

Antipsychotic prescribing in GMS paediatric and young adult population in Ireland 2005–2015: repeated cross-sectional study

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Objectives: To examine the rates of antipsychotic prescribing in the Irish paediatric and young adult population enrolled in the Irish General Medical Services Scheme pharmacy claims database from the Health Service Executive Primary Care Reimbursement Services database, with a focus on age and sex differences. To examine concomitant prescribing of certain other related medicines in this population.

Methods: Data were obtained from the Irish General Medical Services (GMS) scheme pharmacy claims database from the Health Service Executive (HSE) – Primary Care Reimbursement Services (PCRS). Participants included children aged <16 years and youth aged 16–24 years availing of medicines under the HSE-PCRS GMS scheme between January 2005 and December 2015. Outcome measures included prescribing rates of antipsychotics from 2005 to 2015, differences in prescribing rates between different ages and sexes, and percentage of concomitant prescriptions for antidepressants, psychostimulants, anxiolytics and hypnotosedatives.

Results: Overall the trend in prescribing rates of antipsychotic medications was stable at 3.94/1000 in 2005 compared with 3.97/1000 in 2015 for children <16 years, and 48.37/1000 eligible population in 2005 compared to 39.64/1000 in 2015 for those aged 16–24. There was a significant decrease in prescribing rates for males in the 16–24 age group.

Conclusions: While rates of antipsychotic prescribing have decreased or remained stable over the timeframe of the study, we did find a significant proportion of this population were prescribed antipsychotics. This study also shows that co-prescribing of antidepressants increased and highlights the need for guidelines for antipsychotic prescribing in children and youth in terms of clinical indication, monitoring, co-prescribing and treatment duration.

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Introduction

Antipsychotic medications (APs) are major tranquilisers used primarily in the treatment of psychotic disorders but also increasingly for treatment of non-psychotic disorders, such as mixed or manic episodes in bipolar disorder, irritability in autism spectrum disorder (ASD) and conduct disorder. They are classified broadly as first and second generation, also referred to as typical and atypical APs respectively. APs result in dopamine blockade in the main dopaminergic pathways in the brain. The different APs have variable receptor binding profiles, with different APs acting

on serotonin, histamine and dopamine receptors (Reynolds & Kirk, 2010). A trend towards increased prescribing rates of APs, particularly atypical APs, has been attributed to several factors including the reduced rate of extra-pyramidal side effects, the broadening clinical indications for their use, and off label prescribing, such as attention deficit hyperactivity disorder, and other disruptive behaviour disorders (Olfson *et al.* 2012; Ronsley *et al.* 2013; Verdoux *et al.* 2010). Although atypical APs have reduced extrapyramidal side-effects compared with typical antipsychotics, it is now widely recognised that they confer greater risks of weight gain and the metabolic syndrome which are associated with significant morbidity (Clarke, 2004).

In the Irish paediatric population, a number of APs are used in the treatment of psychosis and bipolar disorder, including risperidone, aripiprazole, quetiapine and olanzapine. AP licensing is however quite limited

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compared to other countries as they are not licensed for the management of irritability in ASD even though they are commonly prescribed for this indication. There are currently no all-encompassing guidelines for AP prescribing in the paediatric population in Ireland. In Ireland, aripiprazole is licensed for the treatment of schizophrenia in children 15 years and older, and for acute manic episodes in children 13 years and older. Risperidone is licensed for the short-term symptomatic treatment of persistent aggression associated with conduct disorder or learning disability in children aged 5–18 (Health Products Regulatory Authority, 2020). In the US, the FDA have licensed low-dose risperidone and aripiprazole for the treatment of irritability in autism spectrum disorders (ASD) and conduct disorder, for mixed or manic episodes in the context of bipolar disorder and Tourette's disorder (Olsson *et al.* 2012).

The evidence from a number of community surveys indicates that AP prescribing in paediatric populations is growing internationally (Ronsley *et al.* 2013). Studies in the US of Medicaid enrolled youth indicated that they were four times more likely to be prescribed APs compared with the privately insured population (Wilson, 2009). A study comparing Medicaid-insured youth who were in foster care found that the children in foster care were prescribed APs at more than three times the rate of Medicaid-insured youth who were not in the foster care system (Harrison *et al.* 2012).

