PASS Information

Title	Strattera patient exposures and adherence in the United Kingdom, Germany, the Netherlands, and Sweden: 2016 Bi-annual assessment report (B4Z-MC-B025)
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Product reference:	UK/H/0686/002-008
Procedure number:	N/A
Marketing authorisation holder(s)	Eli Lilly and Company
Joint PASS	No
Research question and objectives	The objective of this study is to describe atomoxetine (Strattera) utilisation patterns for patients treated in Germany, the Netherlands, United Kingdom (UK), and Sweden by: • Estimating number of patients exposed to Strattera, stratified by age group based on years of available data • Estimating duration of exposure, medication possession ratio, and dose over the most recent 24 months of data available • Estimating the number of patients who restarted, gap between, and duration of use in additional exposures over the most recent 24 months, for the patients who stopped taking Strattera • Describing population being treated with Strattera in terms of common comorbidities and concomitant medications.
Countries of study	Germany, the Netherlands, UK, and Sweden
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1. Abstract

Title: Strattera patient exposures and adherence in the United Kingdom, Germany, the Netherlands, and Sweden: 2016 Bi-annual assessment report (B4Z-MC-B025)

Keywords: Atomoxetine, ADHD, drug utilisation, Europe

Rationale and background: In 2003, Eli Lilly and Company (Lilly) launched Strattera (atomoxetine), which was the first attention-deficit/hyperactivity disorder (ADHD) medication indicated for adult use. The adult indication was approved in the European Union (May 2013). The use of ADHD medications, including nonstimulant Strattera has been increasing over-time among children, adolescents and among adults (Castle et al. 2007; Habel et al. 2011; Zoega et al. 2011). There has also been a change in the duration of use in more recent years (Castle et al. 2007; Habel et al. 2011).

Research question and objectives: The main objective of this retrospective database study is to describe Strattera utilisation patterns for patients treated in the United Kingdom (UK), Germany, the Netherlands, and Sweden, by age group. This includes 1) estimating number of patients exposures to Strattera on years of available data, 2) estimating duration of exposure, medication possession ratio, and dose over the most recent 24 months of data available, 3) for those who stopped taking Strattera, estimating the number that restarted, gap time between, and duration of use in additional exposures over the most recent 24 months, and 4) describing the Strattera population in terms of common comorbidities and concomitant medications. This protocol describes the updated drug utilisation study for the studies previously conducted in Europe (B4Z-MC-B019, submitted November 2011 and B4Z-MC-B022, submitted April 2014).

Study design: Retrospective cohort study using secondary data.

Setting: This study included all patients, including children, adolescents, and adults, with prescriptions of Strattera for the longest available duration in each selected database from the UK, Germany, the Netherlands, and Sweden.

Subjects and study size, including dropouts: Patients needed at least two consecutive prescriptions to be eligible for inclusion.

Variables and data sources: The data sources for this study included: the longitudinal prescription (LRx) data in Germany and the Netherlands; the Disease Analyser (DA) and the Clinical Practice Research Datalink (CPRD) datasets in the UK; and the National Drug and Patient Register in Sweden. Variables drawn from these data sources included those related to Strattera exposure (dose, duration), outcomes related to patient counts and drug utilization measures of persistence, discontinuation and restarting patterns, mean daily dose (MDD), medication possession ratios, and length of therapy. Outcomes were assessed by various patient characteristics including country, age, and gender. Counts were also extracted for ADHD diagnoses, comorbidities, and concomitant medication usage.

Results: Among the prevalent cohort of Strattera users from 2008 to 2014, the majority of patients treated with Strattera in each of the countries were 13 to 17 years old. Use among

children 0 to 5 years old and adults 65+ years old continues to remain low (0 to 1%) across countries in each year. There was a trend towards increased use of Strattera among adults in recent years, as expected after EU approval of the ADHD indication in adults in 2013. While the majority of patients treated with Strattera were male, the proportion of use among females increased in Germany, Netherlands, and Sweden between 2008 and 2014. Among the incident user cohort, the majority of new users were male and <18 years old. However, new female users tended towards higher ages in all countries. This was most apparent in Sweden where among new female users, more than half were between 18 to 64 years old. The MDD ranged from approximately 27 mg (Germany) to 47 mg (UK). In all countries, as expected, the highest MDD was among patients ≥18 years old. The mean length of treatment supplied over 24 months ranged from approximately 262 days (Netherlands) to 405 days (UK) and the medication possession ratio (MPR) ranged from 40% (Netherlands) to 60% (UK). In all countries, over 80% of new user patients were treated with 1 episode over the 24-month follow-up period. The overall Strattera persistence patterns in these EU countries show that, on average, persistence beyond 1 year was low. The most frequent diagnoses and medications listed among Strattera-treated patients were not associated with comorbid cardiovascular conditions.

Discussion: This drug utilisation study found mean length of treatment episodes for Strattera patients in UK, Germany, the Netherlands, and Sweden varied, but were approximately 1 year and the majority of patients are treated with 1 episode. The overall Strattera persistence patterns in these EU countries are lower than those reported in the US. Patterns of usage show that, on average, persistence past 1 year is low. Taking into account MPR and mean days treated, even with persistence of more than 1 year, the patient is not necessarily being treated continuously during this period. Therefore, the utilisation patterns in the EU do not suggest any different potential risks of long-term severe cardiovascular outcomes related to Strattera treatment would be expected from those reported in large cohort studies conducted in the US.

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2. List of abbreviations

Term	Definition
ADHD	Attention-deficit/hyperactivity disorder
ATC	Anatomical Therapeutic Chemical classification system
BNF	British National Formulary
CPRD	Clinical Practice Research Datalink
DA	Disease Analyser
EU	European Union
FDA	Food and Drug Administration
HCPs	Healthcare professionals
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th revision
LRx	longitudinal prescription
LOT	length of therapy
MAH	marketing authorisation holder
MDD	mean daily dose
MHRA	Medicines and Healthcare Products Regulatory Agency
MPR	medication possession ratio
NHS	National Health Service
SAP	Statistical Analysis Plan
SmPC	Summary of Product Characteristics
SPDR	Swedish Patient and Drug Register
SSRI	selective serotonin reuptake inhibitor
UK	United Kingdom
US	United States

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European Union QPPV details available on file.

5. Milestones

Milestone	Planned date	Actual date	Comments
Start of data collection	01 October 2015	01 October 2015	
End of data collection	31 January 2016	1 February 2016	
Registration in the EU PAS register	28 September 2015	29 September 2015	
Final report of study results	31 March 2016	31 March 2016	

6. Rationale and background

In 2003, Lilly launched Strattera (atomoxetine), which was the first attention deficit/ hyperactivity disorder (ADHD) medication indicated for adult use. It belongs to the class of selective norepinephrine reuptake inhibitors. The patterns in ADHD medication use have changed over time and vary by country. The use of ADHD medications, including nonstimulant Strattera has been increasing over-time among children, adolescents and among adults (Castle et al. 2007; Habel et al. 2011; Zoega et al. 2011). There has also been a change in the duration of use in more recent years (Castle et al. 2007; Habel et al. 2011).

IMS Health executed the analysis of data assessing the utilisation of Strattera in a multicountry study, in, Germany, the Netherlands, United Kingdom (UK), and Sweden. The analysis included an assessment of adherence patterns among users of Strattera and obtained more information on Strattera use patterns in the European Union (EU), which may have implications for the risk of increased blood pressure and increased heart rate, by virtue of dose/time on treatment and overall exposure/age.

Use of Strattera in the current report is limited to the use of capsules given the late approval and commercialisation (2015) of Strattera Oral Solution in the EU in relation to this study. The final iteration of the drug utilisation study planned for 2018 will include data use through 2016 (describing use of capsules and the oral solution). The current report includes patients with at least 2 consecutive dispensings of Strattera in Germany, Netherlands, and Sweden or 2 consecutive prescriptions of Strattera in the UK in any calendar year from January 2008 through December 2014.

This protocol describes the updated drug utilisation study for the studies previously conducted in Europe (B4Z-MC-B019, submitted November 2011 and B4Z-MC-B022, submitted April 2014), as requested by EU regulatory bodies. A final drug utilisation study (B4Z-MC-B026) will be conducted in 2018.

7. Research question and objectives

The objective of this study is to describe Strattera utilisation patterns for patients treated in the Germany, the Netherlands, UK, and Sweden by:

- Estimating the number of patients exposed to Strattera, stratified by age group (paediatric, adolescent, adult and elderly) based on years of available data.
- Estimating the duration of exposure, medication possession ratio, and dose over the most recent 24 months of data available.
- Estimating the number of patients who restarted, the gap time in between, and duration of use in additional exposures over the most recent 24 months, for those patients who stopped taking Strattera.
- Describing the population being treated with Strattera in terms of common comorbidities, and concomitant medications.

This is a descriptive study and no formal hypotheses are being tested.

8. Amendments and updates

Not applicable.

9. Research methods

9.1. Study design

This is a retrospective cohort database study looking at drug utilisation among users of Strattera in the Germany, the Netherlands, UK, and Sweden.

9.2. Setting

This study included patients with at least two consecutive dispensings of Strattera in Germany, the Netherlands, and Sweden or prescriptions of Strattera in the UK in any calendar year from January 2008 through December 2014. This reflects the 7 most recent full calendar years from which data was available. From this cohort of prevalent users, an incident user cohort for each country was identified from within the most recent 24 month period (1 July 2013 to 30 June 2015) to assess patient discontinuation and adherence.

9.3. Subjects

The source population for analyses of drug utilisation is the prevalent user cohort as defined above: patients with at least 2 consecutive dispensings of/prescriptions for Strattera in any calendar year from January 2008 through December 2014 in Germany, the Netherlands, UK, and Sweden. This prevalent user cohort was used to assess patient counts, as well as for assessment of comorbidities and concomitant medication usage.

To estimate measures of patient utilisation and adherence, an incident user cohort of patients was identified from within the most recent 24 month period of data available. Incident users were defined by the first of 2consecutive prescriptions between 1 January 2013 and 30 June 2013. These new users were followed for a 24-month period (last possible date of follow-up is 30 June 2015). The incident user (new user) cohort is used to assess mean daily dose, treatment patterns (number of episodes, days between episodes), and persistence patterns with the 24 months of follow-up.

9.4. Variables

Variable	Definition
Exposure	
Atomoxetine use	≥2 consecutive atomoxetine (Strattera) prescription dispatches, with a 90 day allowable gap between.
Outcomes	
Treatment duration	the number of days between the date of the first and the last recorded prescription
Duration of exposure	percentage of patients remaining on therapy over time in monthly intervals
Drug dose	package size multiplied by package dose **Please note that in the database, package size can be a proportion of the package size. Thus, this proportion will also be used in the calculations
Total treatment dose	sum of the drug doses for all purchases (apart from the last purchase)
Mean daily dose	total treatment dose/treatment duration
Length of therapy	Sum of days supplied in treatment episodes, not allowing for treatment gaps.

Variable	Definition
Other characteristics	
Comorbid diagnoses	International Classification of Diseases (ICD)-10 diagnoses, at the four-digit level, which have been recorded in the database during follow-up
Concomitant medications	Codes for medications reported during treatment period (either Anatomical Therapeutic Chemical [ATC] or British National Formulary [BNF] codes)

9.5. Data sources

IMS maintains different sets of longitudinal patient data in 11 countries around the world. For the purpose of this analysis, the datasets included were:

1. **The longitudinal prescription (LRx) data in Germany and the Netherlands**
   - LRx is gathered from pharmacy transactions through coding centres or directly from retail chains. This data source contains anonymised encrypted patient identifiers (IDs) that enable tracking of the patient over time. The LRx panel in Germany represents approximately 60% of all retail prescriptions dispensed in the country. The LRx panel in the Netherlands represents approximately 75% of all retail prescriptions dispensed in the country.
   - The LRx data for Germany and the Netherlands utilise the European Pharmaceutical Market Research Association (EphMRA) Anatomical Therapeutic Chemical (ATC) coding scheme for medications.

2. **The Disease Analyser (DA) and the Clinical Practice Research Datalink (CPRD) datasets in the UK.**
   - The DA is composed of electronic medical records gathered from physician office software and allows the tracking of patients longitudinally.
   - The CPRD, formerly the General Practice Research Database data set in the UK, is the new National Health Service (NHS) observational data and interventional research service that provides large multi-linked observational datasets. The CPRD covers about 5.5 million patients from 675 UK primary care practices throughout the UK accounting for about 8% of the UK population.
   - Drug usage of Strattera from the DA and the CPRD are reflected through prescriptions written by the physician, not from pharmacy claims.
   - Drugs are coded according to the British National Formulary (BNF) chapter in the CPRD and EPhMRA ATC codes in the DA.

3. **The Swedish Prescribed Drug Register and Swedish Patient Register**
   - The Swedish Prescribed Drug Register (SPDR) covers all drugs dispatched at pharmacies in Sweden dating back to 2005. The SPDR contains information for all prescriptions dispensed to the entire population of Sweden (approximately 9 million inhabitants). For prescribed drugs, the register includes data on dispensed item, substance, brand name, formulation, package size, dispensed package count, strength, date of prescribing and

dispensing, as well as, prescriber's profession and practice. All drugs are classified according to the ATC.

- In order to evaluate the indication, the SPDR data was linked to the Swedish patient register, which includes ICD-10-SE diagnosis codes associated with all inpatient and outpatient (specialist) health care contacts, also with national coverage.

9.6. Bias

The study used dispensed prescriptions in Germany, the Netherlands, and Sweden, and written prescriptions in the UK as proxies for actual medication use. As a result of the methodology used, it is possible to include persons not taking Strattera. In an effort to address this source of potential bias, inclusion criteria required 2 consecutive dispensings/prescriptions rather than only 1, to increase the probability that patients actually took the medication. Henceforth, all data are described as dispensed medications, and the limitation of the UK data and this potential source of bias is described again in Section 11.2.

