Links between the amount of antipsychotic medication prescribed per population at general practice level, local demographic factors and medication selection

Adrian Hugh Heald (adrian.heald@manchester.ac.uk)
Salford Royal NHS Foundation Trust https://orcid.org/0000-0002-9537-4050
Mike Stedman
Res Consortium, Andover
Sanam Farman
Mersey Deanery Psychiatry Rotation
Chaw Khine
King's Mill Hospital, Mansfield
Mark Davies
Res Consortium, Andover
Marc de Hert
Katholieke Universiteit Leuven
David Taylor
Institute of Psychiatry, London

Research article

Keywords: antipsychotic, prescribing, variations, general practice, demographic, psychosis

Posted Date: February 20th, 2020

DOI: https://doi.org/10.21203/rs.2.24127/v1

Version of Record: A version of this preprint was published on November 7th, 2020. See the published version at https://doi.org/10.1186/s12888-020-02915-3.

Abstract

BACKGROUND Antipsychotic medications are the first-line pharmacological intervention for severe mental illnesses(SMI) such as schizophrenia and other psychoses, while also being used to relieve distress and treat neuropsychiatric symptoms in dementia. Since 2014 many antipsychotic agents have moved to generic provision. In 2017_18 supplies of certain generic agents were affected by substantial price increases. Our aim was to examine factors relating to antipsychotic prescribing in general practices across England and how cost changes in recent years have impacted.

METHODS The study examined over time the prescribing volume/prices paid for antipsychotic medication by agent in primary care. The NHS in England/Wales publishes each month the prescribing in general practice by BNF code. This was aggregated for the year 2018_19 using Defined Daily doses (DDD). Cost of each agent year-on-year was determined. Monthly prescribing in primary care was consolidated over 5 years(2013-2018) and DDD amount from WHO/ATC for each agent was used to convert the amount to total DDD/practice.

RESULTS Description We included 5,750 general practices with practice population >3000 and with >30 people on their SMI register. In 2018_19 there were 10,360,865 prescriptions containing 136 million DDD with costs of £110 million at an average cost of £0.81/DDD issued in primary care. Effect of price In 2017_18 there was a sharp increase in overall prices. There was a gradual increase in antipsychotic prescribing over 2013-2019 which was not perturbed by the drug price increase in 2017/18. Regression Demographic factors The strongest positive relation to increased prescribing of antipsychotics came from higher social disadvantage, higher population density(urban), and comorbidities e.g. chronic obstructive pulmonary disease(COPD). Higher %younger and %older populations, northerliness and non-white (Black and Minority Ethnic (BME)) ethnicity were all independently associated with less antipsychotic prescribing. Prescribing Factors Higher DDD/general practice population was linked with higher %injectable, higher %liquid, higher doses/prescription and higher %zuclopenthixol depot. Less DDD/population was linked with general practices using higher %risperidone and higher spending/dose of antipsychotic.

CONCLUSIONS Levels of antipsychotic prescribing at general practice level are driven by social factors/comorbidities. We found a contrasting link between depot prescriptions with higher DDD and risperidone prescriptions with lower DDD.

Introduction

Antipsychotic medications are the first-line pharmacological intervention for severe mental illnesses (SMI) such as schizophrenia (1) and other psychoses, while also being used to relieve distress and to treat neuropsychiatric symptoms in dementia (2). Oral antipsychotic medication prescribed in primary care is one of the main sources of support to people with a history of psychosis.

The America Psychiatry Assocation (ADA) Clinical Practice guidelines (1) recommend treatment with second generation antipsychotic agents (SGA) first line for psychosis. However first generation antipsychotic (FGA) agents are still widely prescribed, often for historical reasons in the case of a particular individual. The medication is largely recommended by specialist teams and prescribed in general practice, with the exception of Clozapine and depot antipsychotic treatment (3).

It was shown by Marston et al in 2014 (4) using a United Kingdom (UK) Primary Care database that of those receiving first-generation antipsychotics, less than 50% had a diagnosis of psychosis/bipolar disorder. For the second-generation agents, the numbers ranged from 4824 (36%) for quetiapine to 7094 (62%) for olanzapine. In patients without psychosis/bipolar disorder, common diagnoses included anxiety, depression, dementia, sleep and personality disorders. Thus in many cases, these agents are not used for other indications than psychosis.