Studies on rates of prescribing of antidepressant medications, benzodiazepines and psychostimulants in children and adolescents have been undertaken previously in an Irish context (O'Sullivan *et al.* 2015a, 2015b). Rates of psychostimulant prescribing were reported to have increased during the same time period as this study. To date no investigation has been undertaken of AP prescribing in children and young adults in Ireland. Given increases in prescribing of APs reported in other countries and the extension of the license for APs to treat disruptive behaviour disorders in children and adolescents, we hypothesised that AP prescribing rates would also have increased in Ireland.

The aims of the study were to examine: (i) the rates of AP prescribing in a sub-section of the Irish population (children, adolescents and young adults) in Ireland over the time period from January 2005 to December 2015; (ii) the age and sex differences in prescribed antipsychotics and (iii) the proportion of co-prescribing of antidepressants, psychostimulants used in the treatment of ADHD, anxiolytics and hypnotosedatives.

Methodology

Study population and design

Data were obtained from the Irish Health Service Executive Primary Care Reimbursement Services (HSE-PCRS) pharmacy claims database. For a subset of the population who are eligible for the General Medical Services (GMS) scheme, health services are provided without cost, except for a small co-payment for medicines introduced in October 2010. Eligibility for the scheme is based on means testing with a higher threshold for those aged 70 years and over. The GMS pharmacy claims database contains basic demographic information (age and sex) and details on monthly dispensed medications coded using the WHO's Anatomical Therapeutic Chemical (ATC) classification system for each individual within the scheme.

The GMS scheme represents 28% of Irish children (<15 years old) but over-represents socially deprived and female populations (Health Service Executive, 2015). Regarding numbers of children and young adults in the PCRS scheme, in 2005 there were 77,133 aged <5 years; 105,532 aged 5–11 years; 58,558 aged 12–15 years and 98,502 aged 16–24 years. In 2015 there were 101,146 aged <5 years; 187,677 aged 5–11 years; 101,907 aged 12–15 years and 170,146 aged 16–24 years. No information on diagnosis or disease condition or outcomes of medications is available. Ethical approval for this study was not required as permission was given by the data controller (HSE-PCRS) to use the pseudo-anonymised GMS pharmacy claims data for the purpose of this study.

Children (<16 years) and young adults (16–24 years) eligible and receiving medicines under the GMS scheme between January 2005 and December 2015 were included in the study. All authorised AP medicines (N05A) were identified from the GMS database. In addition, dispensing of concomitant psychotropic medications was also examined and included anxiolytics [N05B], hypnotics and sedatives [N05C], antidepressants [N06A] and psychostimulants [N05BA].

Data analysis

The prescribing rates per 1000 GMS eligible population and associated 95% confidence intervals (CIs) for any antipsychotic medication was examined across years, by age groups (0–15 and 16–24 years) and sex. The number and percentage of concomitant psychotropic medications (antidepressants, psychostimulants (ADHD medications), anxiolytics and hypnotosedatives) in those in receipt of AP medications was calculated within each year.

