EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Trends in prescriptions of valproate and valpromide for bipolar disorder in IMS France and IMS Germany between 2010 and June 2016 and in UK THIN between 1999 and 2015

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1. General information

Title	Trends in prescriptions of valproate and valpromide for bipolar disorder in IMS France and IMS Germany between 2010 and June 2016 and in UK THIN between 1999 and 2015
Date of last version of the protocol	30/01/2017
Active substance	Valproate/valpromide
Product reference:	N/A
Procedure number:	N/A
Initiator	Surveillance and Epidemiology Unit, EMA
Research question and objectives	How are valproate/valpromide products being prescribed in France, Germany and the UK for bipolar disorder?
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2. Rationale and background

There is a concern that the benefit risk balance for valproate may be less favourable in women of child bearing potential.

Research questions:

- To what extent is valproate being prescribed in the general population, and in particular in patients with bipolar disorder?
- What are the trends in prescribing of valproate in the general population, and in particular in patients with bipolar disorder?

3. Aim

The aim of the study is to report the prevalence of prescribing of valproate and valpromide in patients in France, Germany and the UK, and in particular in patients with bipolar disorder:

- as a proportion of all patients in IMS and THIN databases
- as a proportion of all patients with a diagnosis of bipolar disorder

Further aims in IMS France and IMS Germany are:

- to provide 6-monthly prevalence of prescribing of valproate and valpromide since 2010, per 1000 active patients in the population
- to compare trends of 6-monthly prevalence of prescribing of valproate and valpromide, per 1000 active patients in the population with overall prevalence of prescribing of valproate and valpromide.

For UK data, prescribing trends have also been reported for people with epilepsy and migraine. This was not possible to do for IMS France and IMS Germany as no further data was available within the time period for analysis.

4. Methods

4.1. Patients with bipolar disorder and overall patients in IMS and THIN

4.1.1. IMS France and IMS Germany

Patients with a diagnosis of bipolar disorder were identified by ICD code F31. Patients with an ICD code for acute mania (ICD code F30) were also included as the majority of manias occur in the context of bipolar disorder. The date of first occurrence of one of the included ICD codes was noted for the patient and considered as the diagnosis date. All consultation dates for patients with bipolar disorder from the diagnosis date and forward, between 1 January 2010 and 30 June 2016, were identified.

4.1.2. UK THIN

In the UK THIN database, patients with a diagnosis of bipolar disorder were identified by Read codes for bipolar disorder (including mania). In THIN, cohort entry for the bipolar cohort was defined as the date of the first Read code for bipolar disorder recorded in the electronic medical record in patients registered with a general practice for at least 1 year. Cohort exit for the bipolar cohort was defined as date of death or date patients transferred out of the general practice.

The prevalence of valproate prescribing was also assessed using the entire population contained within the THIN database (i.e. the cohort entry and exit criteria was not applied and codes for bipolar disorder, epilepsy and migraine were not taken into account). In this analysis the mid-year counts of all patients in THIN were used as the denominator. For assessing the prevalence of valproate prescribing in patients with epilepsy , all patients with at least one Read code for epilepsy recorded within the calendar year were used as the denominator for subsequent analysis.

4.2. Prescriptions of valproate and valpromide

4.2.1. IMS France and IMS Germany

Valproate and valpromide were identified by substance name. All patients with a prescription of valproate or valpromide between 1 January 2010 and 30 June 2016 were identified, and all prescription dates for valproate or valpromide during this time period were noted.

In patients with bipolar disorder, all prescription dates that occurred from the diagnosis date and forward were identified.

In addition, all patients with a prescription for valproate or valpromide during the study period were identified that had a diagnosis of:

- Epilepsy as identified by ICD codes G40 and G41
- Migraine or other vascular headache as identified by ICD codes G43, G44.0 and G44.1
- Any diagnosis belonging to ICD codes F (Mental or behavioural disorders) or G (Diseases of the nervous system)

before or on the same day as the valproate or valpromide prescription.

There were no prescriptions for valpromide in IMS Germany.

4.2.2. UK THIN

Valproate prescriptions were identified by substance name. All patients with a prescription of valproate between 1 January 2000 and 31 December 2015 were identified, and all prescription dates for valproate during this time period were noted. In patients with bipolar disorder, all prescription dates that occurred from the diagnosis date and forward were identified. The same time period was applied for overall valproate prescribing using all patients in THIN.

4.3. Population denominator

4.3.1. IMS France and IMS Germany

All patients with a consultation date between 1 January 2010 and 30 June 2016 were identified.

4.3.2. UK THIN

Population denominators used for the analysis of valproate prescribing trends in THIN are defined as follows:

a) All patients with bipolar disorder meeting cohort entry and exit criteria described above.
b) All patients in the THIN database.
c) All patients with a Read code for epilepsy recorded in each calendar year in THIN.
d) All patients with a Read code for migraine recorded in each calendar year in THIN.

Different cohort denominators were used for epilepsy and migraine to reflect active management of patients as opposed to bipolar disorder which is a more pervasive chronic illness. In this regard, it was noted that inclusion of people simply with a past history of

epilepsy and migraine lead to an underestimation of the prevalence of valproate prescribing over time (due to the accrual of non-active patients).

4.4. Analysis

4.4.1. IMS France and IMS Germany

IMS Disease Analyser France version October 2016 and IMS Disease Analyser Germany version October 2016 were used for the analyses. Data were analysed by 6-monthly intervals, stratified by gender and the following age groups: 10-29 years, 30-49 years and ≥50 years. In IMS Germany, general practitioner (GP) patients and neurologist patients were included in the analyses as most prescriptions of valproate were issued by GPs and neurologists. Results were analysed separately for GP patients and for neurologist patients.

In IMS Germany, patients older than 99 years are presented as age unknown. For this reason, patients with unknown age have been included in the age group ≥50 years in IMS Germany.

4.4.1.1. Prevalence calculations

Prevalence of patients treated with valproate or valpromide for bipolar disorder was calculated as proportion of patients with a diagnosis of bipolar disorder:

- All patients with a prescription for valproate or valpromide during the time period that had a diagnosis of bipolar disorder before or on the same day as the valproate or valpromide prescription were considered in the numerator. All patients with a consultation during the time period and diagnosis of bipolar disorder before or during the time period were considered in the denominator.

Prevalence of patients treated with valproate or valpromide as proportion of all active patients in the population:

- All patients with a prescription for valproate or valpromide during the time period were considered in the numerator. All patients with a consultation during the time period were considered in the denominator.

4.4.2. UK THIN

4.4.2.1. Prevalence calculations

Three prevalence calculationThe prevalence of valproate prescribing in people with bipolar disorder were analysed by quarterly intervals, stratified by gender and the following age groups: 10-29 years, 30-49 years and ≥50 years. The numerator consisted of the number of patients with a valproate prescription in each quarter, by age group and gender, and the denominator consisted of all patients with bipolar disorder present in the same quarter, by age group and gender.

For overall valproate prescribing using all patients in THIN, the proportion of patients with one or more Read codes for epilepsy, migraine and bipolar disorder ever recorded within their electronic medical record was measured. Yearly trends in valproate prescribing (measured as prescriptions per 100 patients) were plotted by gender and age group. Yearly trends in valproate prescribing for people with epilepsy and migraine were similarly plotted by gender and age group (quarterly trends are not reported due to significant variability between data points).

5. Results

5.1. IMS France

A total of 12484 patients received valproate or valpromide in IMS France between 1 January 2010 and 30 June 2016. Of those patients:

- 7630 patients (61%) had a diagnosis belonging to ICD codes F (Mental or behavioural disorders) or G (Diseases of the nervous system) prior to or on the day of the prescription
- 1449 patients (12%) had bipolar disorder as defined above (ICD codes F30 or F31) prior to or on the day of the prescription
- 2525 patients (20%) had epilepsy (ICD codes G40 or G41) prior to or on the day of the prescription
- 432 patients (3%) had vascular headache/migraine (ICD codes G43, G44.0 or G44.1) prior to or on the day of the prescription

The total number of patients with bipolar disorder in IMS France was 6839 with 4149 female patients (61%). The overall prevalence of prescribing of valproate or valpromide in patients with bipolar disorder did not change markedly between 1 January 2010 and 30 June 2016. Overall prevalences were higher in male compared with female patients. The trend was stable to slightly increasing in the oldest age group. In the middle age group, there was an overall decrease from with slight fluctuations during the period and the lowest value recorded at the end of the period. In the youngest age group there were large fluctuations during the period. Trends by age group were somewhat similar in male and female patients. Results are shown in Figures 1-4.

Overall prevalence of prescribing of valproate or valpromide per 1000 active patients in the population slightly decreased. Overall prevalences were higher in male compared with female patients. Prevalence remained stable in the oldest age group, and decreased in the middle and lowest age groups. Decreases were slightly more pronounced in female compared with male patients. Results are shown in Figures 5-8.

The proportion of all patients with a prescription of valproate or valpromide that had bipolar disorder varied from 11% at the beginning of the period to 12% at the end of the period.

Figure 1 Proportion of patients with bipolar disorder with a prescription for valproate or valpromide by 6-monthly periods in IMS France

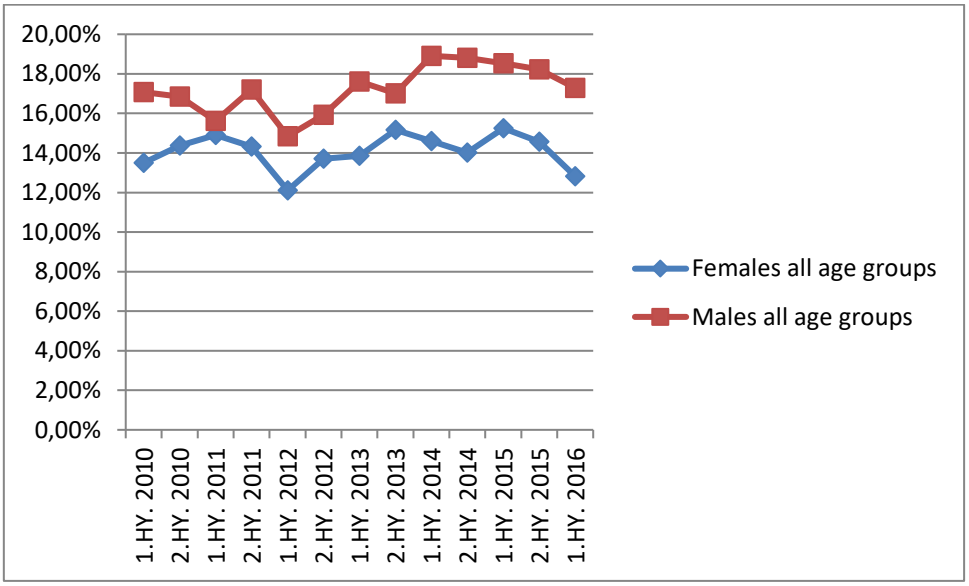


Figure 2 Proportion of patients with bipolar disorder with a prescription for valproate or valpromide by age group and 6-monthly periods in IMS France

