Mark Drakeford AC / AM
Y Gweinidog Iechyd a Gwasanaethau Cymdeithasol
Minister for Health and Social Services

Llywodraeth Cymru
Welsh Government

Ein cyf/Our ref MA(P)MD-0805-16

Ann Jones
Chair
Children, Young People and Education Committee
National Assembly for Wales
Cardiff Bay
CF99 1NA

26 February 2016

Dear Ann,

Further to my appearance before the Committee to discuss Child and Adolescent Mental Health Service (CAMHS) I undertook to provide some further information.

You requested copies of the Welsh Health Circular relating to prescribing antidepressants to children and young people; the final report by Swansea University on the analysis of antipsychotics; and the January *Together for Children and Young People* programme report. These are all attached with this letter.

As far as the antipsychotic report is concerned, it paints a similar picture as the earlier reports on ADHD and antidepressant medication, in as much as it supports studies elsewhere which show an increase in prescribing across the western world. Following receipt of the report I have asked my officials to issue a Welsh Health Circular reiterating to GPs, CAMHS clinicians and pharmacists the requirements of NICE guidance and the British National Formulary for Children in relation to prescribing practice. I will also ask the NHS's CAMHS Planning Network to consider the report and what further work may be required as a result of the issues it raises.

You also asked for details on the psychological therapies available to young people and whether they will be available across Wales. You are aware we are investing over £1m of the new CAMHS funding to expand psychological therapies, creating almost 19 new whole time equivalent posts. In time I would hope this will ensure less reliance on medication as access to these therapies expands. Such therapies have always formed a core part of CAMHS provision and the main ones employed include Cognitive Behavioural Therapy, Systemic Family Therapy, Dialectical Behaviour Therapy, Eye Movement Desensitization and Reprocessing, and brief solution focussed therapies. I understand these are routine across all services.

Bae Caerdydd • Cardiff Bay
Caerdydd • Cardiff
CF99 1NA

English Enquiry Line 0300 0603300
Llinell Ymholiadau Cymraeg 0300 0604400
Correspondence.Mark.Drakeford @wales.gsi.gov.uk

During the session on 10 February you also asked for further detail on the availability of data collected at secondary care level on prescription drugs for children and young people with ADHD. Professor Ann John who led the prescribing analysis has confirmed that SAIL does not have access to secondary care prescribing. However, there are proposals for some pilots to take place and SAIL is looking at Abertawe Bro Morgannwg University Health Board data from Morriston, though this is in its early stages of development. Elsewhere, data is available for supplies of ADHD drugs within secondary care. It is possible to differentiate between outpatient and inpatient supplies, however inpatient supplies may be made to the ward as stock rather than for individual patients. For both outpatient and inpatient supplies, where supplies are made on an individual patient basis data is not available which identifies whether the patient was a child or young person.

We also agreed I would provide a response to several questions that were not reached during the session. My response to each is as follows:

Q1 - In what way does the Minister envisage the Together for Children and Young People review will move away from the existing clinic based 9-5 model of delivering specialist CAMHS, given that this approach was the subject of much criticism in evidence to the original inquiry.

Together for Children and Young People is all about addressing the needs of young people in the most appropriate setting, keeping them out of specialist CAMHS if at all possible. We are seeking to promote provision of other services, which will naturally be held in settings appropriate to the service provided. For example, schools counselling, where services are not only available in schools but other community settings. Data published on 18 February (SDR18/2016) showed over 11,500 pupils received counselling in the 2014/15 academic year, with 89% completing their counselling without the need for onward referral.

However, I also want to ensure NHS services are available in the community, which is why I am pleased that during 2015 the NHS achieved all-Wales coverage for CAMHS community intensive treatment teams. This means many more contacts and face-to-face work with young people completed in their homes and local community, without the need to attend clinic. Nevertheless, we also need to recognise there is a place for the clinic model. In particular for young people experiencing severe mental illness attending regular clinics can be the most appropriate, effective and efficient way of providing their care. Both for the young person and health professionals involved, which may include a multidisciplinary team. During my evidence to Committee I mentioned the recent ‘Making Sense’ report by young CAMHS service users and in particular their view that specialist CAMHS should support much smaller numbers with the highest need; and that young people would prefer to receive support from friends, educational counselling and teachers. My officials have shared the report with health boards and asked them to reflect its findings and key messages in their work.

Q2 - How will the review address the wide range of concerns about access to CAMHS in an emergency or out of hours CAMHS provision.

To improve provision for all young people who present in crisis, whether at an emergency department, via the police or other route we have made available £2.7m to expand and improve crisis and out of hours provision. Health boards intend to recruit over 40 new whole time equivalent specialist staff in CAMHS to provide this service. Generally these young people tend to be older adolescents, it is therefore important these new CAMHS staff also work closely with adult psychiatric liaison services, in which we are also investing a further £4m. Services will be available over extended hours, though delivery models will differ across health boards in line with local need. I expect health boards to keep these services under review to ensure they are available in line with demand.

In December 2015 I launched the Crisis Care Concordat signed by the Welsh Government, police forces, the NHS, councils and other agencies. It commits organisations to working together to intervene early and reduce the likelihood of people posing a risk to themselves or others as a result of a mental health condition. Crucially it reiterates that people under 18 experiencing a mental health crisis should never be held in police custody, unless in exceptional circumstances. When these incidents do occur, case reviews will be held to determine whether this could have been avoided and to learn from the incident.

When such presentations require hospital admittance this will be in line with our admissions guidance, published in May 2015. The guidance was developed by CAMHS and adult mental health practitioners and widely consulted on. It distinguishes between cases where admission to an adult ward is unavoidable but undesirable, and those where for that individual it may be preferable. Where admission is unavoidable the overriding concern must be safeguarding the young person. They should be cared for by suitably qualified staff and, as soon as practicable, they should be moved to a more appropriate facility. It is also important that unavoidable admissions are recorded and reviewed to ensure the correct processes have been followed and that lessons can be learned.

Q3 - What tangible changes does the Minister envisage the review will deliver in respect of concerns about the transition from child to adult services.

Transition has long been an area where we have sought improvements in current practice and is a specific work-stream under Together for Children and Young People. The work-stream includes wide representation from CAMHS, adult mental health, adoption, third sector, social services and, importantly, service users.

As a start the work-stream is reviewing, for consistency and to identify good practice, health board transition protocols, which need to have been jointly agreed between CAMHS and adult services. The intention is to develop a resource pack for professionals to help ensure a smooth transition. The group has also highlighted a lack of information for service users and their representatives and plan to explore this issue further via some limited service user engagement events in the spring. The intention is to developing an information pack for the individual to help them understand and engage in the process.

I also agreed that some of the new CAMHS investment should be targeted at developing services for early intervention in psychosis, where a weight of evidence suggests future outcomes can be significantly improved by early intensive treatment. These most severe mental illnesses develop between the ages of 15 and 25. The funding of £800,000 will create over 18 wte posts in CAMHS, which will need to work across both CAMHS and adult service boundaries to improve transition for those who require ongoing care.

Best wishes

Mark Drakeford

Mark Drakeford AC / AM
Y Gweinidog Iechyd a Gwasanaethau Cymdeithasol
Minister for Health and Social Services

WHC (2015) 048

WELSH HEALTH CIRCULAR

Llywodraeth Cymru
Welsh Government

Issue Date: 8 October 2015

STATUS: INFORMATION

CATEGORY: HEALTH PROFESSIONAL LETTER

Title: Prescribing for children and young people in relation to antidepressants.

Date of Expiry / Review
N/A

For Information to:
CAMHS consultants
Paediatricians
General Practitioners
Pharmacists

Action required by:
N/A

Sender:
Dr Sarah Watkins, Senior Medical Officer

HSSG Welsh Government Contact(s) :
Richard Hockey, Health and Social Service Group, Cathays Park, Cardiff, CF10 3NQ
MentalHealthandVulnerableGroups@wales.gsi.gov.uk

Enclosure(s): Letter and current guidance

Dear Colleague

In January 2015 Welsh Government commissioned Swansea University to analyse prescribing data for children and young people in relation to ADHD medication, antidepressants and antipsychotics. The first phase of the work covered the prescribing of antidepressants and reported in May.

The analysis of antidepressant use identified that fluoxetine was being prescribed as a first line therapeutic agent. However, the report also found that citalopram, which is not licensed for use in children and young people, was prescribed in almost as many cases. The prescribing data analysed covered 2013 when advice from NICE was more supportive of the use of citalopram. This is no longer the case.

Doctors are reminded that when prescribing for depressive illness in children and adolescents only fluoxetine has been shown to be effective and when initiated should be carefully monitored in line with current guidance (see current BNF for advice, which is replicated on the reverse of this letter). Use of other medication to treat depressive illness should be initiated by a specialist and only when ongoing monitoring has been put in place.

Yours faithfully,

Dr Sarah Watkins

Dr Sarah Watkins
Senior Medical Officer

“Depressive illness in children and adolescents

The balance of risks and benefits for the treatment of depressive illness in individuals under 18 years is considered unfavourable for the SSRIs citalopram, escitalopram, paroxetine, and sertraline, and for mirtazapine and venlafaxine. Clinical trials have failed to show efficacy and have shown an increase in harmful outcomes. However, it is recognised that specialists may sometimes decide to use these drugs in response to individual clinical need; children and adolescents should be monitored carefully for suicidal behaviour, self-harm or hostility, particularly at the beginning of treatment.

Only fluoxetine has been shown in clinical trials to be effective for treating depressive illness in children and adolescents. However, it is possible that, in common with the other SSRIs, it is associated with a small risk of self-harm and suicidal thoughts. Overall, the balance of risks and benefits for fluoxetine in the treatment of depressive illness in individuals under 18 years is considered favourable, but children and adolescents must be carefully monitored as above.**”**

Source: British National Formulary (online) London: BMJ Group and Pharmaceutical Press Link. [Accessed on 6 October 2015].

Report on prescribing of antipsychotic medication in Wales for children and young people, 2003-2013

Study coordinators and lead authors

Ann John, Associate Professor Public Mental Health, Swansea University Medical School; Consultant in Public Health, Public Health Wales

Amanda Marchant, Research Analyst, Swansea University Medical School

Rest of study team

Keith Lloyd, Professor of Psychiatry, Dean and Head of College, Swansea University Medical School

Dave Williams, Divisional Director Family and Therapies

Aneurin Bevan University Health Board; Specialist Adviser to Chief Medical Officer and Welsh Government – Child & Adolescent Mental Health

Role of funder

This work was funded by Welsh Government. The funding source did not have any influence on study design, collection, analysis or interpretation of data, or the preparation, review or approval of the manuscript except to request CI were removed from some tables to aid the lay reader.

