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Abstract

Background: Little is known about trends in prescribing of anxiolytics (antidepressants, benzodiazepines, beta-blockers, anticonvulsants, antipsychotics) for the treatment of anxiety. Several changes may have affected prescribing in recent years, including changes in clinical guidance.

Aim: To examine trends in prescribing for anxiety in UK primary care between 2003-2018.

Design and Setting: Population-based cohort study using Clinical Practice Research Datalink (CPRD) data.

Methods: Analysis of data from adults (n=2,569,153) registered at CPRD practices between 2003-2018. Prevalence and incidence rates were calculated for prescriptions of any anxiolytic, and each drug class. Treatment duration was also examined.

Results: Between 2003-2018, prevalence of any anxiolytic prescription increased from 24.9/1000 person-years-at-risk (PYAR) to 43.6/1000PYAR, driven by increases in those starting treatment, rather than more long-term use. Between 2003-2008, incidence of any anxiolytic prescription decreased from 12.8/1000PYAR to 9.3/1000PYAR; after which incidence rose to 13.1/1000PYAR in 2018. Similar trends were seen for antidepressant prescriptions. Incident beta-blocker prescribing increased over the 16-years, whilst incident benzodiazepine prescriptions decreased. Long-term prescribing of benzodiazepines declined, yet 44% of prescriptions in 2017 were longer than the recommended four weeks. Incident prescriptions in each drug class rose substantially in young adults in recent years.

Conclusion: Recent increases in incident prescribing, especially in young adults, may reflect better detection of anxiety, increasing acceptability of medication, or an earlier unmet need. However, some prescribing is not based on robust evidence of effectiveness, may contradict guidelines, and there is limited evidence on the effect of taking antidepressants long-term. As such, there may be unintended harm.

How this fits in

Previous studies have found substantial increases in the prescribing of antidepressants for any indication, and for depression, over the past two decades. Our study found increases in incident prescribing for anxiety in most anxiolytic drug classes, and this increase in the number of new patients starting treatment is more likely to explain the overall increase, rather than increases in long-term use. Increases in prescribing were most notable in young adults, with a marked rise in benzodiazepine prescriptions for this group. Increases in incident prescribing may reflect better detection of anxiety or an earlier unmet need, however, some of this prescribing is not based on robust evidence of effectiveness, some may contradict guidelines, and there is limited evidence on the effect of taking antidepressants long-term, and therefore, there may be unintended harm.

Introduction

Anxiety disorders are common and usually managed in primary care (1). The National Institute for Health and Care Excellence (NICE) stepped care guidelines recommend psychological therapy at step 2, followed by the option of medication at step 3 (2). If patients' progress to medication, NICE guidelines recommend antidepressant treatment. Antidepressant prescribing for any indication has substantially increased over the past two decades, which has been attributed to increasing long-term use, rather than increases in those starting medication (3, 4). Antidepressant prescribing for generalised anxiety disorder (GAD) has also increased over the same period, however it is not known if long-term use has similarly increased (5).

Other drugs are prescribed for anxiety. Due to their potential for dependency, benzodiazepines are not recommended for long-term use (6). Since 2008, the number of patients prescribed a benzodiazepine in the year after a GAD diagnosis has declined (5). However, no data have been published on prescribing for anxiety disorders in general over time. Furthermore, the 2011 NICE guidelines recommended that antipsychotics should not be prescribed for treatment of GAD (2). Yet, there are no data on the prescribing of antipsychotics for anxiety (with the exception of GAD (5)), or on other drugs used for anxiety – beta-blockers and anticonvulsants – in recent years.

This study examines trends in prescribing for anxiety in UK primary care between 2003-2018 using Clinical Practice Research Datalink (CPRD) data. The specific objectives were to:

- Examine trends in prevalence and incidence of prescriptions - overall and by drug class - between 2003-2018, and to investigate potential differences over time according to age and gender.
- Determine whether any changes in prescribing over time were due to: (i) increases in incident prescriptions; and/or (ii) changes in the duration of treatment.