9.7. Study size

The study sample included all identified users of Strattera during the study time period with at least 2 consecutive Strattera dispensings/prescriptions as inclusion criteria.

9.8. Data transformation

Persistence curves were calculated per month and patient from the index prescription up until the 24th month of follow-up. Reinitiation was also accounted for and separately reported. Follow-up time is normalized in relation to the index date of each patient; the total population size remained constant across the months. Persistence curves were reported, in addition to patient counts, on the number that discontinue and reinitiate. In the Sweden data, the number of days supplied is not included so persistence curves and length of therapy were calculated using a dispatch duration of 30 days and 90 day allowable gap. Any patient with a dispatch that is not preceded by a new dispatch within 120 days was considered discontinued. When a patient discontinued or reinitiated therapy, they were considered compliant during the period up until 120 days. The mean length of therapy (LOT) was used to calculate the patient years (# patients * mean LOT)/365.

9.9. Statistical methods

9.9.1. Main statistical methods

9.9.1.1. Patient counts and descriptive analyses

For each country, counts of prevalent Strattera users were provided for the most recent 7 full calendar years. Counts and proportions were tabulated by country, year (2008 to 2014), age group (0-5, 6-9, 10-12, 13-17, 18-34, 35-64, 65+ years of age, as well as <18 or 18-64 years of age), and gender (female/male). The observed numbers and age-gender proportions of Strattera patients in the LRx datasets from Germany and the Netherlands were used to estimate the

projected counts of Strattera users weighted to the entire population of the respective country. These projected counts are provided for Germany and the Netherlands.

In addition to Strattera counts, frequencies and proportions were provided for ADHD diagnosies, 30 most common comorbidities (defined by 4 digit ICD-10 codes), and concomitant medication usage within 24 months of follow-up in the prevalent cohort.

9.9.1.2. Patient Exposures, Discontinuation, Adherence

Within the incident user cohort, the following measures of drug utilization were estimated:

- Treatment duration, duration of exposure, daily average dose were estimated (where available).
- The percentage of patients reinitiating therapy and persistence curves showing the percentage of patients remaining on therapy at monthly time intervals.
- A mean and median LOT, including the standard deviation. The mean LOT was used to calculate patient years (# patients * mean LOT)/365. The method for obtaining the standard deviation varied for each data source.
    - Note that the difference between persistence and LOT is that therapy gaps are counted in persistence and not LOT, where only the actual day's supply prescribed/dispensed are included.
- Mean daily dose (MDD): Within the CPRD database, the variables numeric daily dose were used to estimate the MDD. For each of the other databases, the MDD was estimated using the following formula: (quantity dispensed/day's supply)*strength.
- A distribution of the percentage of patients having undergone 1 or more treatment episodes over the 24-month observation period. A single episode was defined as the aggregate of all prescriptions refilled, with a 90-day allowed gap after exhausting days supplied in prior prescription.
- The percentage of Strattera patients who stopped taking Strattera and then reinitiated therapy, the gap in between, and the duration of the use in additional exposures.
- The medication possession ratio (MPR), a measure of patient compliance. The MPR was estimated by dividing the number of day's supply equivalent by the number of days available in a 24-month period.

9.9.1.3. Treatment patterns

- Persistence curves showing the percentages of patients remaining on, or discontinuing, or restarting therapy in 1-month intervals. A 90-day gap (grace period) was used when determining persistence. The persistence curves show the patients who stopped taking Strattera, the patients who reinitiated therapy, the gap in between treatment episodes, and the duration.
- Treatment episodes over the 24-month observation period for each patient were reported by aggregating all prescriptions refilled with a 90-day allowable gap after exhausting days supplied in the prior prescription. The number of treatment episodes in the 24 month period, as well as the mean, standard deviation, and median LOT for each treatment episode stratified by age group are provided.

- LOT was calculated by summing days supplied in each prescription in a given treatment episode. Mean, standard deviation, and median LOT are reported and stratified by age group.
- Notes:
    - If the days supplied was not available, the number of days supplied was calculated as the total dose (strength x package size x package count; where strength = medication strength; package size = number of pills in package, and package count = number of packages) contained in dispensed packages divided by the daily dose ordered in the prescription. If daily dose was not available, the strength prescribed was used instead based on the suggested dosing frequency of once-daily provided in the full prescribing information of Strattera. Patients were excluded from the analysis if they didn't have complete information on strength, package size, or package counts.
- MPR was used to measure patient compliance and calculated as the number of day's supply equivalent divided by the number of days available in the 24-month period (24-month period defined as 30 day month * 12 months in a year * 2 years = 720 days).
    - Note: In the Swedish prescription register, days supplied per dispatch is not available. Because the recommended dose for Strattera is weight-dependent (1.2 mg per kg and day), Swedish average weights were extracted across age groups. A weighted average weight was calculated for the age groups based on the representation across ages. A weighted average weight was used to calculate the expected daily dose for the age group, which in turn is related to the total dose prescribed at the individual level, in order to calculate days supplied. Days supplied was calculated by the total dose (strength x package size x package count) dispensed in each dispatch divided by a patient's expected daily dose (1.2 x weighted average weight in Sweden nationally). Patients were excluded from the analysis if they didn't have complete information on strength, package size, or package count.
- MDD was defined as total treatment dose divided by treatment duration. Drug dose per prescription was calculated by multiplying package size by package dose in each prescription. Total treatment dose was calculated as the sum of drug doses in each prescription except the last prescription. Treatment duration was calculated as the number of days between the first and last recorded dispatch date. At least 2 prescriptions were required for the calculation of average daily dose. To avoid stochastic results, individuals that had fewer than 7 days between their first and last dispatch were excluded.

Note: Dosage was assumed to be once daily, therefore strength was used as daily dose for UK CPRD data and daily dosage was used for UK DA.

9.9.2. Missing values

Missing values were treated as unknown and were reported as such.

9.9.3. Sensitivity analyses

Sensitivity analyses were not completed for this study.

9.9.4. Amendments to the statistical analysis plan

None.

9.10. Quality Control

The study adhered strictly to standards consistent with the International Society for Pharmacoepidemiology's Guidelines for Good Pharmacoepidemiology Practices (http://www.pharmacoepi.org). These standards included storage of sensitive data on a server with restricted access. Accuracy and completeness of study data were assessed by IMS. IMS followed its internal policies and procedures to ensure that all data and results were confirmed against the source and the final deliverables have been quality reviewed by a person external to the report author.

IMS confirmed the correctness of programming and cohort selection of the recent update and that the methodologies were aligned with the current statistical analysis plan (SAP).

10. Results

10.1. Descriptive data among prevalent and new users of Strattera users between 2008 and 2014

Counts of patient users of Strattera were estimated among prevalent users between 2008 through 2014, stratified by age group, country, and gender. Counts were also estimated among incident users (i.e., new users) of Strattera. Incident users were those initiating their first prescription sometime between 1 January 2013 and 30 June 2013.

10.1.1. Germany

In Germany, the overall number of patients treated with Strattera is declining (Table 1). In 2008, there were more than 31000 patients treated with Strattera and in 2014, this decreased to 20643 users. The largest proportion of patients treated with Strattera was patients 13 to 17 years of age (23.51% to 33.15%) annually and overall, the majority of Strattera-treated patients were 10 to 17 years of age (i.e., in either the 10 to 12 or 13 to 17 years of age categories). The proportion of adult users between 18 to 64 years of age has increased; 7.58% were in this age category in 2008 and 23.39% in 2014. The proportion of users between 6 to 9 years of age is slowly decreasing (15.86% in 2008 to 11.29% in 2014). The proportion of users being among the very young (0 to 5 years of age) or the very old (65 years of age and older) was consistently less than 1%, in each age group in each year between 2008 and 2014.

In Germany, many patient records did not include gender or age information (Table 2). For those with the recorded information, the majority of patients treated with Strattera were male. Strattera use among males was approximately 2 to 3 times higher than among females. The proportion of female users increased over time; in 2008 15.60% of users were female whereas in 2014, 21.55% were female.

The age and gender distribution among males and females for new users of Strattera was similar (Table 3). Overall the majority (78.39%) of initiators were <18 years of age. Approximately 80.06% of male and 72.86% of female new users were younger than 18 and 8.29% of new users were between 18 to 64 years of age.

10.1.2. Netherlands

In the Netherlands, overall, the data show a decline in the number of Strattera users over time. In 2008, there were 6780 patients treated with Strattera and in 2014 this decreased to approximately 4948 users. The largest portion of Strattera use was among adolescents 13 to17 years of age (30.91% to 38.36%) (Table 4). This trend was consistent over time. The use of Strattera among adults (18 to 64 years of age) increased over time from 23.69% to 36.30% whereas the proportion of users under 18 gradually declined. The proportion of users 6 to 9 years of age decreased the most from 20.31% of users in 2008 to 8.16% of users in 2014. Annually, the use among children 0 to 5 and the elderly 65 years of age and older was less than 1% in each age group.

The majority of patients (74.05% to 78.69%) treated with Strattera in the Netherlands were male (Table 5). While this has been consistent over time, the proportion of female users slightly increased; in 2008 21.31% of users were female and 25.95% in 2014.

Among females in the Netherlands, the majority of Strattera initiation was in those 13 years of age and older (71.92%) (Table 6). Only 26.59% of females initiating Strattera were between 6 to 12 years of age. Among males, age of initiation of Strattera was more evenly distributed across age categories, peaking among those aged 10 to 12 and 13 to 17 years of age (21.89% and 29.94%, respectively). Overall, 62.46% of new users were <18 years of age.

10.1.3. United Kingdom

In the UK, the majority of Strattera use was among adolescents 13 to 17 years of age (39.6% to 45.2%). Over time, the proportion of users <18 years of age has decreased from 89.9% in 2008 to 68.10% in 2014. As such, the proportion of users 18 to 64 years of age has increased over time; 10.10% of users were 18 to 64 years of age in 2008 and 31.90% were between 18-64 years of age in 2014. Annually, the use among children 0 to 5 and the elderly 65 years of age and older was either 0 or too few to report (i.e., <5; Table 7).

The majority of patients treated with Strattera, approximately 80%, in the UK were male (Table 8). This trend remained consistent over time.

Among males in the UK, the majority of new Strattera users were <18 years of age (78.40%); 21.60% of new male users were between 18 to 34 years of age (Table 9). Among females, the majority of new Strattera users were <18 years of age (69.20%); 30.80% of new female users were between 18 to 34 years of age. There were no new users of Strattera aged 0 to 5 years of age or over 65 years of age. For patients over the age of 34, there were too few to report on gender and age distributions.

10.1.4. Sweden

In Sweden, the overall number of patients treated with Strattera is increasing (Table 10). In 2008, there were 4102 patients treated with Strattera and by 2014, this increased to 10 871 users. The largest proportion of Strattera use was among adolescents 13 to 17 years of age; however, use within this age group has declined over time from 33.23% in 2008 to 21.21% in 2014. Approximately 20% of users were 10 to 12 years of age in each year. The proportion of patients between 6 to 9 years of age gradually increased from 14.48% in 2008 to 19.05% in 2014. The gradual increase in use was also observed in those aged 35 to 64 years of age (12.26% in 2008 to 16.19% in 2014). Strattera use among the elderly 65 years of age and older, and children 0 to 5 years of age was less than 1%. The majority of patients treated with Strattera were 6 to 17 years of age (Table 10).

The majority of patients in Sweden treated with Strattera were male (63.86 to 71.28%). Over time, the proportion of female users increased (Table 11). In 2008, 28.72% of users were female and in 2014, 36.14% of users were female.

In Sweden, more than half of new Strattera users were 13 to 34 years of age (Table 12). Among females, new users were more likely between 18 to 64 years of age (59.87%). Whereas among males, new users were more likely <18 years of age (59.41%).

10.2. Mean daily dose, length of therapy, and number of treatment episodes in new users of Strattera

Drug utilisation measures including MDD, average length of therapy and the number of treatment episodes were estimated within the incident user cohort, also referred to as the new user cohort. These were users of Strattera initiating their first prescription sometime between 01 January 2013 and 30 June 2013. Data for drug utilisation were then estimated from a 24-month period of follow-up after initiation, for a last possible date of follow-up being 30 June 2015.

10.2.1. Germany

Overall, the MDD among new Strattera users in the German population was 27.0 mg. The highest MDD was recorded among Strattera-treated patients aged 18 to 34 years (35.3 mg). Among new users 35 to 64 years of age, the MDD was 31.6 mg and among adults 65 years of age and older, the MDD was reduced to 22.7 mg. Overall, the mean days supplied was 306.4 days within a 24-month window. The overall MPR was 0.42 or 42% of days within a 24-month period (Table 13). The MDD, mean number of days supplied, and mean MPR for the days supplied were relatively consistent across age categories.

Of the 1495 new Strattera users, 1227 (82%) were treated with 1 episode and 228 (15%) were treated with 2 episodes. Only 33 (2.2%) of the patients were treated with 3 episodes and 7 (0.5%) of 1495 patients had 4 episodes of treatment. In Germany, the mean number of days for the patients treated was 306.4 days (Table 14).

10.2.2. Netherlands

Overall, the MDD among users of Strattera was 38.7 mg (Table 15). The highest MDD was recorded among patients treated with Strattera 35 to 64 years of age (51.1 mg). Overall, the mean days supplied was 262 days within a 24-month window. The overall MPR was 0.40 or 40% of days within a 24-month period.

Of the 416 new Strattera–treated patients, 380 (91%) had 1 episode of treatment, 29 (7%) were treated with 2 episodes, 6 (1%) were treated with 3 episodes, and 1 (0.2%) had 4 episodes of treatment (Table 16). The mean number of days for the patients treated was 262 days. Children 10 to 12 years of age had the highest mean length of treatment (301.7 days) followed by children 6 to 9 years of age (284.7 days). The lowest mean days of treatment was among children 0 to 5 (172.5 days for n=2 patients aged 0 to 5 years).

