Adjustment disorder with mixed disturbance of emotions and conduct in remission	44784531		SNOMED
Behavioural disorder	Conduct disorder in remission	44782933		SNOMED
Behavioural disorder	Childhood onset conduct-dissocial disorder with limited prosocial emotions	37110480		SNOMED
Behavioural disorder	Childhood onset conduct-dissocial disorder with normal prosocial emotions	37110481		SNOMED
Behavioural disorder	Adolescent onset conduct-dissocial disorder	37110482		SNOMED
Behavioural disorder	Adolescent onset conduct-dissocial disorder with limited prosocial emotions	37110483		SNOMED
Behavioural disorder	Adolescent onset conduct-dissocial disorder with normal prosocial emotions	37110484		SNOMED
Behavioural disorder	Conduct disorder, solitary aggressive type	4254395		SNOMED
Behavioural disorder	Childhood onset conduct-dissocial disorder	42538606		SNOMED
Behavioural disorder	Adjustment disorder with disturbance of conduct	435799		SNOMED
Behavioural disorder	Intermittent explosive disorder	440989		SNOMED
Behavioural disorder	Disruptive mood dysregulation disorder	37396201		SNOMED
Behavioural disorder	Socialized behavior disorder	432877		SNOMED
Behavioural disorder	Sibling jealousy	4100089		SNOMED
Behavioural disorder	Group delinquency	4099964		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Behavioural disorder	Unsocial childhood truancy	4146721		SNOMED
Behavioural disorder	Neurotic delinquency	4099966		SNOMED
Behavioural disorder	Adjustment reaction with antisocial behavior	4103571		SNOMED
Behavioural disorder	Adjustment reaction with aggression	4103570		SNOMED
Behavioural disorder	Adjustment reaction with destructiveness	4102970		SNOMED
Major depressive disorder	Recurrent major depressive episodes	432285		SNOMED
Major depressive disorder	Recurrent major depressive episodes, moderate	432883		SNOMED
Major depressive disorder	Recurrent major depression in remission	433991		SNOMED
Major depressive disorder	Recurrent major depressive episodes, severe, with psychosis	434911		SNOMED
Major depressive disorder	Severe recurrent major depression without psychotic features	435220		SNOMED
Major depressive disorder	Severe major depression, single episode, with psychotic features	438406		SNOMED
Major depressive disorder	Recurrent major depressive episodes, mild	438998		SNOMED
Major depressive disorder	Single major depressive episode, severe, with psychosis	439259		SNOMED
Major depressive disorder	Severe major depression, single episode, without psychotic features	441534		SNOMED
Major depressive disorder	Chronic major depressive disorder, single episode	4031328		SNOMED
Major depressive disorder	Severe recurrent major depression with psychotic features, mood-incongruent	4034842		SNOMED
Major depressive disorder	Moderate major depression, single episode	4049623		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Major depressive disorder	Severe major depression, single episode, with psychotic features, mood-incongruent	4067409		SNOMED
Major depressive disorder	Moderate recurrent major depression	4077577		SNOMED
Major depressive disorder	Major depressive disorder, single episode with postpartum onset	4093584		SNOMED
Major depressive disorder	Chronic recurrent major depressive disorder	4094358		SNOMED
Major depressive disorder	Severe recurrent major depression with psychotic features, mood-congruent	4141292		SNOMED
Major depressive disorder	Recurrent major depression in partial remission	4141454		SNOMED
Major depressive disorder	Severe major depression with psychotic features, mood-congruent	4144233		SNOMED
Major depressive disorder	Major depression in partial remission	4148630		SNOMED
Major depressive disorder	Severe recurrent major depression with psychotic features	4154309		SNOMED
Major depressive disorder	Major depression, melancholic type	4154391		SNOMED
Major depressive disorder	Major depression in remission	4176002		SNOMED
Major depressive disorder	Major depressive disorder, single episode with atypical features	4181807		SNOMED
Major depressive disorder	Mild major depression, single episode	4195572		SNOMED
Major depressive disorder	Recurrent major depressive disorder with melancholic features	4205471		SNOMED
Major depressive disorder	Recurrent major depressive disorder with catatonic features	4220023		SNOMED
Major depressive disorder	Mild recurrent major depression	4228802		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Major depressive disorder	Severe major depression with psychotic features, mood-incongruent	4243822		SNOMED
Major depressive disorder	Severe major depression with psychotic features	4250023		SNOMED
Major depressive disorder	Major depressive disorder, single episode with melancholic features	4270907		SNOMED
Major depressive disorder	Major depression, single episode	4282096		SNOMED
Major depressive disorder	Recurrent major depression	4282316		SNOMED
Major depressive disorder	Major depressive disorder, single episode with catatonic features	4287238		SNOMED
Major depressive disorder	Severe major depression, single episode, with psychotic features, mood-congruent	4299785		SNOMED
Major depressive disorder	Recurrent major depressive disorder with atypical features	4304140		SNOMED
Major depressive disorder	Moderate major depression	4307111		SNOMED
Major depressive disorder	Major depression single episode, in partial remission	4323418		SNOMED
Major depressive disorder	Recurrent major depressive disorder with postpartum onset	4324959		SNOMED
Major depressive disorder	Severe major depression without psychotic features	4327337		SNOMED
Major depressive disorder	Mild major depression	4336957		SNOMED
Major depressive disorder	Recurrent mild major depressive disorder co-occurrent with anxiety	35615151		SNOMED
Major depressive disorder	Recurrent severe major depressive disorder co-occurrent with anxiety	35615152		SNOMED
Major depressive disorder	Recurrent moderate major depressive disorder co-occurrent with anxiety	35615153		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Major depressive disorder	Recurrent major depressive disorder in partial remission co-occurrent with anxiety	35615155		SNOMED
Major depressive disorder	Moderately severe major depression	36714389		SNOMED
Major depressive disorder	Minimal recurrent major depression	36714997		SNOMED
Major depressive disorder	Moderately severe recurrent major depression	36714998		SNOMED
Major depressive disorder	Minimal major depression single episode	36714999		SNOMED
Major depressive disorder	Minimal major depression	36715000		SNOMED
Major depressive disorder	Moderately severe major depression single episode	36717389		SNOMED
Major depressive disorder	Mild major depressive disorder co-occurrent with anxiety single episode	37109052		SNOMED
Major depressive disorder	Moderate major depressive disorder co-occurrent with anxiety single episode	37109053		SNOMED
Major depressive disorder	Severe major depressive disorder co-occurrent with anxiety single episode	37109054		SNOMED
Major depressive disorder	Major depression with psychotic features	37111697		SNOMED
Major depressive disorder	Postpartum major depression in remission	42534817		SNOMED
Major depressive disorder	Severe major depression, single episode	42872411		SNOMED
Major depressive disorder	Severe major depression	42872722		SNOMED
Major depressive disorder	Severe recurrent major depression	43531624		SNOMED
Major depressive disorder	Recurrent major depressive episodes, severe	44805542		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Major depressive disorder	Recurrent major depressive episodes, in partial remission	44805549		SNOMED
Major depressive disorder	Single major depressive episode, in remission	44805550		SNOMED
Major depressive disorder	Single major depressive episode, severe, with psychosis, psychosis in remission	44805668		SNOMED
Major depressive disorder	Recurrent major depressive episodes, severe, with psychosis, psychosis in remission	44805669		SNOMED
Major depressive disorder	Recurrent major depressive episodes, in remission	44813499		SNOMED
Mood disorders	Severe mixed bipolar I disorder without psychotic features	372599		SNOMED
Mood disorders	Organic mood disorder	373176		SNOMED
Mood disorders	Mild bipolar I disorder, single manic episode	432290		SNOMED
Mood disorders	Bipolar I disorder, single manic episode	432866		SNOMED
Mood disorders	Bipolar I disorder	432876		SNOMED
Mood disorders	Dysthymia	433440		SNOMED
Mood disorders	Mixed bipolar I disorder in remission	433743		SNOMED
Mood disorders	Prolonged depressive adjustment reaction	433751		SNOMED
Mood disorders	Bipolar affective disorder, currently manic, moderate	433992		SNOMED
Mood disorders	Depressed bipolar I disorder in full remission	435225		SNOMED
Mood disorders	Bipolar affective disorder, current episode mixed	435226		SNOMED
Mood disorders	Reactive depressive psychosis	435520		SNOMED
Mood disorders	Bipolar disorder in partial remission	436072		SNOMED
Mood disorders	Adjustment disorder with anxious mood	436075		SNOMED
Mood disorders	Mood disorder caused by drug	436079		SNOMED
Mood disorders	Manic bipolar I disorder in full remission	436086		SNOMED
Mood disorders	Severe depressed bipolar I disorder with psychotic features	436386		SNOMED
Mood disorders	Bipolar disorder	436665		SNOMED
Mood disorders	Recurrent manic episodes	437249		SNOMED
Mood disorders	Mild depressed bipolar I disorder	437250		SNOMED
Mood disorders	Severe mood disorder without psychotic features	437522		SNOMED
Mood disorders	Bipolar affective disorder, currently depressed, moderate	437528		SNOMED
Mood disorders	Mixed bipolar I disorder in partial remission	437529		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Recurrent manic episodes, severe, with psychosis	437532		SNOMED
Mood disorders	Recurrent manic episodes, in full remission	437831		SNOMED
Mood disorders	Recurrent manic episodes, mild	438119		SNOMED
Mood disorders	Severe manic bipolar I disorder with psychotic features, mood-congruent	438129		SNOMED
Mood disorders	Recurrent manic episodes, moderate	438405		SNOMED
Mood disorders	Atypical depressive disorder	438727		SNOMED
Mood disorders	Severe mixed bipolar I disorder with psychotic features	439001		SNOMED
Mood disorders	Mixed bipolar affective disorder, in full remission	439245		SNOMED
Mood disorders	Mixed bipolar affective disorder, severe, with psychosis	439246		SNOMED
Mood disorders	Mixed bipolar affective disorder, moderate	439248		SNOMED
Mood disorders	Mixed bipolar affective disorder, mild	439249		SNOMED
Mood disorders	Mixed bipolar affective disorder	439250		SNOMED
Mood disorders	Bipolar affective disorder, currently depressed, in full remission	439251		SNOMED
Mood disorders	Bipolar affective disorder, currently depressed, mild	439253		SNOMED
Mood disorders	Bipolar affective disorder, current episode depression	439254		SNOMED
Mood disorders	Bipolar affective disorder, currently manic, in full remission	439255		SNOMED
Mood disorders	Bipolar affective disorder, currently manic, severe, with psychosis	439256		SNOMED
Mood disorders	Single manic episode in full remission	439261		SNOMED
Mood disorders	Single manic episode, severe, with psychosis	439262		SNOMED
Mood disorders	Single manic episode, moderate	439272		SNOMED
Mood disorders	Single manic episode, mild	439273		SNOMED
Mood disorders	Moderate mixed bipolar I disorder	439785		SNOMED
Mood disorders	Moderate bipolar I disorder, single manic episode	440067		SNOMED
Mood disorders	Bipolar affective disorder, current episode manic	440078		SNOMED
Mood disorders	Mild mixed bipolar I disorder	440079		SNOMED
Mood disorders	Depressive disorder	440383		SNOMED
Mood disorders	Cyclothymia	440696		SNOMED
Mood disorders	Brief depressive adjustment reaction	440698		SNOMED
Mood disorders	Atypical manic disorder	440980		SNOMED
Mood disorders	Bipolar affective disorder, currently manic, mild	441834		SNOMED
Mood disorders	Depressed bipolar I disorder	441836		SNOMED
Mood disorders	Adjustment disorder with depressed mood	442306		SNOMED
Mood disorders	Severe depressed bipolar I disorder without psychotic features	442570		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Manic bipolar I disorder in partial remission	442600		SNOMED
Mood disorders	Manic disorder, single episode	443237		SNOMED
Mood disorders	Severe manic bipolar I disorder without psychotic features	443797		SNOMED
Mood disorders	Multi-infarct dementia with depression	443864		SNOMED
Mood disorders	Mixed bipolar I disorder	443906		SNOMED
Mood disorders	Psychoactive substance-induced organic mood disorder	444038		SNOMED
Mood disorders	Mood disorder	444100		SNOMED
Mood disorders	Treatment resistant depression	607540		SNOMED
Mood disorders	Persistent depressive disorder	607543		SNOMED
Mood disorders	Recurrent manic episodes in partial remission	761111		SNOMED
Mood disorders	Recurrent severe manic episodes	761947		SNOMED
Mood disorders	Chronic mood disorder	762060		SNOMED
Mood disorders	Exacerbation of bipolar disorder	1340265		OMOP Extension
Mood disorders	Exacerbation of depressive disorder	1340305		OMOP Extension
Mood disorders	Exacerbation of major depressive disorder	1340392		OMOP Extension
Mood disorders	Exacerbation of mania	1340393		OMOP Extension
Mood disorders	Bipolar disease in pregnancy	3172581		Nebraska Lexicon
Mood disorders	Substance induced mood disorder	3190612		Nebraska Lexicon