Methods

Study population

CPRD Gold is a large database of anonymised UK primary care electronic records. We used data from adults aged 18 and over, registered at a CPRD Gold practice between 1st January 2003 and 31st December 2018. Patient records had to be 'acceptable', and from practices that were 'up-to-standard' for at least one year before study entry date, and had contributed data for the whole 16-years. For the analysis on incident prescriptions, patients had to have been registered with CPRD Gold for one year before the first recorded anxiolytic prescription to ensure high-quality assessment of incident cases.

Codes for Anxiolytics

Anxiolytic prescriptions were identified using British National Formulary (BNF) codes (Supplement 1), compiled according to the British Association for Psychopharmacology's recommendations for treatment of anxiety disorders (7), and the NICE guidelines (2).

The prescription had to have occurred within the three months before an anxiety symptom or diagnosis code date, or the six months afterwards (Supplement 2). This aligns with similar studies (4).

Statistical analysis

Data analysis was conducted using Stata version 15.1. Analyses were conducted for: any anxiolytic; any antidepressant; SSRIs & 'other antidepressants'; benzodiazepines; beta-blockers (propranolol); antipsychotics; anticonvulsants (pregabalin and gabapentin).

Trends in prevalence and incidence of anxiolytic prescriptions

Patients entered the study on the last date of either their current registration date or the 1st January 2003, and stopped contributing person-years-at-risk (PYAR) on the earliest date of either their transfer out date; date of death; 31st December 2018; or date of their (prevalent or incident) anxiolytic prescription. PYAR was calculated separately for prevalence and incidence analyses. For each calendar year we calculated: (i) the number of patients who received at least one prescription (prevalent case); and (ii) the number of patients who started a prescription but had no prior prescriptions of that same drug class during the study period, or in the one year before the study start date (incident case). Annual prevalence/incidence rates were calculated by dividing the number of cases by the total (PYAR) for each calendar year, and are presented per 1000PYAR, with 95% confidence intervals (95%CI) based on the Poisson distribution. Data were stratified by age (<25, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, ≥85 years) and gender.

Univariable Poisson regression models were used to examine associations between year, age, gender and prevalence/incidence of the drug(s) of interest. Prevalence rate ratios (PRRs)/incidence rate ratios (IRRs) and 95%CI are reported. Multivariable Poisson regression models that included year, age and gender were used to examine the independent effects of such factors. Sensitivity analyses were conducted to account for any clustering by practices within the multivariable model. To formally test whether prevalence/incidence varied over time according to age and gender, the multivariable Poisson regression model was repeated including an interaction between gender and year, and age and year.

Changes in trends were examined using joinpoint regression (version 4.7.0.0) (8). By fitting a series of joined lines, the model selects the point(s) where the rate significantly increases/decreases (joinpoints) thus identifying the years (with 95%CI) when changes in trends occurred. Annual percentage change, based on the gradient between joinpoints, was also calculated.

Sensitivity analyses considered anxiolytic medication prescribed within one month before the anxiety code, or one month afterward. Additionally, sensitivity analyses excluded patients prescribed low dose (<75mg) amitriptyline.

Trends in treatment duration

For each drug class, the duration of treatment was calculated for incident prescriptions by dividing the quantity of drug prescribed by the daily dose. If no dosage instructions were entered, then the median of the substance specific prescription duration was used. Similar studies have used this approach (3, 4). A prescription occurring within ≤12 months of the previous prescription ending was considered part of the same treatment episode. Patients not prescribed medication for >12 months were considered as having ended treatment, with any further prescriptions regarded as a new treatment episode. Duration was subdivided into categories (days: <15, 15-30, 31-60, 61-180, 181-365, 366+).