10.2.3. United Kingdom

Overall, the MDD among users of Strattera was 46.5 mg (Table 17). The highest MDD was recorded among the 6 Strattera patients 35 to 64 years of age (70.5mg). Overall, the mean days

supplied was 405.3 days within a 24-month window. The overall medication possession ratio was 0.60 or 60% of days within a 24-month period.

Of the 106 new patients treated with Strattera, 100 (94%) were treated with 1 episode. The remaining 6 patients were treated with either 2 or 3 episodes. No patients were treated with more than 3 episodes. The mean number of days for the patients treated was approximately 405.3 days. The low total number of new users included in this table limits the ability to interpret the findings within each age strata (Table 18). These data reflect no new users of Strattera under 6 and over 64 years of age.

10.2.4. Sweden

Overall, the MDD among users of Strattera was approximately 42.3 mg (Table 19). The MDD among Strattera-treated patients 13 to 17, 18 to 34, or 35 to 64 years of age were similar, ranging from 45.6 to 47.1 mg per day in all 3 of these age categories. Under the age of 6 and 65 years of age and older, there were fewer than 10 patients per group treated with Strattera and, therefore, the numbers could not be reported. Overall, the mean days supplied was 348.6 days within a 24-month window. Users 6 to 9 years of age had the largest mean days supplied (444.4) and those aged 18 to 34years had the smallest mean days supplied (270.2 days). The overall MPR was 48.4% of days within 24-month period.

Of the 2040 new users treated with Strattera, 1801 (88%) patients were treated with 1 episode. A total of 225 (11%) were treated with 2 episodes. A total of 14 (0.7%) of the patients were treated with 3 episodes. The mean number of days for the patients treated with Strattera was 348.6 days (Table 20).

10.3. Persistence and mean gap between episodes in new users of Strattera

Similar to measures of MDD, average length of therapy and the number of treatment episodes, measures of persistence and gaps between episodes were estimated within the incident user cohort. These were users of Strattera initiating their first prescription sometime between 01 January 2013 and 30 June 2013. Data for drug utilisation were then estimated from a 24-month period of follow-up after initiation, for a last possible date of follow-up being 30 June 2015.

10.3.1. Germany

After 24 months, 28.63% of patients were still being treated with Strattera (Table 21). Of the patients who discontinued, 7.89% restarted therapy. In general, persistence on Strattera therapy upon initiation was nearly 100% up through 5 months, keeping in mind persistence calculations allowed for 120 days to utilise a 30-day supply because of the grace period. After 5 months, there was a gradual increase in Strattera treatment discontinuation over time (Figure 1).

In Germany, the mean gap between episodes was approximately 93.9 days. The largest gap between episodes was found among patients 35 to 64 years of age (n=4 patients). Overall, the mean days between episodes decreased with each episode treatment group (Table 22).

10.3.2. Netherlands

After 24 months, approximately 18.27% of patients were still being treated with Strattera in the Netherlands (Table 23). Of the patients who discontinued, 3.37% restarted Strattera therapy. In general, persistence on Strattera therapy upon initiation was nearly 100% up through 4 months. After 4 months there was a gradual increase in treatment discontinuation over time (Figure 2).

In the Netherlands, the mean gap between episodes was approximately 115.6 days (Table 24). The shortest mean gap between episodes was in patients 13 to 17 years of age (44.1 days). The longest gap between episodes was in the 2 patients 6 to 9 years of age (547 days). Those in age categories 10 to 12, 18 to 34, and 35 to 64 years all had a mean gap between episodes of approximately 100 days. There was no observable pattern in the gap between treatment episodes as 91% of patients only had only 1 treatment episode (see Section 10.4.2).

10.3.3. United Kingdom

After 24 months, 30.19% of patients in this study were still being treated with Strattera in the UK. Of the patients who discontinued, 4.72% of patients restarted Strattera therapy (Table 25). At 18 months, discontinuation was greater than 50%. In general, persistence on therapy upon initiation was 100% through 4 months. After 4 months, there was a gradual increase in discontinuation over time (Figure 3).

In the UK, the mean gap between episodes could not be calculated. Of the 106 new users, all had only 1 episode noted, as too few (n<5) restarted therapy to conduct analyses (see Section 10.4.2). Age-specific strata resulted in individual cells with <5 individuals and were therefore obscured (Table 26).

10.3.4. Sweden

After 24 months, 21.08% of patients were still being treated with Strattera in Sweden. Of the patients who discontinued, 11.67% of patients restarted therapy (Table 27). After 17 months, discontinuation was greater than 60%. In general, persistence on Strattera therapy upon initiation was 100% through 3 months. After 3 months, there was a gradual increase in treatment discontinuation over time (Figure 4).

In Sweden, the mean gap between episodes was approximately 235 days (Table 28). The gap was largely consistent across age-groups ranging from 206.2 days in those aged 10 to 12 years, up to 253.9 days in those aged 18 to 34 years. The mean days between the first and second episode were 238.6 days. The mean days between the second and third episode were 177.6 days. In Sweden, numbers <10 cannot be reported; therefore the data were not available for patients treated with 3 or more episodes.

10.4. Diagnoses and concomitant medication use among prevalent Strattera users

Diagnoses and concomitant medications were assessed from a 24-month period of follow-up among the prevalent users of Strattera in the UK and in Sweden. Germany and the Netherlands' LRx data are only pharmacy claims data and do not have medical claims data. Due to the lack of

medical claims data, it was not possible to provide information on ADHD diagnosis and comorbidities for patients in these 2 countries.

10.4.1. Presence of ADHD diagnosis (ICD-10 F90), most frequent diagnosis codes, and concomitant medications*

10.4.1.1. United Kingdom

Table 29 shows that among patients in the UK using Strattera, 24.5% had an ADHD diagnosis recorded within 24-months of follow-up.

Table 30 includes the 30 most frequent ICD – 10 diagnostic codes recorded for a 24-month follow-up period among all patients in the UK (CPRD and DA). Four of the 30 most frequent diagnoses are codes for mental, behavioural, and neurodevelopmental disorders (F900, F909, F840, F845). Not considering an ADHD diagnosis (F900), the top five codes included encounters for medical care (Z518, Z519), acute upper respiratory infection (J069), prophylactic surgery (Z408), and acne vulgaris (L700).

Table 31 includes the 30 most frequent drug/treatment ATC codes recorded for a 24-month follow-up period among Strattera patients in the UK DA database. The tables that follow not only include specific drugs or treatments, but also related procedures used for billing purposes. The nature of using these types of codes including entries for encounters (i.e., visits), procedures, medications, and diagnoses allows for inclusion of codes that do not always describe specific drugs or treatments.

Table 32 includes the 30 most frequent drug/treatment BNF codes recorded for a 24-month follow-up period among Strattera-treated patients in the UK CPRD database.

10.4.1.2. Sweden

Table 33 describes that among patients in Sweden using Strattera, 85.96% have an ADHD diagnosis recorded within 24-months of follow-up.

Table 34 includes the 30 most frequent ICD-10-SE diagnosis codes recorded for a 24-month follow-up period among all patients in Sweden. Nine of the 30 most frequent diagnoses were codes for mental, behavioural, and neurodevelopmental disorders (F900, F419, F329, F412, F845, F321, F100, F909, F192). Not considering an ADHD diagnosis (F900), the top five codes were encounters for pain in the abdomen (R104), anxiety disorder (F419), general psychiatric examination (Z004), major depressive disorder (F329), and observation for other suspected diseases (Z038).

Table 35 includes the 30 most frequent drug/treatment ATC codes recorded for a 24-month follow-up period among Strattera-treated patients in Sweden. As with the UK data sources, the nature of using these codes allows for inclusion of codes that do not describe specific drugs but also describe procedures used for billing purposes.

10.4.2. Trends among new users who restart therapy

Table 36 describes the number of new users in Germany restarting therapy over a period of 24 months of follow-up. In Germany, a total of 268 of 1495 new users (18%) restarted therapy over the 24-month follow-up period. Of those who restarted therapy (n=268), 85% (n=228) had 2 episodes of treatment.

Table 37 describes the number of new users in the Netherlands restarting therapy over a period of 24 months of follow-up. In the Netherlands, a total of 36 of 416 new users (8.6%) restarted therapy over the 24-month follow-up period. Of those who restarted therapy (n=36), 80.6% (n=29) had 2 episodes of treatment, 16.7% (n=6) had 3 episodes of treatment and 2.8% (n=1) had 4 episodes of treatment.

Table 38 describes the number of new users in the UK restarting therapy over a period of 24 months of follow-up. In the UK, there were a total 106 new users of Strattera. The number restarting is not available as small sample size required obscuring data for age-specific stratum with <5 individuals. As previously stated, 94% of Strattera users in the UK had only 1 episode, so restart data is limited.

Table 39 describes the number of new users in Sweden restarting therapy over a period of 24 months of follow-up. In Sweden, a total of 239 of 2040 new users (11.7%) restarted therapy over the 24-month follow-up period. Of those who restarted therapy (n=239), 94.1% (n=225) had 2 episodes of treatment, 5.9% (n=14) had 3 episodes. No users restarted a fourth time.

10.5. Adverse events/adverse reactions

No adverse events were reported in this analysis.

11. Discussion

11.1. Key results

11.1.1. Age

Overall, the number of prevalent Strattera users decreased in Germany and the Netherlands from 2008 to 2014. Whereas the number of prevalent users in the UK and Sweden increased from 2008 to 2014. Regardless of whether the number of users increased or decreased, a universal trend among all four countries was the increasing use among adults (18 to 64 years of age). In Sweden, the increase was more notable in adults aged 35 to 64 years. Despite increasing use among adults, use in adults 65 years and older remained extremely low in all countries (<0.25% of Strattera users). The increased use among adults is a trend which became clear since the previous report (Study B022), with increases most notable in the prevalent user data from 2013 and 2014. This increase among adult users is expected due to the EU ADHD indication approval in adult patients in 2013. Other contributing factors could include that a recent long-term follow-up study revealed that in 40 to 60% of children with ADHD, the disorder persists into adulthood (Volkow and Swanson 2013). Therefore use among adults may in part be due to the transition of adolescent users into adult users. Additionally, changes to the most recent *Diagnostic and Statistical Manual of Mental Disorders* (DSM) update (DSM-5) for diagnosing adult ADHD led to a more inclusive criteria, requiring symptoms be present prior to 12 years of age instead of 7 years of age in the DSM-IV (APA 2013). Furthermore, the number of symptoms for a reliable diagnosis in adults changed from 5, instead of 6. Lastly, examples of ADHD presentation were added to improve the diagnosis across the different ages. These considerations, alongside the EU ADHD indication approval in adult patients in 2013, could contribute to the trends observed towards increased use among adults.

In general, in each of the countries, the majority of patients treated with Strattera were between 13 and 17 years of age. Strattera use among children 0 to 5 years old was 0 to 1% across countries.

11.1.2. Gender

The majority of Strattera users were male, particularly for users younger than 18. This is consistent with Study B022. In some countries, the gender distribution becomes more similar with increased age. While females remain a minority among Strattera users, a new trend observed with the current study was the increasing proportion of female users. In fact, in Sweden, new users of Strattera between the ages of 16 to 64 years were more likely female. This trend was observed in Germany, the Netherlands and Sweden. An increased use among females may not have been noted in the UK because of smaller sample sizes. The increase in use among females, and particularly older females, may be due to various reasons. Differently than in children, where boys are diagnosed with ADHD more than girls, epidemiological studies show that the gender distribution among adults tends to be similar. However, girls may be underdiagnosed in childhood because the ADHD subtype has less hyperactivity and impulsivity symptoms and more often attention problems. Furthermore, the comorbidity patterns in girls

includes more internalizing problems rather than externalizing, which is common in boys. Attention problems in females may be more likely dysfunctional after puberty and in adulthood when the requirements of school, work, and home are demanding and the underachieving becomes problematic. Therefore the increase of Strattera use among females may be due to increasing acceptance of the presence of ADHD in females, alongside an increasing recognition of the symptoms and subsequent dysfunction for females with ADHD in adulthood.

11.1.3. Mean daily dose

Overall, the MDD between countries ranged from approximately 27 mg (Germany) to 47 mg (UK). Among patients 6 to 9 years of age, the MDD ranged from approximately 19 mg (Germany) to 24 mg (Netherlands). Among those 10 to 12 years of age, the MDD range was much greater with a low MDD of 25 mg in Germany and a high MDD of 42.5 mg in the UK. Among those 13 to 17 years of age, Germany again had the lowest MDD of 32 mg, and the UK had the highest with an MDD of approximately 50 mg. These trends were similar among those 18 years of age and older, where Germany had the lowest MDD of 35 mg and the UK had the largest MDD of approximately 60 mg. Overall, for a paediatric population, these mean doses were appropriate for patients with lower weight and may be low for patients who weigh approximately 50 kg. For the adult population, the observed MDD seems to be below the recommended target dose. The overall MDDs were generally consistent with those reported in the previous study, Study B022, but slightly lower.

11.1.4. Mean days supplied over 24 months, the MPR, and persistence.

The mean days supplied ranged from approximately 262 days (the Netherlands) to 405 days (UK), and the MPR ranged from 40% (the Netherlands) to 60% (UK). The mean days supplied in Sweden was 349 and in Germany, 306 days. The MPR is the proportion of days during the treatment period (24 months) that the patient was considered persistent. Overall, the MPR was approximately 40-45% and the mean days supplied was close to 300 days.

11.1.5. Treatment episodes and length of treatment

Overall, the majority of patients were treated with 1 episode and the mean number of days treated ranged from 262 in the Netherlands to 405 in the UK. This range of episode length is similar, but slightly lower, to that observed in Study B022. The previous mean low length of treatment was 304 days in the Netherlands and the mean high length of treatment was 411 days in Sweden.