Mood disorders	Mood disorder with manic symptoms caused by amphetamine and amphetamine derivative	3654786		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by amphetamine and amphetamine derivative	3654787		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by amphetamine and amphetamine derivative	3654788		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive with psychotic features, mood-congruent	4000165		SNOMED
Mood disorders	Chronic bipolar II disorder, most recent episode major depressive	4001733		SNOMED
Mood disorders	Mixed bipolar I disorder in full remission	4009648		SNOMED
Mood disorders	Cocaine-induced mood disorder	4012869		SNOMED
Mood disorders	Single episode of major depression in full remission	4025677		SNOMED
Mood disorders	Mild bipolar disorder	4028027		SNOMED
Mood disorders	Hallucinogen mood disorder	4029464		SNOMED
Mood disorders	Severe bipolar I disorder, single manic episode with psychotic features, mood-congruent	4030102		SNOMED
Mood disorders	Severe bipolar I disorder, single manic episode without psychotic features	4030856		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Severe mixed bipolar I disorder with psychotic features, mood-incongruent	4031928		SNOMED
Mood disorders	Bipolar I disorder, single manic episode with postpartum onset	4033390		SNOMED
Mood disorders	Bipolar II disorder, most recent episode major depressive	4037669		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive, in full remission	4045263		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive with psychotic features, mood-incongruent	4051448		SNOMED
Mood disorders	Late onset dysthymia	4057218		SNOMED
Mood disorders	Bipolar I disorder, most recent episode depressed with catatonic features	4071442		SNOMED
Mood disorders	Bipolar I disorder, most recent episode manic with catatonic features	4073401		SNOMED
Mood disorders	Seasonal affective disorder	4092239		SNOMED
Mood disorders	Severe depressed bipolar I disorder with psychotic features, mood-incongruent	4094507		SNOMED
Mood disorders	Early onset dysthymia	4096229		SNOMED
Mood disorders	Recurrent depression	4098302		SNOMED
Mood disorders	Severe manic bipolar I disorder with psychotic features	4102603		SNOMED
Mood disorders	Mood disorder with manic features due to general medical condition	4102936		SNOMED
Mood disorders	Postviral depression	4102973		SNOMED
Mood disorders	Drug-induced depressive state	4103126		SNOMED
Mood disorders	Chronic depression	4103574		SNOMED
Mood disorders	Sedative, hypnotic AND/OR anxiolytic-induced mood disorder	4103853		SNOMED
Mood disorders	Opioid-induced mood disorder	4105930		SNOMED
Mood disorders	Bipolar I disorder, most recent episode depressed with atypical features	4107538		SNOMED
Mood disorders	Endogenous depression	4114950		SNOMED
Mood disorders	Severe postnatal depression	4129184		SNOMED
Mood disorders	Mild postnatal depression	4129842		SNOMED
Mood disorders	Severe bipolar disorder with psychotic features, mood-incongruent	4131027		SNOMED
Mood disorders	Severe mood disorder with psychotic features	4132144		SNOMED
Mood disorders	Maternity blues	4133073		SNOMED
Mood disorders	Severe manic bipolar I disorder with psychotic features, mood-incongruent	4141603		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Bipolar II disorder, most recent episode major depressive with melancholic features	4144519		SNOMED
Mood disorders	Premenstrual dysphoric disorder in remission	4145216		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive with psychotic features	4147991		SNOMED
Mood disorders	Bipolar I disorder, single manic episode, in full remission	4148842		SNOMED
Mood disorders	Bipolar II disorder, most recent episode major depressive with postpartum onset	4148934		SNOMED
Mood disorders	Mild depression	4149320		SNOMED
Mood disorders	Severe depression	4149321		SNOMED
Mood disorders	Secondary dysthymia early onset	4150047		SNOMED
Mood disorders	Bipolar I disorder, most recent episode hypomanic	4150985		SNOMED
Mood disorders	Moderate depression	4151170		SNOMED
Mood disorders	Major depressive disorder	4152280		SNOMED
Mood disorders	Severe bipolar I disorder	4154283		SNOMED
Mood disorders	Involutional depression	4154805		SNOMED
Mood disorders	Transitory postpartum mood disturbance	4155208		SNOMED
Mood disorders	Severe bipolar disorder	4155798		SNOMED
Mood disorders	Severe bipolar II disorder	4161200		SNOMED
Mood disorders	Manic bipolar I disorder in remission	4166701		SNOMED
Mood disorders	PCP mood disorder	4168298		SNOMED
Mood disorders	Endogenous depression - recurrent	4168858		SNOMED
Mood disorders	Bipolar II disorder, most recent episode hypomanic	4172156		SNOMED
Mood disorders	Minor depressive disorder	4174987		SNOMED
Mood disorders	Organic mood disorder of depressed type	4175329		SNOMED
Mood disorders	Depressed bipolar I disorder in partial remission	4177651		SNOMED
Mood disorders	Severe depressed bipolar I disorder with psychotic features, mood-congruent	4182998		SNOMED
Mood disorders	Amphetamine-induced mood disorder	4184321		SNOMED
Mood disorders	Bipolar II disorder, most recent episode major depressive with atypical features	4185096		SNOMED
Mood disorders	Bipolar I disorder, most recent episode depressed with melancholic features	4192865		SNOMED
Mood disorders	Moderate bipolar disorder	4194222		SNOMED
Mood disorders	Severe bipolar disorder with psychotic features	4195158		SNOMED
Mood disorders	Primary dysthymia late onset	4195680		SNOMED
Mood disorders	Stuporous depression	4197222		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Chronic bipolar I disorder, most recent episode depressed	4197669		SNOMED
Mood disorders	Severe bipolar disorder without psychotic features	4200385		SNOMED
Mood disorders	Depressed bipolar I disorder in remission	4201739		SNOMED
Mood disorders	Alcohol-induced mood disorder	4205002		SNOMED
Mood disorders	Bipolar I disorder, most recent episode manic with postpartum onset	4210024		SNOMED
Mood disorders	Mild manic bipolar I disorder	4215917		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive without psychotic features	4217940		SNOMED
Mood disorders	Amok	4218985		SNOMED
Mood disorders	Severe bipolar I disorder, single manic episode with psychotic features	4220617		SNOMED
Mood disorders	Bipolar disorder in full remission	4220618		SNOMED
Mood disorders	Menopausal depression	4223090		SNOMED
Mood disorders	Secondary dysthymia	4224639		SNOMED
Mood disorders	Schizoaffective disorder, depressive type	4224940		SNOMED
Mood disorders	Recurrent brief depressive disorder	4226155		SNOMED
Mood disorders	Inhalant-induced mood disorder	4232492		SNOMED
Mood disorders	Organic mood disorder of manic type	4237734		SNOMED
Mood disorders	Severe mood disorder with psychotic features, mood-congruent	4239453		SNOMED
Mood disorders	Postpartum depression	4239471		SNOMED
Mood disorders	Moderate mood disorder	4241158		SNOMED
Mood disorders	Premenstrual dysphoric disorder	4242733		SNOMED
Mood disorders	Primary dysthymia early onset	4243308		SNOMED
Mood disorders	Schizoaffective disorder, bipolar type	4244078		SNOMED
Mood disorders	Mood disorder in full remission	4244690		SNOMED
Mood disorders	Bipolar I disorder, most recent episode mixed with catatonic features	4251178		SNOMED
Mood disorders	Mood disorder in partial remission	4253782		SNOMED
Mood disorders	Moderate bipolar II disorder, most recent episode major depressive	4262111		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive, in remission	4262272		SNOMED
Mood disorders	Recurrent major depression in full remission	4263748		SNOMED
Mood disorders	Secondary dysthymia late onset	4263770		SNOMED
Mood disorders	Mild mood disorder	4269143		SNOMED
Mood disorders	Major depression in full remission	4269493		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Bipolar I disorder, most recent episode mixed with postpartum onset	4274957		SNOMED
Mood disorders	Severe mixed bipolar I disorder with psychotic features, mood-congruent	4276670		SNOMED
Mood disorders	Moderate depressed bipolar I disorder	4280361		SNOMED
Mood disorders	Severe bipolar II disorder, most recent episode major depressive, in partial remission	4283219		SNOMED
Mood disorders	Manic bipolar I disorder	4287544		SNOMED
Mood disorders	Severe mood disorder with psychotic features, mood-incongruent	4289751		SNOMED
Mood disorders	Mood disorder due to a general medical condition	4295956		SNOMED
Mood disorders	Mood disorder with major depressive-like episode due to general medical condition	4298317		SNOMED
Mood disorders	Bipolar I disorder, single manic episode, in partial remission	4301106		SNOMED
Mood disorders	Postoperative depression	4305966		SNOMED
Mood disorders	Organic mood disorder of mixed type	4307518		SNOMED
Mood disorders	Moderate manic bipolar I disorder	4307804		SNOMED
Mood disorders	Primary dysthymia	4307951		SNOMED
Mood disorders	Bipolar II disorder	4307956		SNOMED
Mood disorders	Agitated depression	4308866		SNOMED
Mood disorders	Bipolar disorder in remission	4310821		SNOMED
Mood disorders	Severe bipolar I disorder, single manic episode with psychotic features, mood-incongruent	4312736		SNOMED
Mood disorders	Reactive depression (situational)	4314692		SNOMED
Mood disorders	Severe bipolar disorder with psychotic features, mood-congruent	4322477		SNOMED
Mood disorders	Mild bipolar II disorder, most recent episode major depressive	4324945		SNOMED
Mood disorders	Bipolar I disorder, single manic episode, in remission	4327669		SNOMED
Mood disorders	Mood disorder with depressive features due to general medical condition	4328217		SNOMED
Mood disorders	Mood disorder with mixed features due to general medical condition	4329560		SNOMED
Mood disorders	Bipolar II disorder, most recent episode major depressive with catatonic features	4330846		SNOMED
Mood disorders	Post-schizophrenic depression	4332994		SNOMED
Mood disorders	Organic bipolar disorder	4333670		SNOMED
Mood disorders	Mania	4333677		SNOMED
Mood disorders	Hypomania	4333678		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Endogenous depression first episode	4333679		SNOMED
Mood disorders	Right hemispheric organic affective disorder	4335160		SNOMED
Mood disorders	Manic stupor	4335170		SNOMED
Mood disorders	Bipolar I disorder, most recent episode depressed with postpartum onset	4336405		SNOMED
Mood disorders	Generalized neuromuscular exhaustion syndrome	4336980		SNOMED
Mood disorders	Organic emotionally labile disorder	4338019		SNOMED
Mood disorders	Masked depression	4338029		SNOMED
Mood disorders	Mixed anxiety and depressive disorder	4338031		SNOMED
Mood disorders	Bipolar I disorder, single manic episode with catatonic features	4338812		SNOMED
Mood disorders	Recurrent reactive depressive episodes, severe, with psychosis	35609824		SNOMED
Mood disorders	Reactive depression, prolonged single episode	35609842		SNOMED
Mood disorders	Reactive depression, single episode	35609843		SNOMED
Mood disorders	Reactive depression, recurrent	35609844		SNOMED
Mood disorders	Reactive depression, first episode	35609845		SNOMED
Mood disorders	Recurrent depression with current severe episode and psychotic features	35610097		SNOMED
Mood disorders	Recurrent depression with current severe episode without psychotic features	35610108		SNOMED
Mood disorders	Recurrent depression with current moderate episode	35610109		SNOMED
Mood disorders	Mania with mood-congruent psychotic features	35610110		SNOMED
Mood disorders	Mania with mood-incongruent psychotic features	35610111		SNOMED
Mood disorders	Mania with psychotic features	35610112		SNOMED
Mood disorders	Recurrent major depressive disorder co-occurrent with anxiety in full remission	35615154		SNOMED
Mood disorders	Psychosis and severe depression co-occurrent and due to bipolar affective disorder	35622934		SNOMED
Mood disorders	Bipolar disorder, most recent episode depression	35624743		SNOMED
Mood disorders	Bipolar disorder, most recent episode manic	35624744		SNOMED
Mood disorders	Bipolar affective disorder, most recent episode mixed	35624745		SNOMED
Mood disorders	Bipolar I disorder, most recent episode manic	35624747		SNOMED
Mood disorders	Bipolar I disorder, most recent episode depression	35624748		SNOMED
Mood disorders	Adjustment disorder with mixed anxiety and depressed mood	36684319		SNOMED
Mood disorders	Perinatal depression	36712668		SNOMED
Mood disorders	Minimal depression	36713698		SNOMED
Mood disorders	Moderately severe depression	36717092		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Opioid-induced mood disorder due to opioid abuse	37016268		SNOMED
Mood disorders	Acute depression	37016718		SNOMED
Mood disorders	Depressive disorder in mother complicating pregnancy	37018656		SNOMED
Mood disorders	Opioid-induced mood disorder due to opioid dependence	37018689		SNOMED
Mood disorders	Bipolar type I disorder currently in full remission	37109940		SNOMED
Mood disorders	Secondary mood disorder	37109941		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by alcohol	37109950		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by alcohol	37109951		SNOMED
Mood disorders	Mood disorder with mixed manic and depressive symptoms caused by alcohol	37109952		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by hypnotic	37110428		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by anxiolytic	37110429		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by sedative	37110430		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by hypnotic	37110431		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by sedative	37110432		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by hypnotic	37110433		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by cocaine	37110438		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by cocaine	37110439		SNOMED