Table of Contents

Executive summary

Introduction

A recent enquiry into Child and Adolescent Mental Health Services (CAMHS) by the Children, Young People and Education Committee of the National Assembly for Wales raised several concerns about mental health service provision for young people in Wales. This included issues relating to increasing numbers and associated costs of prescription medication and the limited availability of alternatives to pharmacological treatments such as psychological therapies. As a result of this report the Minister for Health and Social Services committed to undertake further analysis of prescribing trends.

Studies in other western cultures have shown an increase in prescribing of antipsychotic medication in children and young people (CYP). It has been suggested that such increases may be related to an increasing tendency to manage behavioural problems with such medications. The aim of this study is to utilise routinely collected healthcare data to explore trends in the incidence and prevalence of antipsychotic prescriptions in CYP in primary care in Wales. In addition the potential indication for which a medication is prescribed and contact with secondary care will also be examined.

Methods

A retrospective e-cohort study was conducted utilising the Secure Anonymised Information Linkage (SAIL) databank at Swansea University. Individuals aged 17 and under, registered with a SAIL supplying GP between 1st January 2003 and 31st December 2013 were identified. Demographic data regarding gender, age and deprivation were collected for each year of the study. Prevalence (new and repeat longer term prescriptions) and incidence (new) of prescriptions for antipsychotic medication were examined for each year of the study period. Incident prescriptions were further examined for the indication for which they were prescribed and for contact with secondary care.

Results

A modest increase in antipsychotic prescribing was seen over the study period. However, a significant increase was seen in those aged 15-17 years. This reflects an underlying decrease in prescriptions for conventional/1st generation/typical antipsychotics alongside a nearly two-fold increase in prescription of second generation/atypical antipsychotics.

While the incidence did not increase in younger children there was a consistent level of antipsychotic prescribing to those aged 0-5 year i.e. 299 prescriptions issued over the 11 year study period. There is an absence of guidance or safety data available for such medication in the age group.

Incident prescriptions were significantly higher in boys than in girls, in older age groups and in the most deprived areas.

Risperidone was the most commonly prescribed antipsychotic to CYP followed by olanzapine and quetiapine. The potential indication for which an antipsychotic was prescribed varied by antipsychotic type, with risperidone being most frequently associated with attention deficit hyperactivity disorder and pervasive developmental disorders (which include autistic spectrum disorders and Asperger syndrome), olanzapine with serious mental illness, and quetiapine with depression. Conventional antipsychotics were the most likely to have no associated diagnosis recorded.

Where at least one year of follow-up data was available following incident prescription, 62% had at least one additional prescription in the subsequent year, with a third receiving five or more prescriptions. Around half of prescriptions over the study period represent prevalent rather than incident cases.

Discussion

Results of this study further support and extend previous work demonstrating an increase in antipsychotic prescriptions in children and young people across western cultures, although in Wales overall this increase was modest. Increases in prescribing for behaviour problems and depression may be at least in part responsible for the increase in prescriptions.

The increase in prescriptions for older adolescents highlights a need for further support for this population. Recent work has demonstrated an increase in both antidepressant and stimulant prescriptions in primary care in this age group.

The consistent level of prescriptions for very young children is in keeping with evidence outlined in the recent CAMHS enquiry. The absence of any guidance on prescription of such medication and the sparseness of data regarding safety and efficacy make this finding a cause for concern and requires further investigation. This highlights the need for guidance for clinicians and an increase in service provision such as parent training and psychological therapies for behaviour problems in very young children.

Conclusion

The results of this study further support and extend existing literature and give the first indication of rates of antipsychotic prescription for children and young people in Wales. A significant increase in prescription of antipsychotic medication in children aged 15-17 years was found. For all age groups a decrease in typical and an increase in second-generation atypical antipsychotic prescriptions is evident, representing a shift in prescribing practices.

Key messages

Studies in other western cultures have shown an increase in prescribing of antipsychotic medication, some of which is unlicensed usage, in children and young people (CYP). Little is known about the long-term safety and efficacy of antipsychotic medication or it's effect on the developing nervous system of CYP. Children appear at a greater risk than adults for a number of adverse effects. The British National Formulary for Children provides indications and dosages for use of antipsychotic medication, both licensed and unlicensed in response to individual clinical need, under the close supervision of an appropriate specialist

While rates of antipsychotic prescriptions as a whole have increased only modestly over the study period 2003-2013, a significant increase in prescriptions is seen for those aged 15-17 years. Such trends over time reflect an underlying decrease in prescriptions of typical antipsychotics alongside a nearly two-fold increase in prescriptions of atypical antipsychotics.

Incident (new) prescriptions were significantly higher in boys than in girls, in older age groups and in the most deprived areas.

Risperidone was the most commonly prescribed antipsychotic to CYP followed by olanzapine and quetiapine. Antipsychotics are being prescribed for a range of diagnoses. The potential indication for which an antipsychotic was prescribed varied by antipsychotic type. Risperidone was most frequently associated with attention deficit hyperactivity disorder and pervasive developmental disorders (which include autistic spectrum disorders and Asperger syndrome), olanzapine with serious mental illness and quetiapine with depression. Increases in prescribing for behaviour problems and depression may be at least in part responsible for the increase in prescriptions.

It appears that an increasing proportion of individuals are seen in secondary care around the time of

first prescription. However, this varies by antipsychotic type and associated diagnosis and may be an artefact of improved recording.

These findings confirm a need for further support for older adolescents to be made available at a primary care level. This may be particularly important in this age group given the transition from CAMHS to adult services for those also looked after in secondary care. Good primary care support may assist in this transition.

1. Introduction

In a recent enquiry into Child and Adolescent Mental Health Services (CAMHS) through the Children, Young People and Education Committee [1] several concerns were raised about the care of children and young people (CYP) with mental health difficulties in Wales. One related to the increasing use of prescription medications to manage mental health conditions. The evidence outlined suggested that the numbers of prescriptions and associated costs are increasing. The limited availability of alternatives to pharmacological treatment was highlighted, in particular limited access to psychological therapies.

Increases in the prescribing of psychotropic medication to children and young people has been seen across western countries including America [2], Europe [3], and the UK [4] in the past three decades. Increases in antipsychotic prescriptions have been seen across different cultures and this is being linked with managing behavioural problems associated with attention deficit hyperactivity disorder (ADHD), conduct disorder and autism [5, 6].

In the UK, routinely collected data from the THIN and General Practice Research Database (GPRD) databanks in England has been utilised to examine trends over time in antipsychotic prescriptions in the population as a whole (both children and adults) [7] and for children and young people alone [8]. A 60 fold increase in atypical/ 2nd generation antipsychotic prescriptions (amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, rispiridone) from 1992 to 2005 in children and young people was found alongside a decrease in typical/ 1st generation prescriptions (phenothiazine derivatives: chlorpromazine hydrochloride, levomepromazine, promazine hydrochloride, pericyazine, perphenazine, prochlorperazine, trifluoperazine; butyphenones: e.g. haloperidol; diphenylbutylpiperidines: pimozide; substituted benzamides: sulpiride) from 2000 onwards [8]. Compared to the adult population few under 18s received antipsychotic medication [7]. When antipsychotics were prescribed in CYP, risperidone was prescribed far more commonly than other

antipsychotics. Some of this may be due to the use of risperidone to manage behavioural difficulties associated with conditions such as ADHD and autism. A recent study in England, also utilising the THIN database, found that the use of antipsychotics in individuals with autism is much higher than in the general population [9].

The increasing use of antipsychotics in CYP warrants further investigation, particularly as research from Europe and America suggests that these medications are being prescribed for conditions off license and research supporting their efficacy and safety is sparse [5, 6]. In particular little is known about the long-term effects of antipsychotic medication on the developing nervous system. In 2009 the results of an evidence review on the efficacy and safety of antipsychotic medication in CYP, by an expert panel of the European College of Neuro-psychopharmacology, was reported. It concluded that controlled studies support the short-term efficacy of several second-generation antipsychotics for treating psychosis, mania and aggression in CYP. However children appear to be at a greater risk than adults for a number of adverse effects such as extra--pyramidal symptoms, sedation, weight gain as well as metabolic and endocrine abnormalities such as prolactin elevation [10].

While risperidone is approved by the Federal Drugs Agency in the United States of America for treatment of irritability associated with autism in 5-16 year olds, approval for this use in the UK was submitted but subsequently withdrawn by the licence holder in 2006. This occurred following an offer limiting the indication of risperidone to the symptomatic treatment of severe aggression and violence in children with autism, with additional safety monitoring through a treatment register [11]. NICE currently recommend that risperidone is considered for the short-term management of severely aggressive behaviour in conduct disorder and antisocial behaviour only in those who have not responded to psychosocial interventions such as parental psycho---education training [13]. The latter intervention is limited by its availability.

In the UK the National Institute of Clinical Excellence (NICE) recommends that antipsychotic treatment for psychosis or bipolar disorder is always initiated by specialist mental health services and not in primary care, particularly since many may be being used off license [12]. Second generation/atypical anti psychotics such as risperidone, olanzapine, amisulpride and quetiapine are not licensed for use in the management of psychosis and schizophrenia in CYP. Aripiprazole is licensed for use in those aged over 15 years and clozapine in those aged over 16 years. Use of first generation/typical antipsychotics such as chlorpromazine, benperidol, flupentixol, promazine and thioridazine is generally avoided, due to concerns over extrapyramidal side effects, including tardive dyskinesia, elevated prolactin and QTc prolongation. Haloperidol is licensed for the treatment of childhood behavioural disorders associated with hyperactivity and aggression. Pimozide is licensed for schizophrenia and other psychoses in patients aged over 12 years. Both current NICE guidance and the British Association for Psychopharmacology evidence based guidance on the use of medication in bipolar disorder in CYP suggest that adult treatment guidelines should be followed due to the limited evidence base available in the under 18 age group. The severity of any mania present will dictate whether an antipsychotic or valproate or lithium is used. None of the atypical antipsychotics available are licensed for bipolar disorder in patients under the age of 18 years. Typical antipsychotics are of limited use due to side effects.

It should be noted however that the British National Formulary for Children (http://www.pharmpress.com/product/9780857111647/bnfc) also provides indications and dosages for use of antipsychotic medication licensed and unlicensed under the close supervision of an appropriate specialist for schizophrenia, other psychoses, severe mental or behavioural disorders, Tourette's syndrome, psychomotor agitation, mania and, in the short term, to calm disturbed children whatever the underlying psychopathology which may be schizophrenia, brain damage, mania, toxic delirium or agitated depression. They may be used to alleviate severe anxiety but this too should be a short-term measure.