Results

Sample characteristics

The dataset included 176 practices with 2,569,153 eligible patients registered across 2003-2018, and 17.7 million person-years-at-risk (PYAR). There were 546,154 anxiolytic prescribing events, of which 194,049 were incident prescriptions (References

1. Wittchen. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol.* 2011;21(9):655-79.
2. NICE. Generalised anxiety disorder and panic disorder in adults: management Clinical guideline [CG113]. 2011. Available from: <https://www.nice.org.uk/guidance/cg113> [Accessed 25th November 2021].
3. Mars B, Heron J, Kessler D, et al. Influences on antidepressant prescribing trends in the UK: 1995–2011. *Soc Psychiatry Psychiatr Epidemiol.* 2017;52(2):193-200.
4. Moore M, Yuen HM, Dunn N, et al. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *Bmj.* 2009;339:b3999.
5. Snee A, Nazareth I, Freemantle N, Horsfall L. Trends in generalised anxiety disorders and symptoms in primary care: UK population-based cohort study. *Br J Psychiatry.* 2020:1-7.
6. NICE. Anxiety Disorders - Quality standard [QS53]. 2014. Available from: <https://www.nice.org.uk/guidance/qs53> [Accessed 25th November 2021].
7. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol.* 2014;28(5):403-39.
8. National Cancer Institute. Joinpoint Trend Analysis Software 2020 [Available from: <https://surveillance.cancer.gov/joinpoint/>. [Accessed 25th November 2021].
9. Lockhart P, Guthrie B. Trends in primary care antidepressant prescribing 1995-2007: a longitudinal population database analysis. *Br J Gen Pract.* 2011;61(590):e565-e72.
10. Archer C, Kessler D, Wiles N, Turner K. GPs' and patients' views on the value of diagnosing anxiety disorders in primary care: a qualitative interview study. *Br J Gen Pract.* 2021.
11. Archer C, Turner K, Kessler D, et al. Trends in the recording of anxiety in UK primary care: a multi-method approach. *Soc Psychiatry Psychiatr Epidemiol.* 2021.
12. MHRA. Benzodiazepines Learning Module 2015 Available from: https://cpd.mhra.gov.uk/benzodiazepines/CON234573_20. [Accessed 25th November 2021].
13. openprescribing.net. Propranolol Hydrochloride (0204000R0) 2020 [Available from: <https://openprescribing.net/chemical/0204000R0/>. [Accessed 25th November 2021].
14. Royal Pharmaceutical Society of Great Britain. British national formulary 79. London: Royal Pharmaceutical Society; 2020. Available from: <https://bnf.nice.org.uk/> [Accessed 25th November 2021].
15. Brudkowska Ż, Tomczyk M, Jusiak K, et al. The role of beta-adrenolytic drugs in treating anxiety disorders. *Curr Probl Psychiatry.* 2018;19(3):209-24.
16. Steenen SA, van Wijk AJ, Van Der Heijden GJ, et al. Propranolol for the treatment of anxiety disorders: Systematic review and meta-analysis. *J Psychopharmacol.* 2016;30(2):128-39.
17. Montastruc F, Loo SY, Renoux C. Trends in first gabapentin and pregabalin prescriptions in primary care in the United Kingdom, 1993-2017. *Jama.* 2018;320(20):2149-51.
18. Marston L, Nazareth I, Petersen I, et al. Prescribing of antipsychotics in UK primary care: a cohort study. *BMJ Open.* 2014;4(12):e006135.
19. Martin-Merino E, Ruigomez A, Wallander MA, et al. Prevalence, incidence, morbidity and treatment patterns in a cohort of patients diagnosed with anxiety in UK primary care. *Fam Pract.* 2010;27(1):9-16.
20. Public Health England. Dependence and withdrawal associated with some prescribed medicines: An evidence review. 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940255/PHE_PMR_report_Dec2020.pdf [Accessed 25th November 2021].
21. Lijster JMD, Dierckx B, Utens EM, et al. The age of onset of anxiety disorders: a meta-analysis. *Can J Psychiatry.* 2017;62(4):237-46.
22. Education Policy Institute. Access to child and adolescent mental health services in 2019. 2020. Available from: https://epi.org.uk/wp-content/uploads/2020/01/Access-to-CAMHS-in-2019_EPI.pdf [Accessed 10th December 2021].