Mood disorders	Mood disorder caused by methylenedioxymethamphetamine	37110452		SNOMED
Mood disorders	Mood disorder caused by dissociative drug	37110463		SNOMED
Mood disorders	Mood disorder caused by ketamine	37110464		SNOMED
Mood disorders	Depressive symptoms due to primary psychotic disorder	37110495		SNOMED
Mood disorders	Bipolar type II disorder currently in full remission	37117177		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by sedative	37117211		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by anxiolytic	37117212		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by cocaine	37117214		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by anxiolytic	37119148		SNOMED
Mood disorders	Depressive disorder caused by amphetamine	37209503		SNOMED
Mood disorders	Bipolar disorder caused by drug	37209504		SNOMED
Mood disorders	Depressive disorder caused by methamphetamine	37309680		SNOMED
Mood disorders	Mood disorder caused by methamphetamine	37309775		SNOMED
Mood disorders	Mood disorder caused by cannabis	37311915		SNOMED
Mood disorders	Antenatal depression	37312479		SNOMED
Mood disorders	Synthetic cannabinoid induced mood disorder	37312550		SNOMED
Mood disorders	Rapid cycling bipolar II disorder	37312578		SNOMED
Mood disorders	Chronic depressive personality disorder	40481798		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by opioid	42538584		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by opioid	42538585		SNOMED
Mood disorders	Mood disorder caused by stimulant	42538589		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by stimulant	42538590		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by stimulant	42538591		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by hallucinogen	42538595		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by hallucinogen	42538596		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by hallucinogen	42538597		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by volatile inhalant	42538598		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by volatile inhalant	42538599		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by volatile inhalant	42538600		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by dissociative drug	42538603		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by dissociative drug	42538604		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by dissociative drug	42538605		SNOMED
Mood disorders	Mood disorder caused by synthetic cathinone	42538735		SNOMED
Mood disorders	Mood disorder with depressive symptoms caused by synthetic cathinone	42538736		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Mood disorders	Mood disorder with manic symptoms caused by synthetic cathinone	42538737		SNOMED
Mood disorders	Mood disorder with manic symptoms caused by opioid	42539145		SNOMED
Mood disorders	Mood disorder with mixed depressive and manic symptoms caused by synthetic cathinone	42539371		SNOMED
Mood disorders	Severe mixed bipolar I disorder	42872412		SNOMED
Mood disorders	Severe depressed bipolar I disorder	42872413		SNOMED
Mood disorders	Severe manic bipolar I disorder	43020451		SNOMED
Mood disorders	Reactive depressive psychosis, single episode	43020483		SNOMED
Mood disorders	Rapid cycling bipolar I disorder	43021847		SNOMED
Mood disorders	Mood disorder of manic type	43021849		SNOMED
Mood disorders	Adjustment disorder with depressed mood in remission	44782518		SNOMED
Mood disorders	Severe seasonal affective disorder	44782720		SNOMED
Mood disorders	Cyclothymia in remission	44782932		SNOMED
Mood disorders	Depressive disorder in remission	44782943		SNOMED
Mood disorders	Adjustment disorder with anxious mood in remission	44784526		SNOMED
Mood disorders	Episodic mood disorder	44784632		SNOMED
Mood disorders	Mixed bipolar affective disorder, in partial remission	44804961		SNOMED
Mood disorders	Mixed bipolar affective disorder, severe	44805540		SNOMED
Mood disorders	Recurrent manic episodes, severe	44805543		SNOMED
Mood disorders	Single manic episode, severe	44805545		SNOMED
Mood disorders	Recurrent manic episodes, in partial remission	44805547		SNOMED
Mood disorders	Recurrent manic episodes, in remission	44805548		SNOMED
Mood disorders	Single manic episode in partial remission	44805552		SNOMED
Mood disorders	Single manic episode in remission	44805553		SNOMED
Mood disorders	Major depressive disorder in mother complicating childbirth	45757195		SNOMED
Mood disorders	Major depressive disorder in mother complicating pregnancy	45757196		SNOMED
Mood disorders	Depressive disorder in mother complicating childbirth	45757213		SNOMED
Dementia	Aggression due to dementia	37312036		SNOMED
Dementia	Agitation due to dementia	37312035		SNOMED
Dementia	Altered behavior in Alzheimer's disease	44784643		SNOMED
Dementia	Altered behavior in Huntington's dementia	44784620		SNOMED
Dementia	Alzheimer's disease	378419		SNOMED
Dementia	Alzheimer's disease co-occurrent with delirium	37395572		SNOMED
Dementia	Amyotrophic lateral sclerosis, parkinsonism, dementia complex	3654598		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Dementia	Amyotrophic lateral sclerosis with dementia	4041685		SNOMED
Dementia	Anxiety due to dementia	37312031		SNOMED
Dementia	Apathetic behavior due to dementia	37312030		SNOMED
Dementia	Arteriosclerotic dementia with delirium	376094		SNOMED
Dementia	Arteriosclerotic dementia with depression	374326		SNOMED
Dementia	Arteriosclerotic dementia with paranoia	4100252		SNOMED
Dementia	Behavioral and psychological symptoms of dementia	35608576		SNOMED
Dementia	Behavioral disturbance co-occurrent and due to late onset Alzheimer dementia	37117145		SNOMED
Dementia	Behavioral variant of frontotemporal dementia	37399020		SNOMED
Dementia	Cerebral degeneration presenting primarily with dementia	4092747		SNOMED
Dementia	CHMP2B-related frontotemporal dementia	45771254		SNOMED
Dementia	Cortical vascular dementia	3654434		SNOMED
Dementia	Delirium co-occurrent with dementia	37111242		SNOMED
Dementia	Delusions in Alzheimer's disease	44782726		SNOMED
Dementia	Dementia	4182210		SNOMED
Dementia	Dementia associated with AIDS	4228133		SNOMED
Dementia	Dementia associated with alcoholism	378726		SNOMED
Dementia	Dementia associated with another disease	374888		SNOMED
Dementia	Dementia associated with cerebral anoxia	44784607		SNOMED
Dementia	Dementia associated with cerebral lipidosis	44784472		SNOMED
Dementia	Dementia associated with multiple sclerosis	44784474		SNOMED
Dementia	Dementia associated with Parkinson's Disease	4314734		SNOMED
Dementia	Dementia co-occurrent with human immunodeficiency virus infection	37017549		SNOMED
Dementia	Dementia due to chromosomal anomaly	36716797		SNOMED
Dementia	Dementia due to Creutzfeldt Jakob disease	4180284		SNOMED
Dementia	Dementia due to disorder of central nervous system	37110513		SNOMED
Dementia	Dementia due to Huntington chorea	40483103		SNOMED
Dementia	Dementia due to metabolic abnormality	36716796		SNOMED
Dementia	Dementia due to multiple sclerosis with altered behavior	44782559		SNOMED
Dementia	Dementia due to Parkinson's disease	44782422		SNOMED
Dementia	Dementia due to Pick's disease	44782710		SNOMED
Dementia	Dementia due to prion disease	42538609		SNOMED
Dementia	Dementia due to Rett's syndrome	43020422		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Dementia	Dementia of frontal lobe type	441002		SNOMED
Dementia	Dementia of the Alzheimer type with behavioral disturbance	43530664		SNOMED
Dementia	Dementia with behavioral disturbance	43530666		SNOMED
Dementia	Dementia with Down syndrome	37116469		SNOMED
Dementia	Depressed mood in Alzheimer's disease	44782727		SNOMED
Dementia	Dialysis dementia	4244346		SNOMED
Dementia	Diffuse Lewy body disease	380701		SNOMED
Dementia	Disinhibited behavior due to dementia	37311665		SNOMED
Dementia	Early onset Alzheimer's disease with behavioral disturbance	44782432		SNOMED
Dementia	Epilepsy co-occurrent and due to dementia	37110677		SNOMED
Dementia	Epileptic dementia with behavioral disturbance	37018608		SNOMED
Dementia	Familial Alzheimer-like prion disease	36717455		SNOMED
Dementia	Familial Alzheimer's disease of early onset	4043241		SNOMED
Dementia	Familial Alzheimer's disease of late onset	4043243		SNOMED
Dementia	Focal Alzheimer's disease	4043377		SNOMED
Dementia	Frontotemporal dementia	4043378		SNOMED
Dementia	Frontotemporal dementia with parkinsonism-17	45765480		SNOMED
Dementia	GDS level 4 - moderate cognitive decline	4250118		SNOMED
Dementia	GDS level 5 - moderately severe cognitive decline	4233045		SNOMED
Dementia	GDS level 6 - severe cognitive decline	4236296		SNOMED
Dementia	GDS level 7 - very severe cognitive decline	4236297		SNOMED
Dementia	GRN-related frontotemporal dementia	45765477		SNOMED
Dementia	Hallucinations co-occurrent and due to late onset dementia	37109222		SNOMED
Dementia	Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia	45766396		SNOMED
Dementia	Ischemic vascular dementia	36717248		SNOMED
Dementia	Language disorder of dementia	4044415		SNOMED
Dementia	Lewy body dementia with behavioral disturbance	44782763		SNOMED
Dementia	Mild dementia	762497		SNOMED
Dementia	Mixed cortical and subcortical vascular dementia	4046090		SNOMED
Dementia	Mixed dementia	43021816		SNOMED
Dementia	Moderate dementia	762704		SNOMED
Dementia	Multi-infarct dementia	379778		SNOMED
Dementia	Multi-infarct dementia due to atherosclerosis	37395562		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Dementia	Multi-infarct dementia, uncomplicated	377254		SNOMED
Dementia	Multi-infarct dementia with delirium	444091		SNOMED
Dementia	Multi-infarct dementia with delusions	443790		SNOMED
Dementia	Multi-infarct dementia with depression	443864		SNOMED
Dementia	Non-amnestic Alzheimer disease	36716558		SNOMED
Dementia	Non-familial Alzheimer's disease of early onset	4043242		SNOMED
Dementia	Non-familial Alzheimer's disease of late onset	4043244		SNOMED
Dementia	Organic dementia associated with AIDS	4224860		SNOMED
Dementia	Parkinsonism with dementia of Guadeloupe	37396063		SNOMED
Dementia	Patchy dementia	4047748		SNOMED
Dementia	Predominantly cortical dementia	35610098		SNOMED
Dementia	Predominantly cortical vascular dementia	35610099		SNOMED
Dementia	Presenile dementia	378125		SNOMED
Dementia	Presenile dementia associated with AIDS	4224240		SNOMED
Dementia	Presenile dementia co-occurrent with human immunodeficiency virus infection	37017247		SNOMED
Dementia	Presenile dementia with delirium	381832		SNOMED
Dementia	Presenile dementia with delusions	44782771		SNOMED
Dementia	Presenile dementia with depression	377527		SNOMED
Dementia	Presenile dementia with paranoia	4098163		SNOMED
Dementia	Presenile dementia with psychosis	35610096		SNOMED
Dementia	Primary degenerative dementia	43020444		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, presenile onset	4218017		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, presenile onset, uncomplicated	4277444		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, presenile onset, with delirium	4277746		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, presenile onset, with delusions	4182539		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, presenile onset, with depression	4019705		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset	4220313		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset, uncomplicated	4278830		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset, with behavioral disturbance	762578		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset, with delirium	4167839		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset, with delusions	4204688		SNOMED
Dementia	Primary degenerative dementia of the Alzheimer type, senile onset, with depression	4097384		SNOMED
Dementia	PRKAR1B-related neurodegenerative dementia with intermediate filaments	36674472		SNOMED
Dementia	Progressive aphasia in Alzheimer's disease	4043379		SNOMED
Dementia	Psychological symptom due to dementia	37311890		SNOMED
Dementia	Rapidly progressive dementia	37109635		SNOMED
Dementia	Semantic dementia	4046091		SNOMED
Dementia	Senile dementia	4048875		SNOMED
Dementia	Senile dementia of the Lewy body type	4196433		SNOMED
Dementia	Senile dementia with delirium	376946		SNOMED
Dementia	Senile dementia with delusion	380986		SNOMED
Dementia	Senile dementia with depression	379784		SNOMED
Dementia	Senile dementia with depressive or paranoid features	4101137		SNOMED
Dementia	Senile dementia with paranoia	4100250		SNOMED
Dementia	Senile dementia with psychosis	4159643		SNOMED
Dementia	Severe dementia	765653		SNOMED
Dementia	Subcortical dementia	42538857		SNOMED
Dementia	Subcortical vascular dementia	4047747		SNOMED
Dementia	Uncomplicated arteriosclerotic dementia	439276		SNOMED
Dementia	Uncomplicated presenile dementia	376085		SNOMED
Dementia	Uncomplicated senile dementia	375791		SNOMED
Dementia	Vascular dementia	443605		SNOMED
Dementia	Vascular dementia of acute onset	4046089		SNOMED
Dementia	Vascular dementia with behavioral disturbance	37018688		SNOMED
Dementia	Vascular dementia without behavioral disturbance	37109056		SNOMED
Dementia	Wandering due to dementia	37312577		SNOMED
Apathy	Indifference	4071366		SNOMED
Apathy	Apathetic behavior due to dementia	37312030		SNOMED