Since 2014 many antipsychotic agents have moved to generic provision. In 2017_18 supplies of certain generic agents were affected by substantial price increases (5).

We have previously looked at the factors related to prescribing of antidepressants in England and show that the quality of patient-general practice relationship influences the antidepressant prescribing rate (6). Our analysis utilised the same modelling paradigm. Our aim was to examine the factors that relate to antipsychotic prescribing in general practices across England.

Methods

The study examined over time the amount and prices paid in antipsychotic medication by agent in primary care and considered if this affected selection of agents by prescribers. We also looked at the general practice characteristics including disorder registers and local demography as potential determinants of antipsychotic prescribing. Antipsychotic agents were looked at individually.

The National Health Service (NHS) in England and Wales publishes publicly each month (7) the prescribing in general practice by each British National Formulary (BNF) code which distinguishes between the various prescribed agents. This was aggregated for the year 2018_19 using Defined Daily doses (DDD) as published by the World Health Organisation Annual Therapeutic Classification WHO/ATC (8) and analysed by delivery method (oral/intramuscular) and dose level for agents to treat psychosis or behaviour felt to put the individual or those around them at risk.

Monthly prescribing in primary care was consolidated over 5 years and DDD amount from WHO/ATC for each agent was used to convert the amount to total DDD/practice. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. Cost of each agent year on year was determined (5).

We examined 3 different classes of possible factors that could influence the antipsychotic prescribing rate.

a) Location & Demographic

- Population Age distribution & Gender
- Social Deprivation
- Ethnicity % Black and Minority Ethnicity (BME)
- Latitude (Northerliness)
- Population Density (urban/rural)

b) Practice Characteristics

- List Size
- Practice level Comorbidities (Depression, Diabetes, Chronic Obstructive Pulmonary disease (COPD))

c) Practice mental health prescribing behaviour

- Use of Antipsychotic DDD/pop
- Use Anxiolytic & Hypnotic DDD/pop
- Number of different types of antipsychotic (Chem/Dose/Method)
- Antipsychotic Doses/Prescription by individual agent
- Antipsychotic Average Cost / Dose by individual agent

Multivariate regression analysis was used to establish the link of these factors to the antipsychotic prescribing rate.

Results

We included 5,750 general practices with population > 3000 and with more than 30 people on their severe enduring mental illness (SMI) register. In 2018_19 there were 10,360,865 million prescriptions containing 136 million DDD with costs of £110 million at an average costs of £0.81 / DDD issued in primary care.

Figure 1 shows the progression of prescribing over a 5 year period. The unforeseen price rises in 2017_18 caused a sharp increase in overall prices and they had not reduced to the expected levels by the end of the 2018_19 evaluation year. There was a gradual increase in antipsychotic prescribing which was not perturbed by the increase in drug price in 2017/18.

General practice characteristics vs antipsychotic prescribing

Figure 2 shows the results of the regression analysis (r^2 = 17.4%). The strongest positive relation to increased prescribing of antipsychotics DDD/practice list came from higher social disadvantage, higher population density (urban), and comorbidities for example chronic obstructive pulmonary disease

(COPD), while less antipsychotic prescribing was associated with higher % younger and % older populations, northerliness and higher proportion of non-white (Black and Minority Ethnic (BME)) ethnicity.

Prescribing factors vs antipsychotic prescribing

Higher antipsychotic prescribing DDD/population was linked with higher % injectable, higher % liquid, higher doses/prescription and % zuclopenthixol depot use, while less DDD/population was linked with general practices using higher % risperidone and higher spending/dose of antipsychotic.

Discussion

The levels of antipsychotic prescribing at general practice level in the UK are associated with social factors and with comorbidities. The regression analysis that we undertook indicated that particular drivers are high population density and socioeconomic deprivation. Furthermore transcultural factors (BME ethnicity associated with less antipsychotic prescribing) need to be considered in relation both treatment of psychosis (9).