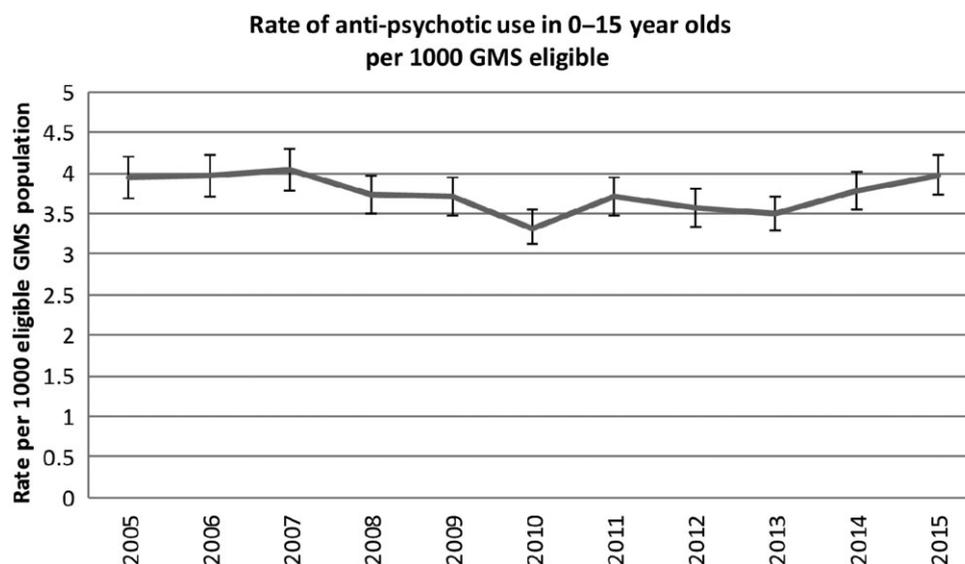


Fig. 1. Rate of antipsychotic use per 1000 eligible population in 0–15 year olds.

A negative binomial regression model was used to examine trends in rates of AP medication. The log of the GMS population was used as the offset term. Separate models for males and females were conducted with year, age group (excluding the age group 0–4 years), and the interaction included in each model. In the presence of a significant interaction results are presented by separate age groups. Prevalence rate ratios (RRs) and 95% confidence intervals (CIs) are presented.

To determine the likelihood of any concomitant psychotropic medication (yes *v.* no) a multivariable logistic regression analysis was performed including age (reference 0–15 years), sex (reference F) and year of concomitant medicine use (reference 2005) as predictors. Separate models for each age group <16 years and 16–24 years were used to examine the effect of year, sex and the interaction in relation to each concomitant medicine. Odds ratios (OR) and 95% CIs are presented. The 0–4 year age group were included in this analysis.

The maximum duration of any AP medicine use was determined by calculating the maximum number of consecutive dispensing (number of months of continual dispensing) at any time from January 2005 to December 2015 in all those in receipt of at least one item. The duration was categorized as <6 months, 6–11, 12–17, 18–23 and 24+ months.

Data analysis was performed using SAS version 9.3 (SAS Institute Inc. Cary, NC, USA). Significance at $p < 0.05$ was assumed.

Results

Study population

In 2005 there were a total of 339,725 youth aged 0–24 on the GMS list or 26.45% of the population. In 2015 there

were a total of 560,876 youth aged 0–24 on the GMS list or 36.83% of the population. The number of those aged under 16 years in receipt of at least one AP increased from 950 in 2005 (3.94/1000 eligible population) to 1552 in 2015 (3.97/1000 eligible population (Fig. 1). Figure 1 presents the rate of AP use in those aged 0–15 years over the 11 years of the study with no significant change in the rate over this period.

The proportion of males in receipt of APs also remained stable at 52.1% of the total use in 2005 compared to 57.2% in 2015. The rate of all children and adolescents in receipt of any antipsychotic aged between 12 and 15 years increased from 5.99/1000 in 2005 to 6.88/1000 in 2015, and in those under 5 years decreased from 0.82/1000 in 2005 to 0.35/1000 in 2015.

The number of young adults aged 16–24 years in receipt of any AP increased from 4822 in 2005 to 7518 in 2015, or a rate of 48.37/1000 eligible population in 2005 compared to 39.64/1000 in 2015.

Prescribing trends

Figure 2 shows the trends in the rate of AP prescribing by sex and age groups including age groups 5–11 years, 12–15 years and 16–24 years. There was a significant age by year interaction for males ($p = 0.008$) and females ($p = 0.043$); therefore, results are presented by separate age groups. The trend over time was non-significant for males aged 5–11 and 12–15 years, but there was a significant decline over time for males aged 16–24 years (RR = 0.97; 95% CI 0.96, 0.98; $p < 0.001$). For females there was a significant decline in the yearly rate of prescribing in all ages; for those aged 5–11 years (RR = 0.95; 95% CI 0.937, 0.972 $p < 0.001$), 12–15 years (RR = 0.987;