Intellectual disability	Intellectual disability	40277917		SNOMED
Intellectual disability	X-linked intellectual disability hypotonic face syndrome	608002		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Intellectual functioning disability	4041136		SNOMED
Intellectual disability	Profound intellectual disability	438733		SNOMED
Intellectual disability	Hyperphosphatasemia with intellectual disability	4141891		SNOMED
Intellectual disability	Severe intellectual disability	432898		SNOMED
Intellectual disability	Intellectual disability, congenital heart disease, blepharophimosis, blepharoptosis and hypoplastic teeth	4133527		SNOMED
Intellectual disability	X-linked intellectual disability with marfanoid habitus	4173610		SNOMED
Intellectual disability	Moderate intellectual disability	436682		SNOMED
Intellectual disability	CASK related intellectual disability	45766270		SNOMED
Intellectual disability	Alpha thalassemia X-linked intellectual disability syndrome	37399441		SNOMED
Intellectual disability	Early onset parkinsonism and intellectual disability syndrome	37399497		SNOMED
Intellectual disability	Female restricted epilepsy with intellectual disability syndrome	37396778		SNOMED
Intellectual disability	FRAXE intellectual disability syndrome	37399013		SNOMED
Intellectual disability	Microphthalmia with ankyloblepharon and intellectual disability syndrome	37397173		SNOMED
Intellectual disability	Spondyloepiphyseal dysplasia, craniosynostosis, cleft palate, cataract and intellectual disability syndrome	36713803		SNOMED
Intellectual disability	X-linked intellectual disability with ataxia and apraxia syndrome	36713853		SNOMED
Intellectual disability	X-linked recessive intellectual disability and macrocephaly with ciliary dysfunction syndrome	36717325		SNOMED
Intellectual disability	X-linked intellectual disability Seemanova type	36717679		SNOMED
Intellectual disability	Syndromic X-linked intellectual disability type 11	36713896		SNOMED
Intellectual disability	X-linked intellectual disability Shrimpton type	36713900		SNOMED
Intellectual disability	X-linked intellectual disability Siderius type	36713902		SNOMED
Intellectual disability	X-linked intellectual disability Stevenson type	36713903		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	X-linked intellectual disability Stocco Dos Santos type	36713904		SNOMED
Intellectual disability	X-linked intellectual disability Stoll type	36713905		SNOMED
Intellectual disability	X-linked intellectual disability Turner type	36713906		SNOMED
Intellectual disability	X-linked intellectual disability Van Esch type	36713908		SNOMED
Intellectual disability	X-linked intellectual disability Wilson type	36717686		SNOMED
Intellectual disability	X-linked intellectual disability Schimke type	36713963		SNOMED
Intellectual disability	X-linked intellectual disability Pai type	36713964		SNOMED
Intellectual disability	X-linked intellectual disability Miles Carpenter type	36713965		SNOMED
Intellectual disability	X-linked intellectual disability Cilliers type	36713966		SNOMED
Intellectual disability	X-linked intellectual disability Cantagrel type	36713967		SNOMED
Intellectual disability	X-linked intellectual disability Armfield type	36713968		SNOMED
Intellectual disability	X-linked intellectual disability Abidi type	36713969		SNOMED
Intellectual disability	Uveal coloboma with cleft lip and palate and intellectual disability syndrome	36713988		SNOMED
Intellectual disability	X-linked intellectual disability with cerebellar hypoplasia syndrome	36714051		SNOMED
Intellectual disability	X-linked intellectual disability with cubitus valgus and dysmorphism syndrome	36714053		SNOMED
Intellectual disability	X-linked intellectual disability and epilepsy with progressive joint contracture and facial dysmorphism syndrome	36714067		SNOMED
Intellectual disability	X-linked intellectual disability with hypogammaglobulinemia and progressive neurological deterioration syndrome	36714068		SNOMED
Intellectual disability	X-linked intellectual disability and hypotonia with facial dysmorphism and aggressive behavior syndrome	36714069		SNOMED
Intellectual disability	Syndromic X-linked intellectual disability type 7	36714072		SNOMED
Intellectual disability	Syndromic X-linked intellectual disability due to JARID1C mutation	36714073		SNOMED
Intellectual disability	Pterygium colli with intellectual disability and digital anomaly syndrome	36714144		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Disorder of sex development with intellectual disability syndrome	36714286		SNOMED
Intellectual disability	X-linked intellectual disability with seizure and psoriasis syndrome	36714528		SNOMED
Intellectual disability	X-linked intellectual disability Cabezas type	36714529		SNOMED
Intellectual disability	X-linked intellectual disability with plagiocephaly syndrome	36717758		SNOMED
Intellectual disability	X-linked intellectual disability, macrocephaly, macroorchidism syndrome	36714541		SNOMED
Intellectual disability	X-linked intellectual disability with acromegaly and hyperactivity syndrome	36714542		SNOMED
Intellectual disability	Congenital hypoplasia of ulna and intellectual disability syndrome	36714554		SNOMED
Intellectual disability	Aniridia and intellectual disability syndrome	36715012		SNOMED
Intellectual disability	Arachnodactyly with abnormal ossification and intellectual disability syndrome	36715036		SNOMED
Intellectual disability	Arachnodactyly and intellectual disability with facial dysmorphism syndrome	36715037		SNOMED
Intellectual disability	Ataxia with deafness and intellectual disability syndrome	36715050		SNOMED
Intellectual disability	Coloboma, congenital heart disease, ichthyosiform dermatosis, intellectual disability ear anomaly syndrome	36715141		SNOMED
Intellectual disability	Alopecia, contracture, dwarfism, intellectual disability syndrome	36717431		SNOMED
Intellectual disability	Alopecia, psychomotor epilepsy, periodontal pyorrhea, intellectual disability syndrome	36715349		SNOMED
Intellectual disability	Alopecia and intellectual disability with hypergonadotropic hypogonadism syndrome	36715350		SNOMED
Intellectual disability	Alport syndrome, intellectual disability, midface hypoplasia, elliptocytosis syndrome	36715351		SNOMED
Intellectual disability	Aniridia, ptosis, intellectual disability, familial obesity syndrome	36715355		SNOMED
Intellectual disability	Hair defect with photosensitivity and intellectual disability syndrome	36715367		SNOMED
Intellectual disability	Deafness and intellectual disability Martin Probst type syndrome	36715416		SNOMED
Intellectual disability	Dentinogenesis imperfecta, short stature, hearing loss, intellectual disability syndrome	36717441		SNOMED
Intellectual disability	Intellectual disability, epilepsy, bulbous nose syndrome	36715461		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Seizure, sensorineural deafness, ataxia, intellectual disability, electrolyte imbalance syndrome	36715509		SNOMED
Intellectual disability	Hypogonadism with mitral valve prolapse and intellectual disability syndrome	36716030		SNOMED
Intellectual disability	Lipodystrophy, intellectual disability, deafness syndrome	36716108		SNOMED
Intellectual disability	Intellectual disability with cataract and kyphosis syndrome	36716124		SNOMED
Intellectual disability	Osteogenesis imperfecta, retinopathy, seizures, intellectual disability syndrome	36716191		SNOMED
Intellectual disability	Osteopenia, myopia, hearing loss, intellectual disability, facial dysmorphism syndrome	36716192		SNOMED
Intellectual disability	Spastic paraplegia, intellectual disability, palmoplantar hyperkeratosis syndrome	36716260		SNOMED
Intellectual disability	Severe X-linked intellectual disability Gustavson type	36716264		SNOMED
Intellectual disability	Agenesis of corpus callosum, intellectual disability, coloboma, micrognathia syndrome	36717547		SNOMED
Intellectual disability	Congenital cataract with hypertrichosis and intellectual disability syndrome	36716388		SNOMED
Intellectual disability	Intellectual disability, craniofacial dysmorphism, hypogonadism, diabetes mellitus syndrome	36717215		SNOMED
Intellectual disability	Intellectual disability, hypoplastic corpus callosum, preauricular tag syndrome	36716446		SNOMED
Intellectual disability	Intellectual disability, developmental delay, contracture syndrome	36716447		SNOMED
Intellectual disability	Male hypergonadotropic hypogonadism, intellectual disability, skeletal anomaly syndrome	36716449		SNOMED
Intellectual disability	Skeletal dysplasia with intellectual disability syndrome	36716463		SNOMED
Intellectual disability	Microcephaly, seizure, intellectual disability, heart disease syndrome	37118888		SNOMED
Intellectual disability	Fallot complex with intellectual disability and growth delay syndrome	37109597		SNOMED
Intellectual disability	Hypotrichosis and intellectual disability syndrome Lopes type	37109617		SNOMED
Intellectual disability	Non-progressive cerebellar ataxia with intellectual disability	37118953		SNOMED
Intellectual disability	Spastic tetraplegia, retinitis pigmentosa, intellectual disability syndrome	37109775		SNOMED
Intellectual disability	Severe intellectual disability, epilepsy, anal anomaly, distal phalangeal hypoplasia syndrome	37118973		SNOMED
Intellectual disability	Seizures and intellectual disability due to hydroxylysinuria	37109991		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Retinitis pigmentosa, intellectual disability, deafness, hypogenitalism syndrome	37109996		SNOMED
Intellectual disability	Laryngeal abductor paralysis with intellectual disability syndrome	37110103		SNOMED
Intellectual disability	X-linked spasticity, intellectual disability, epilepsy syndrome	37110783		SNOMED
Intellectual disability	Intellectual disability Buenos Aires type	37111245		SNOMED
Intellectual disability	X-linked intellectual disability Brooks type	37111251		SNOMED
Intellectual disability	Intellectual disability, cataract, calcified pinna, myopathy syndrome	37111654		SNOMED
Intellectual disability	X-linked intellectual disability Hedera type	37111663		SNOMED
Intellectual disability	X-linked intellectual disability Nascimento type	37111667		SNOMED
Intellectual disability	X-linked intellectual disability, limb spasticity, retinal dystrophy, diabetes insipidus syndrome	37115758		SNOMED
Intellectual disability	Cortical blindness, intellectual disability, polydactyly syndrome	37118457		SNOMED
Intellectual disability	Osteopenia, intellectual disability, sparse hair syndrome	37117739		SNOMED
Intellectual disability	Branchial dysplasia, intellectual disability, inguinal hernia syndrome	37116296		SNOMED
Intellectual disability	Marfanoid habitus with autosomal recessive intellectual disability syndrome	37116372		SNOMED
Intellectual disability	Preaxial polydactyly, colobomata, intellectual disability syndrome	37116391		SNOMED
Intellectual disability	Ichthyosis, intellectual disability, dwarfism, renal impairment syndrome	37116399		SNOMED
Intellectual disability	Thumb stiffness, brachydactyly, intellectual disability syndrome	37116413		SNOMED
Intellectual disability	Metaphyseal dysostosis, intellectual disability, conductive deafness syndrome	37116641		SNOMED
Intellectual disability	Spastic paraplegia, glaucoma, intellectual disability syndrome	37116656		SNOMED
Intellectual disability	Hereditary congenital hypomelanotic and hypermelanotic cutaneous macules, growth retardation, intellectual disability syndrome	37116668		SNOMED
Intellectual disability	Megalocornea with intellectual disability syndrome	37116706		SNOMED
Intellectual disability	Ectodermal dysplasia, intellectual disability, central nervous system malformation syndrome	37118763		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Alpha-thalassemia intellectual disability syndrome linked to chromosome 16	42539413		SNOMED
Intellectual disability	Charcot-Marie-Tooth disease, deafness, intellectual disability syndrome	35621875		SNOMED
Intellectual disability	Cerebellar ataxia, intellectual disability, oculomotor apraxia, cerebellar cysts syndrome	35622032		SNOMED
Intellectual disability	Intellectual disability, obesity, brain malformation, facial dysmorphism syndrome	35622038		SNOMED
Intellectual disability	Ichthyosis, alopecia, eclabion, ectropion, intellectual disability syndrome	35622087		SNOMED
Intellectual disability	Aortic arch anomaly, facial dysmorphism, intellectual disability syndrome	35622247		SNOMED
Intellectual disability	Intellectual disability due to nutritional deficiency	35622258		SNOMED
Intellectual disability	Craniodigital syndrome and intellectual disability syndrome	35622278		SNOMED
Intellectual disability	Intellectual disability, alacrima, achalasia syndrome	35622323		SNOMED
Intellectual disability	Intellectual disability, polydactyly, uncombable hair syndrome	35622324		SNOMED
Intellectual disability	Intellectual disability, spasticity, ectrodactyly syndrome	35622325		SNOMED
Intellectual disability	Intellectual disability, brachydactyly, Pierre Robin syndrome	35622326		SNOMED
Intellectual disability	Intellectual disability Wolff type	35622327		SNOMED
Intellectual disability	Pachygyria, intellectual disability, epilepsy syndrome	35607971		SNOMED
Intellectual disability	Intellectual disability Birk-Barel type	35622702		SNOMED
Intellectual disability	Cryptorchidism, arachnodactyly, intellectual disability syndrome	35622769		SNOMED