There have been significant fluctuations in the cost of many antipsychotic preparations in the last 3 years and these rapid changes can put pressure on clinical decision making, with impact on patient outcomes with regards to stability of mental state over time. Interestingly however, despite the price fluctuation, we saw a consistent steady rise in antipsychotic prescribing over the 5 year period (2013–2018) that we examined. This was also reported by Roberts et al in 2019 looking (9). They described a consistent increase in the proportion of atypical antipsychotics prescribed, compared to typical antipsychotics, between 2007 and 2014, with atypicals accounting for 79.9% of total antipsychotics prescribed in 2014 in England and Wales.

In the Marston et al study (4) in a large primary care database representative of the UK, approximately half of the prescriptions for first-generation and second-generation antipsychotics are issued to people who have no record of SMI, defined as schizophrenia, bipolar affective disorder or other non-organic psychosis in their clinical notes. Furthermore, they were more likely to be prescribed to older people who may be more sensitive to adverse effects such as movement disorders and cardiometabolic risk. As shown by Szczepura et al, in 2016, individuals with dementia are sometime treated with antipsychotics in order to reduce/attenuate challenging behaviour. When antipsychotics are prescribed to people without SMI, they tend to be given in lower doses and for slightly shorter periods, with the exception of people with ADHD and dementia who receive these drugs for relatively long periods. In our study, we were not able to examine dose prescribed by specific condition

While the growth in generic medication brings substantial cost advantages it also brings significant risks in supply and cost forecasting which may affect the recommendations made by medicines management committees (12).

The association between lower overall antipsychotic prescribing vs DDD for risperidone, and high overall prescribing vs DDD for depot antipsychotics is an important finding. The development of receptor

supersensitivity in relation to long-term exposure to first generation antipsychotic agents was described in a seminal paper by Prien in 1969 (13). Whether this is a contributory phenomenon here is not something that our methodology can address.

General practice prescribing in England and Wales is generally in accordance with National Institute for Clinical Excellence (NICE) guidance (14) in relation to antipsychotic prescribing for psychosis and behavioural disturbance. Depot medication is still a significant treatment option for many patients.

Further database work could explore symptoms associated with these antipsychotic prescriptions, and the treatment decisions pre-dating the choice of an antipsychotic agent.

Strength/Weaknesses

We have analysed national prescribing data over a 5 year period. However this is at general practice not individual level. Nevertheless that can enable visibility of trends that would be more difficult to elucidate at individual patient level.

Conclusion

The level of antipsychotic prescribing at a general practice level are driven by social changes and comorbidities. Despite the price fluctuations, we saw a consistent steady rise in antipsychotic prescribing over the 5 year period (2013- 2018) that we examined.

Declaration

Ethics approval and consent to participate: The analysis used nationally available general practice level data with no patient identifiable data. Therefore we felt that Ethics Permission was not required.

Consent for publication: All authors consent to the publication of this article

Competing interests: None

Funding: This work was self funded

Authors' contributions: Adrian Heald and Mike Stedman conceived the study and led on the paper. Sanam Farman and Chaw Khine assisted in the data analysis as did Mark Davies. Professors Mark de Hert and David Taylor gave expert advice on prescribing and provided editorial input.

Acknowledgements: None

References

1. https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines: accessed 31 January 2020

2. Tifratene K, Manera V, Fabre R, Gros A, Thummler S, Pradier C, Robert P, David R. Antipsychotic prescribing for Alzheimer's disease and related disorders in specialized settings from 2010 to 2014 in France: a repeated cross-sectional study. Alzheimers Res Ther2017; 9: 34

3. Heald A, Livingston M, Yung A, De Hert MA. Prescribing in schizophrenia and psychosis: Increasing polypharmacy over time. Hum Psychopharmacol2017; 32(2)

4. MarstonL, Nazareth I, Petersen I, Walters K, Osborn DP. Prescribing of antipsychotics in UK primary care: a cohort study. BMJ Open 2014; 4(12)