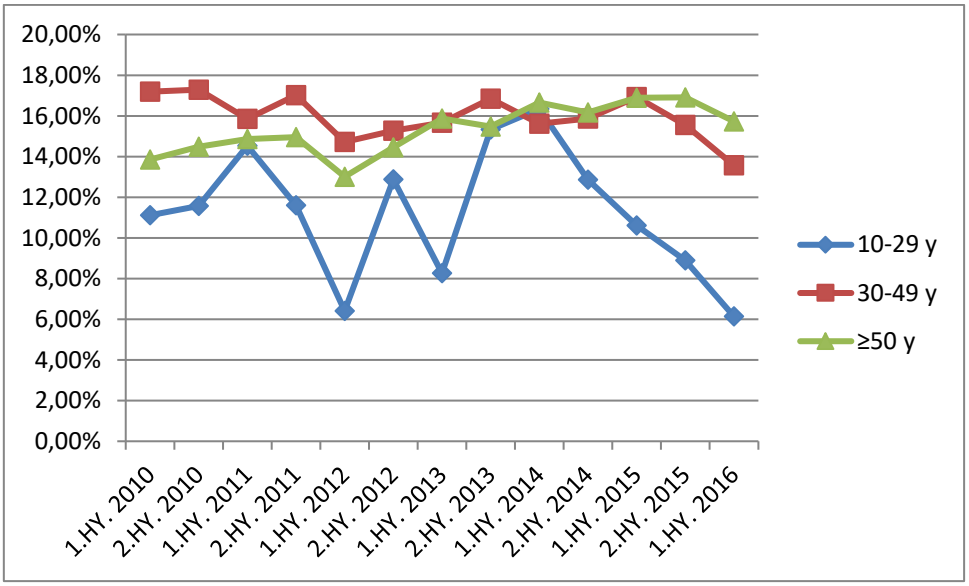


Figure 3 Proportion of male patients with bipolar disorder with a prescription for valproate or valpromide by age group and 6-monthly periods in IMS France

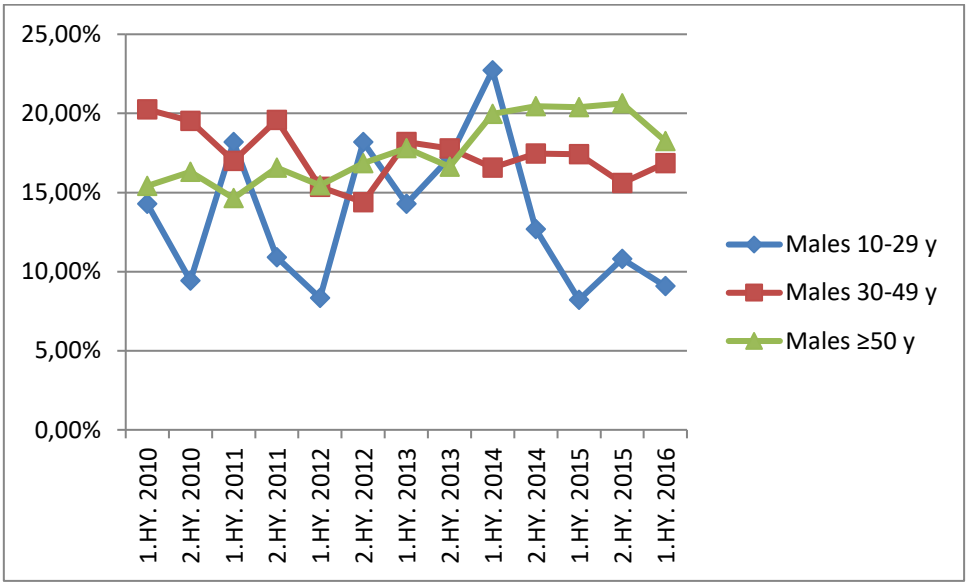


Figure 4 Proportion of female patients with bipolar disorder with a prescription for valproate or valpromide by age group and 6-monthly periods in IMS France

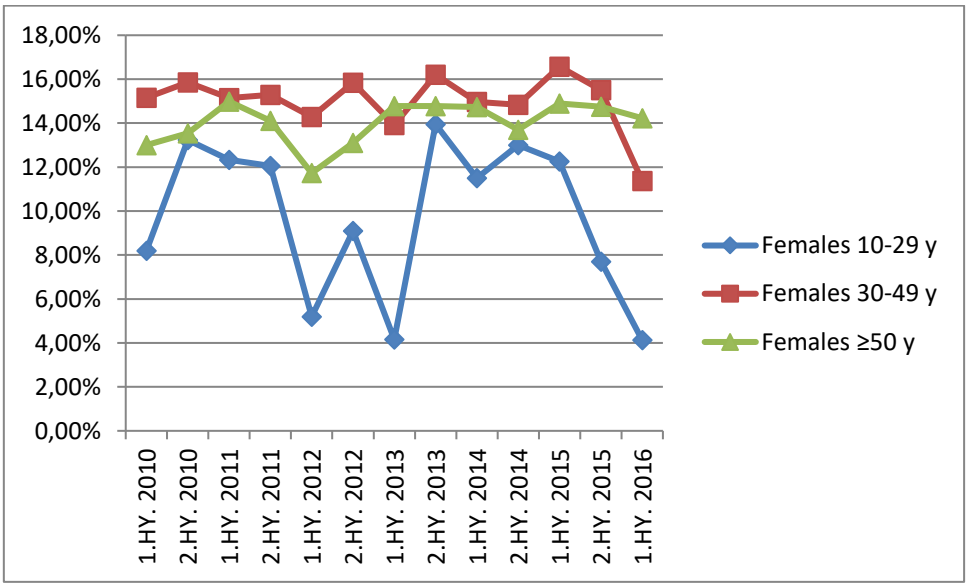


Figure 5 Prevalence of valproate or valpromide per 1000 active patients in IMS France by 6-monthly periods

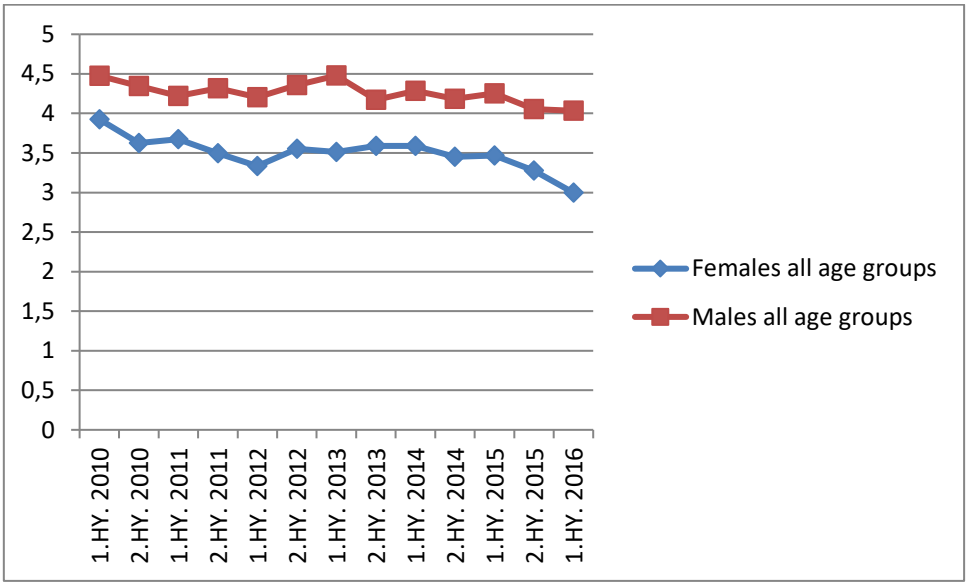


Figure 6 Prevalence of valproate or valpromide per 1000 active patients in IMS France by age group and 6-monthly periods

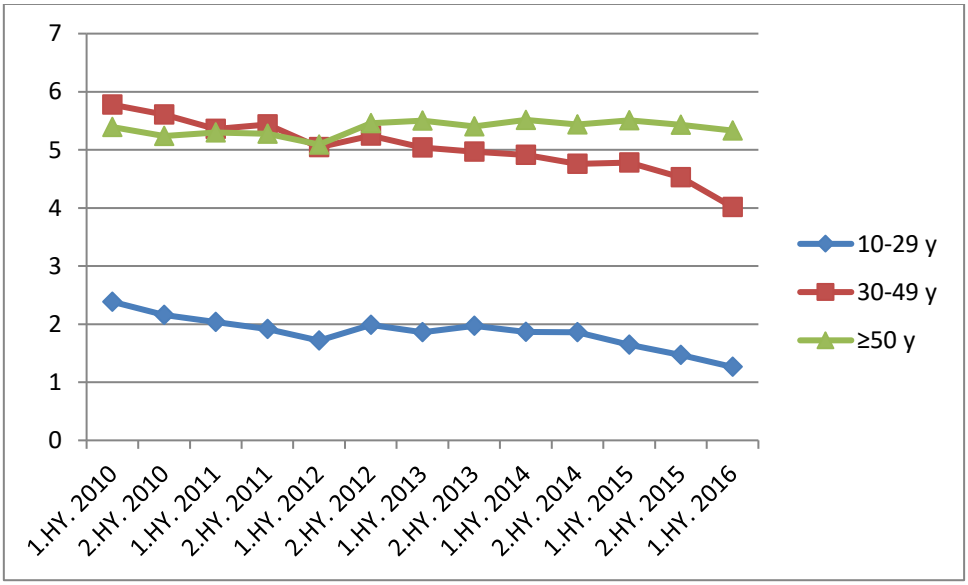


Figure 7 Prevalence of valproate or valpromide per 1000 active male patients in IMS France by age group and 6-monthly periods