11.1.6. Recorded medication use and medical conditions

In the UK, between the 2 databases (CPRD and DA) used to assess medication use among Strattera-treated patients, many of the listed drugs were associated with treatment of psychiatric disorders. Many others include treatment for infections and various common conditions. Neither cardiovascular conditions nor medication for cardiovascular disease were listed among the 30 most common conditions/medications. Of the 30 most common conditions, several were related to neurodevelopmental disorders, such as disturbance activity/attention (24%), hyperkinetic disorder (7%), autism (4%), and Asperger's syndrome (3%). Table 29 shows that

in the UK, approximately 25% have a recorded ADHD diagnosis within the 24-month follow-up period. This low percentage of ADHD diagnoses can be attributed to various causes. One of which is that the diagnosis may have occurred outside of the 24-month observation window for collecting the data. For example, a diagnosis of ADHD prior to a patient receiving the first Strattera prescription would not have been captured in the data. This may be particularly true within the CPRD, which is an electronic health record and unlike a claims database tied to billing, a diagnosis does not necessarily occur again when a prescription occurs.

In Sweden, a high proportion of medications listed were for treating psychiatric disorders. Eighty-three percent of patients in the cohort were taking centrally acting sympathomimetics. Many other medications for treating psychiatric conditions were listed, including: selective serotonin reuptake inhibitor (SSRI; 41%); melatonin receptor agonists (39%); benzodiazepine-related drugs (26%). Of the listed medical conditions, mental health-related or general medical conditions were common. Neither cardiovascular conditions nor medication for cardiovascular disease were listed among the 30 most common conditions/medications. Table 33 shows that among patients new to Strattera, 86% have a recorded ADHD diagnosis within the 24-month follow-up period. This proportion is notably higher than the findings in the UK. One can speculate that these findings could also be attributed to differences in the way ADHD is coded and treated in Sweden. It is also possible that in the Swedish cohort, the actual diagnoses may have occurred outside of the 24-month observation window.

11.2. Limitations

Limitations to the methodology used for this study include:

- The types of data sources used for each country varied. Germany and the Netherlands used claims data, whereas Sweden used the most comprehensive combined pharmacy data with national healthcare data. The UK combined CPRD clinical data with the DA patient database, both of which contained data on written prescriptions, not dispensed prescriptions. Care should be taken when comparing the data from these different data sources.
- The sample size in the UK was notably smaller than the other countries. This is a reflection of the limited coverage in the UK data sources. Therefore, the findings may not be representative of the entire country.
- ADHD diagnoses from claims and encounter databases is limited (Habel et al. 2011). This was apparent within this report by the discrepant results from the UK and Sweden. Furthermore, understanding the common comorbidities more generally is limited because administrative and procedural codes were included.

11.3. Interpretation

This study assessed prevalent use of Strattera from 2008 through 2014 and drug utilisation patterns from a 24-month period among new users of Strattera initiating their prescription between 01 January 2013 and 30 June 2013 in Germany, the Netherlands, the UK, and Sweden. Patterns of treatment assessed with MPR, mean days treated, discontinuation, and persistence show that, on average, persistence past 1 year was approximately 50% overall. Among users in

the UK and Sweden, neither cardiovascular outcomes nor use of medication for the treatment of cardiovascular outcomes were listed among the 30 most common conditions/medications. This is reassuring and may be the result of appropriate assessment for preexisting cardiovascular conditions, as recommended in the Summary of Product Characteristics (SmPC), among patients being assessed for ADHD treatment with Strattera. These findings are consistent with the literature and findings from a recent risk minimisation assessment survey (B4Z-MC-B024) conducted in Europe among healthcare professionals (HCPs). This survey found that the majority of physicians participating in the survey were aware of, and adhered to, the recommendation to monitor blood pressure and heart rate in all patients at baseline and during treatment with Strattera, indicating that core risk minimisation activities, particularly appropriate labelling, are effective in managing these cardiovascular risks.

Overall, duration of treatment was relatively short (1 year on average), patients receive 1 episode of treatment, and the MPR showed that treatment is generally not continuous over time. Overall, the measured key usage parameters were lower than those in the US (Winterstein et al. 2008; Christensen et al. 2010; Schellemen et al. 2011). Additionally, data from short-term and long-term Strattera clinical trials showed that increases in blood pressure and heart rate observed during treatment with Strattera do not persist after the drug was discontinued. These factors may explain why observational studies conducted in the United States (US) have reported no significant difference in cardiovascular outcomes in children (Cooper et al. 2011; Schelleman et al. 2011) or adults (Cooper et al. 2011; Habel et al. 2011) with the use of ADHD medications, which includes Strattera compared to non-users. One study comparing the rate of severe cardiovascular events and death in children aged 3 to 17 years treated with ADHD medications compared to nonusers, found the rate of cardiovascular events in exposed children was, in general, no higher than among controls (Schelleman et al. 2011). A retrospective cohort study, conducted by Agency for Healthcare Research and Quality and Food and Drug Administration (FDA) funded, used data from 4 health plans assessed the risk of serious cardiovascular events (sudden cardiac death, acute myocardial infarction, and stroke) in children and young adults between the ages of 2 and 24 years (Cooper et al. 2011). This study did not find evidence that current use of an ADHD medication was associated with an increased risk of serious cardiovascular events (Cooper et al. 2011). A retrospective, population-based cohort study of adults aged 25 through 64 years compared current or new use of an ADHD medication to non- or remote use and found no increased risk of serious cardiovascular events (Habel et al. 2011).

11.4. Generalisability

The countries included in this study represent a large proportion of Strattera use in the EU. As a result, these study findings should be representative of patients and treatment patterns in the EU. However, the limited sample size from the UK should be considered.

12. Other information

None.

13. Conclusion

In conclusion, the most frequent diagnoses and medications listed among Strattera-treated patients were not associated with cardiovascular conditions. This drug utilisation study found mean treatment episodes for Strattera patients in UK, Germany, the Netherlands, and Sweden varied, but were approximately 1 year and the majority of patients are treated with 1 episode. The overall Strattera persistence patterns in these EU countries are lower than those reported in the US. Patterns of usage show that, on average, persistence past 1 year is low. Taking into account MPR and mean days treated, even with persistence of more than 1 year, the patient is not necessarily being treated continuously during this period. Taken together, the utilisation patterns in the EU do not suggest any different potential risks of long-term severe cardiovascular outcomes related to Strattera treatment would be expected in the EU from those reported in large cohort studies conducted in the US. This conclusion is the same as noted in the previous study, Study B022.

14. References

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Annex 1. Tables and Figures

Tables for Section 10.1

Table 1. Germany: Annual Projected Age Distribution for all Prevalent Patients

	2008		2009		2010		2011		2012		2013		2014	
Age in Years	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
0-5 years	297	0.96%	144	0.55%	40	0.16%	33	0.14%	30	0.13%	26	0.12%	23	0.11%
6-9 years	4920	15.86%	3904	15.05%	3616	14.26%	3154	13.25%	2757	12.26%	2475	11.87%	2331	11.29%
10-12 years	7107	22.91%	6443	24.84%	6510	25.66%	6134	25.76%	6089	27.09%	5397	25.88%	4633	22.44%
13-17 years	7293	23.51%	6990	26.95%	7653	30.17%	6845	28.75%	6520	29.00%	6914	33.15%	6454	31.26%
18-34 years	1683	5.42%	1997	7.70%	2050	8.08%	1649	6.93%	1330	5.92%	2052	9.84%	3395	16.45%
35-64 years	669	2.16%	572	2.21%	305	1.20%	212	0.89%	207	0.92%	473	2.27%	1434	6.95%
65+ years	190	0.61%	131	0.51%	42	0.17%	21	0.09%	19	0.09%	43	0.21%	40	0.19%
<18 years	19618	63.23%	17481	67.41%	17818	70.25%	16167	67.90%	15396	68.49%	14812	71.02%	13441	65.11%
18-64 years	2352	7.58%	2569	9.91%	2355	9.28%	1861	7.82%	1537	6.84%	2525	12.11%	4829	23.39%
Unknown	8867	28.58%	5752	22.18%	5150	20.30%	5760	24.19%	5528	24.59%	3476	16.67%	2333	11.30%
Total	31026	100.00%	25933	100.00%	25365	100.00%	23808	100.00%	22480	100.00%	20857	100.00%	20643	100%

Table 2. Germany: Annual Projected Gender Distribution for all Prevalent Patients

	2008		2009		2010		2011		2012		2013		2014	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Female	4840	15.60%	4283	16.51%	4285	16.89%	4140	17.39%	4022	17.89%	3970.62	19.04%	4448.2	21.55%
Male	14740	47.51%	12444	47.99%	11452	45.15%	9812	41.21%	8815	39.21%	8582.15	41.15%	8774.48	42.51%
Unknown	11447	36.89%	9206	35.50%	9628	37.96%	9856	41.40%	9643	42.90%	8303.77	39.81%	7420.68	35.95%
Total	31026	100.00%	25933	100.00%	25365	100.00%	23808	100.00%	22480	100.00%	20856.5	100.00%	20643.4	100.00%

Table 3. Germany: Annual Projected Age and Gender Distribution for New Users

Age in Years	All		Female		Male		Unknown	
	N	%	N	%	N	%	N	%
0-5 years	6	0.20%	2	0.29%	2	0.16%	2	0.19%
6-9 years	623	19.46%	98	13.57%	274	20.41%	250	22.12%
10-12 years	939	29.36%	197	27.14%	404	30.14%	338	29.87%
13-17 years	939	29.36%	231	31.86%	394	29.35%	314	27.79%
18-34 years	227	7.09%	56	7.67%	98	7.34%	73	6.43%
35-64 years	39	1.20%	13	1.77%	15	1.12%	11	0.95%
65+ years	9	0.27%	4	0.59%	2	0.16%	2	0.19%
<18 years	2507	78.39%	528	72.86%	1074	80.06%	905	79.96%
18-64 years	265	8.29%	68	9.44%	113	8.45%	83	7.37%
Unknown	417	13.04%	124	17.11%	152	11.32%	141	12.48%
Total	3198	100.00%	725	100.00%	1341	100.00%	1132	100.00%

Table 4. Netherlands: Annual Projected Age Distribution for all Prevalent Patients

Age in Years	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
0-5 years	22	0.32%	14	0.23%	29	0.50%	12	0.22%	17	0.31%	8	0.16%	4	0.08%
6-9 years	1377	20.31%	1013	16.79%	723	12.42%	653	11.79%	560	10.17%	430	8.54%	404	8.16%
10-12 years	1651	24.35%	1512	25.06%	1480	25.43%	1295	23.38%	1282	23.29%	980	19.46%	885	17.89%
13-17 years	2096	30.91%	1997	33.10%	1935	33.25%	1913	34.53%	1977	35.92%	1932	38.36%	1844	37.27%
18-34 years	994	14.66%	943	15.63%	1023	17.58%	1050	18.95%	1006	18.28%	1065	21.14%	1119	22.62%
35-64 years	612	9.03%	544	9.02%	608	10.45%	602	10.87%	593	10.77%	591	11.73%	677	13.68%
65+ years	17	0.25%	8	0.13%	11	0.19%	12	0.22%	35	0.64%	19	0.38%	8	0.16%
<18 years	5146	75.90%	4536	75.17%	4167	71.61%	3873	69.91%	3836	69.69%	3350	66.51%	3137	63.40%
18-64 years	1606	23.69%	1487	24.64%	1631	28.03%	1652	29.82%	1599	29.05%	1656	32.88%	1796	36.30%
Unknown	11	0.16%	3	0.05%	10	0.17%	3	0.05%	34	0.62%	12	0.24%	7	0.14%
Total	6780	100.00%	6034	100.00%	5819	100.00%	5540	100.00%	5504	100.00%	5037	100.00%	4948	100.00%

Table 5 Netherlands: Annual Projected Gender Distribution for all Prevalent Patients.

	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Female	1445	21.31%	1344	22.27%	1330	22.86%	1270	22.92%	1240	22.53%	1225	24.32%	1284	25.95%
Male	5335	78.69%	4690	77.73%	4489	77.14%	4270	77.08%	4264	77.47%	3812	75.68%	3664	74.05%
Unknown	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Total	6780	100.00%	6034	100.00%	5819	100.00%	5540	100.00%	5504	100.00%	5037	100.00%	4948	100.00%

Table 6. **Netherlands: Annual Projected Age and Gender Distribution for New Users.**

Age in Years	All		Female		Male	
	N	%	N	%	N	%
0-5 years	4	0.41%	2	0.75%	2	0.28%
6-9 years	134	13.74%	33	12.36%	101	14.27%
10-12 years	193	19.79%	38	14.23%	155	21.89%
13-17 years	278	28.51%	66	24.72%	212	29.94%
18-34 years	198	20.31%	63	23.60%	135	19.07%
35-64 years	161	16.51%	63	23.60%	98	13.84%
65+ years	0	0.00%	0	0.00%	0	0.00%
<18 years	609	62.46%	139	52.06%	470	66.38%
18-64 years	359	36.82%	126	47.19%	233	32.91%
Unknown	7	0.72%	2	0.75%	5	0.71%
Total	975	100.00%	267	100.00%	708	100.00%

Table 7. UK: Annual Age Distribution for all Prevalent Patients

	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
0-5 years	<5	-	<5	-	<5	-	0	0.00%	0	0.00%	<5	-	<5	-
6-9 years	131	17.60%	106	13.60%	107	13.40%	92	10.40%	87	9.90%	115	13.00%	94	11.00%
10-12 years	220	29.50%	209	26.80%	203	25.40%	238	26.90%	221	25.10%	187	21.10%	149	17.50%
13-17 years	319	42.80%	352	45.10%	361	45.20%	385	43.50%	386	43.80%	352	39.70%	337	39.60%
18-34 years	63	8.50%	96	12.30%	104	13.00%	146	16.50%	159	18.00%	192	21.70%	219	25.70%
35-64 years	12	1.60%	18	2.30%	23	2.90%	24	2.70%	28	3.20%	40	4.50%	53	6.20%
65+ years	0	0.00%	0	0.00%	0	0.00%	<5	-	0	0.00%	0	0.00%	<5	-
<18 years	670	89.90%	667	85.40%	671	84.10%	715	80.80%	694	78.80%	654	73.80%	580	68.10%
18-64 years	75	10.10%	114	14.60%	127	15.90%	170	19.20%	187	21.20%	232	26.20%	272	31.90%
Unknown	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Total	745	100.00%	781	100.00%	798	100.00%	885	100.00%	881	100.00%	886	100.00%	852	100.00%

Table 8. UK: Annual Gender Distribution for all Prevalent Patients.