2. Aims

In light of the findings of the recent report, the aim of this study is to utilise routinely collected healthcare data to explore trends in the incidence and prevalence of antipsychotic prescriptions in children and young people (CYP) in primary care in Wales. In addition the potential indication for which a medication is prescribed and contact with secondary care will also be examined.

3. Methods

3.1 Design

A retrospective electronic cohort study was conducted utilizing the Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com) developed in the Health Information Research Unit (HIRU) at the College of Medicine, Swansea University.

3.2 Ethical approval

Approval was granted from the Information Governance Review Panel (IGRP). This is an independent body consisting of a range of government, regulatory and professional agencies. The IGRP oversees study approvals in line with permissions already granted to the analysis of data in the SAIL databank [14, 15]. The key points of the MRC/welcome Trust data sharing policy were followed.

3.3 Data source

The SAIL databank is an expanding repository of anonymised person based linkable data for use supporting research. SAIL was established at Swansea University in 2004 and forms part of the Health e-Research Collaboration UK (HeRC UK), led by the Medical Research Council (MRC) and is based in the Centre for the Improvement of Population Health through e-Records Research (CIPHER). CIPHER is a UK Clinical Research Collaboration (UKCRC) Public Health Research Centre of Excellence set within the Farr Institute at the Swansea University Medical School. Two authors (AJ, KL) are Farr investigators.

Policies, structures and controls are in place to protect patient confidentiality, along with a high performance computing infrastructure and a reliable matching, anonymisation and encryption process, which is achieved in conjunction the NHS Wales Informatics Service. A split file method is employed to ensure anonymisation and confidentiality, whilst maintaining the facility of data linkage at the level of the individual to any of the datasets housed in SAIL [14, 15]. This allows data from sources including general practice records, hospital admissions and demographic information to be linked at patient level whilst maintaining anonymity.

For the purpose of this study data were utilised from several datasets linked at patient level.

- The Welsh Demographic Service (WDS) is a core data set available within the SAIL databank and part of a set of services to manage administrative information (demographic data) for NHS patients in Wales. The WDS was introduced in 2009 replacing a similar service known as the NHS Wales Administrative Register (NHS AR). The WDS is a register of all individuals who have at some point in time been registered with a Welsh GP or required some form of NHS healthcare provision in Wales.

- The General Practice Database (GPD) contains attendance and clinical information for all general practice interactions including symptoms, investigations, diagnoses and prescribed medication. Currently data is collected from approximately 40% of practices i.e. 195 practices (out of 474 in Wales) covering a population of over 1.9 million with regularly updated data

- Deprivation indices were taken from the Welsh Index of Multiple Deprivation 2011 (WIMD). This score is derived from eight separate domains of deprivation including income, employment and education. This dataset assigns all 1909 Lower Super Output Areas in Wales (average population 1500; range 1000 – 3000) a deprivation score. LSOAs are ranked for deprivation and divided into quintiles.

- The Patient Episode Database for Wales (PEDW) contains data on NHS Wales hospital admissions (inpatients and day cases) and contains information on attendance and clinical information including diagnoses and operations performed.

- The Outpatients Dataset (OPD) contains attendance information for all NHS Wales hospital outpatient appointments.

The SAIL databank was interrogated using structured query language (SQL).

3.4 Study population and setting

Individuals aged 17 or under between the 1st January 2003 and 31st December 2013 were identified. There was no lower age limit and individuals born during the study period were included. Data collection began either six months from GP registration or at the study onset whichever was the later to exclude the risk of retrospective recording. Data collection ended at the end of registration with a SAIL supplying GP, date of death, 18th birthday or the study end, whichever was the sooner. Individuals supplying a minimum of six months of data based on these criteria (and therefore registered with a SAIL supplying GP for a minimum of one year) were included in the cohort. Each individual could supply more than one period of data provided the above criterions were met. For each year, data were collected between the start and end dates identified when constructing the original cohort or, between the 1st of January and the 31st of December if an individual's period of data collection spanned beyond these dates.

3.5 Measures

Age, gender and area based deprivation quintile data were collected. Age and deprivation information for each individual was collected based upon the onset of data collection for each year. Age was broken down into four groups: 0-5, 6-10, 11-14 and 15-17 years.

The primary care database was queried using db2 structured query language, implementing Read

Codes Version 2 (5-byte set). The primary care dataset in SAIL (GPD) contains Read codes for each registered individual in a SAIL supplying practice. Read codes are a hierarchical nomenclature used to record clinical summary information. Primary care physicians enter medical diagnoses and symptoms using Read codes. The GPD does not contain any accompanying free text on referral or discharge to or from secondary/tertiary care. The Read codes used in this study were developed by clinical members of the study team (list of codes available on request). They were used to create an algorithm to identify those with a prescription of any antipsychotic medication in the primary care dataset.

Defining incidence

An individual was regarded as an incident case if no other record of an antipsychotic prescription was found in the previous twelve months. Participants may have more than one episode recorded as long as a period of at least twelve months exists between entries. This is in keeping with previous routine data studies conducted in England [16-18]. Incident prescriptions may be thought of as new prescriptions.

Incident prescriptions were examined for antipsychotics as a group of medications, so if an individual changed from one drug to another it was not counted as a new incident case (e.g. an individual who began treatment with a typical antipsychotic and then switched to an atypical with less than a year between subsequent prescriptions would be counted as one case and not two).

Defining prevalence

An annual prevalent case was defined as an individual with any record of a prescription in the target year. This included both those with a history of previous prescriptions and incident cases [19]. Hence prevalent prescriptions include new and repeat longer term prescriptions.

Identifying potential indications for prescription

Routine data does not explicitly link medication prescription with diagnosis. The records of individuals with an incident antipsychotic prescription were further explored in an attempt to identify the indication for which the medication was prescribed. Potential indications for antipsychotic medication include both relapsing and remitting conditions such as depression and anxiety where multiple diagnoses may be recorded and enduring conditions such as pervasive developmental disorder (PDD) i.e. autistic spectrum disorders, Asperger's, Rett syndrome, where a diagnosis may be recorded only once. As such an individual's GP record was searched for potential indications at any time during the study period. This method has been employed previously with routine data studies in England [7].

In keeping with previous research [7] records were searched at any point for the presence of severe mental illness (SMI) defined as schizophrenia-like disorders, bipolar disorder and other psychoses such as delusional disorder. If any record of these was found then it was assumed that this was the indication for which an antipsychotic was prescribed and no other indications were searched. If a serious mental illness diagnosis was not found then an individual's GP record was searched for the following diagnosis in keeping with previous research: depression, anxiety, sleep disorders, ADHD, personality disorders, post---traumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD). In addition due to the young age of our cohort we have also included eating disorders, PDD, Tourette's/tic disorders and conduct disorder.

Secondary care data for all individuals with an incident antipsychotic prescription (both with and without a serious mental illness diagnosis) was investigated in order to identify contact with specialist services in which a diagnosis may be made and treatment initiated. Hospital admissions or attendance at an outpatient clinic under a consultant specialising in paediatrics, child and adolescent mental health, mental illness, mental handicap or psychotherapy in the year before or six months following an incident prescription were examined.

3.6 Statistical Analysis

Annual incidence rates were calculated using person years at risk (PYAR) as a denominator. For example a person who supplied six months of data to the study would contribute 0.5 years to the denominator. Annual prevalence rates were also calculated utilising PYAR as a denominator. This is a more appropriate unit rather than number of registered cases because the period of follow up will vary between individuals [19]. Poisson regression was undertaken to investigate the adjusted associations between incidence of antipsychotic prescription on the one hand and, year of record, gender, age and deprivation on the other. The significance of variables in the Poisson regression modelling was assessed using Wald tests. Robust standard errors for the estimated incidence rate ratios (IRRs) were utilised to account for clustering within practices. Analysis was conducted using SPSS version 20 for Windows (syntax available on request).

4. Results

4.1 Study population

A total of 457,943 individuals aged 17 and under between 1st January 2003 and 31st December 2013 contributed 2,649,108 person years of data.

4.2 Prevalence of antipsychotic prescriptions

The prevalence (repeat longer term prescriptions) of antipsychotic medication is shown in Table 1. This includes new and longer term repeat prescriptions.

Table 1: Number of events and prevalence[a] of antipsychotic prescriptions in GP data over time

Year	Events	Antipsychotic Prescription prevalence
2003	356	1.43
2004	416	1.63
2005	416	1.61
2006	432	1.68
2007	444	1.73
2008	423	1.65
2009	369	1.55
2010	402	1.61
2011	439	1.87
2012	399	1.91
2013	277	1.64

a. Prevalence calculated as number of individuals with any record of a given subtype recorded in the target year as rate per 1000 person years at risk.

4.3 Incidence of antipsychotic prescriptions

A total of 1685 individuals received 1846 incident (new) antipsychotic prescriptions during the study period. Of these 296 (21%; 95% Confidence Interval [CI] 10-23) represent prescription of typical antipsychotics and 1454(79%; 95% CI 77-81) represent atypical prescriptions.

The number of prescriptions and incidence of antipsychotic prescriptions over the study period is shown in Table 2. Trends over time broken down into typical and atypical prescriptions are shown in Figure 1. The incidence of antipsychotic prescriptions showed an initial increase from 0.64 cases per 1000 PYAR to 0.83 cases in 2006 before decreasing to 0.56 cases in 2009 after which point incidence

began increasing again resulting in an overall modest increase to 0.66 cases per 1000 PYAR in 2013 (IRR = 1.21, 95% CI 0.95 – 1.52; see Table 3 for IRR). When split into typical and atypical antipsychotics results show and a significant decrease in incident prescriptions of typical antipsychotics from 0.19 cases per 1000 PYAR in 2003 to 0.04 in 2013 (IRR = 0.29, 95% CI 0.13---0.64). In contrast prescriptions of atypical antipsychotics have shown a significant increase from 0.45 to 1.62 cases per 1000 PYAR from 2003 to 2013 (IRR = 1.56, 95% CI = 1.22 – 2.00) with the largest increase evident from 2009 onwards.