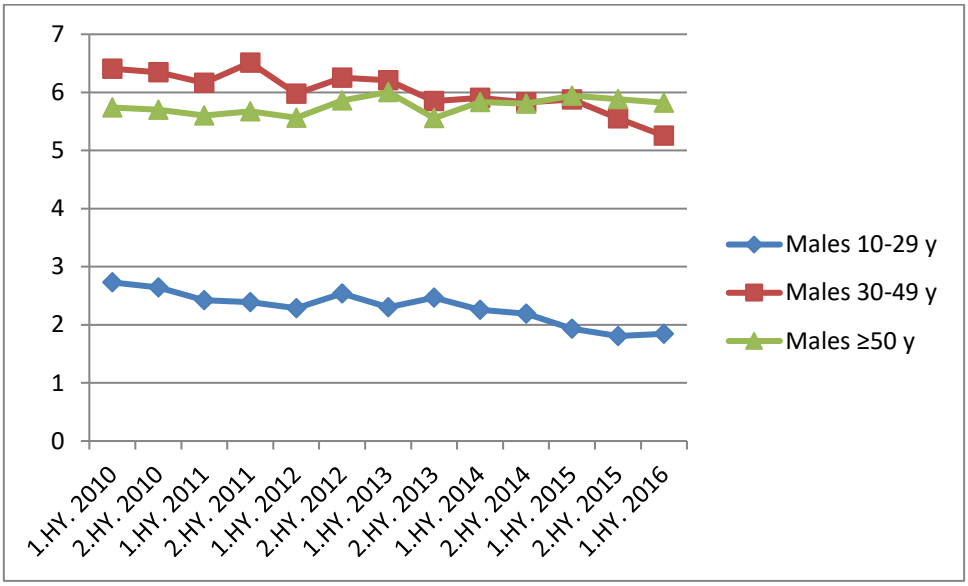
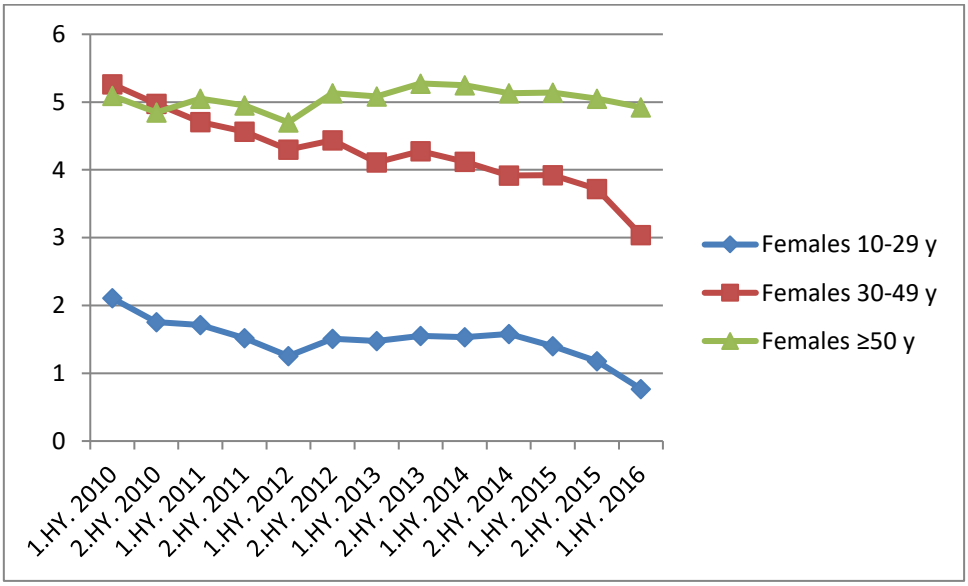


Figure 8 Prevalence of valproate or valpromide per 1000 active female patients in IMS France by age group and 6-monthly periods



5.2. GP patients in IMS Germany

A total of 13221 GP patients received valproate or valpromide in IMS Germany between 1 January 2010 and 30 June 2016. Of those patients:

- 12315 patients (93%) had a diagnosis belonging to ICD codes F (Mental or behavioural disorders) or G (Diseases of the nervous system) prior to or on the day of the prescription
- 727 patients (5%) had bipolar disorder as defined above (ICD codes F30 or F31) prior to or on the day of the prescription
- 8230 patients (62%) had epilepsy (ICD codes G40 or G41) prior to or on the day of the prescription
- 605 patients (5%) had vascular headache/migraine (ICD codes G43, G44.0 or G44.1) prior to or on the day of the prescription

The total number of GP patients in IMS Germany with bipolar disorder was 13259 with 7867 (59%) female patients. The overall prevalence of prescribing of valproate (valpromide was not prescribed in IMS Germany) in patients with bipolar disorder between 1 January 2010 and 30 June 2016 decreased slightly in female patients. It remained almost unchanged in male patients, albeit with marked fluctuations during the time period. The overall prevalence was higher in male compared with female patients. Prevalence by age group showed a slight decrease in the middle age group and no clear changes in the oldest and youngest age groups, albeit with marked fluctuations in the lowest age group. The gender specific prevalence by age group showed even more marked fluctuations. In male patients, the highest age group showed an increase with no apparent change in the middle age group. In female patients, prevalence decreased slightly in the oldest and middle age groups. Trends by gender could not be assessed in the lowest age groups. Results are shown in Figures 9-12.

Overall prevalence of prescribing of valproate per 1000 active patients in the population decreased. Prevalence was higher in male compared with female patients. Decreases were seen in all age groups in both genders. Results are shown in Figures 13-16.

The proportion of all patients with a prescription of valproate that had bipolar disorder varied from 3% at the beginning of the period to 6% at the end of the period.

Figure 9 Proportion of GP patients with bipolar disorder with a prescription for valproate by 6-monthly periods in IMS Germany

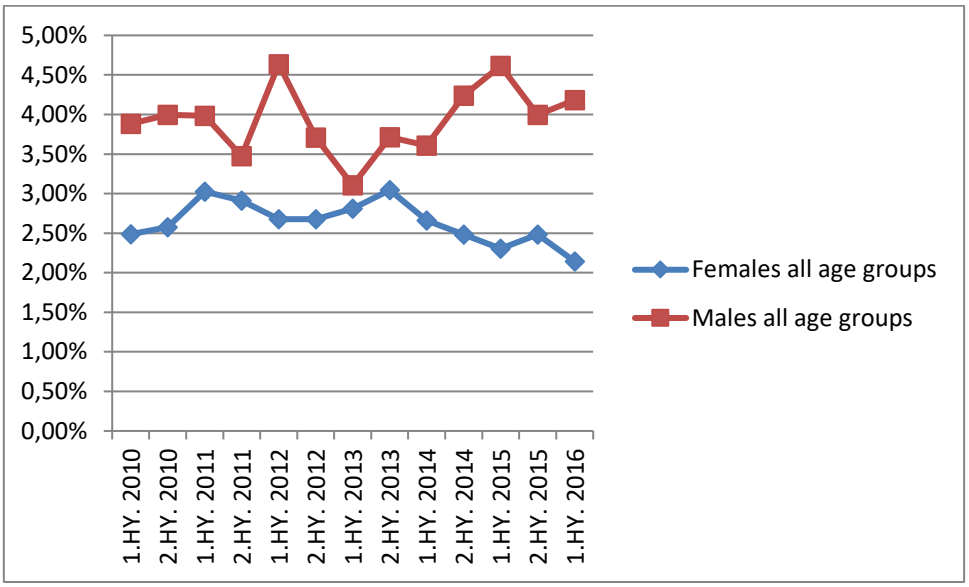


Figure 10 Proportion of GP patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

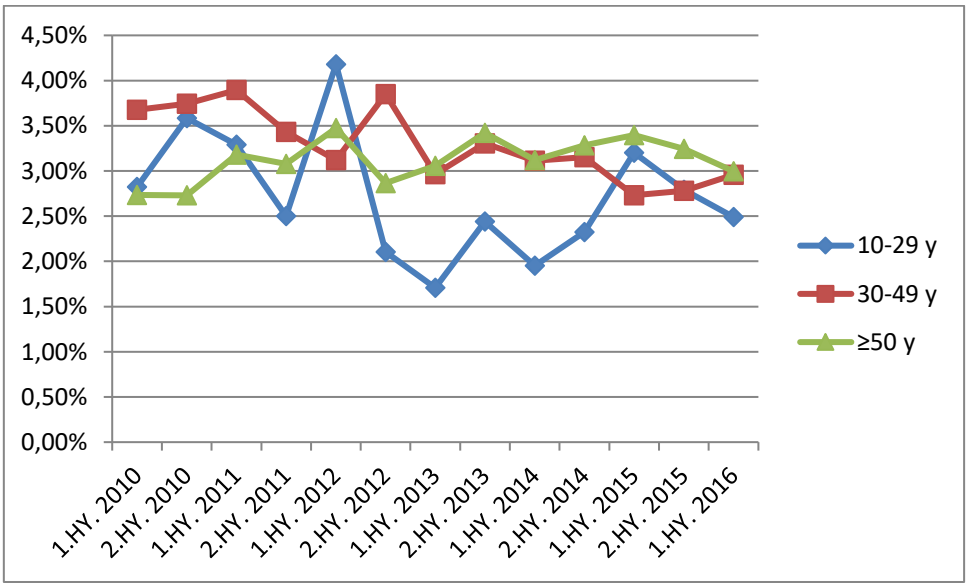


Figure 11 Proportion of male GP patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

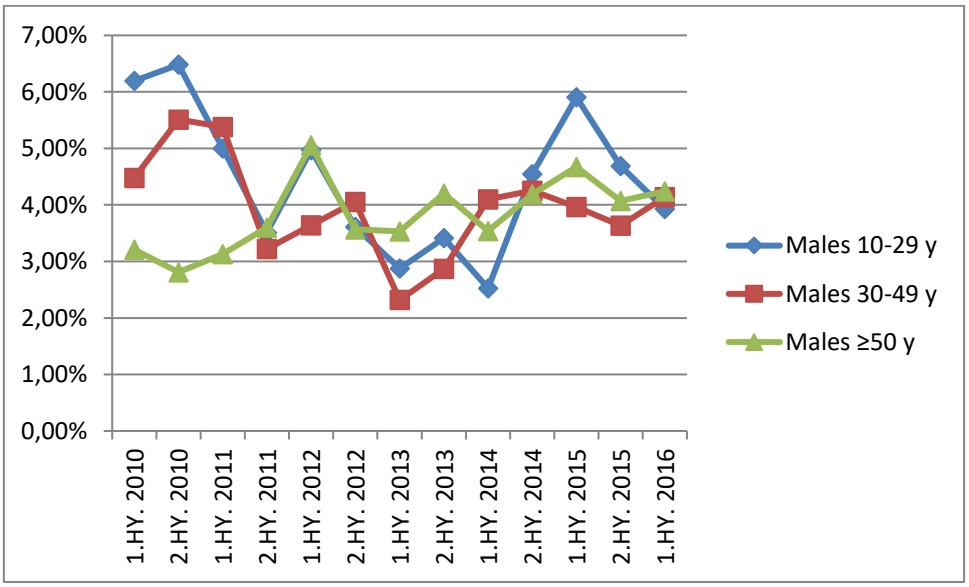


Figure 5 Proportion of female GP patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

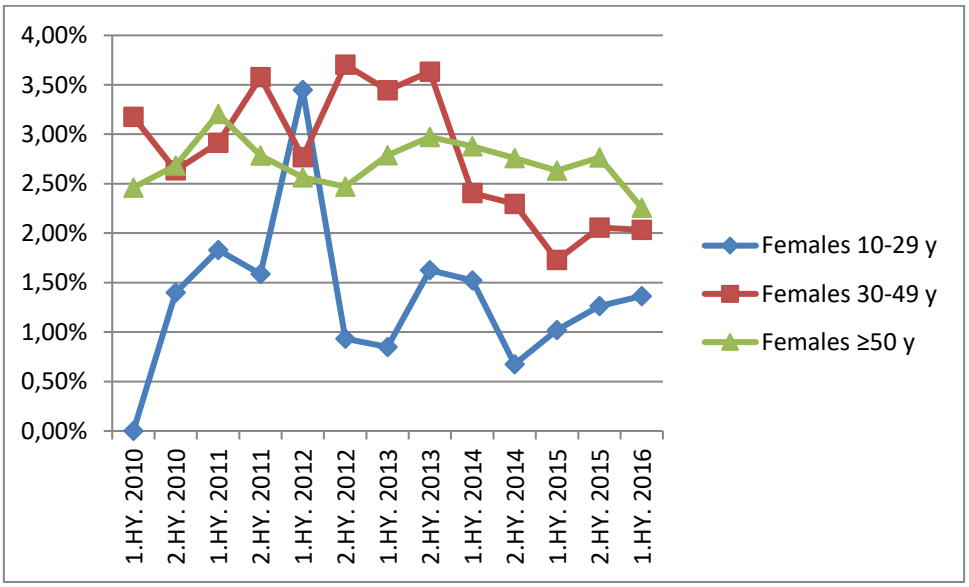


Figure 13 Prevalence of valproate per 1000 active GP patients in IMS Germany by 6-monthly periods