	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Female	123	16.50%	129	16.50%	132	16.50%	163	18.40%	165	18.70%	175	19.80%	171	20.10%
Male	622	83.50%	652	83.50%	666	83.50%	722	81.60%	716	81.30%	711	80.20%	681	79.90%
Unknown	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Total*	745	100.00%	781	100.00%	798	100.00%	885	100.00%	881	100.00%	886	100.00%	852	100.00%

* The totals of this table are calculated to exclude the small numbers reported as <5 in Table 7.

Table 9. UK: Annual Age and Gender Distribution for New Users

	All		Female		Male	
	N	%	N	%	N	%
0-5 years	0	0.00%	0	0.00%	0	0.00%
6-9 years	28	28.00%	6	23.10%	22	29.70%
10-12 years	20	20.00%	7	26.90%	13	17.60%
13-17 years	28	28.00%	5	19.20%	23	31.10%
18-34 years	24	24.00%	8	30.80%	16	21.60%
35-64 years	<5	—	<5	—	<5	—
65+ years	0	0.00%	0	0.00%	0	0.00%
<18 years	76	76.00%	18	69.20%	58	78.40%
18-64 years	24	24.00%	8	30.80%	16	21.60%
Unknown	0	0.00%	0	0.00%	0	0.00%
Total*	100	100.00%	26	100.00%	74	100.00%

* Please note that to avoid the recalculation of the small numbers, the number of female and male patients aged 35-64 years have been obscured and excluded from the calculation of the totals.

Table 10. Sweden: Annual Age Distribution for all Prevalent Patients

	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
0-5 years	14	0.34%	21	0.4	31	0.47	55	0.68	65	0.76	67	0.68	79	0.73
6-9 years	594	14.48%	805	15.32	1130	17	1451	17.96	1655	19.23	1871	18.97	2071	19.05
10-12 years	809	19.72%	1016	19.34	1267	19.06	1550	19.19	1750	20.33	1972	20	2148	19.76
13-17 years	1363	33.23%	1624	30.91	1889	28.42	2161	26.75	2152	25.01	2309	23.41	2306	21.21
18-34 years	819	19.97%	1077	20.5	1393	20.96	1700	21.05	1786	20.75	2144	21.74	2482	22.83
35-64 years	503	12.26%	700	13.32	927	13.95	1141	14.13	1182	13.73	1480	15.01	1760	16.19
65+ years	<10	—	11	0.21	9	0.14	19	0.24	16	0.19	19	0.19	25	0.23
<18 years	2780	67.77%	3466	65.97	4317	64.96	5217	64.59	5622	65.33	6219	63.06	6604	60.75
18-64 years	1322	32.23%	1777	33.82	2320	34.91	2841	35.17	2968	34.49	3624	36.75	4242	39.02
Unknown	<10	—	<10	—	<10	—	<10	—	<10	—	<10	—	<10	—
Total*	4102	100.00%	5254	100.00%	6646	100.00%	8077	100.00%	8606	100.00%	9862	100.00%	10871	100.00%

* Patients presented only for groups of sufficient size (N ≥10).

Table 11. Sweden: Annual Gender Distribution for all Prevalent Patients

	2008		2009		2010		2011		2012		2013		2014	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Female	1180	28.72%	1619	30.81%	2092	31.48%	2720	33.68%	2929	34.03%	3545	35.95%	3929	36.14%
Male	2929	71.28%	3635	69.19%	4554	68.52%	5357	66.32%	5677	65.97%	6317	64.05%	6942	63.86%
Unknown	<10	—	<10	—	<10	—	<10	—	<10	—	<10	—	<10	—
Total*	4109	100.00%	5254	100.00%	6646	100.00%	8077	100.00%	8606	100.00%	9862	100.00%	10871	100.00%

* Patients presented only for groups of sufficient size (N ≥10).

Table 12. Sweden: Annual Age and Gender Distribution for New Users

	All		Female		Male	
	N	%	N	%	N	%
0-5 years	<10	—	<10	—	<10	—
6-9 years	245	12	57	7.50%	188	14.68%
10-12 years	331	16.22%	76	10	255	19.91%
13-17 years	483	23.66%	170	22.37%	313	24.43%
18-34 years	585	28.66%	275	36.18%	310	24.20%
35-64 years	386	18.91%	180	23.68%	206	16.08%
65+ years	<10	—	<10	—	<10	—
<18 years	1065	52.18%	304	40.00%	761	59.41%
18-64 years	971	47.57%	455	59.87%	516	40.28%
Unknown	<10	—	<10	—	<10	—
Total*	2041	100.00%	760	100.00%	1281	100.00%

* Patients presented only for groups of sufficient size (N ≥10).

Tables for Section 10.2

Table 13. Germany: Mean Daily Dose and Medication Possession Ratio in New Users

	Mean Daily Dose (MDD), mg				Days Supplied		Medication Possession Ratio (MPR) for Days Supplied	
	No. patients	Mean	Standard deviation	Median	Mean	Median	Mean	Median
0-5 years	3	15.9	10.8	16.1	153.3	56.0	0.21	0.08
6-9 years	291	18.7	8.5	18.0	294.8	224.0	0.40	0.31
10-12 years	439	25.1	11.3	23.7	330.3	307.0	0.45	0.42
13-17 years	439	32.0	15.3	31.3	302.5	242.0	0.41	0.33
18-34 years	106	35.3	18.0	33.1	313.8	242.0	0.43	0.34
35-64 years	18	31.6	22.1	32.0	342.1	259.5	0.47	0.36
65+ years	4	22.7	7.9	23.6	212.0	154.0	0.29	0.21
<18 years	1172	26.1	13.5	23.2	310.6	259.0	0.43	0.35
18-64 years	124	34.8	18.6	33.1	317.9	242.0	0.44	0.34
Unknown	195	27.3	14.1	25.2	275.7	224.0	0.38	0.31
Total	1495	27.0	14.2	23.7	306.4	247.0	0.42	0.34

Table 14. Germany: Length of Treatment and Number of Episodes in New Users

		Treatment Episodes										Cumulative length of treatment (Days)	
		One episode		Two episodes		Three episodes		Four episodes		Five or more episodes		Patient-Level	
	N	n	%	n	%	n	%	n	%	n	%	Mean	Median
0-5 years	3	3	0.24%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	153.3	56.0
6-9 years	291	235	19.15%	47	20.61%	8	24.24%	1	14.29%	0	0.00%	294.8	224.0
10-12 years	439	361	29.42%	67	29.39%	9	27.27%	2	28.57%	0	0.00%	330.3	307.0
13-17 years	439	357	29.10%	70	30.70%	9	27.27%	3	42.86%	0	0.00%	302.5	242.0
18-34 years	106	82	6.68%	20	8.77%	4	12.12%	0	0.00%	0	0.00%	313.8	242.0
35-64 years	18	14	1.14%	4	1.75%	0	0.00%	0	0.00%	0	0.00%	342.1	259.5
65+ years	4	3	0.24%	1	0.44%	0	0.00%	0	0.00%	0	0.00%	212.0	154.0
<18 years	1172	956	77.91%	184	80.70%	26	78.79%	6	85.71%	0	0.00%	310.6	259.0
18-64 years	124	96	7.82%	24	10.53%	4	12.12%	0	0.00%	0	0.00%	317.9	242.0
Unknown	195	172	14.02%	19	8.33%	3	9.09%	1	14.29%	0	0.00%	275.7	224.0
Total	1495	1227	100.00%	228	100.00%	33	100.00%	7	100.00%	0	0.00%	306.4	247.0

Table 15. Netherlands: Mean Daily Dose and Medication Possession Ratio in New Users

	Mean Daily Dose (MDD), mg				Days Supplied			Medication Possession Ratio (MPR) for Days Supplied	
	No. patients*	Mean	Standard deviation	Median	No. patients	Mean	Median	Mean	Median
0-5 years	2	10.1	10.1	10.1	2	172.5	172.5	0.20	0.20
6-9 years	57	23.9	11.5	24.3	58	284.7	147.0	0.40	0.20
10-12 years	83	32.1	16.4	30.4	84	301.7	216.0	0.40	0.30
13-17 years	117	41.7	19.9	40.6	119	271.1	157.0	0.40	0.20
18-34 years	77	42.8	23.2	40.0	83	203.4	106.0	0.30	0.20
35-64 years	67	51.1	23.6	49.8	67	258.3	115.0	0.40	0.20
65+ years	0	0.0	0.0	0.0	0	0.0	0.0	0.00	0.00
<18 years	259	34.4	18.7	32.1	263	283.1	159.0	0.40	0.20
18-64 years	144	46.6	23.7	45.2	150	227.9	111.5	0.30	0.20
Unknown	3	22.9	29.5	7.0	3	110.0	115.0	0.20	0.20
Total*	406	38.7	21.5	35.6	416	262.0	142.0	0.40	0.20

* Patients with 7 days between their first and last prescription are excluded from results in this table to avoid stochastic results.

Table 16. Netherlands: Length of Treatment and Number of Episodes in New Users

		One episode		Two episodes		Three episodes		Four episodes		Five or more episodes		Cumulative length of therapy (days), Patient-level	
	N	n	%	n	%	n	%	n	%	n	%	Mean	Median
0-5 years	2	2	0.53%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	172.5	172.5
6-9 years	58	56	14.74%	2	6.90%	0	0.00%	0	0.00%	0	0.00%	284.7	147.0
10-12 years	84	77	20.26%	4	13.79%	3	50.00%	0	0.00%	0	0.00%	301.7	216.0
13-17 years	119	108	28.42%	10	34.48%	1	16.67%	0	0.00%	0	0.00%	271.1	157.0
18-34 years	83	74	19.47%	9	31.03%	0	0.00%	0	0.00%	0	0.00%	203.4	106.0
35-64 years	67	62	16.32%	3	10.34%	2	33.33%	0	0.00%	0	0.00%	258.3	115.0
65+ years	0	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0.0	0.0
<18 years	263	243	63.95%	16	55.17%	4	66.67%	0	0.00%	0	0.00%	283.1	159.0
18-64 years	150	136	35.79%	12	41.38%	2	33.33%	0	0.00%	0	0.00%	227.9	111.5
Unknown	3	1	0.26%	1	3.45%	0	0.00%	1	100.00%	0	0.00%	110.0	115.0
Total	416	380	100.00%	29	100.00%	6	100.00%	1	100.00%	0	0.00%	262.0	142.0

Table 17. United Kingdom: Mean Daily Dose and Medication Possession Ratio in New Users

	Mean Daily Dose (MDD), mg				Days Supplied		Medication Possession Ratio (MPR) for Days Supplied	
	No. patients	Mean	Standard deviation	Median	Mean	Median	Mean	Median
0-5 years	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
6-9 years	28	30.5	9.1	30.6	357.5	262.5	0.5	0.4
10-12 years	20	42.5	16.0	44.8	378.6	297.5	0.5	0.4
13-17 years	28	50.9	13.5	51.0	408.3	448.0	0.6	0.6
18-34 years	24	57.2	20.8	58.5	443.6	308.0	0.6	0.4
35-64 years	6	70.5	27.2	66.2	550.8	549.5	0.8	0.8
65+ years	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
<18 years	76	41.1	15.4	40.0	381.7	346.5	0.5	0.5
18-64 years	30	59.9	22.3	60.0	465.1	406.0	0.7	0.6
Unknown	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total	106	46.5	19.5	40.4	405.3	350.0	0.6	0.5

Table 18. United Kingdom: Length of Treatment and Number of Episodes in New Users

		One episode		Two episodes*		Three episodes*		Four episodes		Five or more episodes		Cumulative length of therapy (days), Patient-level	
	N	n	%	n	%	n	%	n	%	n	%	Mean	Median
0-5 years	0	0	0.0	<5	—	<5	—	0	0.0	0	0.0	0.0	0.0
6-9 years	28	27	27.0	<5	—	<5	—	0	0.0	0	0.0	357.5	262.5
10-12 years	20	19	19.0	<5	—	<5	—	0	0.0	0	0.0	378.6	297.5
13-17 years	28	28	28.0	<5	—	<5	—	0	0.0	0	0.0	408.3	448.0
18-34 years	24	20	20.0	<5	—	<5	—	0	0.0	0	0.0	443.6	308.0
35-64 years	6	6	6.0	<5	—	<5	—	0	0.0	0	0.0	550.8	549.5
65+ years	0	0	0.0	<5	—	<5	—	0	0.0	0	0.0	0.0	0.0
<18 years	76	74	74.0	<5	—	<5	—	0	0.0	0	0.0	381.7	346.5
18-64 years	30	26	26.0	<5	—	<5	—	0	0.0	0	0.0	465.1	406.0
Unknown	0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0.0	0.0
Total	106	100	100.0	<5	—	<5	—	0	0.0	0	0.0	405.3	350.0

* Results for two episodes and three episodes are over-masked (i.e., the small numbers and the number reported as 0 are reported as <5) to avoid recalculation of small numbers in other tables.