Table 2 Number of events and incidence[a] of antipsychotic prescriptions in GP database over time

Year	All Antipsychotics		Typical Antipsychotics		Atypical Antipsychotics	
	Events	Incidence	Events	Incidence	Events	Incidence
2003	160	0.64	47	0.19	113	0.45
2004	189	0.74	55	0.21	135	0.53
2005	180	0.70	57	0.22	123	0.48
2006	213	0.83	56	0.22	159	0.62
2007	179	0.70	31	0.12	148	0.58
2008	152	0.59	34	0.13	119	0.46
2009	143	0.56	31	0.12	112	0.44
2010	175	0.70	30	0.12	145	0.58
2011	189	0.80	23	0.10	166	0.71
2012	155	0.74	25	0.12	130	0.62
2013	111	0.66	7	0.04	104	0.62

a. Incidence calculated as number of individuals with an incident record in the target year as rate per 1000 person years at risk

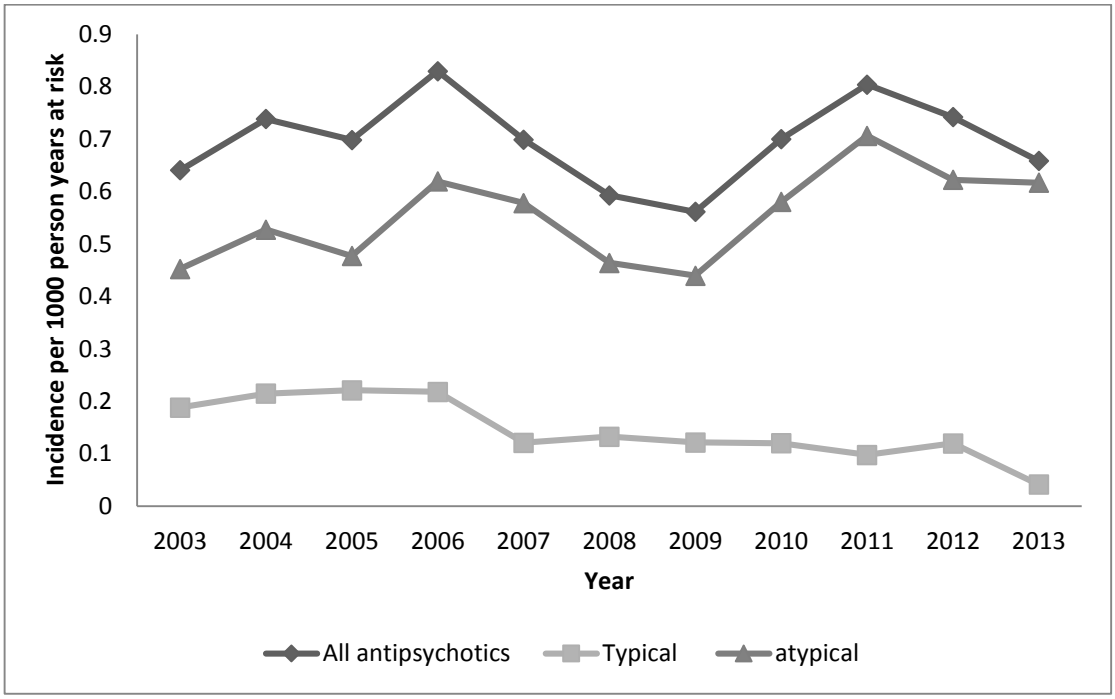

Figure 1 Incidence of antipsychotic prescriptions in GP database over time

4.4 Incident prescriptions by antipsychotic type

The most commonly prescribed antipsychotics over the study period were risperidone, olanzapine and quetiapine, which made up 42%, 17% and 12% of prescriptions respectively. Prescriptions of olanzapine have remained relatively stable over time while quetiapine shows the most marked increase from 0.02 cases in 2003 to 0.11 cases per 1000 PYAR in 2013. Trends over time for risperidone largely reflect that of antipsychotics overall with an initial increase followed by a drop from 2006 before increasing again from 2009 onwards (Figure 2).

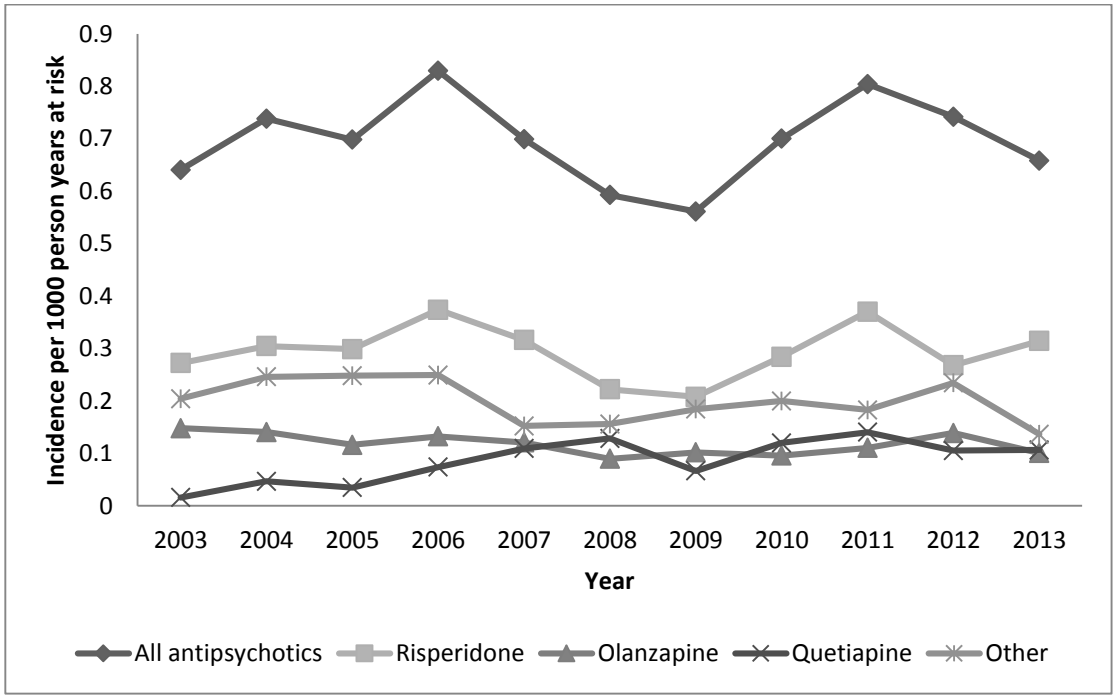

Figure 2 Incident antipsychotic prescriptions by antipsychotic type over time

4.5 Incidence and prevalence of antipsychotic prescriptions over time

Of the 2035 incident prescriptions 1382 had at least one year's follow-up data available. Of this group 855 (62%) had at least one additional prescription in the subsequent year and 453(33%) had five or more prescriptions.

Incident prescriptions represent 42% of all prescriptions during the study period. While the overall number of prevalent prescriptions is larger than the number of incident prescriptions, trends over time appear to be largely similar for both new and existing prescriptions (Figure 3).

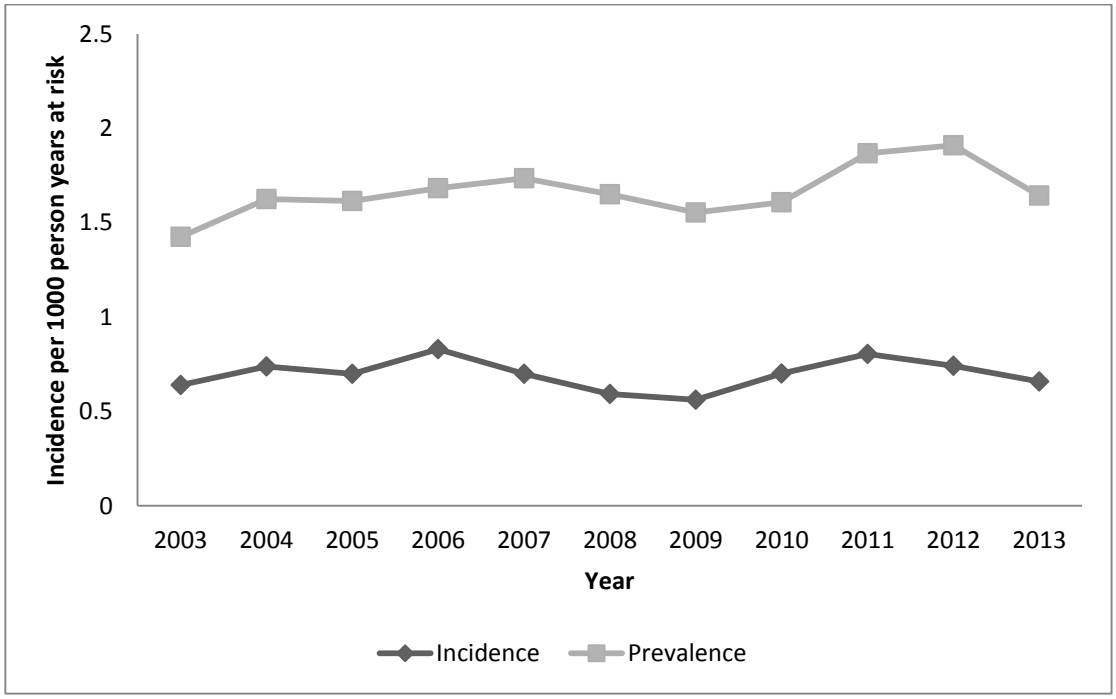

Figure 3 Incidence and prevalence of antipsychotic prescriptions in GP data over time

Age, gender and deprivation

Adjusted incident rate ratios for year, gender, age group and deprivation for antipsychotic prescriptions are shown in Table 3. Incidence of antipsychotic prescriptions as a whole was significantly higher in boys than in girls (IRR = 1.40, 95% CI 1.28---1.53). However, when looking at typical and atypical medications separately there was no significant difference between males and females for typical antipsychotics (IRR = 1.02, 95% CI 0.84 – 1.24) while the boys received significantly more incident atypical prescriptions than girls (IRR = 1.52, 95% CI 1.37 – 1.69). Antipsychotic prescriptions were significantly higher in the most deprived compared with the least deprived areas (IRR = 1.59, 95% CI 1.38 – 1.82).

For all subtypes incidence was the highest in those ages 15-17 years, however the difference between age groups was greater with atypical antipsychotics where prescribing in 15-17 year olds were nearly five times that of 0-5 year olds (all antipsychotics IRR = 3.69, 95% Cl 3.23 – 4.22, typical antipsychotics IRR = 1.93, 95% Cl 1.49 – 2.50, atypical antipsychotics IRR = 4.55, 95% Cl 3.88 – 5.34). While those aged 0-5 years made up the smallest number of prescriptions overall, during the study period they received 299 incident prescriptions.