Table 1).

Prevalence of anxiolytic prescriptions

Estimates of the prevalence of anxiolytic prescriptions are presented in Figure 1 (and Supplement 3-5). Between 2003-2008, the prevalence of any anxiolytic prescription was steady at 25-26/1000PYAR, rising sharply to 43.6/1000PYAR in 2018 (Figure 1; Supplement 3). Similar patterns were seen for all antidepressants, and SSRI and 'other antidepressants' (Figure 1; Supplement 3). Prevalence of prescriptions for benzodiazepines was lower but remained steady over the 16-years (Figure 1; Supplement 4), whilst beta-blockers gradually increased from 3.8/1000PYAR in 2008 to 8.7/1000PYAR in 2018 (Figure 1; Supplement 4). Antipsychotics and anticonvulsants were prescribed infrequently (Figure 1; Supplement 4 and 5).

The best-fitting joinpoint models for any anxiolytic, all antidepressants, and SSRIs and 'other antidepressants', included two joinpoints - one in 2008 (95% CI 2006-2011), after which prevalence of prescribing increased, and one in 2014 (95% CI 2011-2016), with substantial increases to 2018 (Figure 3 and Supplement 6). The best-fitting models included one join point for prescriptions of benzodiazepines (2005 (95% CI 2005-2006)), beta-blockers (2008 (95% CI 2007-2009)) and antipsychotics (2007 (95% CI 2005-2010)), whilst anticonvulsants included two joinpoints in 2010 (95% CI 2009-2012), and 2016 (95% CI 2015-2016) (Figure 3 and Supplements 7-10).

Prescribing of anxiolytics in women was over twice that of men, excluding antipsychotics (~50% higher in women compared to men (PR: 1.46 (95% CI 1.42-1.49)) (Supplement 11). Prescribing of any anxiolytic, all antidepressants, beta-blockers (Supplement 11) and SSRIs and 'other antidepressants' (Supplement 11) was less prevalent in older adults. In contrast, the prevalence of benzodiazepine and anticonvulsant prescriptions in those aged 25+ was two to three times that of those aged<25 (Supplement 11). The prevalence of antipsychotic prescribing for 25-54-year-olds was ~40% higher than those aged<25 (Supplement 11).

The overall pattern of trends over time (any anxiolytic and most drug classes) were similar for men and women. There was no evidence of an interaction between year and gender for antipsychotics (p value for interaction=0.44), and weak evidence for anticonvulsants (p=0.07). There was evidence of an interaction between year and gender for any anxiolytic (p=0.02); all antidepressants (p=0.007); SSRIs & 'other antidepressants' (p=0.006); benzodiazepines (p=0.03); and beta-blockers (p=0.009), however these results need to be interpreted with some caution. For the years where the interaction parameters were driving the interaction effect, there was little temporal increase in prescribing for men, such that slight increases in women represented a large relative increase, and it was this relative difference which the interaction terms were estimating. Such differences were therefore unlikely to be clinically meaningful. Prevalence rates were stratified by age (Figure 2; Supplement 12-17). Prevalence increased substantially in 18-34-year-olds in later years of the study, across all drug classes. There was strong evidence of an interaction between year and age in all models (p values for interaction<0.001) (Figure 2).