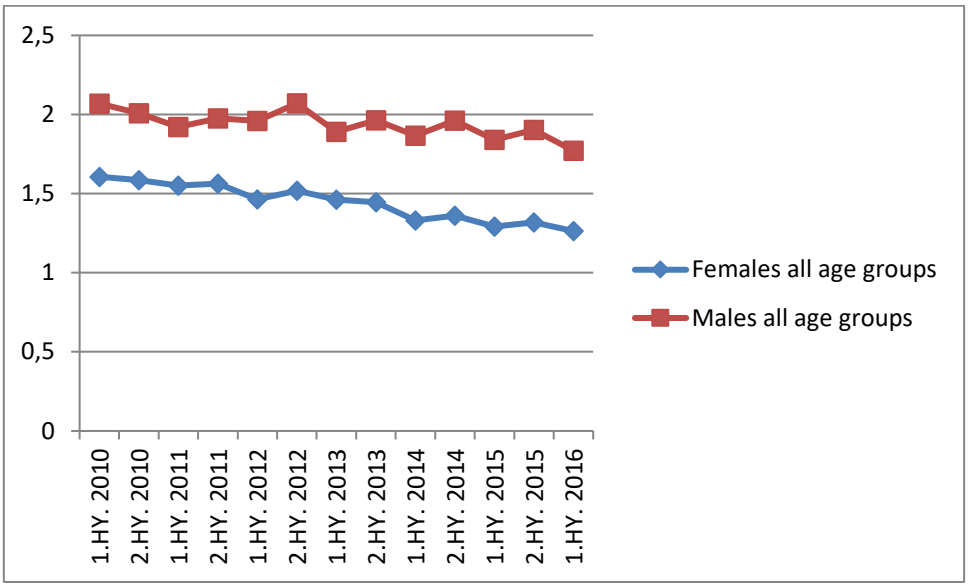


Figure 14 Prevalence of valproate per 1000 active GP patients in IMS Germany by age group and 6-monthly periods

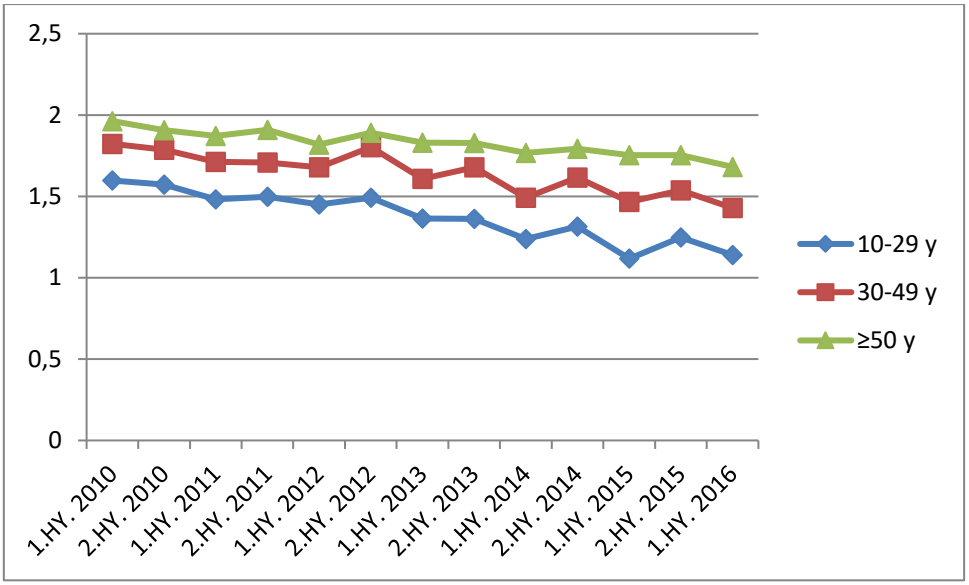


Figure 15 Prevalence of valproate per 1000 active male GP patients in IMS Germany by age group and 6-monthly periods

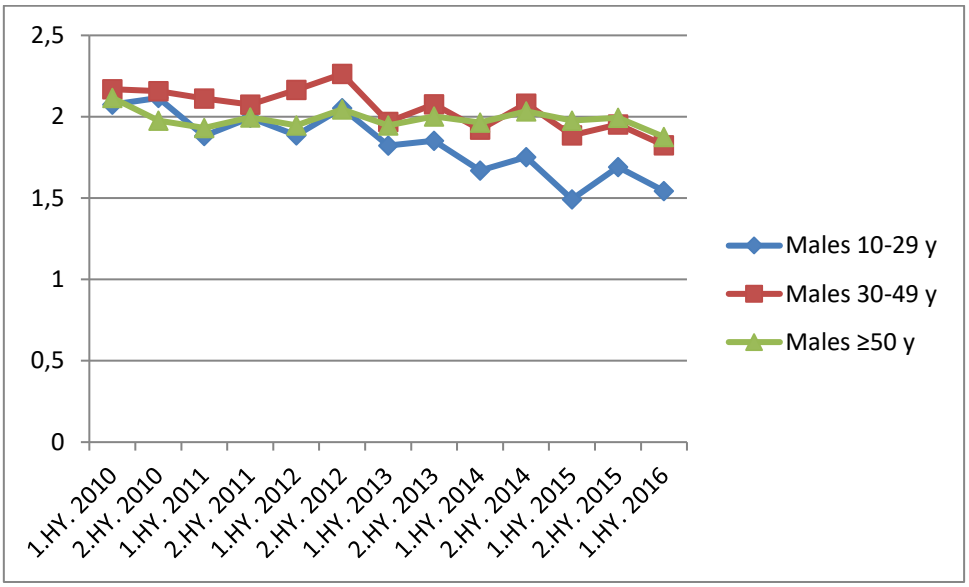
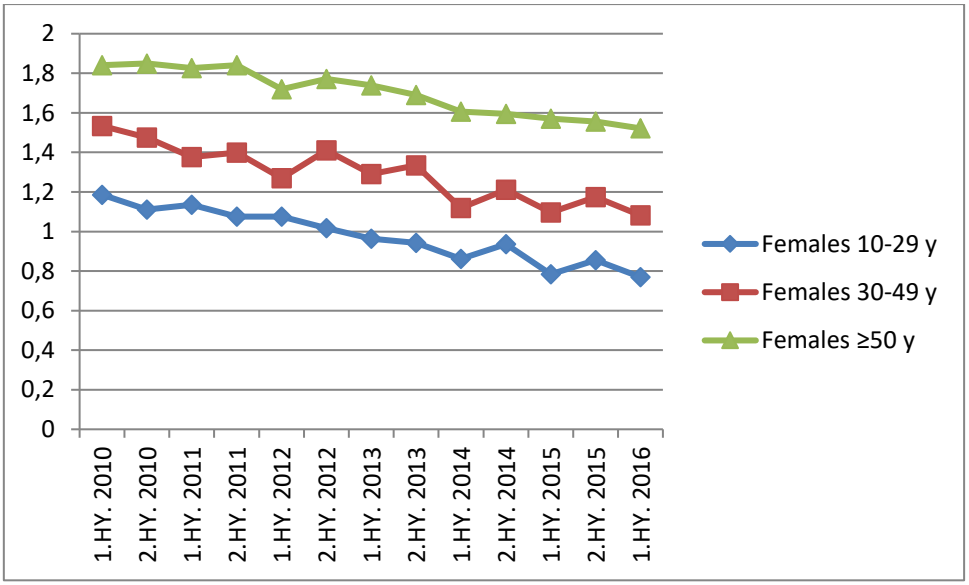


Figure 16 Prevalence of valproate per 1000 active female GP patients in IMS Germany by age group and 6-monthly periods



5.3. Neurologist patients in IMS Germany

A total of 16588 neurologist patients received valproate or valpromide in IMS Germany between 1 January 2010 and 30 June 2016. Of those patients:

- 16198 patients (98%) had a diagnosis belonging to ICD codes F (Mental or behavioural disorders) or G (Diseases of the nervous system) prior to or on the day of the prescription
- 1501 patients (9%) had bipolar disorder as defined above (ICD codes F30 or F31) prior to or on the day of the prescription
- 10958 patients (66%) had epilepsy (ICD codes G40 or G41) prior to or on the day of the prescription
- 1339 patients (8%) had vascular headache/migraine (ICD codes G43, G44.0 or G44.1) prior to or on the day of the prescription

Among neurologist patients in IMS Germany, the total number of patients with bipolar disorder was 11892 with 7041 female patients (59%). Overall prevalence of prescribing of valproate between 1 January 2010 and 30 June 2016 in patients with bipolar disorder decreased slightly. Prevalence was higher in male compared with female patients. There was a slight decrease in the oldest and middle age groups and a more marked decrease in the youngest age group, albeit with more marked fluctuations. The gender specific prevalence by age group showed different trends. In male patients the youngest age groups showed marked fluctuations with no trend, the oldest age group showed a slight decrease, and the middle age group showed a slight increase. In female patients, the middle and youngest age groups showed decreases, and the oldest age group showed almost no change. Results are shown in Figures 17-20.

Overall prevalence of prescribing of valproate per 1000 active patients in the population decreased in both genders. The decrease was more pronounced in female patients. Prevalence was higher in male compared with female patients. Prevalence by age group showed the greatest decrease in the youngest age group, where prevalence decreased in both genders. In the oldest and middle age groups, prevalence decreased in female patients and remained almost stable in male patients. Results are shown in Figures 21-24.

The proportion of all patients with a prescription of valproate that had bipolar disorder varied from 8% at the beginning of the period to 9% at the end of the period.