5. GP Practice Prescribing Presentation-level Data. NHS Digital. https://digital.nhs.uk/catalogue. Accessed 23 January 2020

6. Heald AH, Stedman M, Davies M, Farman S, Taylor D, Bailey S, Gadsby R. Quantifying the Impact of Patient-Practice Relationship Quality on the Levels of the Average Annual Antidepressant Practice Prescribing Rate in Primary Care in England. Prim Care Companion CNS Disord 2020; 22(1)

7. https://digital.nhs.uk/data: accessed 25 January 2020

8. Defined Daily Dose (DDD); ATC/WHO. http://www.whocc. no/atc_ddd_index: Accessed 25 January 2020

9. Das-Munshi J, Bhugra D, Crawford MJ. Ethnic minority inequalities in access to treatments for schizophrenia and schizoaffective disorders: findings from a nationally representative cross-sectional study. BMC Med 2018 18; 16:55

10. Roberts R, Neasham A, Lambrinudi C, Khan A. A quantitative analysis of antipsychotic prescribing trends for the treatment of schizophrenia in England and Wales. JRSM Open 2018; 9 (4)

11. Szczepura A, Wild D, Khan AJ, Owen DW, Palmer T, Muhammad T, Clark MD, Bowman C. Antipsychotic prescribing in care homes before and after launch of a national dementia strategy: an observational study in English institutions over a 4-year period. BMJ Open 2016; 6(9)

12. Maudsley Prescribing Guidance file:///Users/macbookpro/Downloads/9780429103629_googlepreview.pdf: Accessed 31 January 2020

13. Prien RF, Cole JO, Belkin NF. Relapse in chronic schizophrenics following abrupt withdrawal of tranquillizing medication. Br J Psychiatry 1969; 115: 679-86

14. Psychosis and schizophrenia in adults: prevention and management. https://www.nice.org.uk/guidance/cg178: Accessed 31 January 2020