Table 19. Sweden: Mean Daily Dose and Medication Possession Ratio in New Users

	Mean Daily Dose (MDD), mg				Days Supplied		Medication Possession Ratio (MPR) for Days Supplied	
	No. patients	Mean	Standard deviation	Median	Mean	Median	Mean	Median
0-5 years	<10	—	—	—	—	—	—	—
6-9 years	245	27.7	11.4	25.1	444.4	420.0	61.7	58.3
10-12 years	331	35	15	34.3	434.7	406.0	60.4	56.4
13-17 years	483	47.1	18.4	45.6	354.6	280.0	49.3	38.9
18-34 years	584	46.7	19.6	46	270.2	168.0	37.5	23.3
35-64 years	386	45.6	21.2	40	323.3	206.5	44.9	28.7
65+ years	<10	—	—	—	—	—	—	—
<18 years	1065	38.8	17.9	36.7	400.6	336.0	55.6	46.7
18-64 years	970	46.2	20.2	43.2	291.3	169.8	40.5	23.6
Unknown	<10	—	—	—	—	—	—	—
Total* †	2040	42.3	19.4	39.9	348.6	252.0	48.4	35.0

* There are 2040 patients in this table because one patient bought Strattera and later returned the dispatch (prescription); therefore they were not included in analyses.

† Patients presented only for groups of sufficient size (N ≥10).

Table 20. Sweden: Length of Treatment and Number of Episodes in New Users

		One episode		Two episodes		Three episodes		Four episodes		Five or more episodes		Cumulative length of therapy (days), Patient-level	
	N	n	%	n	%	n	%	n	%	n	%	Mean	Median
0-5 years	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%	—	—
6-9 years	245	219	12.16%	25	11.11%	<10	—	0	0.00%	0	0.00%	444.4	420.0
10-12 years	331	303	16.82%	26	11.56%	<10	—	0	0.00%	0	0.00%	434.7	406.0
13-17 years	483	419	23.26%	59	26.22%	<10	—	0	0.00%	0	0.00%	354.6	280.0
18-34 years	584	511	28.37%	70	31.11%	<10	—	0	0.00%	0	0.00%	270.2	168.0
35-64 years	386	338	18.77%	45	20.00%	<10	—	0	0.00%	0	0.00%	323.3	206.5
65+ years	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%	—	—
<18 years	1065	947	52.58%	110	48.89%	<10	—	0	0.00%	0	0.00%	400.6	336.0
18-64 years	970	849	47.14%	115	51.11%	<10	—	0	0.00%	0	0.00%	291.3	169.8
Unknown	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%	—	—
Total* †	2040	1801	100.00%	225	100.00%	14	100.00%	0	0.00%	0	0.00%	348.6	252.0

* There are 2040 patients in this table because one patient bought Strattera and later returned the dispatch (prescription) therefore they were not included in analyses.

† Patients presented only for groups of sufficient size (N ≥10).

Tables/Figures Section 10.3

Table 21. Germany: Proportion of New Users Persistent by Month, over a 24-month Follow-up Period

Month	1	2	3	4	5	6	7	8	9	10	11	12
Persistence	100.00%	100.00%	100.00%	100.00%	99.13%	91.30%	83.01%	74.31%	68.43%	61.07%	56.92%	53.24%
Discontinuation	0.00%	0.00%	0.00%	0.00%	0.87%	8.70%	16.72%	24.95%	29.83%	36.52%	39.80%	42.47%
Reinitiation	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.27%	0.74%	1.74%	2.41%	3.28%	4.28%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Month	13	14	15	16	17	18	19	20	21	22	23	24
Persistence	49.97%	46.76%	44.48%	41.87%	39.87%	37.99%	35.65%	33.78%	32.11%	30.77%	29.77%	28.63%
Discontinuation	45.35%	48.09%	49.70%	52.24%	53.91%	55.38%	57.59%	59.46%	61.07%	61.67%	62.41%	63.48%
Reinitiation	4.68%	5.15%	5.82%	5.89%	6.22%	6.62%	6.76%	6.76%	6.82%	7.56%	7.83%	7.89%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

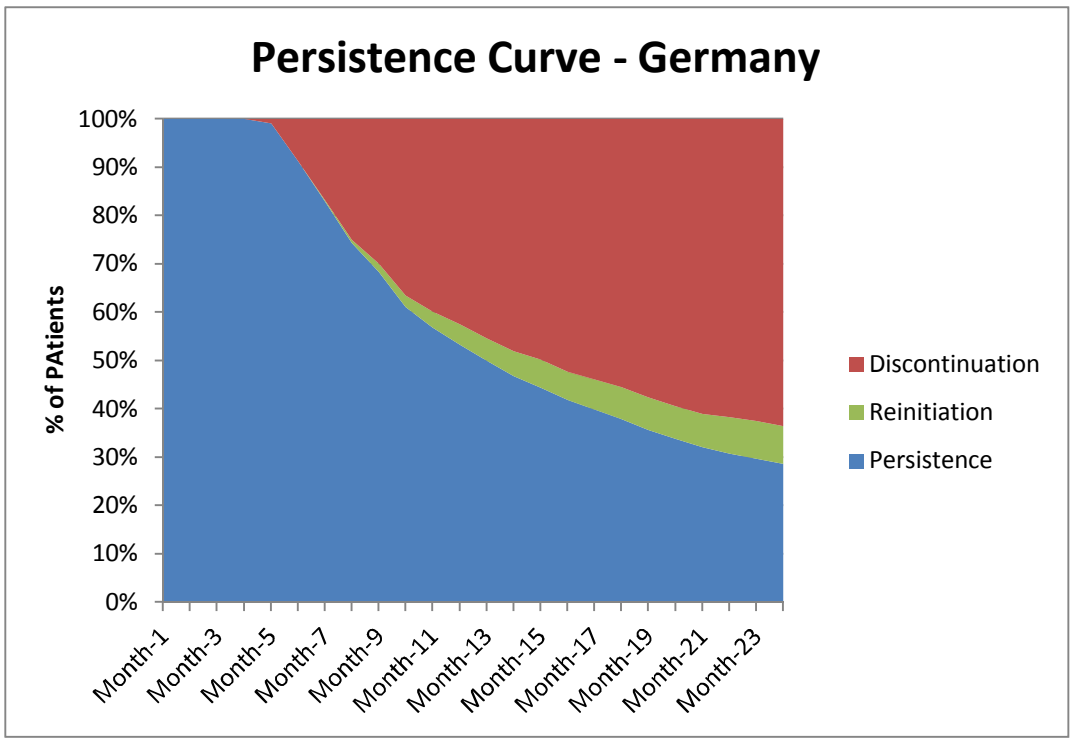

Figure 1. **Germany: Persistence over a 24-month period among patients between 30 June 2013 through 30 June 2015.**

Table 22. Germany: Mean Gap (in Days) between Treatment Episodes in New Users during the 24-month Follow-up Period, by age group

	All the episode gaps			Gap between episode 1 and 2			Gap between episode 2 and 3			Gap between episode 3 and 4		
	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥3 episodes	Mean	Median	No. patients with ≥4 episodes	Mean	Median
0-5 years	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
6-9 years	56	103.0	45.0	56	105.6	44.5	9	98.1	85.0	1	1.0	1.0
10-12 years	78	89.6	53.0	78	93.5	58.0	11	73.1	44.0	2	31.5	31.5
13-17 years	82	100.1	71.0	82	109.0	81.5	12	58.8	49.5	3	24.0	22.0
18-34 years	24	68.3	36.0	24	72.1	36.5	4	45.3	29.0	0	0.0	0.0
35-64 years	4	147.3	155.5	4	147.3	155.5	0	0.0	0.0	0	0.0	0.0
65+ years	1	78.0	78.0	1	78.0	78.0	0	0.0	0.0	0	0.0	0.0
<18 years	216	97.1	60.0	216	102.5	68.5	32	74.8	49.5	6	22.7	17.5
18-64 years	28	78.2	36.5	28	82.9	38.5	4	45.3	29.0	0	0.0	0.0
Unknown	23	83.1	34.0	23	99.0	42.0	4	12.0	11.5	1	1.0	1.0
Total	268	93.9	50.0	268	100.0	56.0	40	65.5	44.0	7	19.6	13.0

Table 23. Netherlands: Proportion of New Users Persistent by Month, over a 24-month Follow-up Period

Month	1	2	3	4	5	6	7	8	9	10	11	12
Persistence	100.00%	100.00%	100.00%	99.52%	88.46%	72.36%	61.54%	54.09%	47.36%	43.27%	41.59%	38.46%
Discontinuation	0.00%	0.00%	0.00%	0.48%	11.06%	26.92%	37.02%	43.99%	50.24%	53.85%	55.29%	57.93%
Reinitiation	0.00%	0.00%	0.00%	0.00%	0.48%	0.72%	1.44%	1.92%	2.40%	2.88%	3.13%	3.61%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Month	13	14	15	16	17	18	19	20	21	22	23	24
Persistence	37.50%	35.58%	32.21%	29.81%	27.64%	24.28%	23.08%	21.88%	20.19%	19.71%	18.75%	18.27%
Discontinuation	59.62%	61.54%	64.18%	67.31%	69.47%	72.36%	73.56%	74.52%	75.96%	76.20%	76.68%	78.37%
Reinitiation	2.88%	2.88%	3.61%	2.88%	2.88%	3.37%	3.37%	3.61%	3.85%	4.09%	4.57%	3.37%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

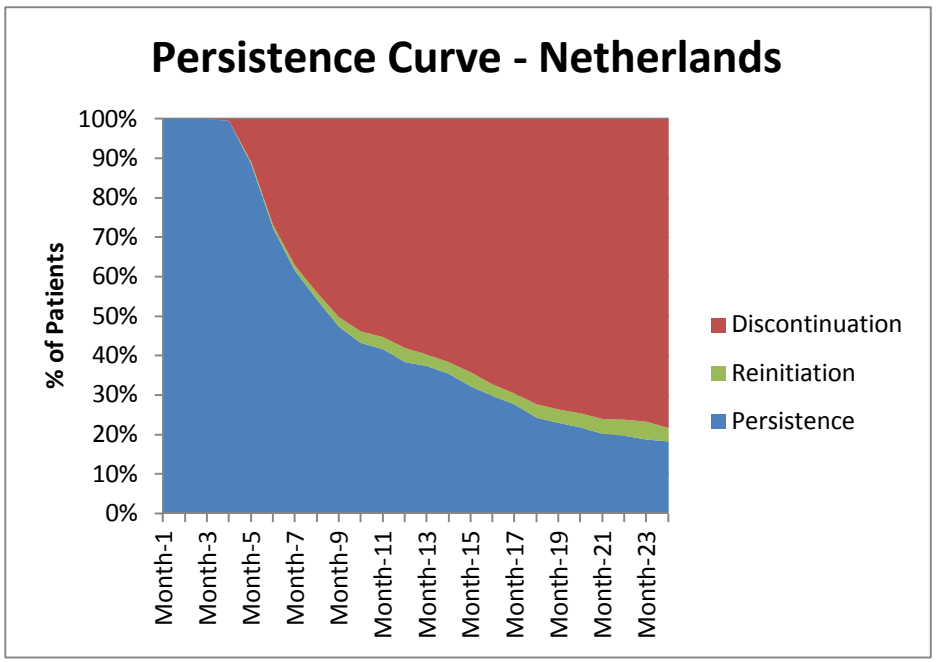

Figure 2. **Netherlands: Persistence over a 24-month period among patients between 30 June 2013 through 30 June 2015.**

Table 24. **Netherlands: Mean Gap (in Days) between Treatment Episodes in New Users during the 24-month Follow-up Period, by Age Group**

	All the episode gaps			Gap between episode 1 and 2			Gap between episode 2 and 3			Gap between episode 3 and 4		
	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥3 episodes	Mean	Median	No. patients with ≥4 episodes	Mean	Median
0-5 years	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
6-9 years	2	547.0	547.0	2	547.0	547.0	0	0.0	0.0	0	0.0	0.0
10-12 years	7	98.0	54.5	7	51.3	39.0	3	207.0	87.0	0	0.0	0.0
13-17 years	11	44.1	38.5	11	44.9	42.0	1	35.0	35.0	0	0.0	0.0
18-34 years	9	100.9	41.0	9	100.9	41.0	0	0.0	0.0	0	0.0	0.0
35-64 years	5	91.9	53.0	5	115.6	71.0	2	32.5	32.5	0	0.0	0.0
65+ years	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
<18 years	20	108.5	47.5	20	97.4	44.5	4	164.0	78.0	0	0.0	0.0
18-64 years	14	96.9	47.0	14	106.1	62.0	2	32.5	32.5	0	0.0	0.0
Unknown	2	233.3	151.5	2	348.5	348.5	1	232.0	232.0	1	4.0	4.0
Total	36	115.6	48.5	36	114.7	48.5	7	136.1	69.0	1	4.0	4.0

Table 25. United Kingdom: Proportion of New Users Persistent by Month, over a 24-month Follow-up Period

Month	1	2	3	4	5	6	7	8	9	10	11	12
Persistence	100.00%	100.00%	100.00%	100.00%	95.28%	90.57%	84.91%	75.47%	72.64%	66.98%	63.21%	57.55%
Discontinuation	0.00%	0.00%	0.00%	0.00%	4.72%	9.43%	15.09%	19.81%	22.64%	28.30%	32.08%	37.74%
Reinitiation	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	4.72%	4.72%	4.72%	4.72%	4.72%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Month	13	14	15	16	17	18	19	20	21	22	23	24
Persistence	53.77%	51.89%	50.00%	47.17%	48.11%	44.34%	42.45%	38.68%	35.85%	33.96%	31.13%	30.19%
Discontinuation	41.51%	43.40%	45.28%	48.11%	47.17%	50.94%	52.83%	56.60%	59.43%	61.32%	64.15%	65.09%
Reinitiation	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%	4.72%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