Incidence of anxiolytic prescriptions

The number of patients starting anxiolytics are shown in Figure 3 (and Supplement 18-20). Between 2003-2006, incident prescriptions for any anxiolytic decreased from 12.8/1000PYAR to 10.0/1000PYAR, after which incidence remained steady until 2012, before rising to 13.1/1000PYAR in 2018 (Figure 3; Supplement 18). Similar trends were seen for all antidepressants, and SSRI and 'other antidepressants' (Figure 3; Supplement 18). For benzodiazepines, incident prescribing declined from 6.4/1000PYAR to

4.6/1000PYAR between 2003-2018 (Figure 3; Supplement 19). In contrast, incident prescribing of beta-blockers rose from 2.3/1000PYAR to 4.1/1000PYAR between 2003-2018 (Figure 3; Supplement 19). The incidence of antipsychotic prescriptions was between 0.5-0.7/1000PYAR across the 16-years (Figure 3; Supplement 19), whilst anticonvulsants slightly increased from 0.1/1000PYAR to 1.3/1000PYAR (Figure 3; Supplement 20).

The best-fitting joinpoint model for any anxiolytic included two joinpoints at 2006 (95% CI 2005-2009) and 2012 (95% CI 2009-2015), with similar patterns seen for all antidepressants and SSRIs and 'other antidepressants' (Figure 5 and Supplement 21). For benzodiazepine prescriptions, the best-fitting model had a single joinpoint in 2008 (95%CI 2006-2011) (Supplement 22). The best-fitting model had one joinpoint for beta-blockers (2008 (95% CI 2007-2009)) and for antipsychotics (2007 (95% CI 2005-2009)) and included two joinpoints for anticonvulsants (2010 (95% CI 2009-2011); 2016 (95% CI 2015-2016)) (Figure 5 and Supplements 23-25).

Incident anxiolytic prescriptions in women were twice that of men, excluding antipsychotics (44% higher in women compared with men (adjusted IRR: 1.44 (95% CI 1.39-1.50))) (Supplement 26). Incident prescriptions of any anxiolytic, all antidepressants, SSRIs and 'other antidepressants' and beta-blockers decreased with age (Supplement 26). Incident antipsychotic prescriptions were slightly lower in older individuals compared with younger individuals (Supplement 26). In contrast, those aged 25+ had between a 16%-48% increased rate of incident benzodiazepine prescriptions compared with those aged<25 (Supplement 26). Incident anticonvulsant prescriptions in those aged 25+ were two to three times that of those aged<25 (Supplement 26).

The overall pattern of trends over time (any anxiolytic and most drug classes) were similar for men and women. There was no evidence of an interaction between year and gender for beta-blockers (p value for interaction=0.40) and antipsychotics (p=0.53), and weak evidence for anticonvulsants (p= 0.11). There was evidence of an interaction between year and gender for any anxiolytic (p<0.001); all antidepressants (p<0.001); SSRIs & 'other antidepressants' (p<0.001); and benzodiazepines (p<0.001), however as previously for prevalent prescribing, differences were small and unlikely to be clinically meaningful. Incidence rates were stratified by age (Figure 4; Supplement 27-32). Incidence increased in 18-34-year-olds in later years of the study (2013/2014-2018), across all drug classes. There was strong evidence of an interaction between year and age for all models (p value for interaction<0.001) (Figure 4).

Sensitivity analyses

Sensitivity analyses examined the potential impact of clustering within GP practices, and the impact on findings when prescriptions were restricted to one month either side of an anxiety code, or when low-dose amitriptyline was excluded. Trends were comparable to the main analysis.

Trends in treatment duration for patients starting anxiolytics by drug class

For all antidepressants, SSRIs & 'other antidepressants' and beta-blockers, prescription duration remained relatively stable between 2003-2018, with year-to-year fluctuations in the duration of antipsychotic and anticonvulsant prescriptions (Supplements 33-37). In contrast, the proportion of short-term benzodiazepine prescriptions increased with time, whilst long-term use decreased (Figure 5). However, 44% of the prescriptions in 2017 were longer than the recommended maximum (four weeks) (2) (Figure 5).