Intellectual disability	Intellectual disability, myopathy, short stature, endocrine defect syndrome	35622777		SNOMED
Intellectual disability	Focal epilepsy, intellectual disability, cerebro-cerebellar malformation syndrome	35622869		SNOMED
Intellectual disability	HIVEP2-related intellectual disability	35623128		SNOMED
Intellectual disability	X-linked intellectual disability, hypogonadism, ichthyosis, obesity, short stature syndrome	35623139		SNOMED
Intellectual disability	Brachydactyly, mesomelia, intellectual disability, heart defect syndrome	35623289		SNOMED
Intellectual disability	ADNP-related multiple congenital anomalies, intellectual disability, autism spectrum disorder	35624210		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	PPP2R5D-related intellectual disability	35625633		SNOMED
Intellectual disability	Early-onset epileptic encephalopathy and intellectual disability due to GRIN2A mutation	36674712		SNOMED
Intellectual disability	Polyneuropathy, intellectual disability, acromicria, premature menopause syndrome	36674826		SNOMED
Intellectual disability	Microcephaly, thin corpus callosum, intellectual disability syndrome	36674865		SNOMED
Intellectual disability	Optic atrophy, intellectual disability syndrome	36674867		SNOMED
Intellectual disability	Intellectual disability, seizures, macrocephaly, obesity syndrome	36674893		SNOMED
Intellectual disability	Intellectual disability, seizures, hypotonia, ophthalmologic, skeletal anomalies syndrome	36674191		SNOMED
Intellectual disability	Autosomal recessive cerebellar ataxia, epilepsy, intellectual disability syndrome due to WWOX deficiency	36674914		SNOMED
Intellectual disability	Autosomal recessive intellectual disability, motor dysfunction, multiple joint contracture syndrome	36674915		SNOMED
Intellectual disability	Microcephaly, short stature, intellectual disability, facial dysmorphism syndrome	36674971		SNOMED
Intellectual disability	Intellectual disability, short stature, hypertelorism syndrome	36674974		SNOMED
Intellectual disability	X-linked colobomatous microphthalmia, microcephaly, intellectual disability, short stature syndrome	36674995		SNOMED
Intellectual disability	Hepatic fibrosis, renal cyst, intellectual disability syndrome	36674996		SNOMED
Intellectual disability	Borderline intellectual disability	4299505		SNOMED
Intellectual disability	X-linked intellectual disability, craniofacioskeletal syndrome	36676400		SNOMED
Intellectual disability	Intellectual disability with strabismus syndrome	36676502		SNOMED
Intellectual disability	Intellectual disability, facial dysmorphism, hand anomalies syndrome	36676513		SNOMED
Intellectual disability	Severe intellectual disability, short stature, behavioral abnormalities, facial dysmorphism syndrome	36676516		SNOMED
Intellectual disability	Autosomal recessive cerebellar ataxia, epilepsy, intellectual disability syndrome due to TUD deficiency	36676588		SNOMED
Intellectual disability	Early-onset epileptic encephalopathy, cortical blindness, intellectual disability, facial dysmorphism syndrome	36676621		SNOMED
Intellectual disability	Severe intellectual disability, poor language, strabismus, grimacing face, long fingers syndrome	36676624		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Intellectual disability, feeding difficulties, developmental delay, microcephaly syndrome	36676625		SNOMED
Intellectual disability	Hypohidrosis, enamel hypoplasia, palmoplantar keratoderma, intellectual disability syndrome	36676626		SNOMED
Intellectual disability	Short ulna, dysmorphism, hypotonia, intellectual disability syndrome	36676629		SNOMED
Intellectual disability	Spondylocostal dysostosis, hypospadias, intellectual disability syndrome	36676634		SNOMED
Intellectual disability	Intellectual disability, craniofacial dysmorphism, cryptorchidism syndrome	36676637		SNOMED
Intellectual disability	Aphonia, deafness, retinal dystrophy, bifid halluces, intellectual disability syndrome	36676639		SNOMED
Intellectual disability	X-linked intellectual disability, cardiomegaly, congestive heart failure syndrome	36676642		SNOMED
Intellectual disability	Intellectual disability, hypotonia, brachycephaly, pyloric stenosis, cryptorchidism syndrome	36676669		SNOMED
Intellectual disability	Late-onset localized junctional epidermolysis bullosa, intellectual disability syndrome	36676715		SNOMED
Intellectual disability	Rare non-syndromic intellectual disability	36676726		SNOMED
Intellectual disability	AHDC1-related intellectual disability, obstructive sleep apnea, mild dysmorphism syndrome	36674471		SNOMED
Intellectual disability	Intellectual disability, obesity, prognathism, eye and skin anomalies syndrome	36674490		SNOMED
Intellectual disability	Severe intellectual disability, progressive postnatal microcephaly, midline stereotypic hand movements syndrome	36676854		SNOMED
Intellectual disability	Intellectual disability, severe speech delay, mild dysmorphism syndrome	36676897		SNOMED
Intellectual disability	Colobomatous microphthalmia, obesity, hypogenitalism, intellectual disability syndrome	36678790		SNOMED
Intellectual disability	Blepharophimosis, intellectual disability syndrome, Verloes type	36680587		SNOMED
Intellectual disability	Severe intellectual disability and progressive spastic paraplegia	36674508		SNOMED
Intellectual disability	SYNGAP1-related intellectual disability	36683256		SNOMED
Intellectual disability	Autosomal recessive cerebellar ataxia, epilepsy, intellectual disability syndrome due to RUBCN deficiency	37204209		SNOMED
Intellectual disability	Severe intellectual disability, progressive spastic diplegia syndrome	37204211		SNOMED
Intellectual disability	Intellectual disability, facial dysmorphism syndrome due to SETD5 haploinsufficiency	37204216		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Intellectual disability, coarse face, macrocephaly, cerebellar hypotrophy syndrome	37204230		SNOMED
Intellectual disability	Primary microcephaly, mild intellectual disability, young-onset diabetes syndrome	37204232		SNOMED
Intellectual disability	Congenital muscular dystrophy with intellectual disability and severe epilepsy	37204238		SNOMED
Intellectual disability	Ophthalmoplegia, intellectual disability, lingua scrotalis syndrome	37204321		SNOMED
Intellectual disability	Severe microbrachycephaly, intellectual disability, athetoid cerebral palsy syndrome	37204364		SNOMED
Intellectual disability	Macrocephaly, intellectual disability, autism syndrome	37204430		SNOMED
Intellectual disability	Congenital muscular dystrophy with intellectual disability	37204504		SNOMED
Intellectual disability	Congenital muscular dystrophy without intellectual disability	37204505		SNOMED
Intellectual disability	DYRK1A-related intellectual disability syndrome due to 21q22.13q22.2 microdeletion	37204735		SNOMED
Intellectual disability	X-linked intellectual disability due to GRIA3 mutations	37204804		SNOMED
Intellectual disability	White matter hypoplasia, corpus callosum agenesis, intellectual disability syndrome	37204805		SNOMED
Intellectual disability	Intellectual disability, hyperkinetic movement, truncal ataxia syndrome	37206827		SNOMED
Intellectual disability	ANK3-related intellectual disability, sleep disturbance syndrome	37206828		SNOMED
Intellectual disability	Alopecia, epilepsy, intellectual disability syndrome Moynahan type	37312387		SNOMED
Intellectual disability	Mild intellectual disability	432612		SNOMED
Intellectual disability	Fragile X syndrome	436803		SNOMED
Intellectual disability	Richieri Costa-da Silva syndrome	37204317		SNOMED
Intellectual disability	Mild intellectual development disorder with minimal impairment of behaviour	35610128		SNOMED
Intellectual disability	Congenital cataract with ataxia and deafness syndrome	36714026		SNOMED
Intellectual disability	Oro-facial digital syndrome type 11	36717662		SNOMED
Intellectual disability	Ossification anomaly with psychomotor developmental delay syndrome	36716189		SNOMED
Intellectual disability	Profound intellectual development disorder with significant impairment of behaviour	35610115		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Shprintzen Goldberg craniosynostosis syndrome	36717691		SNOMED
Intellectual disability	Kagami Ogata syndrome	36674921		SNOMED
Intellectual disability	PPM-X syndrome	45765422		SNOMED
Intellectual disability	SCARF syndrome	37117794		SNOMED
Intellectual disability	Fried syndrome	36713856		SNOMED
Intellectual disability	Profound intellectual development disorder with impairment of behaviour	35610117		SNOMED
Intellectual disability	Severe intellectual development disorder without significant impairment of behaviour	35610118		SNOMED
Intellectual disability	Radioulnar synostosis with developmental delay and hypotonia syndrome	36716048		SNOMED
Intellectual disability	Wolf Hirschhorn syndrome	37397559		SNOMED
Intellectual disability	Radioulnar synostosis with microcephaly and scoliosis syndrome	36714074		SNOMED
Intellectual disability	17q11.2 microduplication syndrome	36714383		SNOMED
Intellectual disability	DOORS syndrome	36714522		SNOMED
Intellectual disability	MEDNIK syndrome	36717524		SNOMED
Intellectual disability	Epilepsy, microcephaly, skeletal dysplasia syndrome	37116354		SNOMED
Intellectual disability	Hyperekplexia epilepsy syndrome	37206121		SNOMED
Intellectual disability	Angelman syndrome	4296631		SNOMED
Intellectual disability	Agenesis of corpus callosum and abnormal genitalia syndrome	35607964		SNOMED
Intellectual disability	15q overgrowth syndrome	36675149		SNOMED
Intellectual disability	Severe feeding difficulties, failure to thrive, microcephaly due to ASXL3 deficiency syndrome	36676500		SNOMED
Intellectual disability	Cooper Jabs syndrome	36715217		SNOMED
Intellectual disability	Intellectual development disorder with significant impairment of behaviour	35610518		SNOMED
Intellectual disability	Facial dysmorphism, macrocephaly, myopia, Dandy-Walker malformation syndrome	37116639		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Martsolf syndrome	36716389		SNOMED
Intellectual disability	Intellectual development disorder with minimal impairment of behaviour	35610519		SNOMED
Intellectual disability	Pitt-Hopkins syndrome	45765412		SNOMED
Intellectual disability	BRESEK syndrome	36713570		SNOMED
Intellectual disability	Autism epilepsy syndrome due to branched chain ketoacid dehydrogenase kinase deficiency	36675122		SNOMED
Intellectual disability	Agammaglobulinemia, microcephaly, craniosynostosis, severe dermatitis syndrome	36716314		SNOMED
Intellectual disability	Cerebrooculonasal syndrome	36715305		SNOMED
Intellectual disability	Microcephalic primordial dwarfism Dauber type	36674736		SNOMED
Intellectual disability	5-amino-4-imidazole carboxamide ribosiduria	37110832		SNOMED
Intellectual disability	Severe intellectual development disorder with significant impairment of behaviour	35610119		SNOMED
Intellectual disability	THOC6-related developmental delay-microcephaly-facial dysmorphism syndrome	36676627		SNOMED
Intellectual disability	Faciocardiorenal syndrome	37109595		SNOMED
Intellectual disability	Infantile choroidocerebral calcification syndrome	37110134		SNOMED
Intellectual disability	Okamoto syndrome	36716160		SNOMED
Intellectual disability	Microcephalic primordial dwarfism Montreal type	35623414		SNOMED
Intellectual disability	Aniridia, renal agenesis, psychomotor retardation syndrome	37116412		SNOMED
Intellectual disability	Epiphyseal dysplasia, hearing loss, dysmorphism syndrome	35624222		SNOMED
Intellectual disability	Fine Lubinsky syndrome	36715332		SNOMED
Intellectual disability	Facial dysmorphism, cleft palate, loose skin syndrome	35621977		SNOMED
Intellectual disability	Myhre syndrome	44783252		SNOMED
Intellectual disability	Kawashima Tsuji syndrome	37396341		SNOMED
Intellectual disability	DNMT3A-related overgrowth syndrome	35625760		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Autism spectrum disorder due to AUTS2 deficiency	36675177		SNOMED
Intellectual disability	Jawad syndrome	36675142		SNOMED
Intellectual disability	Moderate intellectual development disorder without significant impairment of behaviour	35610122		SNOMED
Intellectual disability	Congenital cataract with deafness and hypogonadism syndrome	36716387		SNOMED
Intellectual disability	Kohlschutter's syndrome	4033911		SNOMED
Intellectual disability	Significant learning disability	3657468		SNOMED
Intellectual disability	Renpenning syndrome	44783569		SNOMED
Intellectual disability	Moderate intellectual development disorder with significant impairment of behaviour	35610123		SNOMED
Intellectual disability	9q31.1q31.3 microdeletion syndrome	36676583		SNOMED
Intellectual disability	Developmental delay with autism spectrum disorder and gait instability	36674903		SNOMED
Intellectual disability	Craniofaciofrontodigital syndrome	35622011		SNOMED
Intellectual disability	Cross syndrome	4072144		SNOMED
Intellectual disability	Biemond syndrome type 2	36713523		SNOMED
Intellectual disability	Mild intellectual development disorder with significant impairment of behaviour	35610127		SNOMED
Intellectual disability	Grubben, De Cock, Borghgraef syndrome	35621906		SNOMED
Intellectual disability	Rett's disorder	4288480		SNOMED
Intellectual disability	Atypical hypotonia cystinuria syndrome	36674517		SNOMED
Intellectual disability	Cerebro-facio-thoracic dysplasia	36715139		SNOMED