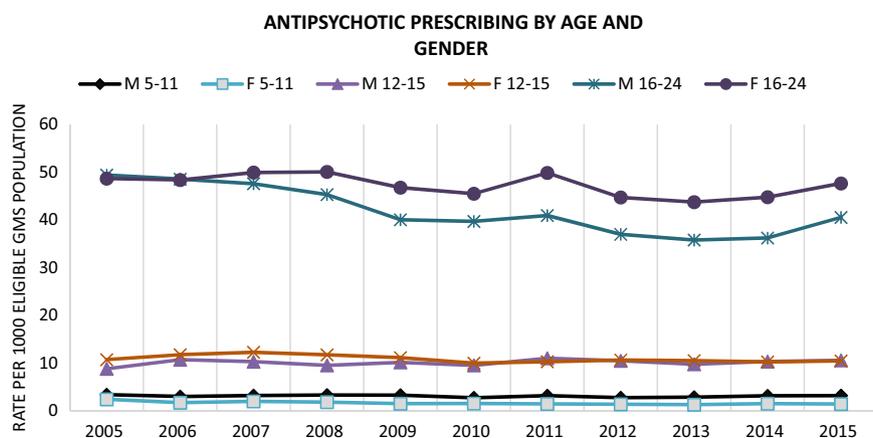


Fig. 2. Rate of antipsychotic use per 1000 eligible population by gender and age groups.

95% CI 0.978, 0.996; $p = 0.006$) and 16–24 years (RR = 0.99; 95% CI 0.984, 0.998; $p = 0.016$).

Co-prescribing trends

The percentage and type of co-prescribed medicines are presented in Fig. 3 for males (5–15 and 16–24 years) and Fig. 4 for females (5–15 and 16–24 years). There was no significant interaction of year by sex for any of the concomitant medicines in those aged <16 years; however, there was a significant year by sex interaction for all concomitant medicines in those aged 16–24 years. In particular, the proportion of any psychostimulant increased in males over time but remained low in females ($p = 0.0054$). The proportion of anxiolytics and hypnotosedatives decreased in males over time but remained stable in females ($p < 0.001$ for both), and the proportion of anti-depressants increased in both males and females over time but at a more accelerated rate in females ($p < 0.001$).

Table 1 shows the OR and 95% CI for factors predicting any concomitant use of psychotropic drugs compared to none in those already in receipt of AP medicines. Males and the older age group (16–24 years) were twice as likely to be prescribed a concomitant psychotropic medicine, and the likelihood of concomitant medicine increased significantly over time from 2010 onwards compared to the base year of 2005. Over the period 2005–2015 there were 62,131 unique cases with any AP use. The maximum duration of consecutive dispensing of any APs is presented in Table 2.

Discussion

Overall, the results of this study indicated that there was no significant increase in the rates of prescription of AP medication in children, adolescents and young adults in Ireland between 2005 and 2015. Initially, we had hypothesised that there would be an increase in

AP prescribing trends. Our hypothesis was based on both the global trend for increase in AP prescribing (Olfson *et al.* 2012; Ronsley *et al.* 2013; Verdoux *et al.* 2010) and on the results of a previous Irish study on prescribing rates of antidepressants in GMS eligible youth in Ireland (O'Sullivan *et al.* 2015), which had reported an increase in concomitant prescribing of APs with antidepressant therapy. This study also reported that prescribing rates of antidepressants in children and adolescents in Ireland decreased between 2002 and 2011; however, we did not find this in children and young adults prescribed AP medications. As the pharmacy claims database provided no access to clinical diagnosis, it is not clear why this might be the case but it may reflect an increased willingness by clinicians to prescribe multiple psychotropics to those with more severe mental health disorders (Staller *et al.* 2005; Baker & Wilens, 2019).

A number of studies have reported an increase in AP prescribing. A multinational study showed similar findings between countries. They examined AP prescribing trends in the UK, USA, Denmark, Germany and the Netherlands between 2005 and 2012 (Kalverdijk *et al.* 2017). Overall, the main findings were an increase in prescribing rates of APs across all age ranges between 2005 and 2012 in the UK, Denmark, Germany and the Netherlands. AP prescribing reduced in the USA over the time period, however rates were significantly higher in the USA initially (Kalverdijk *et al.* 2017). This study had different results to all the countries apart from the US as we also noted a decrease in AP prescribing rates. A study in France found AP prescribing is increasing but the overall rate of AP prescribing remained stable between 2006 and 2013 due to a decline in the prescriptions of typical APs (Hélène Verdoux *et al.* 2015). Other countries have had increased rates of AP prescribing. Prescribing rates for APs were reported to have increased from 1.66/1000 in 1996/97