Figure 17 Proportion of neurologist patients with bipolar disorder with a prescription for valproate by 6-monthly periods in IMS Germany

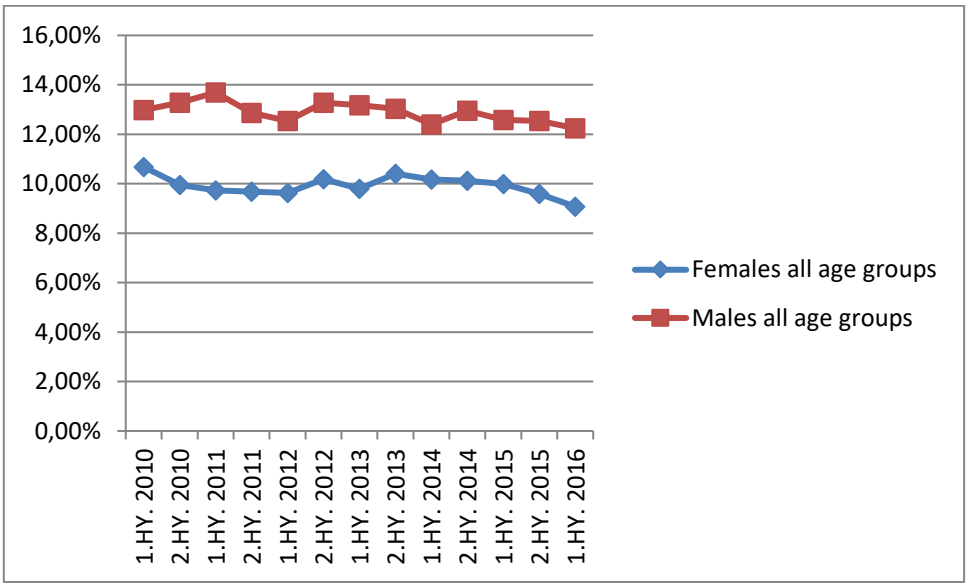


Figure 18 Proportion of neurologist patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

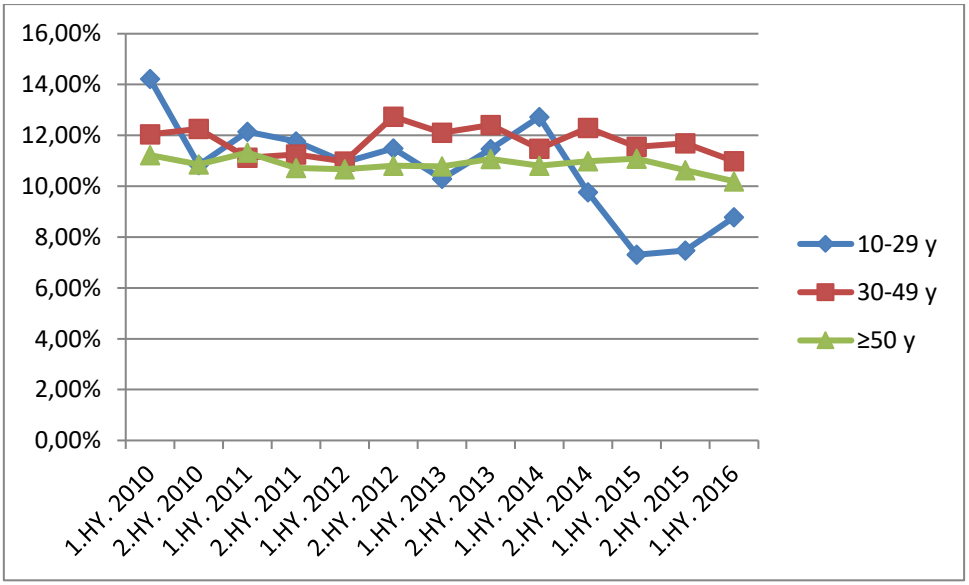


Figure 19 Proportion of male neurologist patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

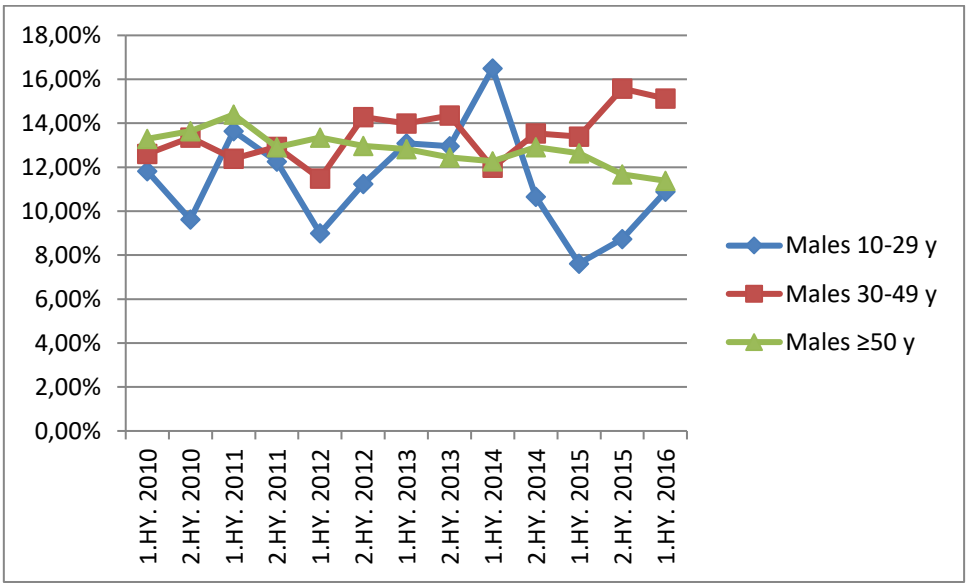


Figure 20 Proportion of female neurologist patients with bipolar disorder with a prescription for valproate by age group and 6-monthly periods in IMS Germany

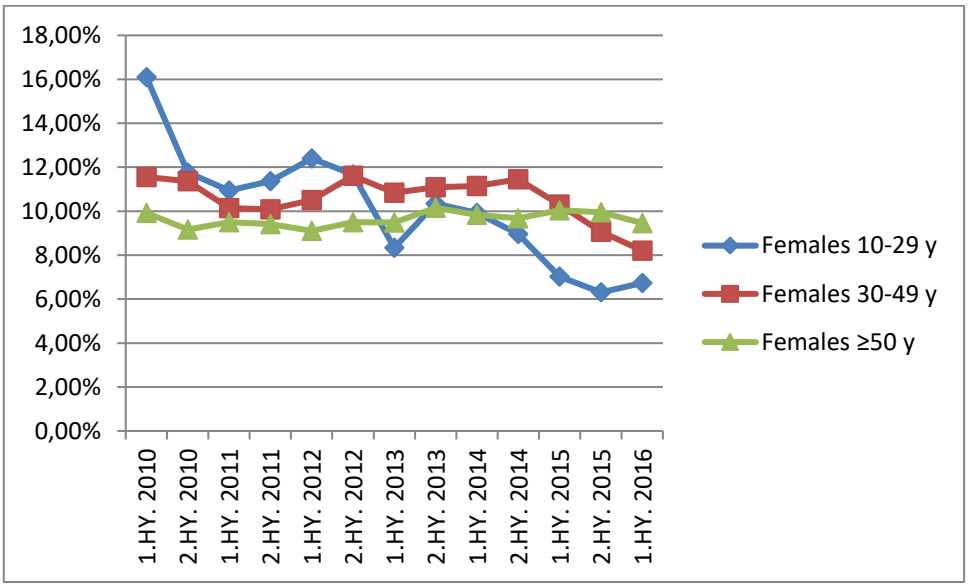


Figure 21 Prevalence of valproate per 1000 active neurologist patients in IMS Germany by 6-monthly periods

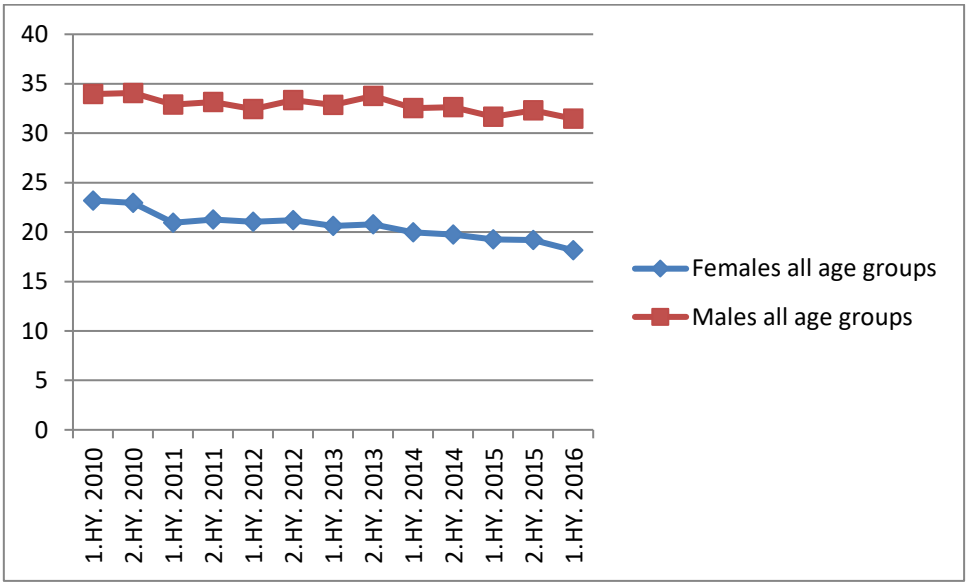


Figure 22 Prevalence of valproate per 1000 active neurologist patients in IMS Germany by age group and 6-monthly periods

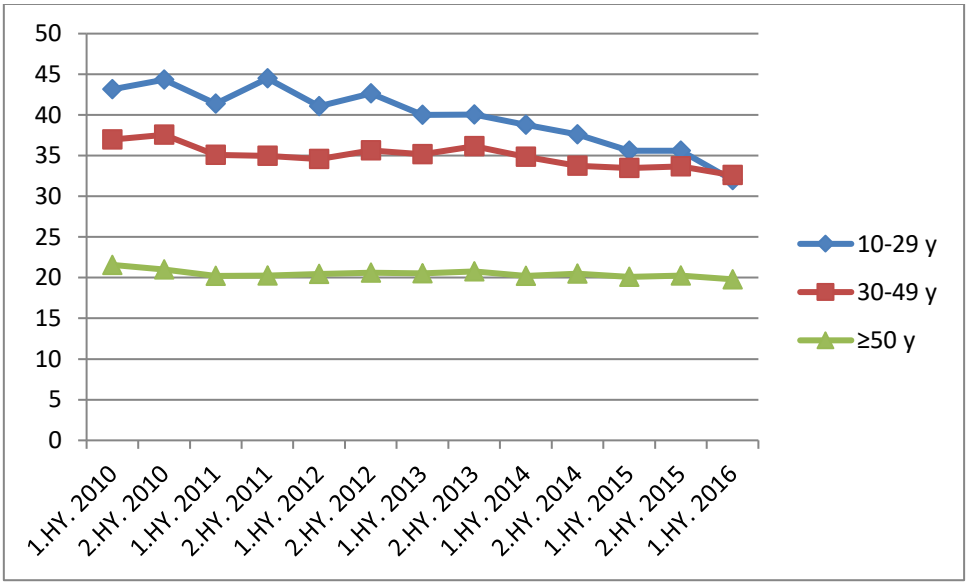


Figure 23 Prevalence of valproate per 1000 active male neurologist patients in IMS Germany by age group and 6-monthly periods