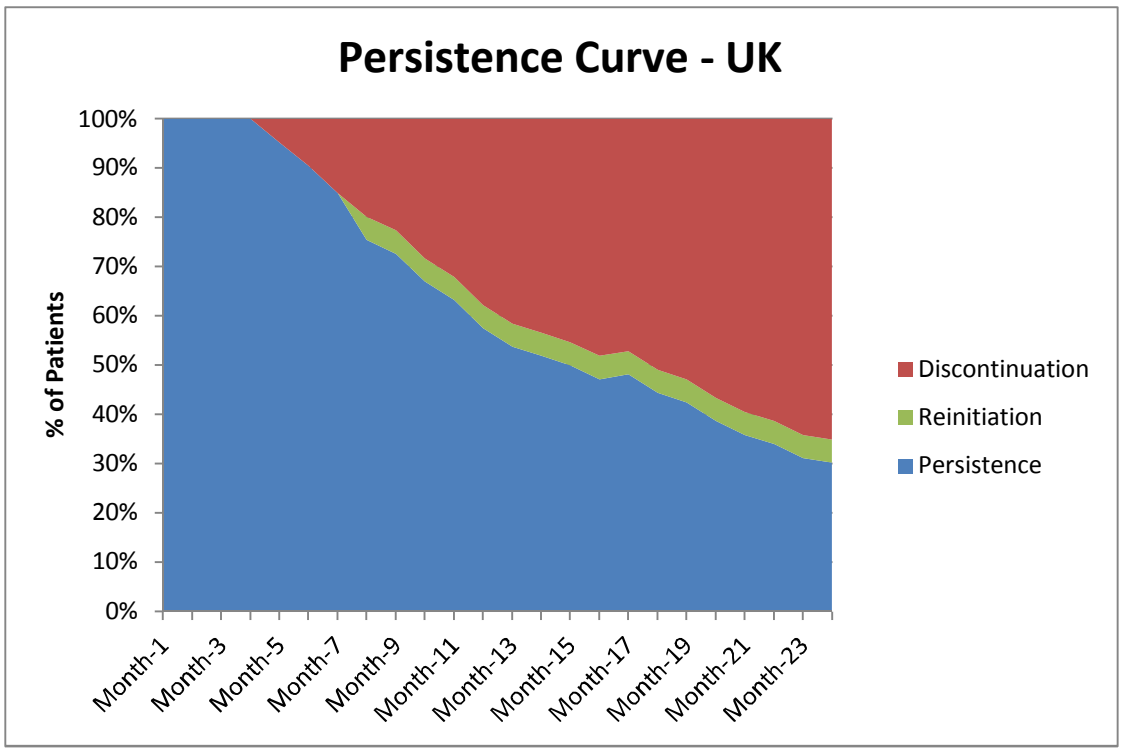

Figure 3. **United Kingdom: Persistence over a 24-month period among patients between 30 June 2013 through 30 June 2015.**

Table 26. United Kingdom: Mean Gap (in Days) between Treatment Episodes in New Users during the 24-month Follow-up Period, by Age Group

	All the episode gaps			Gap between episode 1 and 2			Gap between episode 2 and 3		
	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥3 episodes	Mean	Median
0-5 years	0	—	—	0	—	—	0	—	—
6-9 years	<5	—	—	<5	—	—	0	—	—
10-12 years	<5	—	—	<5	—	—	<5	—	—
13-17 years	0	—	—	0	—	—	0	—	—
18-34 years	<5	—	—	<5	—	—	<5	—	—
35-64 years	0	—	—	0	—	—	0	—	—
65+ years	0	—	—	0	—	—	0	—	—
<18 years	0	—	—	0	—	—	0	—	—
18-64 years	0	—	—	0	—	—	0	—	—
Unknown	0	—	—	0	—	—	0	—	—
Total	0	—	—	0	—	—	0	—	—

Table 27. Sweden: Proportion of New Users Persistent by Month, over a 24-month Follow-up Period

Month	1	2	3	4	5	6	7	8	9	10	11	12
Persistence	100.00%	100.00%	100.00%	95.54%	80.69%	69.90%	61.23%	53.87%	49.85%	45.98%	42.30%	40.29%
Discontinuation	0.00%	0.00%	0.00%	4.41%	18.63%	27.99%	35.64%	41.27%	44.31%	47.55%	50.59%	52.16%
Reinitiation	0.00%	0.00%	0.00%	0.05%	0.69%	2.11%	3.14%	4.85%	5.83%	6.47%	7.11%	7.55%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

Month	13	14	15	16	17	18	19	20	21	22	23	24
Persistence	38.43%	35.88%	33.33%	31.81%	29.66%	28.28%	26.08%	25.00%	24.17%	23.19%	22.25%	21.08%
Discontinuation	53.68%	55.59%	57.60%	58.87%	60.54%	61.47%	63.19%	63.92%	64.41%	65.34%	66.18%	67.25%
Reinitiation	7.89%	8.53%	9.07%	9.31%	9.80%	10.25%	10.74%	11.08%	11.42%	11.47%	11.57%	11.67%
Total	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%

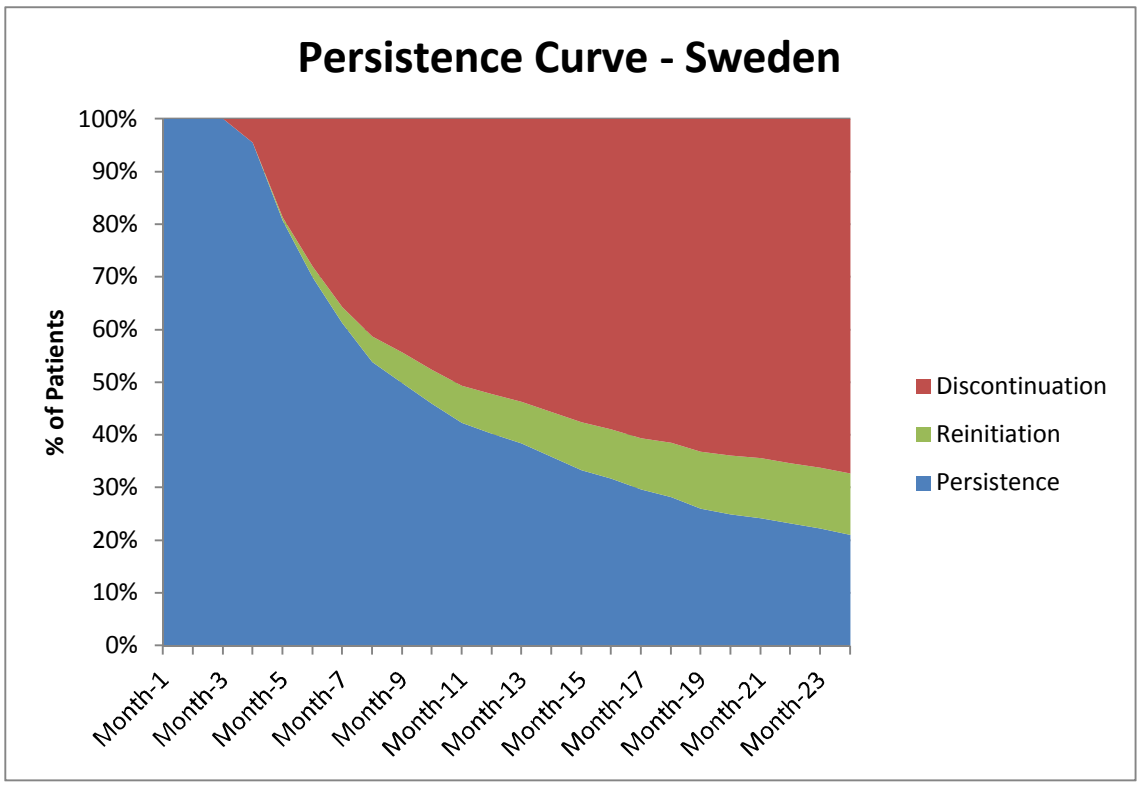

Figure 4. **Sweden: Persistence over a 24-month period among patients between 30 June 2013 through 30 June 2015.**

Table 28. Sweden: Mean Gap (in Days) between Treatment Episodes in New Users during the 24-month Follow-up Period, by Age Group

	All the episode gaps			Gap between episode 1 and 2			Gap between episode 2 and 3		
	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥2 episodes	Mean	Median	No. patients with ≥3 episodes	Mean	Median
0-5 years	<10	—	—	<10	—	—	<10	—	—
6-9 years	26	235.1	211	26	234	205.5	<10	—	—
10-12 years	28	206.2	157.5	28	210.6	158	<10	—	—
13-17 years	64	230	197	64	234	199.5	<10	—	—
18-34 years	73	253.9	212	73	256.5	212	<10	—	—
35-64 years	48	230.5	210	48	236.3	215.5	<10	—	—
65+ years	<10	—	—	<10	—	—	<10	—	—
<18 years	118	225.5	184	118	228.5	184	<10	—	—
18-64 years	121	244.4	211	121	248.5	212	<10	—	—
Unknown	<10	—	—	<10	—	—	<10	—	—
Total*	239	235	200	239	238.6	202	14	177.6	160

* Patients only presented for group of sufficient size (N ≥10).

Tables for Section 10.4

Table 29. United Kingdom: Proportion of Patients in Prevalent User Cohort with ≥1 ICD-10 Code for ADHD and at Least 24-months of Follow-up

	UK Disease Analyser and Clinical Practice Research Datalink		
	Number of atomoxetine users	Number of patients with ADHD	Row %
0-5 years	<5	<5	—
6-9 years	316	81	25.60%
10-12 years	464	118	25.40%
13-17 years	668	139	20.80%
18-34 years	178	61	34.30%
35-64 years	49	11	22.40%
65+ years	0	0	0.00%
<18 years	1448	338	23.30%
18-64 years	227	72	31.70%
Unknown Age	0	0	0.00%
Total	1675	410	24.50%

Abbreviations: ADHD = attention-deficit/hyperactivity disorder; ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th revision; UK = United Kingdom.

Table 30. United Kingdom: 30 Most Frequent Diagnosis Codes among Prevalent Users Cohort with at Least 24-months of Follow-up (CPRD and DA)

ICD10 code (Level 4)	Description	N	%
Z518	OTH SPEC MEDICAL CARE	449	37.67%
F900	DISTURBANCE ACTVTY/ATTEN	282	23.66%
J069	AC UPPER RESPIRATORY INFECT, UNSPECIFIED	181	15.18%
Z408	OTH PROPHYLACTIC SURGERY	169	14.18%
Z519	MEDICAL CARE, UNSPECIFIED	131	10.99%
L700	ACNE VULGARIS	103	8.64%
J039	ACUTE TONSILLITIS UNSP	93	7.80%
F909	HYPERKINETIC DIS UNSP	85	7.13%
M796	PAIN IN LIMB	80	6.71%
R693	NOT STATED DIAG DOC	77	6.46%
J459	ASTHMA UNSPECIFIED	77	6.46%
J220	UNSP AC LOW RESP INFECT	71	5.96%
B070	VIRAL WARTS	69	5.79%
H920	OTALGIA	58	4.87%
F840	CHILDHOOD AUTISM	47	3.94%
L989	DIS SKN/SUBCUT TISS UNSP	44	3.69%
L010	IMPETIGO-ANY ORGNISM/STE	40	3.36%
L089	LOC INF SKN/SC TISS UNSP	43	3.61%
Z000	GENERAL MEDICAL EXAM	42	3.52%
M255	PAIN IN JOINT	40	3.36%
H669	OTITIS MEDIA UNSP	40	3.36%
J301	ALLERG RHINITIS-POLLEN	35	2.94%
L600	INGROWING NAIL	36	3.02%
Z017	LABORATORY EXAMINATION	39	3.27%
J029	ACUTE PHARYNGITIS UNSP	40	3.36%
L209	ATOPIC DERMATITIS UNSP	39	3.27%
F845	ASPERGER'S SYNDROME	36	3.02%
H603	OTH INF OTITIS EXTERNA	33	2.77%
H103	AC CONJUNCTIVITIS UNSP	30	2.52%
Z718	OTH SPEC COUNSELLING	28	2.35%
TOTAL*		1192	

Abbreviations: CPRD = Clinical Practice Research Datalink; DA = Disease Analyser; ICD10 = International Statistical Classification of Diseases and Related Health Problems, 10th revision.

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Table 31. United Kingdom: Top 30 Concomitant Medications in the Prevalent Users Cohort with at Least 24-month Follow-up Period in the DA

ATC code	Description	No. patients*	%
N07X0	ALL OTHER CNS DRUGS	107	90.68%
N06B0	PSYCHOSTIMULANTS	43	36.44%
J01C1	BROAD SPECT PENICILL ORAL	28	23.73%
N05A1	ATYPICAL ANTIPSYCHOTICS	9	7.63%
R03A4	SHORT-ACT B2-STIM,INHAL	10	8.47%
D02A0	EMOLLIENTS & PROTECTIVES	6	5.08%
J01H1	MED/NARROW SPECT PEN PLAI	9	7.63%
N02B0	NON-NARCOTIC ANALGESICS	9	7.63%
M01A1	ANTIRHEUMATICS NON-S PLN	6	5.08%
N05B1	NON-BARBITURATE PLAIN	10	8.47%
R06A0	ANTIHISTAMINES SYSTEMIC	6	5.08%
D07A0	TOP CORTICOSTEROIDS PLAIN	0	0.00%
N01B3	ANAESTH LOCAL TOPICAL	5	4.24%
J01F0	MACROLIDES & SIMILAR TYPE	0	0.00%
D06A0	TOPICAL ANTIBACTERIALS	0	0.00%
N06A4	SSRI ANTIDEPRESSANTS	6	5.08%
D10A0	TOPICAL ANTI-ACNE PREPS	5	4.24%
R03D1	CORTICOIDS INHALANTS	0	0.00%
G03A1	MONOPHAS PREPS<50MCG OEST	5	4.24%
J01A0	TETRACYCLINES & COMBS	5	4.24%
S01A0	ANTI-INFECTIVES-EYE	0	0.00%
D01A1	TOPICAL DERMAT ANTIFUNGAL	0	0.00%
S02C0	STEROID ANTI-INFECT EAR	0	0.00%
Y19A0	SPACERS	0	0.00%
A02B2	ACID PUMP INHIBITORS	0	0.00%
A06A2	STIMULANT LAXATIVES	0	0.00%
A06A6	OSMOTIC LAXATIVES	0	0.00%
H02A2	ORAL CORTICOSTEROID PLAIN	0	0.00%
P01B0	ANTHELMINTICS	0	0.00%
A01B0	MOUTH ANTIFUNGALS	0	0.00%
Total**		118	

Abbreviation: ATC = Anatomical Therapeutic Chemical; DA = Disease Analyser.