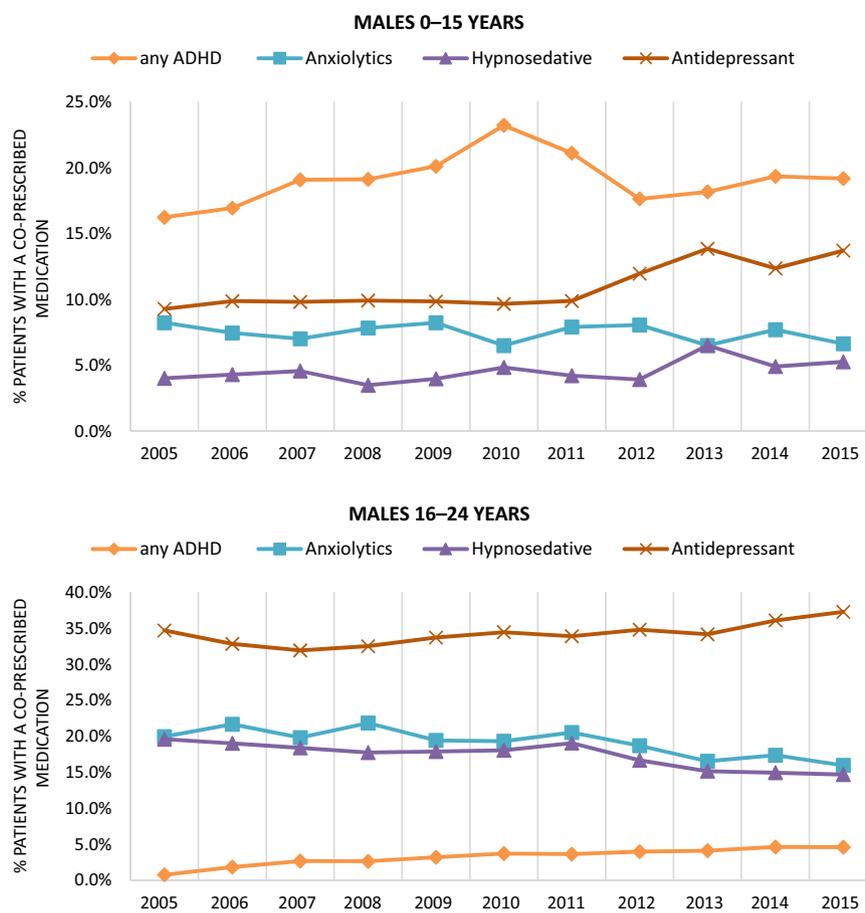


Fig. 3. Percentage and type of co-prescribed medicines in males.

to 6.37/1000 in 2010/11 in British Columbia, Canada, particularly in males aged 6–12 years (2.3–8.6/1000), males 13–18 years (2.8–10.7/1000), and females aged 13–18 years (2.8–10.7/1000). Prescribing of atypical APs increased 18-fold during the period; namely risperidone (48.0%), quetiapine (36.2%) and olanzapine (5.9%) in 2010/11 (Ronsley *et al.* 2013). A study of nationwide health data incorporating approximately 30% of all children in Germany, indicated that AP prescribing increased between 2004 and 2012 from 2.3/1000 to 3.1/1000 largely accounted for by atypical APs. Overall, there was a levelling off of total prescriptions of all neuroleptics and no change in the incidence of new prescriptions, thus the increase is likely explained by longer term prescribing in individuals commenced on APs (Abbas *et al.* 2016).

In the current study we showed that there was a significant decline in overall prescribing rates of APs in 2010, contrary to the results of the studies reported above. This coincided with a significant increase in the prescribing rate of concomitant medications. This could indicate that APs were prescribed less often for other disorders that they may have been prescribed to treat previously, such as ADHD. This trend has also

been seen in other countries due to more judicious use among youth with disorders such as ADHD which have less indication for AP use (Crystal *et al.* 2016).