Table 3 Number of events and incident rate ratios for antipsychotic prescriptions

Variable		All Antipsychotics		Typical		Atypical	
		Events	**IRR[a]**	**Events**	**IRR[a]**	**Events**	**IRR[a]**
Gender	**Female**	741	Reference[b]	190	Reference[b]	555	Reference[b]
	Male	1105	1.40	206	1.02	899	1.52
Age Group	**0-5**	299	Reference[b]	98	Reference [b]	202	Reference [b]
	6-10	315	1.13	86	0.93	229	1.22
	11-14	478	1.85	81	0.95	398	2.28
	15-17	754	3.69	131	1.93	625	4.55
Deprivation[c]	**1**	292	Reference[b]	74	Reference[b]	219	Reference[b]
	2	265	1.09	59	0.96	207	1.13
	3	384	1.19	93	1.12	291	1.21
	4	379	1.39	84	1.19	295	1.45
	5	517	1.59	82	1.00	437	1.79
Year	**2003**	160	Reference[b]	47	Reference[b]	113	Reference[b]
	2004	189	1.12	55	1.14	135	1.12
	2005	180	1.12	57	1.22	123	1.09
	2006	213	1.25	56	1.13	159	1.32
	2007	179	1.11	31	0.68	148	1.28
	2008	152	0.93	34	0.73	119	1.02
	2009	143	0.90	31	0.68	112	0.99
	2010	175	1.11	30	0.67	145	1.30
	2011	189	1.25	23	0.53	166	1.55
	2012	155	1.17	25	0.66	130	1.38
	2013	111	1.21	7	0.29	104	1.56

a. Adjusted for calendar year, gender, age and deprivation, b. based on Wald test, c. Deprivation: 1 = least deprived; 5 = most deprived.

4.6 Trends in incident antipsychotic prescriptions by age-group over time

Incidence of all antipsychotic prescriptions by age group over time is shown in Figure 4. The biggest increase over time is seen in the 15-17 year age group. Incidence initially decreased from 1.47 cases per 1000 PYAR in 2003 to 1.19 in 2009 before increasing to 2.04 cases per 1000 PYAR in 2013 resulting in an overall significant increase over time (IRR = 1.39, 95% CI 1.07 – 1.80). There is a modest non-significant increase in prescribing for 11 to 14 year olds.

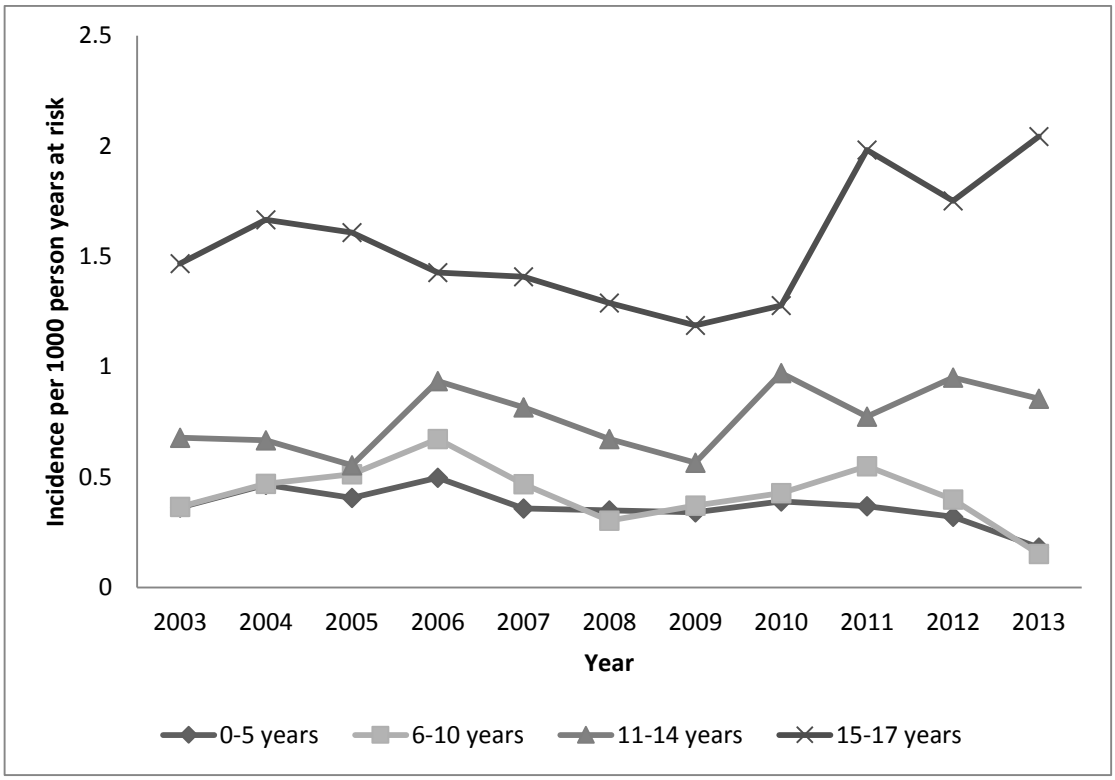

Figure 4 Incident prescriptions of all antipsychotics by age group over time

Incidence of typical antipsychotic prescriptions by age group over time is shown in Figure 5. Overall incidence of typical antipsychotic prescriptions decreased in all age groups with the biggest decrease evident in the 15-17 year age group. Incidence in this age group fluctuated overtime but resulted in an overall significant decrease from 0.33 cases per 1000 PYAR in 2003 to 0.07 in 2013 (IRR= 0.20, 95% CI 0.05-0.76).

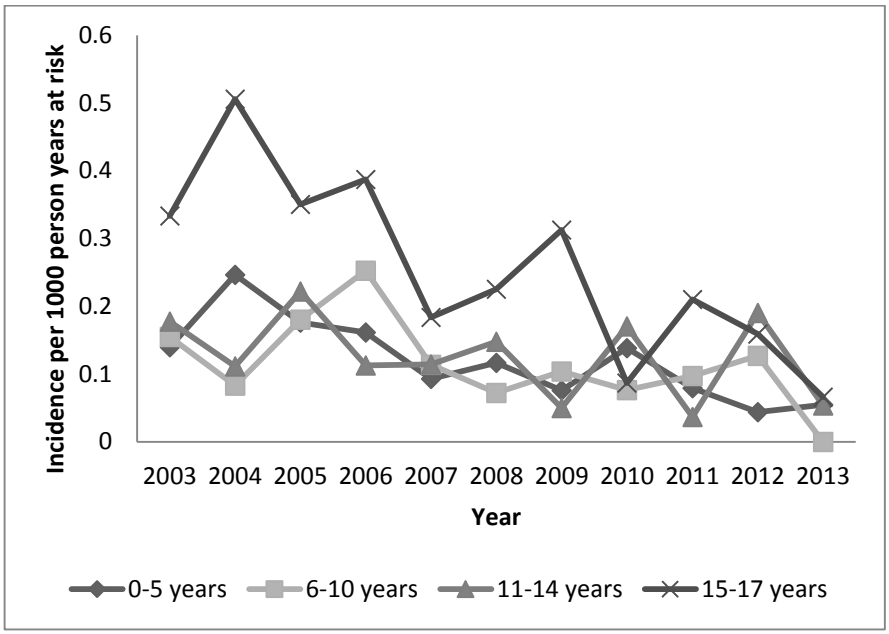

Figure 5 Incident prescriptions of typical antipsychotics by age group over time

Incidence of atypical antipsychotic prescriptions by age group over time is shown in Figure 6. There was no significant change in prescriptions for those aged 0-10 years, with those aged 11 and over receiving significantly more incident prescriptions over time. The largest increase is evident in those aged 15-17. Little change is seen in prescribing trends at the start of the study period with incidence actually decreasing slightly from 1.13 cases per 1000 PYAR in 2003 to 0.88 in 2009 before increasing sharply to 1.98 cases by 2013 (IRR = 1.73, 95% Cl 1.27-2.37).

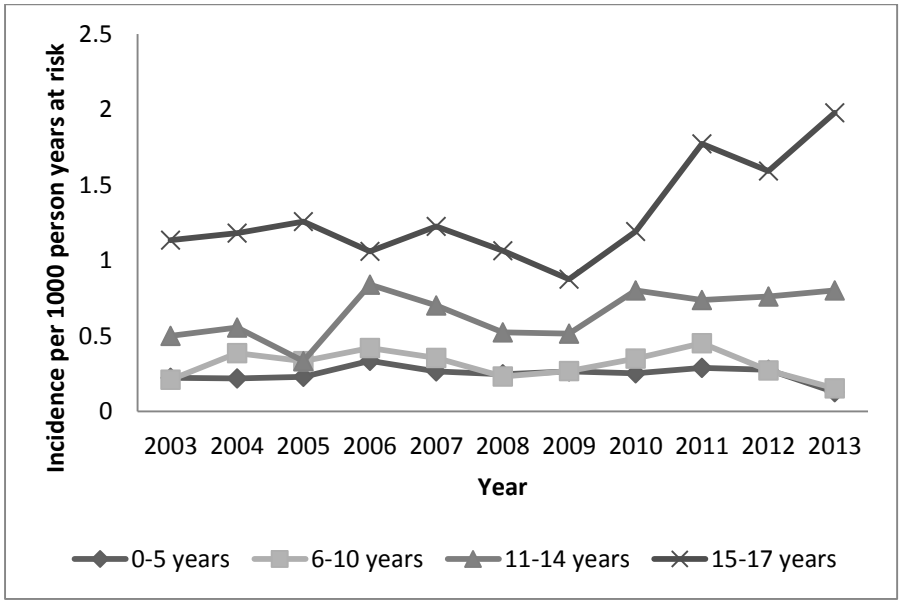

Figure 6 Incident prescriptions of atypical antipsychotics by age group over time

4.7 Contact with secondary care and diagnosis in GP data associated with incident prescriptions

Incidence of contact with secondary care around the time of prescription, recorded diagnosis of SMI in GP data and other potential GP diagnoses in shown in Table 4. Trends over time are shown in Figure 6. Data for outpatients is available from 2004 onwards and, as such, all potential indications data is taken from 2004 – 2013. There are issues relating to the completeness of the OPD.