Figures

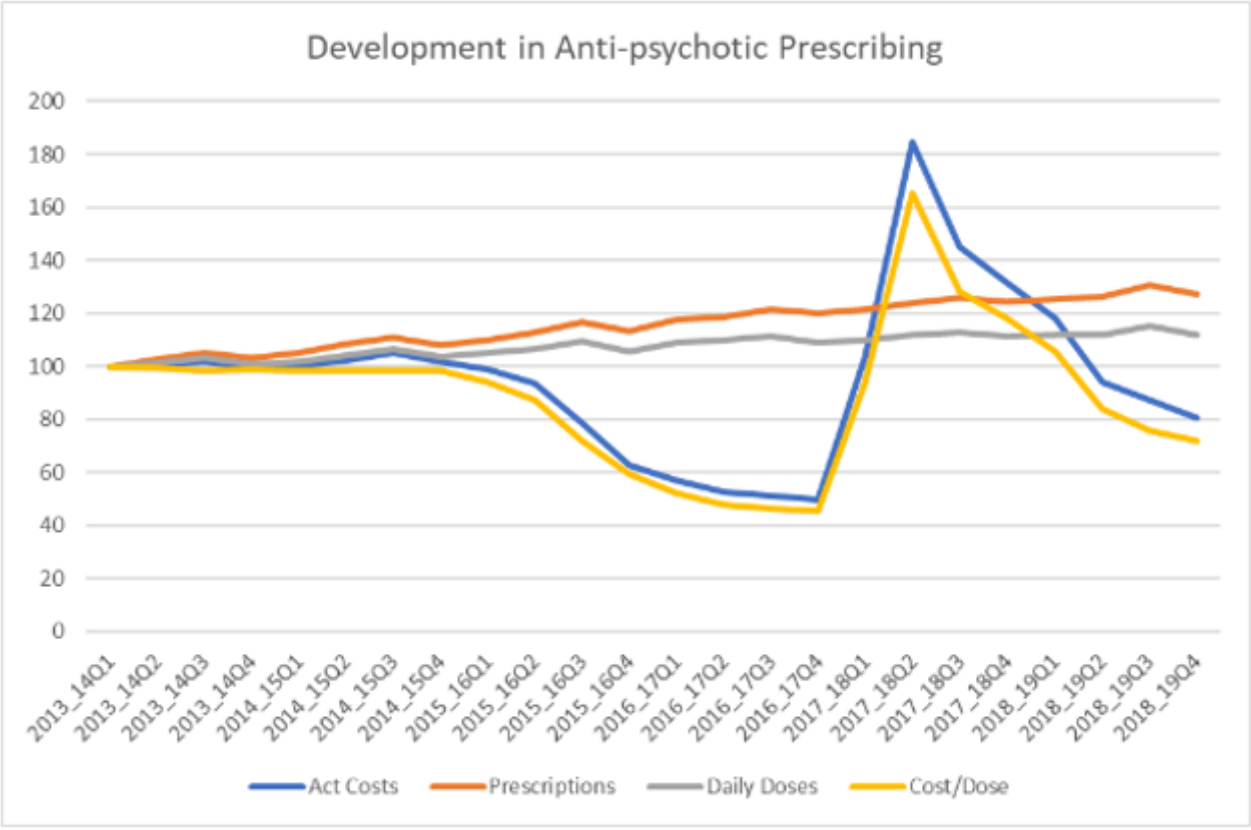

Figure 1

Development of antipsychotic prescribing over 5 years including changes in drug cost. Q = quarter 1, 2, 3 or 4 of the year.

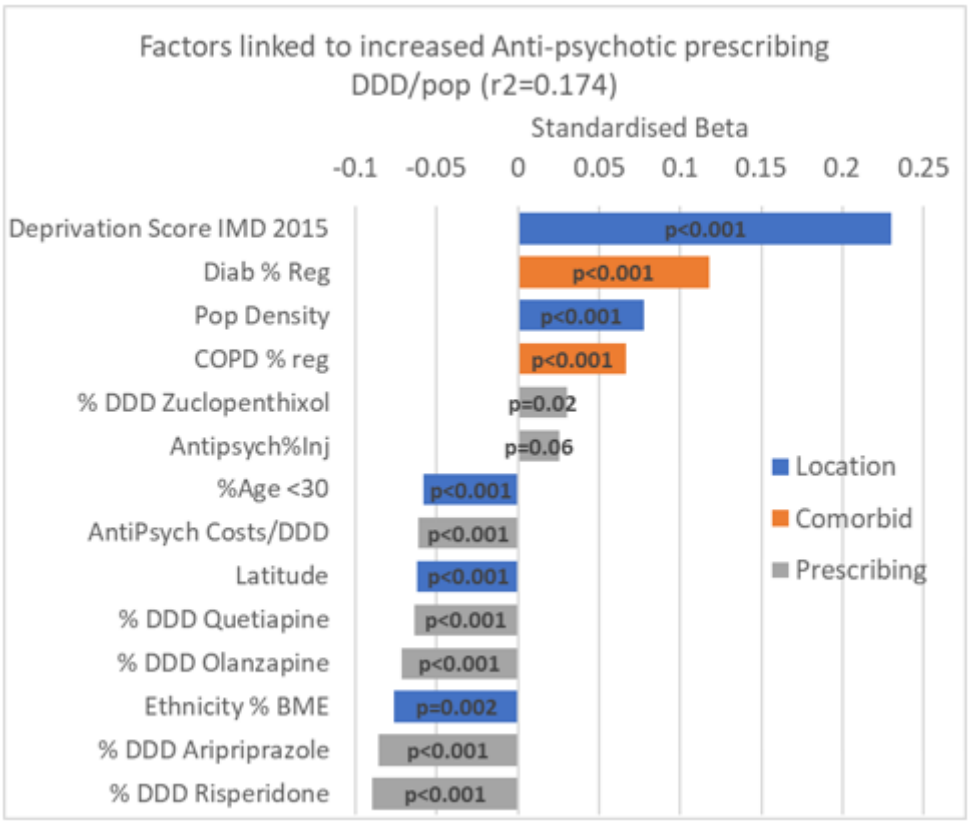

Figure 2

Multivariate regression describing the factors at a general practice level relating to antipsychotic prescribing.