There are a number of reasons why prescription of APs may not have increased in this Irish population. Shortly before the beginning of the study period, in 2004, the American Diabetes Association published a position statement on antipsychotic drugs, obesity and diabetes (Clarke, 2004). This statement stated that there is considerable evidence that APs cause rapid weight gain in the first few months that may not reach a plateau even after one year of treatment. There was also increasing consensus that APs should be treatment of last resort after behavioural treatments have been tried and failed (Gleason *et al.* 2007). In the present study, there was a decline in the prescribing of APs over time for males aged 16–24 and a significant decline in the yearly rate of prescribing in all age groups in females which we did not expect to find. This may be explained in part by the statement of concern about APs from the American Diabetes Association, published in 2004, which may have led to a reluctance in physician prescribing due to an increased knowledge about the short-term effects of APs, in particular the risk

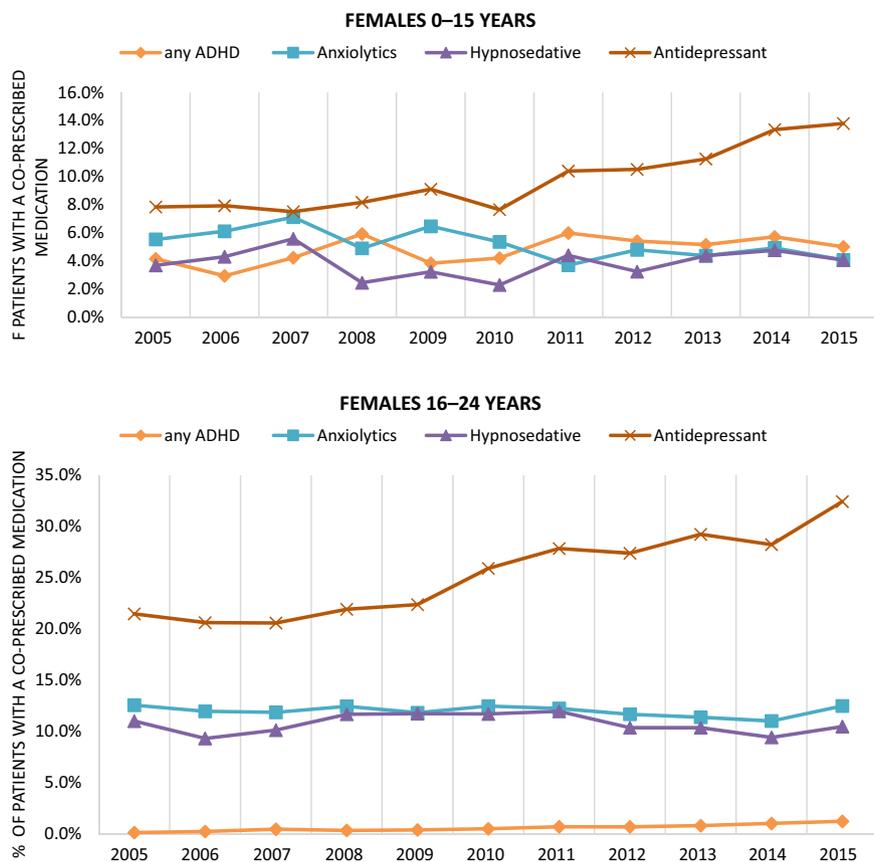


Fig. 4. Percentage and type of co-prescribed medicines in females.

of significant weight gain and metabolic complications. The decline could also possibly be due to a lack of need to prescribe AP medications due to an increase in the prescribing of psychostimulants for ADHD and antidepressants, both used as medications in disorders where APs may previously have been prescribed. However, the lack of knowledge about the clinical indication for the AP prescription makes it difficult to comment on the reasons for the decline over time in prescribing for these two groups. A French study also noted a decline in prescribing rates in the male age group 21–24 (Verdoux *et al.* 2015). Another important factor in relation to the data in the current study is that during the period of the study there was a change in the prescriber of APs in the 16–18 year age group from adult psychiatrists to child and adolescent psychiatrists. This may have had an impact on the rate of AP prescribing in this age group given potential prescribing differences between adult and child and adolescent psychiatrists.