Table 4 Number of events and incidence[a] per 1000 person years of contact with secondary care, SMI diagnosis and other diagnoses in GP data

Year	Contact with secondary care[b]		Diagnosis of SMI[c] in GP data		Other possible indication[d] in GP data	
	Events	Incidence (95% Ci)	Events	Incidence (95% CI)	Events	Incidence (95%CI)
2004	68	0.27(0.21-0.34)	73	0.29(0.22-0.36)	89	0.35(0.28-0.43)
2005	83	0.32(0.26-0.40)	52	0.20(0.15-0.26)	90	0.35(0.28-0.43)
2006	103	0.40(0.33-0.49)	62	0.24(0.19-0.31)	126	0.49(0.41-0.58)
2007	84	0.33(0.26-0.41)	36	0.14(0.10-0.19)	127	0.50(0.41-0.59)
2008	69	0.27(0.21-0.34)	48	0.19(0.14-0.25)	80	0.31(0.25-0.39)
2009	62	0.24(0.19-0.31)	45	0.18(0.13-0.24)	80	0.31(0.25-0.39)
2010	92	0.37(0.30-0.45)	44	0.18(0.13-0.24)	104	0.42(0.34-0.50)
2011	111	0.47(0.39-0.57)	44	0.19(0.14-0.25)	118	0.50(0.42-0.60)
2012	93	0.45(0.36-0.55)	50	0.24(0.18-0.32)	80	0.38(0.30-0.48)
2013	79	0.47(0.37-0.58)	18	0.11(0.06-0.17)	71	0.42(0.33-0.53)

a. Incidence per 1000 person years at risk

b. Contact with secondary care in the year prior and six months following an incident antipsychotic prescription in GP database

c. If an individual had an SMI diagnosis, no other GP diagnoses were searched

d. Those without a diagnosis of SMI searched for all other possible indications in GP data (not mutually exclusive – list in method section)

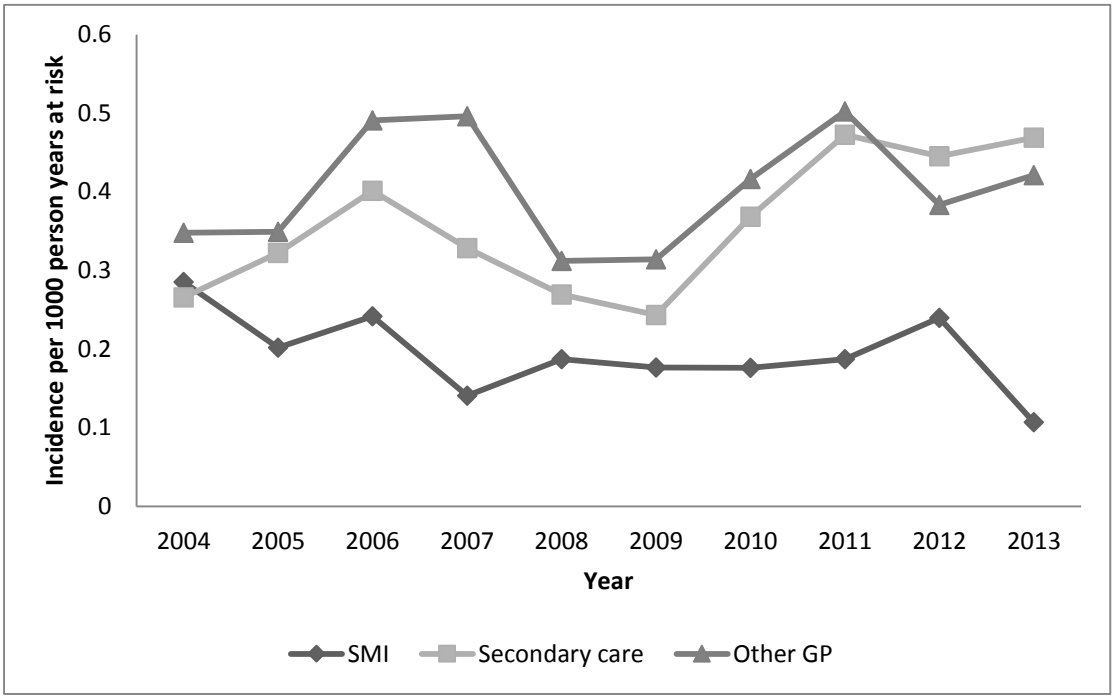

Figure 7 Incidence of antipsychotic prescription by associated contact with secondary care, SMI diagnosis and other diagnoses in GP data over time

There were a total of 1686 incident antipsychotic prescriptions from 2004-2013 in the GP data. Of these 844 (50%; 95% CI 48-52) had contact with secondary care around the time of first prescription. A total of 472 (28%; 95% CI 26-30) had a diagnosis of SMI in the GP data and 965 (57%; 95% CI 55-60) had another associated diagnosis in the GP data. Incidence of antipsychotic prescription associated with SMI in GP data has decreased over time (Figure 7) from 0.29 cases per 100 PYAR in 2004 to 0.11 cases in 2013. In contrast, incident antipsychotic prescription associated with contact with secondary care has increased over the study period particularly since 2009 increasing from 0.24 cases per 1000 PYAR in 2009 to 0.47 in 2013. This most likely reflects improved recording and completeness of the OPD dataset. Incident antipsychotic prescriptions associated with other GP diagnoses showed an initial increase before dropping in 2007 rising again from 2009 onwards resulting in an overall increase over time from 0.35 cases per 1000 PYAR in 2004 to 0.42 cases in 2013.

The percentage of new prescriptions associated with each indication for typical and atypical antipsychotics are shown in Table 5. For antipsychotics overall the most commonly

associated GP diagnosis was SMI followed by depression, sleep disorders and anxiety. However when examining typical and atypical antipsychotics separately, typical antipsychotics are most commonly associated with a diagnosis of depression (34%, 95% CI 29---39) followed by sleep disorders and anxiety with SMI associated with just 13% (95% CI 10---17) of incident prescriptions. Indications for atypical antipsychotics are largely reflective of those of antipsychotics overall.

An absence of any associated GP diagnosis or contact with secondary care is more likely with typical than atypical antipsychotics with 22% (95% Cl 18---27) of typical antipsychotic prescriptions having neither recorded compared with just 5% (95% Cl 4---7) of atypical antipsychotics. This may be partly due to secondary care contact becoming more common over time while the use of typical antipsychotics is most common at the onset of the study.

Table 1 Potential indications, number of events and percentages of associated antipsychotic prescriptions 2004 - 2013

Indication	All Antipsychotics (n = 1686)		Typical antipsychotics (n = 349)		Atypical antipsychotics (n = 1341)	
	Events	Percentage (95% CI)	Events	Percentage (95% CI)	Events	Percentage (95% CI)
Secondary Care[a]	844	50(48-52)	101	29(24-34)	746	56(53-58)
Any GP diagnosis[b]	1437	85(83-87)	237	68(63-73)	1204	90(88-91)
SMI[c]	472	28(26-30)	45	13(10-17)	428	32(29-34)
Other GP diagnosis[d]	965	57(55-60)	192	55(50-60)	776	58(55-60)
Depression	427	25(23-27)	119	34(29-39)	310	23(21-25)
Sleep	328	19(18-21)	92	26(23-31)	237	18(16-20)
Anxiety	245	15(13-16)	72	21(17-25)	174	13(11-15)
ADHD	215	13(11-14)	10	3(2-5)	206	15(14-17)
PDD	211	13(11-14)	14	4(2-7)	197	15(13-17)
Conduct disorder	100	6(5-7)	13	4(2-6)	87	6(5-8)
Eating disorders	81	5(4-6)	<5	<2	77	6(5-7)
Personality disorders	66	4(3-5)	9	3(1-5)	58	4(3-6)
Tic disorders	74	4(4-5)	17	5(3-8)	57	4(3-5)
OCD	55	3(3-4)	<5	<2	50	4(3-5)
PTSD	35	2(1-3)	8	2(1-4)	27	2(1-3)
None of the above[e]	148	9(8-10)	78	22(18-27)	70	5(4-7)

a. Contact with secondary care in the year before or six months following incident antipsychotic prescription in GP data
b. Any diagnosis potentially associated with antipsychotic prescription including serious mental illness
c. If an individual has an SMI diagnosis, any non-SMI diagnoses will not be included in numbers below
d. For those who do not have an SMI diagnosis all non-SMI diagnoses will be shown (i.e. these numbers are not mutually exclusive)
e. No contact with secondary care or potential indication in GP data
f. SMI:serious mental illness, ADHD:attention deficit hyperactivity disorder, PDD: pervasive developmental disorder includes autistic spectrum disorders and aspergers, OCD:obsessive compulsive disorder, PTSD: post traumatic stress disoder

Potential indications for antipsychotic prescriptions broken down into the most commonly prescribed antipsychotics are shown in Table 6. The highest proportion of incident prescriptions with associated secondary care contact is seen with risperidone where 61% (95% CI 57-64) of prescriptions are associated with secondary care contact. Of the three most frequently prescribed antipsychotics risperidone has the lowest proportion of associated SMI diagnosis at only 22% (95% CI 19-25) of prescriptions. In contrast with other antipsychotics ADHD and PDD represent the highest proportion of associated diagnoses for risperidone, with each being associated with nearly a quarter of prescriptions.

Prescriptions for all other GP diagnoses account for a small percentage of prescriptions across antipsychotics with the exception of eating disorders, associated with 13% (95% CI 10---18) of olanzapine prescriptions. The highest proportion of prescriptions associated with SMI is seen for olanzapine where this accounts for nearly half of prescriptions. Quetiapine is most frequently associated with a diagnosis of depression with 42% (95% CI 35---48) of prescriptions associated with such a diagnosis.

Other antipsychotics are the least likely to be associated with secondary care contact (36%, 95% Cl 32-40) with depression representing the most frequent indication associated with such prescriptions followed by SMI, sleep disorders and anxiety. Other antipsychotics are the most likely to have no potential GP indication or secondary care contact recorded with 17% (95% Cl 14-21) of prescriptions having no potential indication found. This compares with only 5% (95% Cl 4-7) of risperidone prescriptions, 3% (95% Cl 1-6) of alanzapine and 8% (95% Cl 5-13) of quetiapine prescriptions.

Table 6 Potential indications, number of events and percentages of associated antipsychotic prescriptions by drug type 2004 -- 2013

Indication	Risperidone (n=709)		Olanzapine (n=276)		Quetiapine (221)		Other (n=482)	
	Events	Percent (95% CI)	Events	Percent (95% CI)	Events	Percent (95% CI)	Events	Percent (95% CI)
Secondary Care[a]	432	61(57-64)	133	48(42-54)	107	48(42-55)	174	36(32-40)
Any GP diagnosis[b]	633	89(87-91)	259	94(90-96)	193	87(82-91)	354	73(69-77)
SMI[c]	158	22(19-25)	133	48(42-54)	65	29(24-36)	116	24(20-28)
Other GP diagnosis[d]	475	67(63-70)	126	46(40-52)	128	58(51-64)	238	49(45-54)
Depression	122	17(15-20)	75	27(22-33)	92	42(35-48)	138	29(25-33)
Sleep	131	18(16-22)	42	15(11-20)	50	23(18-29)	106	22(19-
Anxiety	85	12(10-15)	39	14(11-19)	42	19(14-25)	80	17(14-20)
ADHD	174	25(22-28)	<5	<2	13	6(3-10)	23	5(3-7)
PDD	170	24(21-27)	<5	<2	9	4(2-8)	29	6(4-9)
Conduct disorder	62	9(7-11)	7	3(1-5)	7	3(2-6)	24	5(3-7)
Eating disorders	24	3(2-5)	37	13(10-18)	11	5(3-9)	10	2(1-4)
Personality disorders	20	3(2-4)	14	5(3-8)	21	10(6-14)	11	2(1-4)
Tic disorders	47	7(5-9)	<5	<2	<5	<2	24	5(3-7)
OCD	28	4(3-6)	11	4(2-7)	7	3(2-6)	9	2(1-4)
PTSD	12	2(1-3)	<5	<2	6	3(1-6)	12	2(1-4)
None of the above[e]	38	5(4-7)	8	3(1-6)	18	8(5-13)	84	17(14-21)

a. Contact with secondary care in the year before or six months following incident antipsychotic prescription in GP data

b. Any diagnosis potentially associated with antipsychotic prescription including serious mental illness

c. If an individual has an SMI diagnosis, any non---SMI diagnoses will not be included in numbers below

d. For those who do not have an SMI diagnosis all non---SMI diagnoses will be shown (i.e. these numbers are not mutually exclusive)

e. No contact with secondary care or potential indication in GP data

f. SMI:serious mental illness, ADHD:attention deficit hyperactivity disorder, PDD: pervasive developmental disorder includes autistic spectrum disorders and aspergers, OCD:obsessive compulsive disorder, PTSD: post traumatic stress disoder

Figure 8 shows the percentage of each diagnosis in the GP data associated with secondary care contact around the time of first prescription. Just over half of SMI diagnoses are associated with secondary care contact, with lower proportions of depression, anxiety and sleep disorders associated with secondary care contact. Conduct disorder, pervasive developmental disorder and ADHD have the highest proportions of associated secondary care contact.