Intellectual disability	Cerebrofacioarticular syndrome	35622041		SNOMED
Intellectual disability	12q14 microdeletion syndrome	36713991		SNOMED
Intellectual disability	Temple Baraitser syndrome	37110772		SNOMED
Intellectual disability	McDonough syndrome	37395856		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Ramos Arroyo syndrome	37118960		SNOMED
Intellectual disability	Urban Rogers Meyer syndrome	37396500		SNOMED
Intellectual disability	X-linked cerebral, cerebellar, coloboma syndrome	36674770		SNOMED
Intellectual disability	Atkin Flaitz syndrome	36713653		SNOMED
Intellectual disability	Filippi syndrome	36715331		SNOMED
Intellectual disability	Cleft palate with short stature and vertebral anomaly syndrome	36714301		SNOMED
Intellectual disability	Snyder-Robinson syndrome	45765468		SNOMED
Intellectual disability	Zechi Ceide syndrome	36676430		SNOMED
Intellectual disability	Severe intellectual development disorder with minimal impairment of behaviour	35610120		SNOMED
Intellectual disability	White Sutton syndrome	36675667		SNOMED
Intellectual disability	Weaver Williams syndrome	37111628		SNOMED
Intellectual disability	Oculocerebrofacial syndrome Kaufman type	36716154		SNOMED
Intellectual disability	Ohdo syndrome, Say-Barber-Biesecker-Young-Simpson variant	44783239		SNOMED
Intellectual disability	Developmental delay, facial dysmorphism syndrome due to MED13L deficiency	37204024		SNOMED
Intellectual disability	Mild intellectual development disorder with impairment of behaviour	35610516		SNOMED
Intellectual disability	X-linked complicated corpus callosum dysgenesis	605204		SNOMED
Intellectual disability	Bardet-Biedl syndrome	4209284		SNOMED
Intellectual disability	Intellectual development disorder with impairment of behaviour	35610520		SNOMED
Intellectual disability	Deafness with onychodystrophy syndrome	36674396		SNOMED
Intellectual disability	Hereditary cryohydrocytosis with reduced stomatin	37204308		SNOMED
Intellectual disability	Gillespie syndrome	4100702		SNOMED
Intellectual disability	Borjeson-Forssman-Lehmann syndrome	4065596		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Cognitive impairment, coarse facies, heart defects, obesity, pulmonary involvement, short stature, skeletal dysplasia syndrome	35607999		SNOMED
Intellectual disability	Spondyloepiphyseal dysplasia tarda Kohn type	36714103		SNOMED
Intellectual disability	Seckel syndrome	4240091		SNOMED
Intellectual disability	Perniola Krajewska Carnevale syndrome	37396390		SNOMED
Intellectual disability	Phosphoribosylpyrophosphate synthetase superactivity	37109675		SNOMED
Intellectual disability	Profound intellectual development disorder with minimal impairment of behaviour	35610116		SNOMED
Intellectual disability	21q22.11q22.12 microdeletion syndrome	37206825		SNOMED
Intellectual disability	Brachydactyly and preaxial hallux varus syndrome	37116293		SNOMED
Intellectual disability	Pseudoleprechaunism syndrome Patterson type	36675025		SNOMED
Intellectual disability	Nijmegen breakage syndrome-like disorder	35624153		SNOMED
Intellectual disability	Mowat-Wilson syndrome	45766388		SNOMED
Intellectual disability	Arts syndrome	45765490		SNOMED
Intellectual disability	Extrasystoles, short stature, hyperpigmentation, microcephaly syndrome	36675005		SNOMED
Intellectual disability	Distal Xq28 microduplication syndrome	36676696		SNOMED
Intellectual disability	Blepharophimosis and mental retardation syndrome	37312299		SNOMED
Intellectual disability	Macrocephaly and developmental delay syndrome	35622341		SNOMED
Intellectual disability	Cyclin-dependent kinase-like 5 deficiency	36676367		SNOMED
Intellectual disability	Neurofaciodigitorenal syndrome	37111247		SNOMED
Intellectual disability	Neuronal ceroid lipofuscinosis 8	45771339		SNOMED
Intellectual disability	Achalasia microcephaly syndrome	36717050		SNOMED
Intellectual disability	Severe motor and intellectual disabilities, sensorineural deafness, dystonia syndrome	36674894		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	5p13 microduplication syndrome	36674906		SNOMED
Intellectual disability	MORM syndrome	37395980		SNOMED
Intellectual disability	Microcephalic primordial dwarfism Alazami type	36674735		SNOMED
Intellectual disability	Harrod syndrome	37396321		SNOMED
Intellectual disability	Short stature, unique facies, enamel hypoplasia, progressive joint stiffness, high-pitched voice syndrome	37111630		SNOMED
Intellectual disability	Skeletal dysplasia with epilepsy and short stature syndrome	37398922		SNOMED
Intellectual disability	Wilson Turner syndrome	36714548		SNOMED
Intellectual disability	Goldblatt Wallis syndrome	37396327		SNOMED
Intellectual disability	Microcephalus with brachydactyly and kyphoscoliosis syndrome	36714238		SNOMED
Intellectual disability	Toriello Carey syndrome	36716462		SNOMED
Intellectual disability	Pallister W syndrome	36717687		SNOMED
Intellectual disability	Kapur Toriello syndrome	36716139		SNOMED
Intellectual disability	Van den Bosch syndrome	37116407		SNOMED
Intellectual disability	Kleefstra syndrome	37110119		SNOMED
Intellectual disability	Caudal appendage deafness syndrome	37111590		SNOMED
Intellectual disability	Central nervous system calcification, deafness, tubular acidosis, anemia syndrome	37111627		SNOMED
Intellectual disability	Blepharonasofacial malformation syndrome	36717046		SNOMED
Intellectual disability	Warburg micro syndrome	36675714		SNOMED
Intellectual disability	CK syndrome	36676440		SNOMED
Intellectual disability	Cystic leukoencephalopathy without megalencephaly	36717424		SNOMED
Intellectual disability	Moderate intellectual development disorder with impairment of behaviour	35610125		SNOMED
Intellectual disability	1p21.3 microdeletion syndrome	36717734		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Contracture with ectodermal dysplasia and orofacial cleft syndrome	36715216		SNOMED
Intellectual disability	Facial dysmorphism, developmental delay, behavioral abnormalities syndrome due to 10p11.21p12.31 microdeletion	37204408		SNOMED
Intellectual disability	Temtamy preaxial brachydactyly syndrome	36680576		SNOMED
Intellectual disability	Oro-facial digital syndrome type 5	36716187		SNOMED
Intellectual disability	Oro-facial digital syndrome type 8	36716188		SNOMED
Intellectual disability	Trisomy 10p	37397118		SNOMED
Intellectual disability	Prieto Badia Mulas syndrome	36717698		SNOMED
Intellectual disability	Developmental and speech delay due to SOX5 deficiency	36675144		SNOMED
Intellectual disability	Spondyloepimetaphyseal dysplasia Genevieve type	36676426		SNOMED
Intellectual disability	Piebald trait with neurologic defects syndrome	36674461		SNOMED
Intellectual disability	Lowry MacLean syndrome	36716109		SNOMED
Intellectual disability	Epilepsy telangiectasia syndrome	37116355		SNOMED
Intellectual disability	Savant syndrome	4332239		SNOMED
Intellectual disability	14q32 deletion syndrome	604335		SNOMED
Intellectual disability	Autosomal recessive leukoencephalopathy, ischemic stroke, retinitis pigmentosa syndrome	36675148		SNOMED
Intellectual disability	Macrocephaly, short stature, paraplegia syndrome	36716141		SNOMED
Intellectual disability	Cutis laxa-corneal clouding-oligophrenia syndrome	4241107		SNOMED
Intellectual disability	MASA syndrome	3654718		SNOMED
Intellectual disability	Encephalopathy, intracerebral calcification, retinal degeneration syndrome	37116365		SNOMED
Intellectual disability	Microcephalus cardiomyopathy syndrome	36714240		SNOMED
Intellectual disability	Oro-facial digital syndrome type 9	36713733		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Psychomotor retardation due to S-adenosylhomocysteine hydrolase deficiency	37110022		SNOMED
Intellectual disability	13q12.3 microdeletion syndrome	36676620		SNOMED
Intellectual disability	Mild intellectual development disorder without significant impairment of behaviour	35610126		SNOMED
Intellectual disability	Goldberg Shprintzen megacolon syndrome	36717041		SNOMED
Intellectual disability	14q24.1q24.3 microdeletion syndrome	36676584		SNOMED
Intellectual disability	CAMOS syndrome	37111328		SNOMED
Intellectual disability	Intellectual development disorder without significant impairment of behaviour	35610517		SNOMED
Intellectual disability	Spastic paraplegia with precocious puberty syndrome	37116294		SNOMED
Intellectual disability	GAPO syndrome	36716032		SNOMED
Intellectual disability	Profound intellectual development disorder without impairment of behaviour	35610114		SNOMED
Intellectual disability	Severe intellectual development disorder with impairment of behaviour	35610121		SNOMED
Intellectual disability	Cystic fibrosis with gastritis and megaloblastic anemia syndrome	36714965		SNOMED
Intellectual disability	Moderate intellectual development disorder with minimal impairment of behaviour	35610124		SNOMED
Intellectual disability	Laurence-Moon syndrome	4334252		SNOMED
Intellectual disability	MEHMO syndrome	36716144		SNOMED
Intellectual disability	11p15.4 microduplication syndrome	36674907		SNOMED
Intellectual disability	Pseudoprogeria syndrome	37116389		SNOMED
Intellectual disability	Short stature with webbed neck and congenital heart disease syndrome	36715405		SNOMED
Intellectual disability	Polymicrogyria with optic nerve hypoplasia	36675060		SNOMED
Intellectual disability	Dysmorphism, short stature, deafness, disorder of sex development syndrome	37118645		SNOMED
Intellectual disability	C syndrome	37395832		SNOMED
Intellectual disability	Ataxia, photosensitivity, short stature syndrome	36674412		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	SCN8A-related epilepsy with encephalopathy	35622929		SNOMED
Intellectual disability	Alopecia, progressive neurological defect, endocrinopathy syndrome	36674944		SNOMED
Intellectual disability	Isodicentric chromosome 15 syndrome	37109594		SNOMED
Intellectual disability	Woodhouse Sakati syndrome	37311329		SNOMED
Intellectual disability	3q27.3 microdeletion syndrome	36674863		SNOMED
Intellectual disability	PURA syndrome	35625463		SNOMED
Intellectual disability	19q13.11 microdeletion syndrome	36717093		SNOMED
Intellectual disability	BSG syndrome	36714022		SNOMED
Intellectual disability	Malan overgrowth syndrome	35607962		SNOMED
Intellectual disability	Muscle eye brain disease with bilateral multicystic leukodystrophy	37203915		SNOMED
Intellectual disability	Pitt Hopkins-like syndrome	36676719		SNOMED
Intellectual disability	Congenital microcephaly, severe encephalopathy, progressive cerebral atrophy syndrome	37204234		SNOMED
Intellectual disability	Hall Riggs syndrome	36715368		SNOMED
Intellectual disability	Lowe syndrome	4194065		SNOMED
Intellectual disability	Juberg Marsidi syndrome	36717192		SNOMED
Intellectual disability	Deafness, genital anomaly, metacarpal and metatarsal synostosis syndrome	36715415		SNOMED
Intellectual disability	Infantile cerebral and cerebellar atrophy with postnatal progressive microcephaly	36674869		SNOMED
Intellectual disability	FBLN1-related developmental delay, central nervous system anomaly, syndactyly syndrome	36674473		SNOMED
Intellectual disability	XYLT1-CDG - xylosyltransferase 1 congenital disorder of glycosylation	36676515		SNOMED
Intellectual disability	Coffin-Siris syndrome	4002097		SNOMED
Intellectual disability	Hypotonia, speech impairment, severe cognitive delay syndrome	35622315		SNOMED
Intellectual disability	Microbrachycephaly, ptosis, cleft lip syndrome	37118951		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Prune belly syndrome with pulmonic stenosis, mental retardation and deafness	4030676		SNOMED
Intellectual disability	Oro-facial digital syndrome type 14	35622377		SNOMED
Intellectual disability	MOMO syndrome	37110069		SNOMED
Intellectual disability	Autosomal recessive chorioretinopathy and microcephaly syndrome	36674688		SNOMED
Intellectual disability	Microcephalus, cerebellar hypoplasia, cardiac conduction defect syndrome	35608087		SNOMED
Intellectual disability	Partington syndrome	45765465		SNOMED
Intellectual disability	Roifman syndrome	36676501		SNOMED
Intellectual disability	Mowat-Wilson syndrome due to monosomy 2q22	619073		SNOMED
Intellectual disability	L1 syndrome	37396989		SNOMED
Intellectual disability	Hennekam syndrome	4121804		SNOMED
Intellectual disability	Temtamy syndrome	36714637		SNOMED
Intellectual disability	RAB18 deficiency	36675715		SNOMED
Intellectual disability	Wiedemann Steiner syndrome	35622250		SNOMED
Intellectual disability	Infantile spasms, psychomotor retardation, progressive brain atrophy, basal ganglia disease syndrome	37204292		SNOMED
Intellectual disability	2p13.2 microdeletion syndrome	36674192		SNOMED
Intellectual disability	Karandikar Maria Kamble syndrome	37396247		SNOMED
Intellectual disability	Microcephalus, glomerulonephritis, marfanoid habitus syndrome	37118677		SNOMED
Intellectual disability	Diencephalic mesencephalic junction dysplasia	35608131		SNOMED
Intellectual disability	Fountain syndrome	36715334		SNOMED
Intellectual disability	Chromosome Xp11.3 microdeletion syndrome	36714526		SNOMED
Intellectual disability	Scholte syndrome	36717348		SNOMED
Intellectual disability	Ohdo syndrome, Maat-Kievit-Brunner type	44783238		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Intellectual disability	Oculopalatocerebral syndrome	36716153		SNOMED
Intellectual disability	Oliver syndrome	36715373		SNOMED
Intellectual disability	Ectodermal dysplasia with blindness syndrome	36717454		SNOMED