While the rates of AP prescribing reduced in this study, the rate of concomitant prescribing of antidepressants and psychostimulants increased. We found that males and the older age group (16–24 years) were twice as likely to be prescribed a concomitant

psychotropic medicine. The likelihood of concomitant medicine increased significantly over time from 2010 onwards compared to the base year of 2005. Antidepressant medications were the most commonly co-prescribed medications in both males and females and the rate of prescribing of antidepressant medications increased between 2010 and 2015. Females were more likely to be prescribed an antidepressant than males which is probably due to females being twice as likely to develop depression as males (Kuehner, 2017). Mental health disorders such as mood disorders and anxiety disorders are more common in the 16–24 year age group so it is not surprising that this group were twice as likely to be prescribed a concomitant medication (Piovani *et al.* 2019). Previous studies have shown that overall rates of psychotropic medication prescription increase with age (Piovani *et al.* 2019; Zito *et al.* 2008). The GMS database overly represents patients from socioeconomically deprived areas and youth in lower socioeconomic groups are more likely to be prescribed a psychotropic medication (Kadra *et al.* 2016).

Even though prescribing rates reduced overall, it is important to note that one group in this study had an increase in prescribing rates and there a few factors

Table 1. Logistic regression (GEE adjusting for clustering within patients over years)

	OR	95% CI
Gender (M v. F)	2.04	2.0, 2.1
Age (16–24 v. <16 year)	1.95	1.89, 2.03
2005 (ref year)	1.00	
2006	0.99	0.92, 1.07
2007	0.97	0.90, 1.05
2008	1.02	0.95, 1.10
2009	1.06	0.99, 1.14
2010	1.15	1.07, 1.23
2011	1.20	1.12, 1.29
2012	1.16	1.08, 1.24
2013	1.20	1.12, 1.28
2014	1.21	1.13, 1.44
2015	1.34	1.24, 1.43

Table 2. Duration of consecutive dispensing of anti-psychotics in those aged 0–24 years from 2005 to 2015

	Number of cases (at least one item between 2005 and 2015)	% of all
<6 months	55977	90.1
6–11 months	3226	5.2
12–17 months	1354	2.2
18–23 months	733	1.2
≥24 months	841	1.4
Total	62131	100

which may have impacted this. The largest proportionate increase in prescribed APs was in those aged 12–15 years with an increase from 59.9% in 2005 to 68.8% in 2015. This may reflect the increase in prevalence of mental health disorders in this age group. In July 2009, risperidone was licensed in Ireland for the short-term symptomatic treatment, up to 6 weeks, of persistent aggression in conduct disorder which may have led to increased prescribing rates in this group. There was a decline in the percentage of those under 5 years prescribed APs which could indicate a reluctance to prescribe APs in children under 5 years, given their side effects. This decline has also been found in studies from other countries (Kalverdijk *et al.* 2017; Verdoux *et al.* 2015).

In relation to duration of AP use, more than 90% of consecutive prescriptions for APs appear to have been for a duration of less than 6 months, while 4.8% were consecutively prescribed for a period lasting more than 12 months. Considering all dispensings, the proportion prescribed APs for more than 12 months increased from

4.8% to 8.9%. The short time period of prescribing is possibly due to APs being prescribed for behavioural difficulties with the aim to prescribe them in the short term and possibly due to concerns about side effects. However, the HSE-PCRS GMS data set does not collect information about the indication for prescriptions or about the setting in which the prescription was initiated (e.g. primary care, hospital or specialist setting). Therefore, it is unclear why the AP prescriptions were initiated and why they were mainly used for short periods of time.

A small but significant proportion (8.9%) of those receiving APs received repeat prescriptions for longer than 1 year. This is concerning due to the significant side-effects associated with antipsychotic use. It is possible that these are youth with emerging severe and enduring mental health disorders. However, AP prescribing in children is typically for non-psychotic conditions such as disruptive behavior (Penfold *et al.* 2013). Children and adolescents are more sensitive to the side-effects of APs (Correll & Carlson, 2006). Moreover, there are additional health and safety concerns associated with the longer-term use of AP medications, particularly cardiometabolic side-effects that can predispose to chronic disease in adulthood. Cardiometabolic risks are considerably increased in youth exposed to APs for the first time; weight gain and disturbances in lipid and metabolic parameters are reported (Correll & Carlson, 2006). The impact of overweight and adverse metabolic profiles on morbidity and mortality is well documented (Baker *et al.* 2007), although the long-term impact of exposure to APs in paediatric populations has not been studied. Additionally, some APs (e.g. risperidone) are associated with elevations in the hormone prolactin which has been associated with reductions in bone mineral density, increasing risk for osteopenia (Calarge *et al.* 2013). As a consequence of these and other side effects it is recommended that APs are used judiciously and with close monitoring in the paediatric population (Daviss *et al.* 2016).