* If any age-specific stratum of a prescription had <5 patients, it is treated as 0 to avoid identification of patients with medication. Therefore a 0 for any respective medication means the number of patients with respective medication across all age-groups was <5.

** Number of patients with at least one prescription for one or more of the top 30 cotherapies listed above.

Table 32. United Kingdom: Top 30 Concomitant Medications in the Prevalent Users Cohort with at Least 24-month Follow-up Period in the CPRD

BNF Chapter	No. patients	%
CNS Stimulants And Drugs Used For Attention Deficit	1481	97.56%
Hypnotics	365	24.04%
Broad-spectrum Penicillins	364	23.98%
Selective Beta 2 Agonists	247	16.27%
Non-steroidal Anti-inflammatory Drugs	195	12.85%
Penicillinase-resistant Penicillins	190	12.52%
Second-generation Antipsychotic Drugs	186	12.25%
Non-opioid And Compound Analgesics	181	11.92%
Non-sedating Antihistamines	179	11.79%
Corticosteroids (for Respiratory Conditions)	146	9.62%
Benzylpenicillin And Phenoxymethylpenicillin	124	8.17%
Corticosteroids Used In Nasal Allergy	111	7.31%
Selective Serotonin Re-uptake Inhibitors	103	6.79%
Topical Corticosteroids	100	6.59%
Emollient Skin Preparations	86	5.67%
Topical Corticosteroids With Antimicrobials	85	5.60%
Sedating Antihistamines	72	4.74%
Macrolides	71	4.68%
Sulphonamides And Trimethoprim	72	4.74%
Emollient Bath Additives And Shower Preparations	71	4.68%
Antibacterial Preparations Only Used Topically/Antibacterial Preparations Also Used Systemically (for Skin Conditions)	69	4.55%
Antibacterials (in Eye Preparation)	62	4.08%
Non-opioid And Compound Analgesics/Opioid Analgesics	61	4.02%
Bronchodilators	56	3.69%
Osmotic Laxatives	58	3.82%
Proton Pump Inhibitors	53	3.49%
Control Of Epilepsy	58	3.82%
Unknown	47	3.10%
Macrolides/Oral Antibacterials For Acne	45	2.96%
Other Anti-inflammatory Eye Preparations (for The Eye)	45	2.96%
Total*	1518	

Abbreviations: BNF = British National Formulary; CPRD = Clinical Practice Research Datalink.

* Number of patients with at least one prescription for one or more of the top 30 concomitant medications.

Table 33. Sweden: Proportion of Patients in Prevalent User Cohort with ≥1 ICD-10 Code for ADHD and at Least 24-months Follow-up

	Swedish Prescription Drug Register		
	Number of atomoxetine users	Number of patients with ADHD	Row %
0-5 years	123	95	77.24%
6-9 years	3998	3474	86.89%
10-12 years	4690	4116	87.76%
13-17 years	7435	6537	87.92%
18-34 years	7501	6465	86.19%
35-64 years	4693	3785	80.65%
65+ years	70	34	48.57%
<18 years	16246	14222	87.54%
18-64 years	12194	10250	84.06%
Unknown Age	<10	<10	—
Total	28510	24506	85.96%

Abbreviations: ADHD = attention-deficit/hyperactivity disorder; ICD10 = International Statistical Classification of Diseases and Related Health Problems, 10th revision.

Table 34. Sweden: 30 Most Frequent Diagnosis Codes among Prevalent User Cohort with at Least 24-months of Follow-up for All Patients

ICD-10-SE code* (Level 4)	Description	No. patients	%
F900	Attention-deficit hyperactivity disorder, predominantly inattentive type	24122	84.61%
R104	Other and unspecified abdominal pain	7651	26.84%
F419	Anxiety disorder, unspecified	4758	16.69%
Z004	General psychiatric examination, not elsewhere specified	4634	16.25%
F329	Major depressive disorder, single episode, unspecified	4407	15.46%
Z038	Observation for other suspected diseases	3777	13.25%
F412	Mixed anxiety and depressive disorder	3415	11.98%
Z090	Follow-up examination after surgery for conditions other than malignant neoplasm	3203	11.23%
B349	Viral infection, unspecified	3058	10.73%
J069	Acute upper respiratory infection, unspecified	2974	10.43%
Z011	Encounter for examination of ears and hearing	2948	10.34%
Z032	Observation for suspected mental and other conditions ruled out	2825	9.91%
J459	Other and unspecified asthma	2814	9.87%
F845	Asperger's syndrome	2803	9.83%
Z094	Observation for follow-up for fractures	2756	9.67%
Z010	Encounter for examination of eyes and vision	2650	9.29%
M796	Pain in limb, hand, foot, fingers and toes	2568	9.01%
R699	Irregular breathing, not elsewhere specified under R69	2563	8.99%
S060	Concussion	2563	8.99%
F321	Major depressive disorder, single episode, moderate	2532	8.88%
Z711	Person with feared health complaint in whom no diagnosis is made	2381	8.35%
K590	Constipation	2262	7.93%
F100	Alcohol related disorders	2195	7.70%
R519	Headache, not elsewhere specified under R51	2083	7.31%
F909	Attention-deficit hyperactivity disorder, unspecified type	2063	7.24%
F192	Other psychoactive substance dependence, uncomplicated	2059	7.22%
R074	Chest pain, unspecified	2038	7.15%
Z039	Observation for other suspected diseases	1999	7.01%
H660	Acute suppurative otitis media	1998	7.01%
T509	Poisoning by, adverse effect of and underdosing of other and unspecified drugs, medicaments and biological substances	1988	6.97%
Total		28510	

* International Classification of Diseases, 10th Edition, Sweden (ICD-10-SE) codes were used.

Table 35. Sweden: Top 30 Concomitant Medications among Prevalent User Cohort with at Least 24-months of Follow-up

ATC code	Description	No. patients	%
N06BA	CENTRALLY ACTING SYMPATHOMIMETICS	23775	83.39%
J01CE	BETA-LACTAMASE SENSITIVE PENICILLINS	15213	53.36%
N06AB	SELECTIVE SEROTONIN REUPTAKE INHIBITORS	11681	40.97%
N05CH	MELATONIN RECEPTOR AGONISTS	11126	39.02%
N05BB	DIPHENYLMETHANE DERIVATIVES	9683	33.96%
R06AD	PHENOTHIAZINE DERIVATIVES	9609	33.70%
N06AX	OTHER ANTIDEPRESSANTS	8091	28.38%
N02BE	ANILIDES	7559	26.51%
R05CB	MUCOLYTICS	7345	25.76%
J01CF	BETA-LACTAMASE RESISTANT PENICILLINS	7313	25.65%
N05CF	BENZODIAZEPINE RELATED DRUGS	7303	25.62%
M01AB	ACETIC ACID DERIVATIVES AND RELATED SUBSTANCES	6993	24.53%
M01AE	PROPIONIC ACID DERIVATIVES	6878	24.12%
R03AC	SELECTIVE BETA-2-ADRENORECEPTOR AGONISTS	6800	23.85%
R01AD	CORTICOSTEROIDS	6775	23.76%
N05CM	OTHER HYPNOTICS AND SEDATIVES	6685	23.45%
A02BC	PROTON PUMP INHIBITORS	6537	22.93%
J01CA	PENICILLINS WITH EXTENDED SPECTRUM	5943	20.85%
N02AA	NATURAL OPIUM ALKALOIDS	5854	20.53%
R05FA	OPIUM DERIVATIVES AND EXPECTORANTS	5827	20.44%
N05BA	BENZODIAZEPINE DERIVATIVES	5717	20.05%
R06AX	OTHER ANTIHISTAMINES FOR SYSTEMIC USE	5625	19.73%
J01AA	TETRACYCLINES	5433	19.06%
N03AX	OTHER ANTIEPILEPTICS	5395	18.92%
N05AH	DIAZEPINES, OXAZEPINES, THIAZEPINES AND OXEPINES	4851	17.02%
N05AX	OTHER ANTIPSYCHOTICS	4574	16.04%
A01AA	CARIES PROPHYLACTIC AGENTS	4551	15.96%
A06AD	OSMOTICALLY ACTING LAXATIVES	4465	15.66%
S03CA	CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION	4285	15.03%
R03BA	GLUCOCORTICOIDS	4208	14.76%
Total*		28510	

Abbreviation: ATC = Abbreviation: ATC = Anatomical Therapeutic Chemical.

* Patients only presented only for groups of sufficient size (N ≥10).

Table 36. Germany: Patients Restarting Therapy over a 24-month Period (New Users)

	All new users	All restarters		Restarters with 2 episodes only		Restarters with 3 episodes only		Restarters with 4 episodes only		Restarters with ≥5 episodes	
	No. patients	No. patients	%	No. patients	%	No. patients	%	No. patients	%	No. patients	%
0-5 years	3	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0%
6-9 years	291	56	20.90%	47	20.61%	8	24.24%	1	14.29%	0	0.00%
10-12 years	439	78	29.10%	67	29.39%	9	27.27%	2	28.57%	0	0.00%
13-17 years	439	82	30.60%	70	30.70%	9	27.27%	3	42.86%	0	0.00%
18-34 years	106	24	8.96%	20	8.77%	4	12.12%	0	0.00%	0	0.00%
35-64 years	18	4	1.49%	4	1.75%	0	0.00%	0	0.00%	0	0.00%
65+ years	4	1	0.37%	1	0.44%	0	0.00%	0	0.00%	0	0.00%
<18 years	1172	216	80.60%	184	80.70%	26	78.79%	6	85.71%	0	0.00%
18-64 years	124	28	10.45%	24	10.53%	4	12.12%	0	0.00%	0	0.00%
Unknown	195	23	8.58%	19	8.33%	3	9.09%	1	14.29%	0	0.00%
Total	1495	268	100.00%	228	100.00%	33	100.00%	7	100.00%	0	0.00%

Table 37. Netherlands: Patients Restarting Therapy over a 24-month Period (New Users)

	All new users	All restarters		Restarters with 2 episodes only		Restarters with 3 episodes only		Restarters with 4 episodes only		Restarters with ≥5 episodes	
	No. patients	No. patients	%	No. patients	%	No. patients	%	No. patients	%	No. patients	%
0-5 years	2	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%
6-9 years	58	2	5.56%	2	6.90%	0	0.00%	0	0.00%	0	0.00%
10-12 years	84	7	19.44%	4	13.79%	3	50.00%	0	0.00%	0	0.00%
13-17 years	119	11	30.56%	10	34.48%	1	16.67%	0	0.00%	0	0.00%
18-34 years	83	9	25.00%	9	31.03%	0	0.00%	0	0.00%	0	0.00%
35-64 years	67	5	13.89%	3	10.34%	2	33.33%	0	0.00%	0	0.00%
65+ years	0	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%
<18 years	263	20	55.56%	16	55.17%	4	66.67%	0	0.00%	0	0.00%
18-64 years	150	14	38.89%	12	41.38%	2	33.33%	0	0.00%	0	0.00%
Unknown	3	2	5.56%	1	3.45%	0	0.00%	1	100.00%	0	0.00%
Total	416	36	100.00%	29	100.00%	6	100.00%	1	100.00%	0	0.00%

Table 38. United Kingdom: Patients Restarting Therapy over a 24-month Period (New Users)

	All new users	All restarters		Restarters with 2 episodes only		Restarters with 3 episodes only		Restarters with 4 episodes only		Restarters with ≥5 episodes	
	No. patients	No. patients	%	No. patients	%	No. patients	%	No. patients	%	No. patients	%
0-5 years	0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
6-9 years	28	<5	—	<5	—	0	0.0	0	0.0	0	0.0
10-12 years	20	<5	—	0	0.0	<5	—	0	0.0	0	0.0
13-17 years	28	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
18-34 years	24	<5	—	<5	—	<5	—	0	0.0	0	0.0
35-64 years	6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
65+ years	0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
<18 years	76	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
18-64 years	30	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Unknown	0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Total	106	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 39. Sweden: Patients Restarting Therapy over a 24-month Period (New Users)

	All new users	All restarters		Restarters with 2 episodes only		Restarters with 3 episodes only		Restarters with 4 episodes only		Restarters with ≥5 episodes	
	No. patients	No. patients	%	No. patients	%	No. patients	%	No. patients	%	No. patients	%
0-5 years	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%
6-9 years	245	26	10.88%	25	11.11%	<10	—	0	0.00%	0	0.00%
10-12 years	331	28	11.72%	26	11.56%	<10	—	0	0.00%	0	0.00%
13-17 years	483	64	26.78%	59	26.22%	<10	—	0	0.00%	0	0.00%
18-34 years	584	73	30.54%	70	31.11%	<10	—	0	0.00%	0	0.00%
35-64 years	386	48	20.08%	45	20.00%	<10	—	0	0.00%	0	0.00%
65+ years	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%
<18 years	1065	118	49.37%	110	48.89%	<10	—	0	0.00%	0	0.00%
18-64 years	970	121	50.63%	115	51.11%	<10	—	0	0.00%	0	0.00%
Unknown	<10	<10	—	<10	—	<10	—	0	0.00%	0	0.00%
Total* †	2040	239	100.00%	225	100.00%	14	100.00%	0	0.00%	0	0.00%

* There are 2040 patients in this table because one patient bought Strattera and later returned the dispatch (prescription) therefore they were not included in analyses.

† Patients presented only for groups of sufficient size (N ≥10).

Annex 2. List of standalone documents

Not applicable.