Discussion

Summary

Prevalence of prescriptions of any anxiolytic and all drug classes increased over the study period, with a marked increase from 2008-2018, excluding benzodiazepines which remained steady. Incidence of prescriptions of any anxiolytic, driven by antidepressant prescribing, decreased between 2003-2006, after which rates remained steady, before increasing substantially between 2012-2018. In contrast, incidence of prescriptions for benzodiazepines gradually declined over the 16-years. Whilst prescribed infrequently, incidence of prescriptions of beta-blockers, antipsychotics, and anticonvulsants gradually increased from 2003-2018. The increases in incident prescriptions are more likely to explain the increases in prevalence, rather than longer treatment duration.

Prevalence and incidence of prescriptions in women were nearly twice that of men, for any anxiolytic and each drug class, except for antipsychotics. Trends over time were similar for men and women. Prevalence and incidence of prescriptions of any anxiolytic and each drug class increased substantially in 18-34-year-olds between 2013/2014-2018, with a marked rise in incident benzodiazepine prescribing for this group, despite an overall reduction in incident benzodiazepine prescribing.

Strengths and limitations

The use of a large, nationally representative dataset enabled analysis of trends over a 16-year period in terms of the prevalence/incidence of prescriptions by drug class, and by age and gender. An extensive list of anxiolytic medication was used, and the prescription had to have occurred within the three months before an anxiety code, or the 6 months afterwards.

The study is restricted to patients who have a recorded anxiety code and anxiolytic prescription. Data from patients who have been prescribed an anxiolytic, but do not have an anxiety code, are not captured. Furthermore, whilst prescriptions must have occurred within the defined time-period of an anxiety code, some of these drugs may have been prescribed for other indications. Consequently, the reported figures may be an overestimate. No information was available on dispensing, adherence, or other treatment access.

Comparisons with existing literature

Previous research found substantial increases in prescribing of antidepressants – for any indication and for depression (3, 4, 9) – but this was attributed to increasing long-term use of antidepressants rather than increasing incident prescribing. In contrast, the present study focused on prescribing for anxiety and found increases in incident antidepressant prescribing from 2013-2018. This is consistent with previous research that found increases in antidepressant prescriptions for GAD (issued in the year after diagnosis) between 1998-2018 (5). Qualitative research has found GPs are more likely to use diagnostic codes when anxiety is severe (10) and are more likely to prescribe an anxiolytic when a patient has a diagnosis of anxiety (11). Indeed, the trends in anxiolytic prescribing over time reported in the present study are very similar to trends in diagnostic codes used by GPs over the same period (11). Taken together this may explain the trends observed, although we do not know if the increase in incident prescribing reflects increased awareness of anxiety among GPs, increased awareness of anxiety among patients, or a true increase in anxiety.

Previous data have shown that the prevalence of primary care benzodiazepine prescribing - for all indications - was relatively constant between 2008-2012 (12). In this study, whilst prevalence of benzodiazepine prescribing for anxiety was steady over time, incident prescribing decreased, excluding 18-34-year-olds. Others have reported a similar decline in the year after a GAD diagnosis (5). However, whilst long-term benzodiazepine treatment declined over time, 44% of the prescriptions in 2017 were for longer than the recommended maximum (four weeks) (2).

The increasing prevalence and incidence of beta-blocker prescriptions in this study is consistent with data reporting prescribing trends for all indications (13). Although propranolol is licensed for anxiety (14) there is no conclusive evidence for its effectiveness (15, 16), and it is not recommended in NICE guidance. Previous research on anticonvulsant prescribing - for any indication - found increases in prevalence of prescriptions for anticonvulsants between 2007-2017 (17). We found similar trends in the overlapping years. Whilst the 2011 NICE anxiety guidelines state – “do not offer antipsychotics for treatment of GAD” (page 18) (2), antipsychotic prescribing rates increased after 2011. Whilst some of these prescriptions may have been for other indications, previous research found that ~50% of primary care antipsychotic prescriptions were for non-psychotic disorders, including anxiety (18). In contrast to the present study, others have identified slight declines in antipsychotic prescribing (1998-2018) in the year after a GAD diagnosis (5). However, this latter study linked prescriptions to anxiety codes using a wider interval (one year after incident diagnosis) (5) than the present study.