Intellectual disability	Brachymorphism with onychodysplasia and dysphalangism syndrome	36715092		SNOMED
Intellectual disability	Bullous dystrophy macular type	37111018		SNOMED
Intellectual disability	Stimmler syndrome	37116379		SNOMED
Intellectual disability	Oro-facial digital syndrome type 10	36716167		SNOMED
Intellectual disability	GMS syndrome	37396271		SNOMED
Intellectual disability	Pettigrew syndrome	36714054		SNOMED
Post traumatic brain injury	Traumatic brain injury	4132546		SNOMED
Post traumatic brain injury	Traumatic brain injury with loss of consciousness	4132082		SNOMED
Post traumatic brain injury	Traumatic brain injury with brief loss of consciousness	4132083		SNOMED
Post traumatic brain injury	Traumatic brain injury with moderate loss of consciousness	4133017		SNOMED
Post traumatic brain injury	Traumatic brain injury with prolonged loss of consciousness	4133018		SNOMED
Post traumatic brain injury	Traumatic brain injury with no loss of consciousness	4133715		SNOMED
Post traumatic brain injury	Late effect of traumatic injury to brain	4182419		SNOMED
Post traumatic brain injury	Traumatic brain injury of unknown intent	46270764		SNOMED
Post traumatic brain injury	Concussion injury of brain	4001336		SNOMED
Post traumatic brain injury	Brain injury without open intracranial wound	4234112		SNOMED
Post traumatic brain injury	Post-traumatic epilepsy	4326435		SNOMED
Post traumatic brain injury	Brain stem laceration with open intracranial wound AND no loss of consciousness	443696		SNOMED
Post traumatic brain injury	Focal laceration of cerebellum	36716626		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Laceration of brain	4193520		SNOMED
Post traumatic brain injury	Open fracture of vault of skull with cerebral laceration	3655960		SNOMED
Post traumatic brain injury	Cerebral cortex laceration with concussion	618758		SNOMED
Post traumatic brain injury	Brain stem laceration with concussion	618761		SNOMED
Post traumatic brain injury	Cortex laceration and contusion	4096615		SNOMED
Post traumatic brain injury	Falx laceration	4167919		SNOMED
Post traumatic brain injury	Cerebellar laceration without open intracranial wound AND with loss of consciousness	440560		SNOMED
Post traumatic brain injury	Post-traumatic epilepsy, refractory	762826		SNOMED
Post traumatic brain injury	Multiple focal injuries of cerebellum	36716576		SNOMED
Post traumatic brain injury	Brain stem contusion without open intracranial wound AND with loss of consciousness	443798		SNOMED
Post traumatic brain injury	Brain stem contusion without open intracranial wound AND with concussion	375680		SNOMED
Post traumatic brain injury	Cerebellar contusion without open intracranial wound	434190		SNOMED
Post traumatic brain injury	Open fracture of vault of skull with cerebral contusion	3655961		SNOMED
Post traumatic brain injury	Contusion of cerebellum due to birth trauma	36716737		SNOMED
Post traumatic brain injury	Cortex laceration with open intracranial wound	432476		SNOMED
Post traumatic brain injury	Cerebral laceration and contusion	376552		SNOMED
Post traumatic brain injury	Focal laceration of brainstem	36716575		SNOMED
Post traumatic brain injury	Encephalopathy due to radiation damage	4047767		SNOMED
Post traumatic brain injury	Post-traumatic dementia with behavioral change	44784521		SNOMED
Post traumatic brain injury	Repeated concussion	4235306		SNOMED
Post traumatic brain injury	Cortex contusion with open intracranial wound AND concussion	440550		SNOMED
Post traumatic brain injury	Contusion of cerebral cortex	4034021		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Brain injury with open intracranial wound	438590		SNOMED
Post traumatic brain injury	Left temporal lobe contusion	3184859		Nebraska Lexicon
Post traumatic brain injury	Brain stem laceration with loss of consciousness	618762		SNOMED
Post traumatic brain injury	Open fracture of base of skull with cerebral laceration AND contusion	378264		SNOMED
Post traumatic brain injury	Cortex laceration with open intracranial wound AND concussion	444379		SNOMED
Post traumatic brain injury	Injury of left visual cortex	42538674		SNOMED
Post traumatic brain injury	Dissociative convulsions	4098316		SNOMED
Post traumatic brain injury	Brain stem laceration with open intracranial wound	444217		SNOMED
Post traumatic brain injury	Dementia following injury caused by exposure to ionizing radiation	42535731		SNOMED
Post traumatic brain injury	Traumatic cerebral edema with open intracranial wound	4208505		SNOMED
Post traumatic brain injury	Contusion of right cerebrum	36686191		SNOMED
Post traumatic brain injury	Traumatic cerebral edema	4048796		SNOMED
Post traumatic brain injury	Contusion of cerebrum with open intracranial wound	3663250		SNOMED
Post traumatic brain injury	Cortex contusion with open intracranial wound AND loss of consciousness	434774		SNOMED
Post traumatic brain injury	Contusion of hindbrain	3655953		SNOMED
Post traumatic brain injury	Cortex contusion without open intracranial wound AND with concussion	440868		SNOMED
Post traumatic brain injury	Frontal lobe contusion	3186570		Nebraska Lexicon
Post traumatic brain injury	Spastic paralysis due to intracranial birth injury	4102446		SNOMED
Post traumatic brain injury	Cerebral compression due to injury	4264035		SNOMED
Post traumatic brain injury	Focal injury of brainstem	36716577		SNOMED
Post traumatic brain injury	Hypopituitarism due to radiotherapy	4033376		SNOMED
Post traumatic brain injury	Hind brain laceration with open intracranial wound, with no loss of consciousness	4016975		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Diffuse injury of brainstem	36715608		SNOMED
Post traumatic brain injury	Cortex laceration with open intracranial wound AND loss of consciousness	442114		SNOMED
Post traumatic brain injury	Necrosis of brain caused by exposure to ionizing radiation	602945		SNOMED
Post traumatic brain injury	Radiation injury of brain caused by ionizing radiation following radiotherapy procedure	36716603		SNOMED
Post traumatic brain injury	Crush injury of brain	36715609		SNOMED
Post traumatic brain injury	Cerebral decompression injury	4053307		SNOMED
Post traumatic brain injury	Cerebellar laceration and contusion	4094846		SNOMED
Post traumatic brain injury	Injuries of brain and cranial nerves with injuries of nerves and spinal cord at neck level	4309491		SNOMED
Post traumatic brain injury	Hypoxic ischemic encephalopathy due to strangulation	45766193		SNOMED
Post traumatic brain injury	Focal brain laceration	37311964		SNOMED
Post traumatic brain injury	Cerebellar laceration with open intracranial wound AND concussion	442762		SNOMED
Post traumatic brain injury	Cerebellar contusion without open intracranial wound AND with loss of consciousness	434792		SNOMED
Post traumatic brain injury	Focal brain contusion	37311968		SNOMED
Post traumatic brain injury	Cerebellar contusion with open intracranial wound	434506		SNOMED
Post traumatic brain injury	Concussion injury of cerebrum	40492393		SNOMED
Post traumatic brain injury	Hind brain laceration with open intracranial wound	4016974		SNOMED
Post traumatic brain injury	Brain stem contusion with open intracranial wound AND concussion	442595		SNOMED
Post traumatic brain injury	Concussion with loss of consciousness	375671		SNOMED
Post traumatic brain injury	Focal non-hemorrhagic contusion of brainstem	36716573		SNOMED
Post traumatic brain injury	Laceration of cerebrum	4095993		SNOMED
Post traumatic brain injury	Diffuse injury of cerebellum	36715607		SNOMED
Post traumatic brain injury	Focal laceration of cerebrum	36716568		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Traumatic encephalopathy	4047745		SNOMED
Post traumatic brain injury	Cortex laceration	4133019		SNOMED
Post traumatic brain injury	Brain stem laceration without open intracranial wound	444398		SNOMED
Post traumatic brain injury	Sunstroke	4090535		SNOMED
Post traumatic brain injury	Diffuse brain injury	4096616		SNOMED
Post traumatic brain injury	Cortex contusion with open intracranial wound, with no loss of consciousness	438588		SNOMED
Post traumatic brain injury	Brain stem laceration with open intracranial wound AND concussion	442318		SNOMED
Post traumatic brain injury	Punch drunk syndrome	4046088		SNOMED
Post traumatic brain injury	Open fracture of skull with cerebral contusion	3655962		SNOMED
Post traumatic brain injury	Contusion of left cerebrum	36686192		SNOMED
Post traumatic brain injury	Focal non-hemorrhagic contusion of cerebrum	36717223		SNOMED
Post traumatic brain injury	Contusion of cerebrum	4094847		SNOMED
Post traumatic brain injury	Traumatic focal cerebral edema	4096617		SNOMED
Post traumatic brain injury	Open fracture of vault of skull with concussion	44784467		SNOMED
Post traumatic brain injury	Brain stem contusion without open intracranial wound	442280		SNOMED
Post traumatic brain injury	Contusion of hindbrain with open intracranial wound	3663252		SNOMED
Post traumatic brain injury	Burst lobe of brain	4094848		SNOMED
Post traumatic brain injury	Focal contusion of temporal lobe	37311965		SNOMED
Post traumatic brain injury	Traumatic intracranial subdural hematoma with brief loss of consciousness	4154699		SNOMED
Post traumatic brain injury	Open fracture of vault of skull with loss of consciousness	44784466		SNOMED
Post traumatic brain injury	Focal contusion of parietal lobe	37311966		SNOMED
Post traumatic brain injury	Cerebellar contusion with open intracranial wound AND loss of consciousness	441702		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Cortex laceration with open intracranial wound, with no loss of consciousness	435384		SNOMED
Post traumatic brain injury	Cerebellar laceration with concussion	618760		SNOMED
Post traumatic brain injury	Self-induced non-photosensitive epilepsy	4047907		SNOMED
Post traumatic brain injury	Brain stem laceration with open intracranial wound AND loss of consciousness	443799		SNOMED
Post traumatic brain injury	Postconcussion syndrome	372610		SNOMED
Post traumatic brain injury	Hypothalamic injury	4131328		SNOMED
Post traumatic brain injury	Cerebellar laceration with open intracranial wound	435953		SNOMED
Post traumatic brain injury	Cerebellar laceration without open intracranial wound	434197		SNOMED
Post traumatic brain injury	Visual cortex injury	377439		SNOMED
Post traumatic brain injury	Open fracture of skull with cerebral laceration	3655963		SNOMED
Post traumatic brain injury	Laceration of brain without open intracranial wound	4208112		SNOMED
Post traumatic brain injury	Injury of both visual cortices	42537144		SNOMED
Post traumatic brain injury	Traumatic generalized cerebral edema	4095994		SNOMED
Post traumatic brain injury	Cortex contusion without open intracranial wound	440858		SNOMED
Post traumatic brain injury	Injury of brain stem due to birth trauma	36716540		SNOMED
Post traumatic brain injury	Contusion of brain	4146496		SNOMED
Post traumatic brain injury	Concussion with no loss of consciousness	378001		SNOMED
Post traumatic brain injury	Cortex contusion with open intracranial wound	432751		SNOMED
Post traumatic brain injury	Brain injury without open intracranial wound AND with concussion	373056		SNOMED
Post traumatic brain injury	Contusion of brain due to birth trauma	36716738		SNOMED
Post traumatic brain injury	Concussion with mental confusion AND/OR disorientation without loss of consciousness	4297140		SNOMED
Post traumatic brain injury	Brain stem contusion with open intracranial wound	444248		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Brain stem contusion with open intracranial wound AND loss of consciousness	442616		SNOMED
Post traumatic brain injury	Hind brain laceration with open intracranial wound and loss of consciousness	604740		SNOMED
Post traumatic brain injury	Cerebellar laceration	4133716		SNOMED
Post traumatic brain injury	Diffuse injury of cerebrum	36715606		SNOMED
Post traumatic brain injury	Cerebellar laceration with open intracranial wound AND no loss of consciousness	440235		SNOMED
Post traumatic brain injury	Cerebral dura mater laceration	3179550		Nebraska Lexicon
Post traumatic brain injury	Cerebellar decompression injury	4072639		SNOMED
Post traumatic brain injury	Brain injury with open intracranial wound AND concussion	435681		SNOMED
Post traumatic brain injury	Cerebral injury due to birth trauma	4347416		SNOMED
Post traumatic brain injury	Cerebellar contusion with open intracranial wound AND concussion	439170		SNOMED
Post traumatic brain injury	Cerebellar contusion without open intracranial wound AND with concussion	443931		SNOMED
Post traumatic brain injury	Contusion of brain without open intracranial wound	4236742		SNOMED
Post traumatic brain injury	Cerebellar contusion	4133020		SNOMED
Post traumatic brain injury	Cerebral trauma	4170449		SNOMED
Post traumatic brain injury	Cerebral edema due to birth injury	4048139		SNOMED
Post traumatic brain injury	Focal brain injury	4016540		SNOMED
Post traumatic brain injury	Injury of right visual cortex	42538809		SNOMED
Post traumatic brain injury	Focal traumatic hematoma of brainstem	36716574		SNOMED
Post traumatic brain injury	Post-traumatic epilepsy, non-refractory	762827		SNOMED
Post traumatic brain injury	Cerebellar laceration with open intracranial wound AND loss of consciousness	444257		SNOMED
Post traumatic brain injury	Laceration of brain with open intracranial wound	4038534		SNOMED
Post traumatic brain injury	Brain stem laceration	4132548		SNOMED