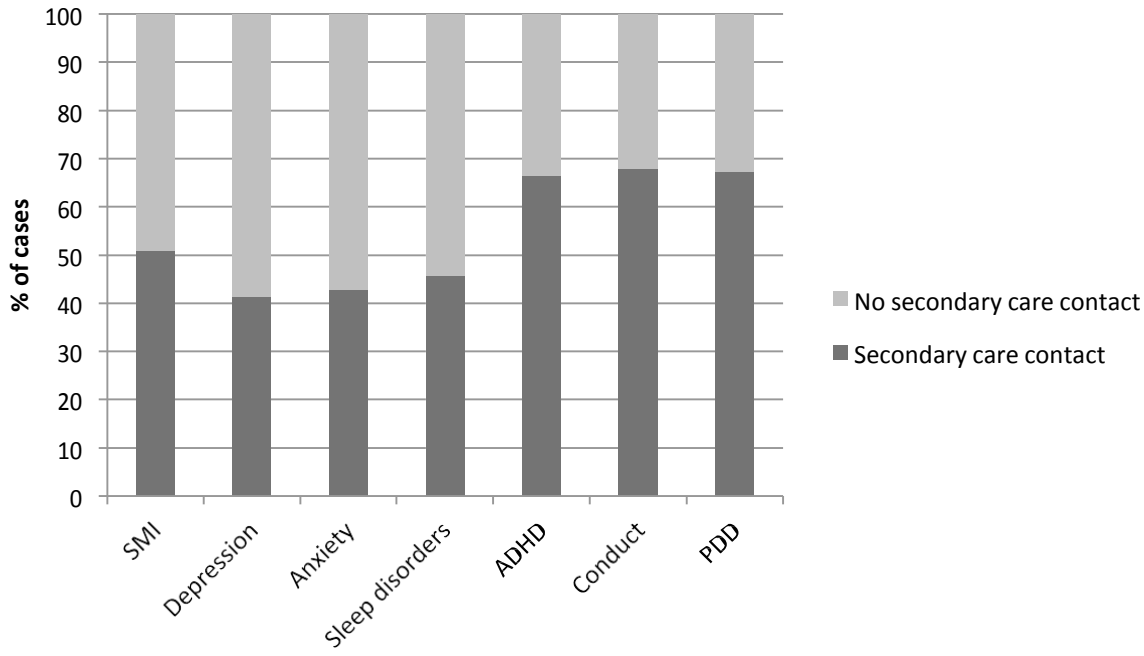

Figure 8 Percentage of diagnoses of GP data associated with secondary care contact

5. Discussion

5.1 Main findings

Over all there was a modest increase in the prevalence and incidence of prescribed antipsychotics over the study period. This reflected a significant increase in prescriptions for atypical antipsychotics and a decrease in those for typical antipsychotics (Figure 1) over time in line with prescribing guidance. When analysed by age group incident antipsychotic prescribing as whole has significantly increased in 15-17 year olds only (not other age groups), reflecting a significant decrease in prescription of typical antipsychotics alongside nearly a two-fold increase in incident prescriptions of atypical antipsychotics. This increase in incident prescriptions is particularly evident from 2009 onwards. Results also show that prescriptions are more frequent in boys than in girls and in the most deprived than least deprived areas.

Results of this report further support research in other western countries demonstrating and increase in prescribing of psychotropic medications for children and young people [2-4] and supports work with routinely collected data in England [7].

Previous research has suggested that increases in antipsychotic prescriptions in western cultures are in part due to the increasing use in managing behavioural problems associated with ADHD, conduct disorder and PDD (including autism and Asperger's) ([5, 6, 8]. Results of this study suggest that the increase seen here may be in part due to prescribing for behavioural problems associated with such diagnoses. Risperidone represented the most popular antipsychotic prescribed in this group for which around a quarter of prescriptions were associated with a diagnosis of ADHD or PDD. Only 8% of incident risperidone prescriptions were associated with conduct disorder. This is interesting given that NICE guidance[13] recommends risperidone in severe cases of aggression associated with conduct disorder and antisocial behaviour (only recommended where the individual has not responded to psychosocial interventions) but not for problems associated with ADHD or PDD.

While it is appears that the increase in prescriptions may be related to behaviour problems, this is

likely only one of several contributing factors. Several other diagnoses are potentially associated with an increase in antipsychotic prescriptions. Overall SMI (defined as schizophrenia-like disorders, bipolar disorder and other psychoses such as delusional disorder) represents the most frequent diagnosis associated with antipsychotic prescriptions followed by depression, sleep disorders and anxiety. This varies by individual antipsychotic. When looking at the most commonly prescribed medications separately the highest proportion of SMI diagnoses is associated with olanzapine with nearly half of incident prescriptions associated with such a diagnosis. Risperidone is more frequently associated with ADHD and PDD and quetiapine is most frequently associated with depression. Quetiapine demonstrated the most consistent increase over the study period, which suggests that incident prescriptions associated with depression, might be partly responsible for the increase in prescribing over time.

NICE guidance for both antisocial behaviour and conduct disorder [13] and psychosis [12] in children and young people state that initiation of antipsychotic use should always be initiated by a specialist and not in primary care as does the BNF for Children. As an indication of adherence to guidelines contact with secondary care under a mental health consultant was also examined. While the outpatients dataset in SAIL does have its limitations, with respect to completeness of data, meaning that contact with secondary care is likely to be underestimated this does give an indication of the proportion of individuals having contact with a mental health specialist in secondary care. Over time it appears that contact with secondary care is increasing alongside a decrease in SMI diagnoses recorded in the GP data. This could be representing a shift in care of individuals with SMI from primary to secondary care. However, it is not possible to confidently conclude that this is the case based on the data available here. An alternative explanation is that the increase in GP diagnoses other than SMI evident alongside this increase in secondary care contact may indicate a change in the indications for which antipsychotics are being prescribed. Overall around half of incident prescriptions are associated with secondary care contact in the year before or six months following incident prescription.

This varies by antipsychotic type with risperidone representing the highest proportion of secondary care contact (61%) and typical antipsychotics representing the lowest (29%).

The proportion of prescriptions for which no potential indication (secondary care or GP diagnosis) could be found also varied dependent on the type of antipsychotic prescribed. No indication could be found for around a fifth of typical antipsychotic prescriptions, compared to just 5% of typical prescriptions. This suggests that typical antipsychotics are less likely to be associated with both secondary care contact and with an associated diagnosis in GP data. It may be that typical antipsychotics are being prescribed for diagnoses outside those analysed here or that GPs are employing different coding behaviour for typical antipsychotics than atypical antipsychotics. It may also be the case that GP coding of associated diagnoses is increasing over time, and that the poorest recording was done at the start of the study period when typical antipsychotic prescribing was more frequent.

When examined by diagnosis type it appears that a diagnosis of ADHD, PDD (includes autistic spectrum disorders and Aspergers) and or conduct disorder is associated with secondary care contact more frequently than a diagnosis of depression, anxiety, sleep disorders or SMI. It is worth noting that since rates of SMI diagnosis in GP data have been found to decrease over the study period this may represent a shift towards individuals being looked after in secondary care. However, around half of incident prescriptions associated with an SMI diagnosis do not appear to have any associated secondary care contact, although this may be an artifact of poor recording. However this may be cause for further research as such diagnoses should not be exclusively looked after in primary care where early intervention in psychosis NICE guidelines should be followed.

The rate of prescribing for children aged five and under is a further cause for concern. While this was not found to increase, 299 incident prescriptions were found for those aged 0-5 over the study period. This suggests a consistent level of prescribing in this age group. While antipsychotics are, for the most part,

unlicensed for use in this age group some are indicated in the BNF for children for use in childhood schizophrenia under expert supervision. There is sparse availability of safety data for children and young people and it has been suggested that this population may be more susceptible to adverse effects [10]. The presence of prescriptions for very young children may be related to issues raised by our previous report where we found a similar rate of stimulant prescribing in this age group and by the findings of the recent inquiry into CAMHS [1]. These include issues of availability of psychosocial interventions for behaviour problems and to medication being seen as an 'easy option' for treatment of this group [1].

5.2 Strengths and limitations

The results of this study reflect trends in presentation to primary care, recognition, recording and treatment by GPs. This is likely to be an underestimate of any diagnoses in the community as routine data does not capture individuals who do not present to their GP or, with whom a problem is discussed but not recorded or treated by the GP. This analysis would not capture those being looked after exclusively by specialist services where no diagnosis or treatment is recorded by the GP. Similarly individuals seen by specialist services in England will not be captured by this analysis. In addition estimates of contact with secondary care are likely to be an underestimate since there are issues with the completeness of the out patient dataset. Such limitations are a common feature of all routinely collected database studies and results are not intended as an estimate of time trends as a whole.

All prescriptions issued in primary care to SAIL supplying general practices are captured by this analysis, however the data available do not make it possible to examine whether such medications were dispensed or taken. The indication for which a medication is prescribed is not explicitly recorded in GP data and can only be inferred based on potential indications for such medication recorded in GP database. This method of inferring indication has been used in routine database studies in England [7]. It is limited since only those with a diagnosis recorded utilising the relevant Read code will be detected by such an analysis. Additionally, examining an individual's GP record for the entire study period (rather than just the time around prescription) while increasing sensitivity for diagnoses such as ADHD or PDD where a diagnosis may only be recorded once, may result in an inflated number of diagnoses unrelated to prescription being inferred as an indication. This technique has been utilised in other routine database studies [7] and represents a limitation of utilising routinely collected data when inferring medication indication.