Anxiolytic use in women was twice that of men and this is consistent with other studies (3, 19, 20). Previous research found that the prescribing of antidepressants (any indication) increased with age (3, 20). In contrast, the present study found that antidepressant prescribing for anxiety was less prevalent in older adults, with the largest increase in young adults, most notably in those aged under 25. This may be because younger patients are more likely to present with anxiety (21), with GP interview data suggesting this increase may be driven by increasing use of social media and increasing pressure on young people (11). It is possible that the increases in prescribing amongst young adults may be the result of earlier unmet need. Referrals to child and adolescent mental health services (CAMHS) have increased in recent years (22). However, in 2018-2019, over a quarter of referrals to CAMHS were rejected, and, for those who access treatment through CAMHS, there is a lack of support during the transition from CAMHS to adult mental health services (22). These factors may, in part, be contributing to the substantial rise in anxiety and its pharmacological treatment amongst young adults over the last decade.

Implications

Increases in incident prescribing for anxiety, especially among young adults, may reflect better detection of anxiety, increasing severity of symptoms or earlier unmet need. However, some of this prescribing is not based on robust evidence of effectiveness, and may contradict guidelines. We know that once people have started taking antidepressants they often continue long-term, and there is increasing evidence that this may be associated with unintended harms. The rise in prescribing of antidepressants for anxiety in young adults (aged under 25) has been substantial in recent years. Although incident benzodiazepine prescribing fell over time, increases have been seen in under 35-year-olds. In 2017, 44% of benzodiazepine prescriptions were longer than the recommended maximum of four weeks. We need research to improve our understanding of why this is happening, and to provide interventions that are acceptable and effective for young adults, that can mitigate the growing reliance on pharmacotherapy for this age group.

Declarations

Declaration of interests

We declare no competing interests.

Ethics statement

The CPRD protocol (19_001) for this study, and a subsequent minor amendment (19_001MnA), was approved by the CPRD's Independent Scientific Advisory Committee (ISAC) prior to undertaking data analysis. The study population was originally defined as those with a recorded anxiety code, in addition to the criteria listed under 'study population'. However, over half of the study population had a prescription on the same date as a recorded anxiety code, and therefore did not contribute any person-years-at-risk. The minor amendment 19_001MnA was approved by CPRD's Independent Scientific Advisory Committee to define those 'at risk' of receiving a prescription for anxiety as individuals listed under 'study population'.

Individual patients can opt-out of sharing their data for research. CPRD does not collect data for these patients.