Phenotype	Concept name	Concept id (including descendants)	Exclude concept id	Vocabulary
Post traumatic brain injury	Focal traumatic hematoma of cerebellum	36716572		SNOMED
Post traumatic brain injury	Focal hemorrhagic contusion of cerebrum	36716567		SNOMED
Post traumatic brain injury	Brain stem contusion	4133021		SNOMED
Post traumatic brain injury	Focal non-hemorrhagic contusion of cerebellum	36716570		SNOMED
Post traumatic brain injury	Brain injury with open intracranial wound AND loss of consciousness	440551		SNOMED
Post traumatic brain injury	Concussion with less than 1 hour loss of consciousness	4019263		SNOMED
Post traumatic brain injury	Cortex contusion without open intracranial wound AND with loss of consciousness	433342		SNOMED
Post traumatic brain injury	Contusion of brain with open intracranial wound	4222768		SNOMED
Post traumatic brain injury	Multiple focal injuries of cerebrum	36716569		SNOMED
Post traumatic brain injury	Brain injury without open intracranial wound AND with loss of consciousness	381978		SNOMED
Post traumatic brain injury	Focal contusion of occipital lobe	37311967		SNOMED

ANNEX V: Glossary

Additional definitions are available in the EMA Glossary of terms https://www.ema.europa.eu/en/about-us/glossaries.

Aggregated Data

Data collected and combined from multiple sources to generate summary information, typically anonymised.

Benefit-Risk Assessment

Evaluation of the positive therapeutic effects of a medicine compared to its risks (e.g., side effects).

Common Data Model (CDM)

A standardized data structure that enables data from multiple sources to be harmonized, making analysis consistent and reproducible. DARWIN EU® utilises the OMOP CDM maintained by the OHDSI community.

Complex Studies (C3)

Studies requiring the development or customisation of specific study designs, protocols, and Statistical Analysis Plans (SAPs), with extensive collection or extraction of data. Examples include etiological studies measuring the strength and determinants of an association between an exposure and the occurrence of a health outcome in a defined population considering sources of bias, potential confounding factors, and effect modifiers.

Coordination Centre (CC)

The central hub responsible for managing and overseeing the activities within DARWIN EU®. It is based at Erasmus University Medical Centre in Rotterdam, the Netherlands.

Data Access

The process of obtaining permission to use specific datasets for regulatory or scientific studies.

Data Quality Framework

A set of standards and procedures to ensure accuracy, completeness, timeliness, and consistency of data used in DARWIN EU®.

Data Source

A database or repository of structured health-related data, such as electronic health records (EHRs), insurance claims, or registries.

DARWIN EU®

The European Medicines Agency's (EMA) federated network of real-world data sources designed to generate evidence to support regulatory decision-making.

EMA (European Medicines Agency)

The regulatory body responsible for the evaluation and supervision of medicinal products in the EU, overseeing DARWIN EU®.

Evidence Generation

The process of analysing real-world data to produce scientific information that can inform healthcare or regulatory decisions.

Federated Network

A data infrastructure where data remain at their original location but can be analysed in a harmonised way across multiple partners using a common model and tools.

GDPR (General Data Protection Regulation)

The EU regulation governing the protection of personal data and privacy, crucial to how DARWIN EU® handles health data.

Health Technology Assessment (HTA)

A systematic evaluation of properties and impacts of health technology, often using DARWIN EU® data to support assessments.

Metadata

Descriptive information about a data source (e.g., its content, quality, and structure), essential for identifying relevant databases in DARWIN EU® studies.

Off-the-Shelf Studies (OTS)

Studies for which a standard protocol per study/analysis type and standardised analytics may be developed and applied or adapted, typically relating to a descriptive research question. This includes studies on disease epidemiology, for example, the estimation of the prevalence or incidence of health outcomes in defined time periods and population groups, or drug utilisation studies at the population or patient level.

OHDSI (Observational Health Data Sciences and Informatics)

An open-science collaborative community that develops tools and standards (including the OMOP CDM) to enable large-scale analytics of observational health data. OHDSI provides the technical and scientific foundation for DARWIN EU®'s analytical ecosystem.

Patient-Level Data

Data related to individuals, de-identified, used for longitudinal or detailed analyses.

OMOP (Observational Medical Outcomes Partnership)

A common data model (CDM) that standardises the structure and content of observational healthcare data, enabling systematic analysis across disparate datasets. DARWIN EU® uses the OMOP CDM to ensure interoperability and consistency in real-world evidence generation.

Real-World Data (RWD)

Data relating to individual health status or healthcare delivery that is collected from routine clinical practice rather than from randomised controlled trials.

Real-World Evidence (RWE)

Clinical evidence derived from the analysis of RWD, used to inform decisions by regulators, payers, or clinicians.

Regulatory Decision-Making

The process by which authorities like EMA assess data to authorise, monitor, or modify the use of medicines in the EU.

Routine Repeated Studies (RR)

Studies that are either Off-the-Shelf or Complex studies repeated on a regular basis, following the same protocol and study code, but with updated data and/or different data partners.

Study Protocol

A detailed plan describing how a specific real-world study will be conducted, including objectives, design, data sources, and analyses.

Very Complex Studies (C4)

Studies which cannot rely only on electronic health care databases, or which would require complex methodological work, for example, due to the occurrence of events that cannot be defined by existing diagnosis codes, including events that do not yet have a diagnosis code, where it may be necessary to combine a diagnosis code with other data such as results of laboratory investigations. These studies might require the collection of data prospectively, or the inclusion of new (not previously onboarded) data sources.