A further limitation of the current research is the lack of information regarding whether and what interventions have been received at secondary and tertiary mental healthcare levels. There are issues relating to the completeness of the OPD dataset and improved electronic prescribing records at secondary care and better recording of diagnosis would improve the utilisation of routine data in Wales. Routinely collected data also does not allow a measure of condition severity. This makes it difficult to assess how appropriate a prescription for any given individual might be.

While routinely collected data does have some limitations, it does have the advantage of allowing research with a large population based cohort. This study covers approximately 40% of practices i.e. 195 practices (out of 474 in Wales) covering a population of over 1.9 million people of all ages.

5.3 Implications

The increase in prescriptions of antipsychotics for 15-17 years olds from primary care may suggest a growing demand in older adolescents or increased management using prescribed medication. The increase in this age group is reflected in other work performed by this research team examining both antidepressant and stimulant prescriptions. There is a need for further support for older adolescents to be made available at a primary care level. This may be particularly important in this age group given the transition from CAMHS to adult services for those also looked after in secondary care. Good primary care support may assist in this transition.

Results of this study suggest that around half of prescriptions issued each year are to those who are already receiving treatment. This may be contributing to the increasing cost of psychotropic prescriptions highlighted by the recent report [1]. Given the doubts over the long-term safety of such medication in CYP and evidence suggesting a greater sensitivity to adverse effects in this population [10] it is important to regularly review medication. This is particularly the case for individuals being treated for behaviour problems where only short-term efficacy is supported [10]. Any medication review should be balanced with the possible consequences of under-treatment or inappropriate discontinuation of medication, particularly for those suffering with serious mental illness.

Antipsychotics may be prescribed for a range of diagnoses. Prescriptions associated with depression, sleep disorders, and anxiety disorders were found to be associated with a high proportion of prescriptions, particularly for quetiapine. While treatment of behaviour problems may be partly responsible for the increase in prescribing, it is important to take other potential indications into account. The high proportion of individuals without any apparent secondary care contact, particularly for SMI, depression, sleep disorders and anxiety is also a potential cause for concern. While results may be partly attributable to patients having treatment initiated outside of Wales, the possibility that GPs are initiating treatment due to barriers in accessing CAMHS services warrants further investigation. The high rate of rejected referrals to CAMHS from primary care has been highlighted in previous research [20].

The range of potential indications found in this study highlights the need for more detailed guidance on appropriate prescribing of antipsychotic medication in children and young people. This is particularly important given the number of very young children being prescribed such medications. Increasing awareness for clinicians combined with improved provision of alternatives to medication, such as parent training, interventions in schools and other psychosocial interventions will support reductions in prescribing in this age group.

6. Conclusion

In conclusion results of this study further support existing literature and give the first indication of the rate of antipsychotic prescribing and associated diagnoses in CYP in Wales. While rates of antipsychotic prescriptions as a whole have increased only modestly, a significant increase in prescriptions is seen for those aged 15-17 years. Such trends over time also reflect a shift from prescription of typical to atypical antipsychotics. It appears that such medications are being prescribed for a range of diagnoses and that increases in prescribing for behaviour problems and depression may be at least in part responsible for the increase in prescriptions. In addition, it appears that an increasing proportion of individuals are seen in secondary care around the time of first prescription. However, this varies by antipsychotic type and associated diagnosis and may be an artefact of improved recording.

References

1. National Assembly for Wales: Children and Young People and Education Comitee, *Inquiry into Child and Adolescent Mental Health Services (CAMHS)*. 2014, National Assembly for Wales: Cardiff.
2. Olfson, M., et al., *National trends in the use of psychotropic medications by children.* Journal of the American Academy of Child & Adolescent Psychiatry, 2002. **41**(5): p. 514---521.
3. Steinhausen, H.C. and C. Bisgaard, *Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark.* Acta Psychiatrica Scandinavica, 2014. **129**(3): p. 221---231.
4. Hsia, Y. and K. Maclennan, *Rise in psychotropic drug prescribing in children and adolescents during 1992–2001: a population---based study in the UK.* European journal of epidemiology, 2009. **24**(4): p. 211---216.
5. Bachmann, C.J., et al., *Antipsychotic prescription in children and adolescents: an analysis of data from a German statutory health insurance company from 2005 to 2012.* Deutsches Ärzteblatt International, 2014. **111**(3): p. 25.
6. Alessi---Severini, S., et al., *Ten years of antipsychotic prescribing to children: a Canadian population---based study.* Canadian journal of psychiatry, 2012. **57**(1): p. 52.
7. Marston, L., et al., *Prescribing of antipsychotics in UK primary care: a cohort study.* BMJ open, 2014. **4**(12): p. e006135.
8. Rani, F., et al., *Epidemiologic features of antipsychotic prescribing to children and adolescents in primary care in the United Kingdom.* Pediatrics, 2008. **121**(5): p. 1002---1009.
9. Murray, M.L., et al., *Pharmacological treatments prescribed to people with autism spectrum disorder (ASD) in primary health care.* Pyschopharmacology, 2013.
10. Vitiello, B., et al., *Antipsychotics in children and adolescents: increasing use, evidence for efficacy and safety concerns.* European Neuropsychopharmacology, 2009. **19**(9): p. 629---635.
11. Morgan, S. and E. Taylor, *Antipsychotic drugs in children with autism.* BMJ: British Medical Journal, 2007. **334**(7603): p. 1069.
12. NICE. *Pyschosis and shizophrenia in children and young people: recognition and management*. 2013; Available from: https://www.nice.org.uk/guidance/cg155.
13. NICE. *Antisocial behaviour and conduct disorders in children and young people: recognition, intervention and management, CG158*. 2013; Available from: http://www.nice.org.uk/guidance/cg158.
14. Lyons, R.A., et al., *The SAIL databank: linking multiple health and social care datasets.* BMC Medical Informatics and Decision Making, 2009. **9**(1): p. 3.
15. Ford, D.V., et al., *The SAIL Databank: building a national architecture for e---health research and evaluation.* BMC Health Services Research, 2009. **9**(1): p. 157.
16. Rait, G., et al., *Recent trends in the incidence of recorded depression in primary care.* The British Journal of Psychiatry, 2009. **195**(6): p. 520---524.
17. Wijlaars, L.P., I. Nazareth, and I. Petersen, *Trends in depression and antidepressant prescribing in children and adolescents: a cohort study in The Health Improvement Network (THIN).* PloS one, 2012. **7**(3): p. e33181.
18. Walters, K., et al., *Recent trends in the incidence of anxiety diagnoses and symptoms in primary care.* PloS one, 2012. **7**(8): p. e41670.
19. Frisher, M., et al., *Prevalence of comorbid psychiatric illness and substance misuse in primary care in England and Wales.* Journal of Epidemiology and Community Health, 2004. **58**(12): p. 1036---1041.
20. Hinrichs, S., et al., *General practitioner experience and perception of Child and Adolescent Mental Health Services (CAMHS) care pathways: a multimethod research study.* BMJ open, 2012. **2**(6): p. e001573.

T4CYP WORK STREAM ACTION PLAN 2016

Work Stream Actions	Timeline
Identification of appropriate membership and approval of individual work stream plans	***Completed 2015***
Resilience, Wellbeing and Early Years	
Develop whole school approaches to promoting mental health (MH) and wellbeing	Spring/Summer 2016
Map existing training and intervention programmes for staff, CYP and families	Spring 2016
Engage with CYP and identified experts to uniform relevant training and interventions	Spring 2016
Develop modular MH and resilience training programme for staff in relevant agencies	Spring 2016
Formally launch all Wales training module for professionals at T4CYP Annual Conference	Summer 2016
Early Intervention and Enhanced Support	
Identify current best practice service models and share with relevant stakeholders	Spring 2016
Identify Communication Strategy, workforce and training issues	Spring 2016
Develop directory of local primary mental health services for children	Spring 2016
Develop service specifications and recommended models of support for vulnerable children including Looked After Children (LAC) and Adopted Children	Spring/Summer 2016
Neurodevelopmental and Co-morbid MH/LD	
Establish Neurodevelopmental Community of Practice	Spring 2016
Undertake initial audit of current health board Neurodevelopmental services and strategic planning groups and share learning	Spring 2016
Develop integrated diagnostic/assessment support packages and a common care pathway for adoption across Wales.	Spring/Summer 2016

Work Stream Actions	Timeline
Specialist CAMHS	
All Wales Baseline Variations Audit	**Completed *2015***
Target areas where significant variation is seen in terms of access and service model	Spring 2016
Complete All Wales Report and share findings	Summer 2016
National Quality and Delivery Framework for Specialist CAMHS	
Develop first draft of Quality Delivery Framework (QDF) to include pathways for: • Crisis Care • Early Interventions in Psychosis • Eating Disorders	Spring 2016
Stakeholder engagement to test the QDF's content	Spring 2016
Produce QDF for formal launch at T4CYP Annual Conference	Summer 2016
Development of QDF; updating content to include additional pathways	Autumn/Winter 2016
Care Transitions	
Review health board transition policies and adherence to ensure effectiveness and consistency	Spring 2016
Consider the volume of young people transitioning across the areas; existing transition models; their appropriateness for use and outcomes of 0-25 service pilots taking place in England and lessons learnt; and the case for transitional support workers/transition champions.	Spring 2016
Hold service user engagement event for those involved in the transition process to identify best practice and lessons learnt.	Spring 2016
Develop first draft 'Transition pack' of resources for professionals setting out models for good transition across the whole process	Spring 2016
Wider consultation and production of final version to include evaluation recommendations	Summer 2016
Evaluation recommendations reported.	Winter 2016
Needs Assessment	
Confirm evidence review questions and agree outline of Needs Assessment with stakeholders	***Completed 2015***
First draft Needs Assessment	Spring 2016
Final Needs Assessment	Summer 2016

Work Stream Actions	Timeline
Workforce, Education and Training	
Consider the recommendations and outcomes from the other work streams and distil from these, key competences that practitioners/ workforce will need.	Spring 2016
Align competences to professional roles, map to national occupational standards and the roles of support staff, and consider how the competences relate to other groups such as practitioners/ workers from third sector organisations.	Spring 2016
Develop core competences that can be applied to the workforce in specific and specialised areas.	Spring 2016
Develop a workforce model that reflects different levels from awareness to specialist skills.	Spring/Summer 2016
Map a model for the development of a flexible education and training framework making recommendations on how this can be delivered in an inter-professional/ interagency way.	Spring 2016
Develop a Continuous Professional Development Framework for CAMHS professionals	Summer /Autumn2016