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References

1. Wittchen. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol.* 2011;21(9):655-79.
2. NICE. Generalised anxiety disorder and panic disorder in adults: management Clinical guideline [CG113]. 2011. Available from: <https://www.nice.org.uk/guidance/cg113> [Accessed 25th November 2021].
3. Mars B, Heron J, Kessler D, et al. Influences on antidepressant prescribing trends in the UK: 1995–2011. *Soc Psychiatry Psychiatr Epidemiol.* 2017;52(2):193-200.
4. Moore M, Yuen HM, Dunn N, et al. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. *Bmj.* 2009;339:b3999.
5. Slee A, Nazareth I, Freemantle N, Horsfall L. Trends in generalised anxiety disorders and symptoms in primary care: UK population-based cohort study. *Br J Psychiatry.* 2020:1-7.
6. NICE. Anxiety Disorders - Quality standard [QS53]. 2014. Available from: <https://www.nice.org.uk/guidance/qs53> [Accessed 25th November 2021].
7. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol.* 2014;28(5):403-39.
8. National Cancer Institute. Joinpoint Trend Analysis Software 2020 [Available from: <https://surveillance.cancer.gov/joinpoint/>. [Accessed 25th November 2021].
9. Lockhart P, Guthrie B. Trends in primary care antidepressant prescribing 1995-2007: a longitudinal population database analysis. *Br J Gen Pract.* 2011;61(590):e565-e72.
10. Archer C, Kessler D, Wiles N, Turner K. GPs' and patients' views on the value of diagnosing anxiety disorders in primary care: a qualitative interview study. *Br J Gen Pract.* 2021.
11. Archer C, Turner K, Kessler D, et al. Trends in the recording of anxiety in UK primary care: a multi-method approach. *Soc Psychiatry Psychiatr Epidemiol.* 2021.
12. MHRA. Benzodiazepines Learning Module 2015 Available from: https://cpd.mhra.gov.uk/benzodiazepines/CON234573_20. [Accessed 25th November 2021].
13. openprescribing.net. Propranolol Hydrochloride (0204000R0) 2020 [Available from: <https://openprescribing.net/chemical/0204000R0/>. [Accessed 25th November 2021].
14. Royal Pharmaceutical Society of Great Britain. British national formulary 79. London: Royal Pharmaceutical Society; 2020. Available from: <https://bnf.nice.org.uk/> [Accessed 25th November 2021].
15. Brudkowska Ż, Tomczyk M, Jusiak K, et al. The role of beta-adrenolytic drugs in treating anxiety disorders. *Curr Probl Psychiatry.* 2018;19(3):209-24.
16. Steenen SA, van Wijk AJ, Van Der Heijden GJ, et al. Propranolol for the treatment of anxiety disorders: Systematic review and meta-analysis. *J Psychopharmacol.* 2016;30(2):128-39.
17. Montastruc F, Loo SY, Renoux C. Trends in first gabapentin and pregabalin prescriptions in primary care in the United Kingdom, 1993-2017. *Jama.* 2018;320(20):2149-51.
18. Marston L, Nazareth I, Petersen I, et al. Prescribing of antipsychotics in UK primary care: a cohort study. *BMJ Open.* 2014;4(12):e006135.
19. Martin-Merino E, Ruigomez A, Wallander MA, et al. Prevalence, incidence, morbidity and treatment patterns in a cohort of patients diagnosed with anxiety in UK primary care. *Fam Pract.* 2010;27(1):9-16.
20. Public Health England. Dependence and withdrawal associated with some prescribed medicines: An evidence review. 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/940255/PHE_PMR_report_Dec2020.pdf [Accessed 25th November 2021].
21. Lijster JMd, Dierckx B, Utens EM, et al. The age of onset of anxiety disorders: a meta-analysis. *Can J Psychiatry.* 2017;62(4):237-46.
22. Education Policy Institute. Access to child and adolescent mental health services in 2019. 2020.

Table 1 Number of prescribing events during the study – for any anxiolytic and by drug class

Drug(s) of interest	Number of prescriptions	
	Total Prescribing events	Total Incident Prescribing events
	Freq.	Freq.
Any anxiolytic	546,154 [∞]	194,049 [∞]
All antidepressants	449,499	163,273
SSRI & 'other antidepressants'	407,229	153,674
Benzodiazepines	210,743	94,927
Beta-blockers	100,146	52,421
Atypical antipsychotics	26,587	10,358
Anticonvulsants	28,601	14,572
[∞] this figure only includes one anxiolytic per year, per patient. Hence, it is not a sum of total prescribing events from each drug class.		

Figure 1 Prevalence of anxiolytic prescriptions (any anxiolytic, and by drug class) per 1000 person years between 2003 and 2018, with joinpoints (with 95% CI).

Figure 2 Prevalence of any anxiolytic prescription per 1000PYAR by age

Figure 3 Incidence of anxiolytic prescriptions (any anxiolytic and by drug class) per 1000 person years between 2003 and 2018, with joinpoints (95% CI).

Figure 4 Incidence of prescriptions of any anxiolytic per 1000PYAR by age

Figure 5 Changes in the proportion of patients with different treatment lengths for benzodiazepines, between 2003 and 2018†

†Data were extracted in July 2019, and therefore it is likely that the figures for 2018 for the longer duration categories are an underestimate and should be interpreted with caution.