Strengths and limitations

This is the first large scale study on the use of APs in a paediatric and young adult population in Ireland. There are a number of limitations, mainly relating to the database used for the study, however it is important to note that this is the only prescribing database in Ireland.

The main limitation is that the HSE-PCRS GMS scheme pharmacy claims database represents approximately one-third of children in Ireland and over-represents more socially disadvantaged children in the population aged under 15 years. This may result

in an overestimation of the true trends in antipsychotic prescription rates, given that children from lower socioeconomic backgrounds are more likely to be prescribed a psychotropic medication. Studies in other countries found that AP prescribing is increased in youth who are publicly insured, particularly in the US (Crystal *et al.* 2016). This study reports on prescribing rates between 2005 and 2015, therefore it is unknown if prescribing rates have increased since then.

Another limitation is that the GMS dataset used in this study does not collect information on the indication for prescribing or about where the medication was prescribed (e.g. primary care, hospital or specialist child and adolescent mental health service). This means that more in-depth clinical interpretation of these data were not possible. It does give us an indication of clinicians prescribing patterns over the period, but it is not possible to comment on the rates of illness.

There were also population changes over the study period that may have impacted the dataset. A different mental health prescription scheme was implemented in one area of Ireland in West Dublin and Kildare during this time period and when these young people transferred to the GMS scheme it may have caused a falsely elevated rate in AP prescribing. However, this represents one area of the country and we think the data are informative as it represents prescribing rates in the PCRS across the rest of the country. In this study, we found that the rates of AP prescribing reduced over time, therefore this issue does not seem to have caused the rates to inflate. It is important to note that there were changes in family economics with a recession in the latter part of the study. This would have led to a higher number of people being eligible for the GMS scheme. However, this did not have an impact on AP prescribing as the rates did not increase over the study period. Taking account of these limitations, we think the data represents prescribing rates in the PCRS for a large proportion of the child and adolescent population.

It is important to note that Irish data is not as comprehensive as data from other countries where all youth have access to publicly funded prescriptions. Therefore, it is difficult to compare prescribing rates in Ireland to other countries that have more comprehensive prescription databases. This study highlights the need for more comprehensive prescribing databases in Ireland.

Implications of findings

This study has demonstrated that a significant proportion of the paediatric population in Ireland were prescribed APs between 2005 and 2015. There is increasing concern about the cardiometabolic side effects of these medications, and the National

Institute for Health and Care Excellence in the UK, the American Diabetes Association and the American Psychiatric Association have all published evidence-based guidelines for monitoring of children and adolescents who are prescribed APs (Findling *et al.* 2011; Hollis, 2016). There is a need for clinicians who prescribe APs to review these guidelines and carefully consider the clinical indication, monitoring requirements, implications of co-prescribing and duration of AP treatment. Initiatives promoting evidence-based prescribing and monitoring practices regarding AP treatment should be implemented in order to reduce the risks of cardiometabolic side effects in this child and adolescent and young adult population. This study highlights the levels of concomitant prescribing with AP medications and the need for coherent prescribing guidelines. Future research in this area and improvement in clinical practice may be possible if clinical indication was a component of the HSE PCRS database. Due to the number of young people prescribed APs and other psychotropic medications, there is a clear need for coherent all-encompassing prescribing guidelines in Ireland for physicians to follow.

Conclusion

Trends of AP prescribing in the GMS population in Ireland show that AP prescribing has remained relatively stable over the study period in 0–15 year olds with a decline in prescribing in 16–24 year olds. A small proportion of youth are prescribed APs for longer than 1 year which increases the risk of long-term cardiometabolic side effects. There was a significant increase in co-prescription of antidepressant medication in female children and young adults. Further research is required to understand the factors that are associated with the longer-term use of APs in youth. National guidelines on antipsychotic use in children and adolescents are desirable to support safe and appropriate prescribing practices. Future studies should examine prescribing trends in association with the clinical indications for initiating and continuing AP medications. There is also an urgent need for better databases for recording of prescribing data in Ireland.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that ethical approval for publication of this paper was not required by their local Ethics Committee.

The study was based on data obtained from the HSE-PCRS.

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