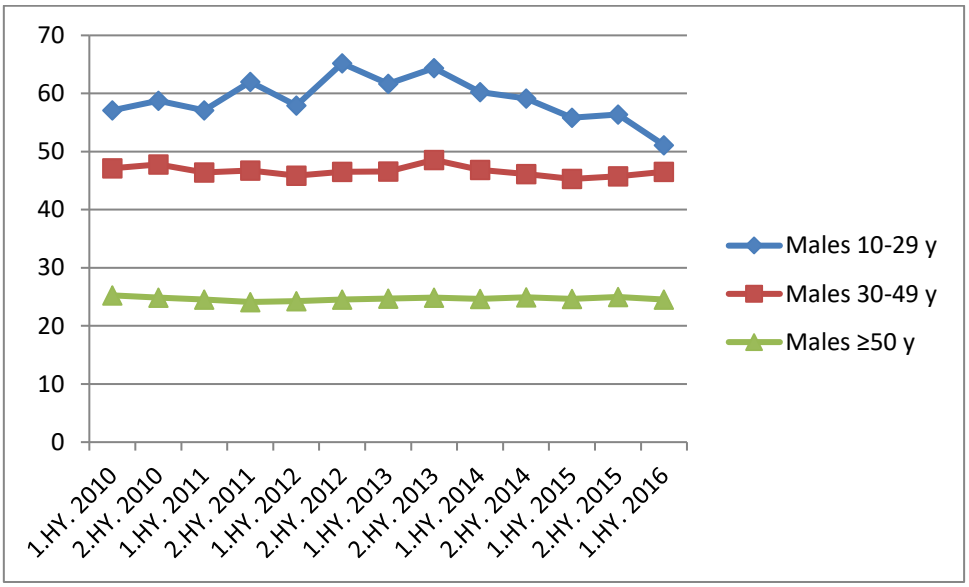
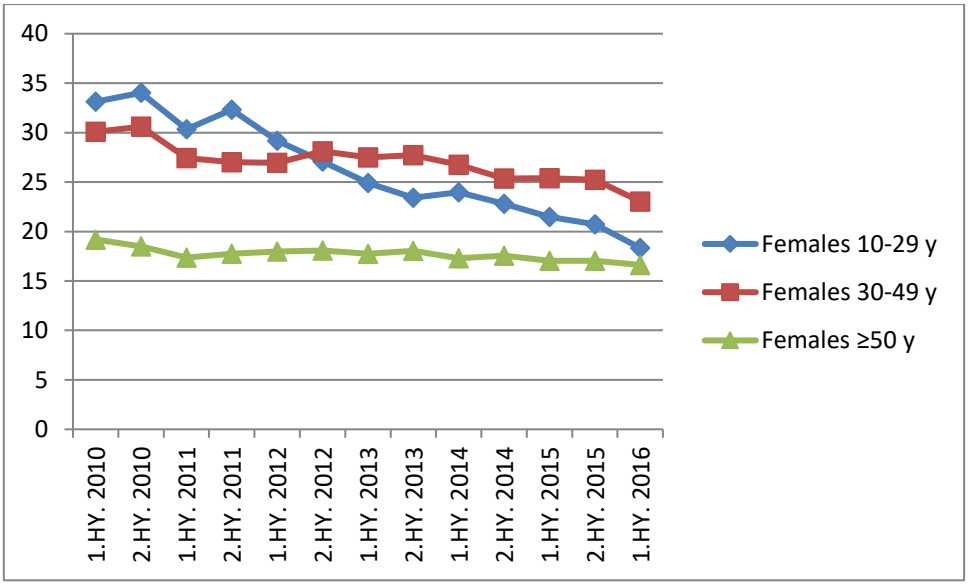


Figure 24 Prevalence of valproate per 1000 active female neurologist patients in IMS Germany by age group and 6-monthly periods



5.4. UK THIN analysis in people with bipolar disorder

The cohort consisted of 41,666 patients with bipolar disorder (60.2 % female, mean duration of follow-up 5.8 years). The overall prevalence of valproate prescribing in people with bipolar disorder rose from 1.8% in 2000 to a high of 12.9% in 2011q3 following which it appeared to fall slightly (figure 37). The prevalence of valproate prescribing was similar for men and women until 2007 when the prevalence of valproate prescribing in women started to fall compared to men (figure 38). In women, the prevalence of valproate prescribing began to fall gradually from a high of 12.2% in 2010q4. In contrast, the prevalence of valproate prescribing in men continued to rise until 2014 when it then began to fall from a high of 14.4% in 2013q4.

The prevalence of valproate prescribing by age group is shown in in figure 39. The prevalence of valproate prescribing in people aged 10 to 29 years increased to a high of 11.3% in 2005q4 and then appeared to gradually fall to a low of 7.4% in 2015q4. The prevalence of valproate prescribing in people aged 30 to 49 years increased to a high of 13.6% in 2010q and then appeared to gradually fall to a low of 10.4% in 2015q4. The prevalence of valproate prescribing in people aged over the age of 50 years increased to 13.4% in 2013q4 when it then appeared to plateau.

The prevalence of valproate prescribing for women of child bearing age is shown in in figure 40 and show similar trends as for age groups with gender combined although with steeper falls in trend. In contrast, trends for men by age group were similar but did start to fall in men aged 10 to 29 years in 2012q2 (figure 41).

Figure 6 Prevalence of valproate prescribing in people with bipolar disorder in the UK

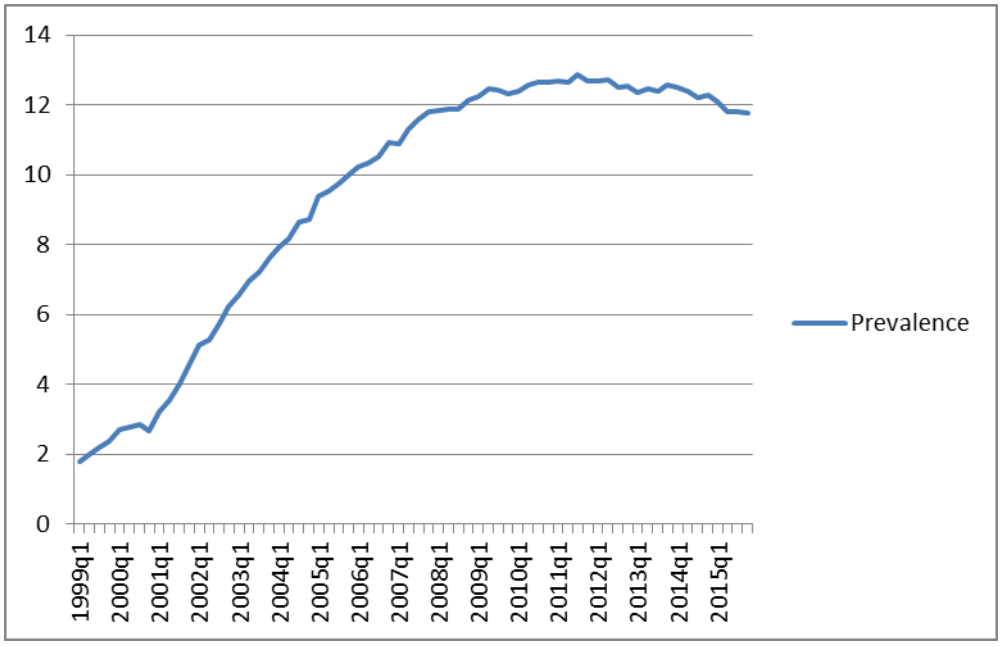


Figure 7 Prevalence of valproate prescribing in people with bipolar disorder in the UK by gender

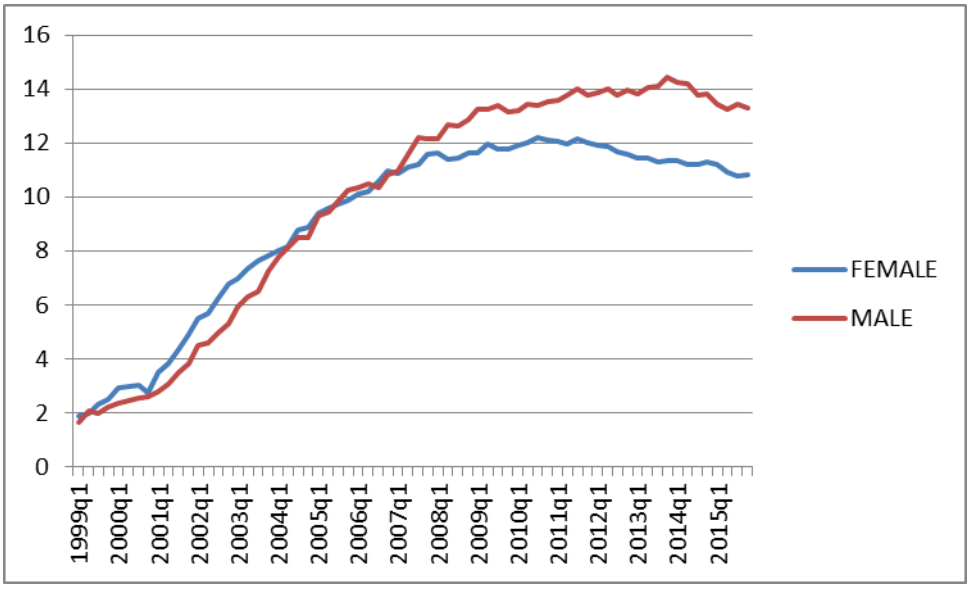


Figure 8 Prevalence of valproate prescribing in people with bipolar disorder in the UK by age

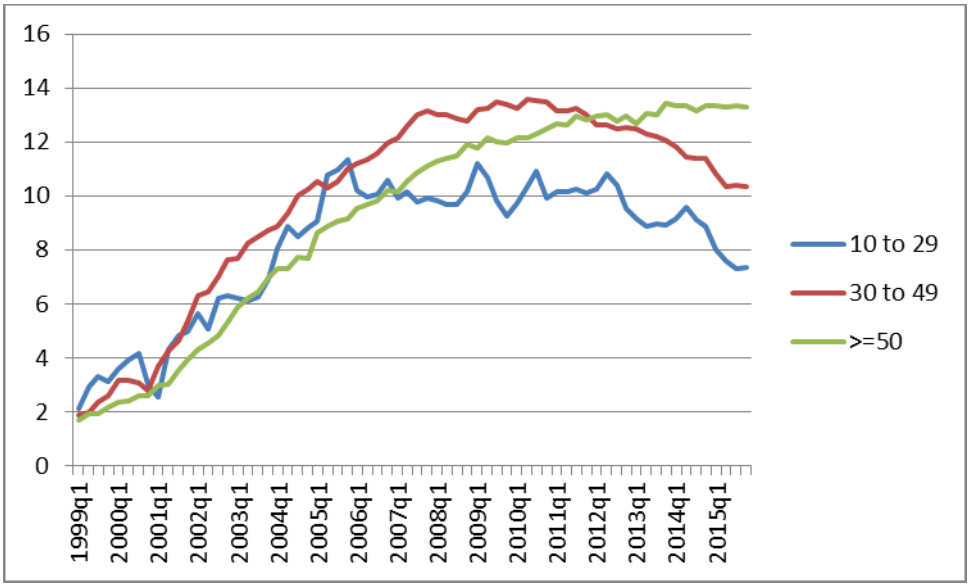


Figure 9 Prevalence of valproate prescribing in women with bipolar disorder in the UK by age

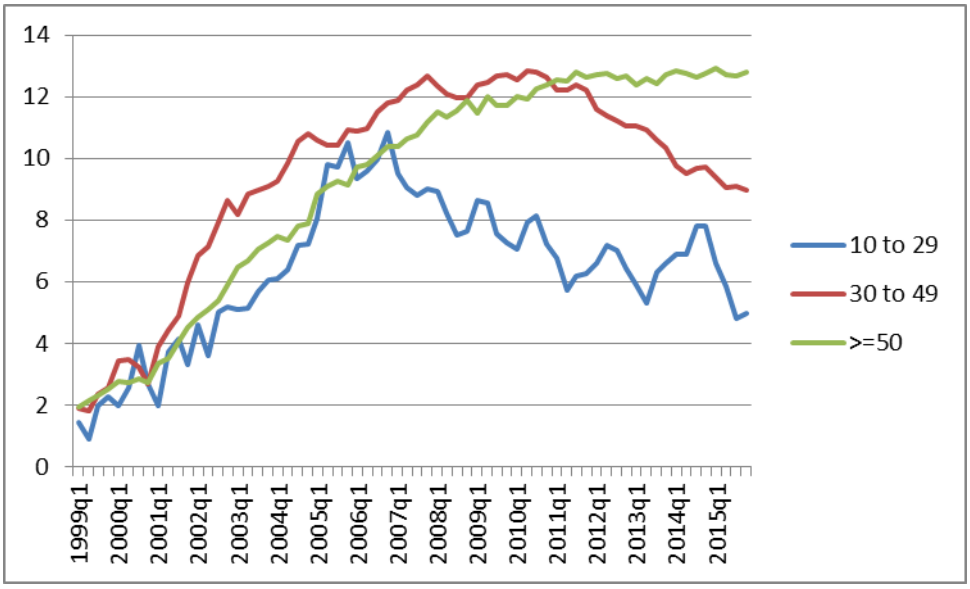
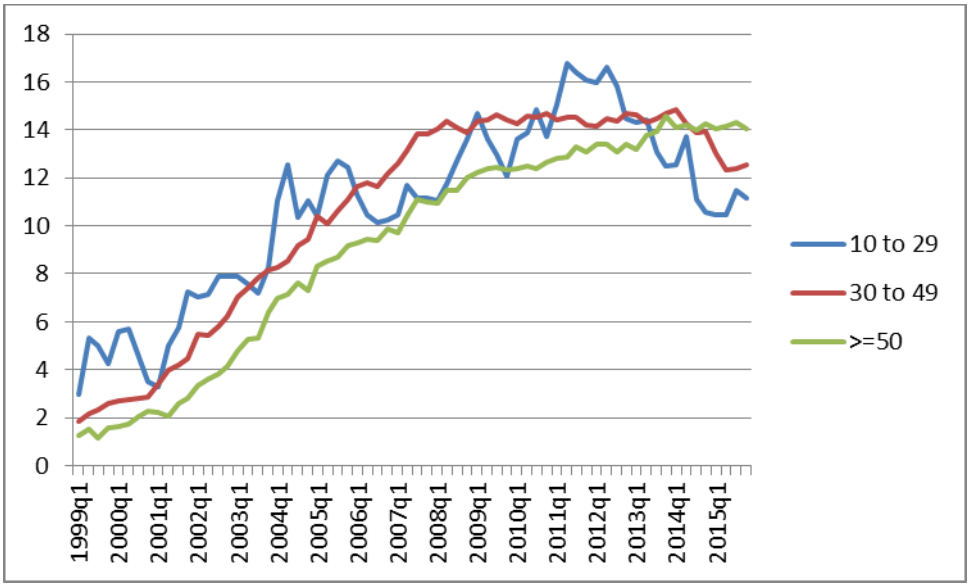


Figure 10 Prevalence of valproate prescribing in men with bipolar disorder in the UK by age



5.5. UK THIN analysis using the total THIN population

This analysis was based upon all patients in the THIN database and did not use the cohort definition as used in bipolar cohort (section 5.4). Among 15,215,057 patients in the THIN database, a total of 4,259,808 prescriptions containing valproate were issued to 106,591 patients in the THIN database (total population 15,215,057 patients). Of patients prescribed valproate, the most commonly recorded condition was for epilepsy (50.7% of patients), followed by migraine (11.6% of patients) had and bipolar disorder (10.2% of patients) based upon codes recorded at any point within their electronic medical record. Around 6% of patients had more than one condition coded within their electronic medical record (table 1).

Condition	Frequency (%)
Epilepsy only	49046 (46.0)
Migraine only	7159 (6.7)
Bipolar disorder only	9036 (8.5)
Epilepsy + migraine	4151 (3.9)
Bipolar disorder + migraine	912 (0.9)
Bipolar disorder + epilepsy	774 (0.7)
Bipolar disorder + epilepsy + migraine	103 (0.1)
Unclassified	35410 (33.2)
Total	106591 (100)

Yearly time trends for valproate prescribing for men and women are presented in figures 42 and 43 below. Overall, valproate prescribing trends increased in women aged 50 years and over during the study period then gradually began to fall in 2012. Valproate prescribing trends progressively fell in women in the 10-29 age group (figure 42). For women in the 30-49 age group, valproate prescribing appeared to increase slightly until 2004, then appeared to plateau and then appeared to fall slightly. In men, valproate prescribed appeared to increase in men aged 30 years and over with prescribing in the 10-29 age group remaining stable during the study period (figure 43).

Figure 42. Proportion of female patients in THIN prescribed valproate per 100 patients

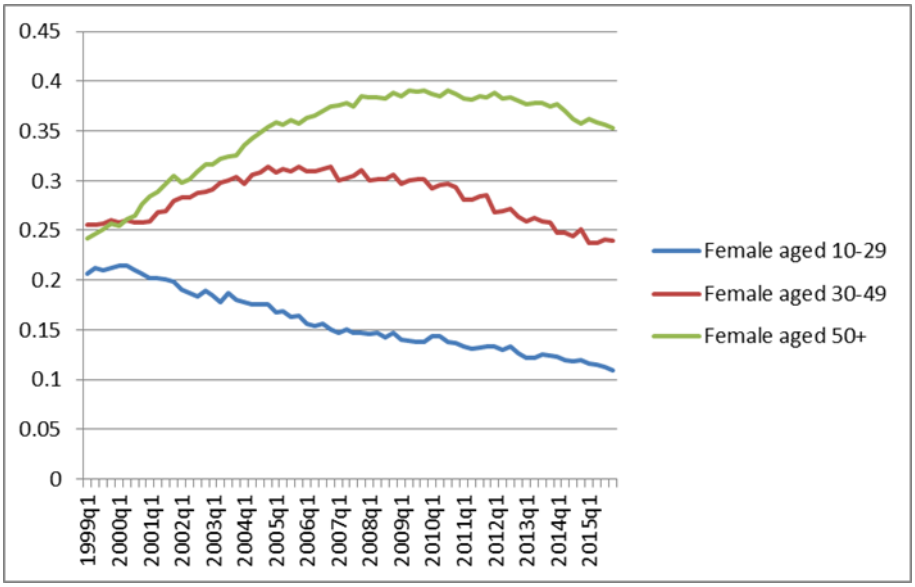
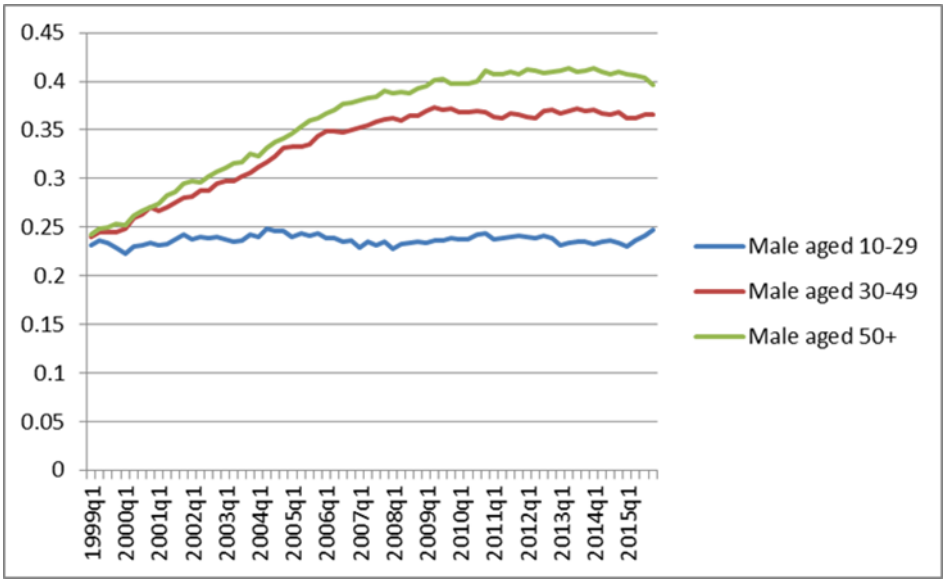


Figure 43. Proportion of men in THIN prescribed valproate per 100 patients



5.6. UK THIN analysis in people with epilepsy

A total of 136,631 patients had one or more Read code for epilepsy within the observation period. Yearly time trends for valproate prescribing for men and women with epilepsy are presented in figures 44 and 45 below. The prevalence of valproate prescribing in women aged 10 to 29 years with epilepsy was 22.8% in 1999 and fell to 12.3% by 2015. The prevalence of valproate prescribing in women aged 30 to 49 years with epilepsy was 27.8% in 1999 and fell to 17.5% by 2015. The prevalence of valproate prescribing in women aged 50+ years with epilepsy was 25.4% in 1999 and was 24.5% in 2015. Overall, valproate prescribing trends increased in women aged 50 years and over until 2012 when they gradually began to fall. Valproate prescribing trends in people with epilepsy appeared to be initially flat and then began to fall in women in the 10-29 and 30-49 age groups from 2004 (figure 44). In men, valproate prescribed trends appeared to increase in all age groups until 2004 when prescribing trends then appeared to flatten (figure 45). From 2012/2013 valproate prescribing trends in older men may have started to fall.

Figure 44. Proportion of women with epilepsy in THIN prescribed valproate

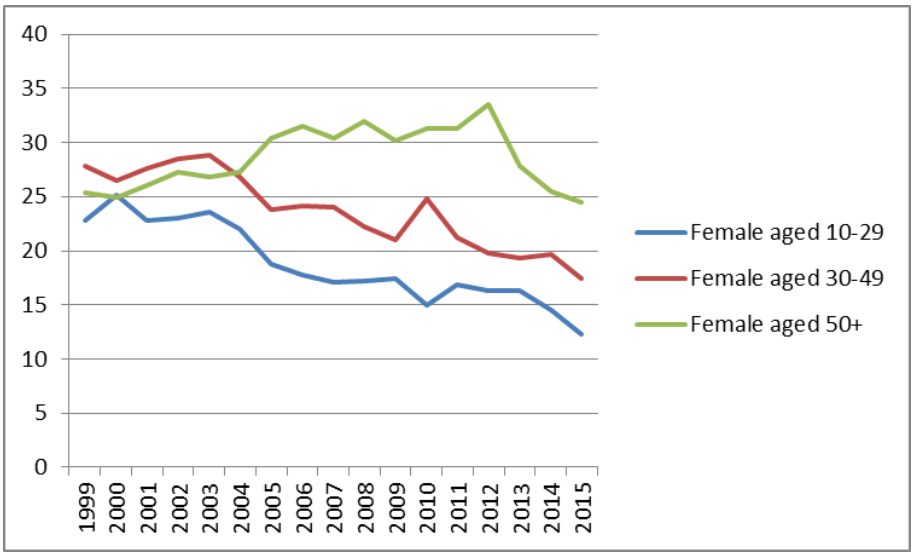
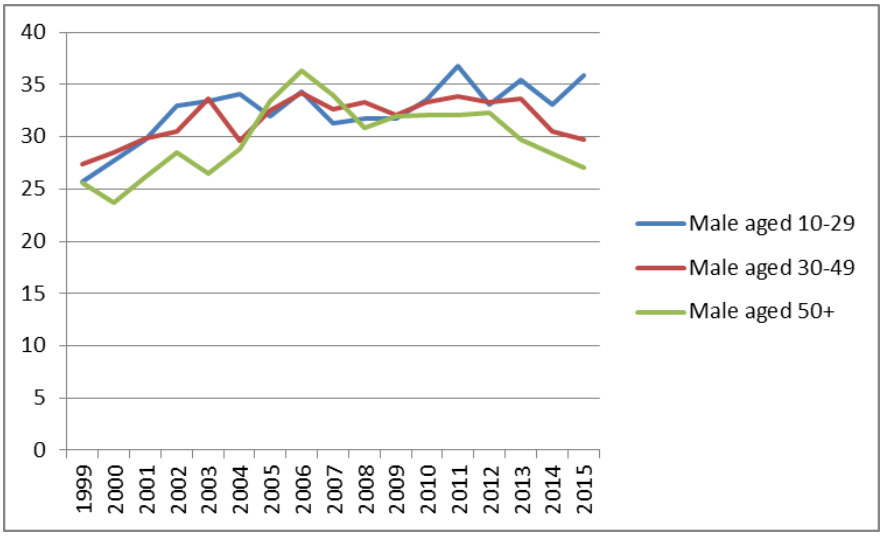


Figure 45. Proportion of men with epilepsy in THIN prescribed valproate



5.7. UK THIN analysis in people with migraine

A total of 541,987 patients had one or more Read code for migraine within the observation period. Yearly time trends for valproate prescribing for men and women with migraine are presented in figures 46 and 47 below. The prevalence of valproate prescribing in women aged 10 to 29 years with migraine was 0.3% in 1999 and 0.2% in 2015. The prevalence of valproate prescribing in women aged 30 to 49 years with epilepsy was 0.8% in 1999 and 1.0% in 2015. The prevalence of valproate prescribing in women aged 50+ years with epilepsy was 0.7% in 1999 and was 1.2% in 2015. Overall, valproate prescribing trends increased in women aged 50 years and over until 2012 when they gradually began to fall. On the whole, valproate prescribing trends remained stable in women in the 10-29 age group although may have fallen from 2014 and where prescribed to only a small proportion of women (figure 46). For women in the 30-49 age group, valproate prescribing trends appeared to increase until around 2009 and then appeared to fall. In men, valproate prescribed trends appeared to increase in older age groups with flat (stable) prescribing trends in men aged 10 to 29 years (figure 47).

Figure 46. Proportion of women with migraine in THIN prescribed valproate

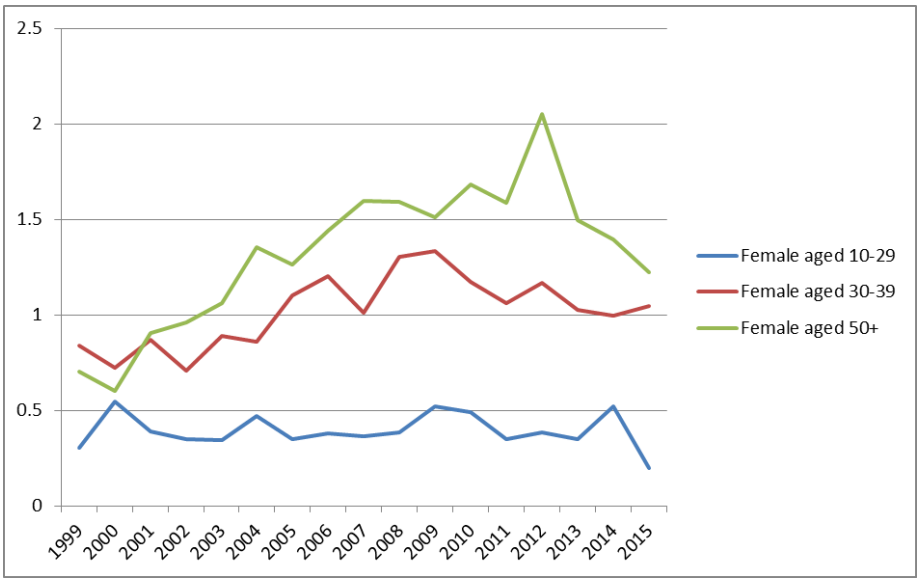
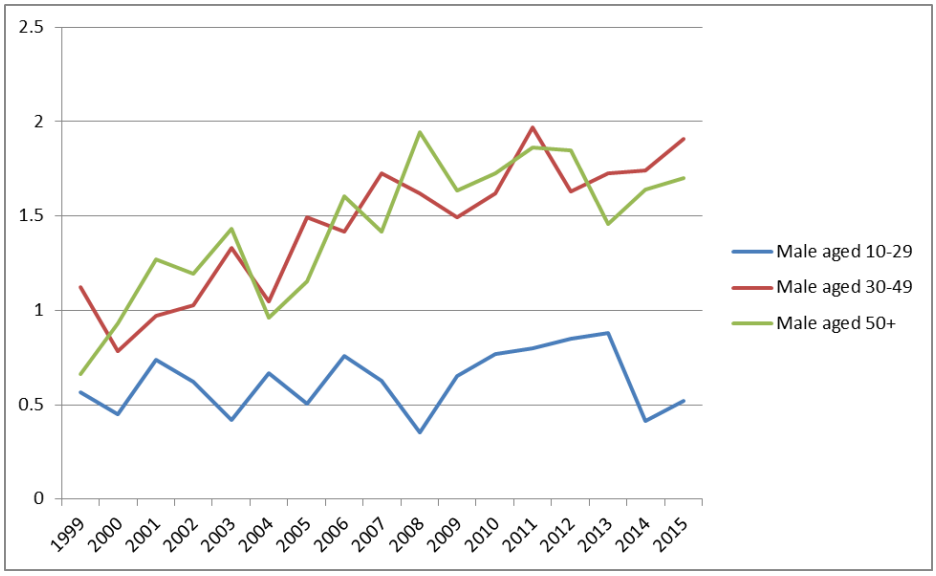


Figure 47. Proportion of men with migraine in THIN prescribed valproate



6. Discussion

6.1. IMS France

In the age groups 10-29 years and 30-49 years, there was a slight decrease in the proportion of patients with bipolar disorder that received a prescription for valproate or valpromide between 1 January 2010 and 30 June 2016. The oldest age group instead showed a slight increase. Results were similar for male and female patients.

Total prescribing of valproate or valpromide per 1000 active patients also decreased in the age groups 10-29 years and 30-49 years. The decreases were more pronounced in female patients.

The data show that there has been a decrease in total prescribing of valproate or valpromide. In patients with bipolar disorder similar decreases can also be identified.

6.2. GP patients in IMS Germany

There was a slight increase in the proportion male patients with bipolar disorder and a slight decrease in the proportion female patients with bipolar disorder that received a prescription for valproate between 1 January 2010 and 30 June 2016, albeit with marked variations. The middle age group showed a slight decrease and the youngest and oldest age groups showed no apparent changes, but fluctuations were marked. Gender specific prevalence by age group showed even more fluctuations. However, there appeared to be a slight decrease in female patients 30-49 years and ≥50 years, and a slight increase in male patients ≥50 years. The youngest age group could not be assessed.

Total prescribing of valproate per 1000 active patients decreased in all age groups in both genders. The data show that the decrease in total prescribing of valproate could only be identified in female patients with bipolar disorder, particularly in the age groups 10-29 years and 30-49 years. In male patients with bipolar disorder, no decrease in prescribing of valproate could be identified. Rather, prescribing appeared to have increased somewhat in male patients.

6.3. Neurologist patients in IMS Germany

There was a slight decrease in the proportion of female and male patients with bipolar disorder that received a prescription for valproate between 1 January 2010 and 30 June 2016, although in male patients the age group 30-49 years showed a slight increase, and in female patients the age group ≥50 years showed almost no change.

Total prescribing of valproate showed a decrease in both genders, which was more pronounced in female patients and in the age group 10-29 years. The age group 10-29 years showed a decrease in both genders, and age groups 30-49 years and ≥50 years showed a decrease in female patients and no apparent change in male patients.

The data show that the decrease in total prescribing of valproate in female patients 10-29 years and 30-49 years could also be identified in patients with bipolar disorder, whereas the decrease in total prescribing of valproate in female patients ≥50 years and in male patients 10-29 years could not be identified in patients with bipolar disorder.

6.4. UK THIN

In UK THIN, the proportion of patients with bipolar disorder that have been prescribed valproate reached a plateau in 2011, and has since then fallen slightly. In patients in the age group 10-29 years, there has been a gradual fall since 2006, and in the age group 30-49 years there has been a gradual fall since 2010. In contrast, there has been no decrease in the age group ≥ 50 years, which has gradually increased and remained stable in the last two years. The decreases noted in age groups 10-29 years and 30-49 years have been steeper in female compared to male patients. The majority of valproate prescribing may be indicated for epilepsy. In contrast to bipolar disorder where the trend in prescribing valproate in younger women initially increased, valproate prescribing in younger women (aged 10-29 years) using the entire THIN cohort appeared to fall in contrast to men where it remained stable. Similar falling trends in valproate prescribing where observed in women aged 30-49 years but this trend began to fall later from around 2008 onwards.

Valproate prescribing trends in people with epilepsy appeared to be initially flat and then began to fall in women in the 10-29 and 30-49 age groups from 2004 in contrast to men where the prescribing trend increased and then flattened around 2005 in all age groups. For people with migraine, vlproate prescribing trends appeared to remain stable in women in the 10-29 age group (although may have started to fall from 2014) and were prescribed in a low proportion of women.

7. Conclusion

In IMS France, total prescribing of valproate or valpromide decreased in the age groups 10-29 years and 30-49 years in both genders. In GP patients in IMS Germany, total prescribing of valproate (valpromide was not prescribed in IMS Germany) decreased in all three age groups in both genders. In neurologist patients in IMS Germany, total prescribing of valproate decreased in the age group 10-29 years in both genders and in age groups 30-49 years and ≥50 years in female patients.

The observed decreases in total prescribing of valproate or valpromide could also be identified in patients with bipolar disorder in IMS France. In IMS Germany, particularly in GP patients, observed decreases in total prescribing of valproate could only be identified in female patients with bipolar disorder.

In the UK, prescribing of valproate to patients with bipolar disorder in the age groups 10-29 years and 30-49 years have gradually decreased during the period 2010 to 2015, particularly in female patients. In the age group ≥50 years prescribing has increased during the period, and plateaued in the last two years. Valproate prescribing in younger women using the entire THIN cohort appeared to show a falling trend in prescribing throughout suggesting that trends in valproate prescribing over time for different indications may not be the same. For people with epilepsy, valproate prescribing appears to have fallen in the at risk age groups over the observation period with the largest reductions in women aged 10 to 29 years of age. Only a small proportion of people with migraine appeared to be prescribed valproate.