

Explaining the variation between practices in the duration of new antidepressant treatment:

a database cohort study in primary care

Abstract

Background

Practices vary in the duration of newly initiated antidepressant treatment, even after adjusting for patient characteristics. It was hypothesised that this may be because of differences between practices in demographic (practice deprivation and antidepressant prescribing rates), organisational (practice size and proportion of female GPs), and clinical factors (proportion of new episodes of depression coded).

Aim

To examine the effect of practice characteristics on the duration of new selective serotonin reuptake inhibitor antidepressant treatment in primary care.

Design and setting

Database cohort study of 28 027 patients from 237 GP practices in Scotland.

Method

Prescription data were used to estimate duration of treatment for individual patients beyond three time points: 30, 90, and 180 days. Data at patient and practice level were analysed by multilevel logistic regression to quantify the variation between practices.

Results

The mean rate of diagnostic coding for depression in patients beginning a course of treatment was 29% (range 0–80%). Practice-level deprivation and rate of new antidepressant prescribing were not associated with duration of treatment. The practice level factor most strongly associated with duration of treatment at practice level was the proportion of patients coded as having depression: odds ratio for continuing beyond 30 days was 1.54 [95% confidence interval (CI) = 1.22 to 1.94]; beyond 90 days, 1.37 (95% CI = 1.09 to 1.71); and beyond 180 days 1.41 (95% CI = 1.10 to 1.82).

Conclusion

Encouraging coding and structured follow-up at the onset of treatment of depression is likely to reduce early discontinuation of antidepressant treatment and improve outcomes.

Keywords

antidepressant treatment; clinical practice variation; depressive disorder; prescribing; primary health care.

INTRODUCTION

Antidepressant drugs, usually selective serotonin reuptake inhibitors (SSRIs), are the most common first-line treatment for depression in primary care.^{1,2} These drugs have been shown to be more effective than placebo in the treatment of depression in primary care.³ Continuation of treatment following remission of depression is associated with a reduced risk of early relapse and in patients who have already experienced depressive episodes, long-term treatment substantially reduces the risk of further episodes.⁴ Consequently, national and international guidelines recommend that antidepressant treatment should be continued for around 6 months after recovery from an initial episode.^{5,6} However, many patients prefer not to take antidepressants and discontinue, or do not even start treatment.^{7,8}

Most new courses of antidepressant treatment fall short of the recommended duration, with at least one-quarter being taken for less than 1 month.^{1,2} Previous research, in a large primary care database cohort, found that duration of treatment was only weakly influenced by patient characteristics including age, sex, socioeconomic deprivation, physical comorbidity, and history of past treatment.⁹ Multilevel analysis in which patients were clustered by GP practice indicated that the GP practice accounted for a similar proportion of variance to the individual characteristics. One factor which may have related to either patient or GP — whether

the GP had recorded a diagnostic code indicating a depressive or other mental health disorder for the episode of care during which antidepressant treatment was initiated — was the variable most strongly associated with duration of treatment. This may have been because more severely affected episodes were coded, or may have reflected differences between practices in liability to code episodes of depression. It was hypothesised that this may be an indicator of adherence to protocols and quality of diagnostic completeness because there was no obligation for practices to enter diagnostic codes for depression. Indeed, doing so meant that the GP had to carry out and record a structured assessment of severity, such as the Patient Health Questionnaire (PHQ-9), Hospital Anxiety and Depression Scale (HADS), or the Beck Depression Inventory (BDI) for the patient.¹⁰

Previous studies of GP diagnosis and treatment of depression have indicated a fivefold difference in rates between practices, with higher rates of depression diagnosis in practices serving areas of greater deprivation and with a higher proportions of GPs who were female.¹¹ No available studies have examined GP practice characteristics in relation to duration of treatment. Thus, this study aimed to examine GP practice characteristics associated with the proportion of patients continuing newly initiated antidepressant treatment beyond 30, 90, and 180 days, using an existing database cohort of patients newly prescribed an antidepressant drug.

C Burton, MD FRCP, senior lecturer; **I Cameron**, PhD, lecturer, Division of Applied Medicine, University of Aberdeen, Aberdeen. **N Anderson**, PhD, senior lecturer, Centre for Population Health Sciences, University of Edinburgh, Edinburgh.

Address for correspondence

Christopher Burton, Division of Applied Health Sciences, University of Aberdeen, Polwarth

Building, Foresterhill, Aberdeen, AB25 2ZD, UK.

E-mail: c.burton@abdn.ac.uk

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How this fits in

While practice variation in the initiation of antidepressant treatment has been described, little is known about practice characteristics associated with duration of new treatment. Performance-related pay for depression management, introduced in the Quality and Outcomes Framework, required GPs who coded patients with a new episode of depression to follow them up at least once after 4–6 weeks. The proportion of patients starting a selective serotonin reuptake inhibitor or similar antidepressant who were coded as having depression varied between practices. The proportion of patients coded was the strongest predictor of the duration of antidepressant treatment at practice level.

METHOD

The study was carried out using the Primary Care Clinical Informatics Unit Research database held by the University of Aberdeen, which comprises anonymised data from patients registered with over 200 GP practices across Scotland. Data were used that related to the 12 months from April 2007 to March 2008. The methods for identifying newly initiated antidepressant treatment have previously been described in detail.⁹ Briefly, eligible patients received one or more prescriptions for an eligible antidepressant — any SSRI, venlafaxine, mirtazapine, lofepramine, or trazodone — in the 12-month period beginning 1 April 2007 and had received no prescriptions for a similar drug in the preceding 12 months. Duration of treatment was estimated from the date, dose, frequency, and quantity characteristics of each prescription, and from the interval between first and last prescriptions. Patients were only included if the duration of treatment assessed by these two methods was similar (difference <60 days). The method permitted dose changes and sequential or concurrent prescribing of different antidepressant drugs to reflect the reality of clinical practice in which antidepressant doses and treatments are commonly changed.

For each patient the following data were collected in addition to estimated duration of treatment: GP practice, age, sex, deprivation (using the Scottish Index of Multiple Deprivation), physical comorbidity (coronary heart disease or diabetes), whether they had ever been prescribed antidepressant treatment before 1 April 2006, and whether a diagnostic code indicating a depressive disorder had been

entered on their record in the study period (the diagnostic codes are available from authors). GP practices were recorded on the database such that they could not be identified by the researchers. For each practice the database included practice size (number of patients and number of doctors), proportion of GP principals who were female (not adjusted for part-time working), and deprivation (Scottish Index of Multiple Deprivation based on the postal code of the main practice premises). For each practice, the proportion of patients prescribed a new course of antidepressant (prescribing rate) and the proportion of those patients prescribed a new course of antidepressant who had a diagnostic code for depression entered in their record (patient coding rate) were also calculated.

Analysis

The effect of patient- and practice-level factors on treatment continuation were examined after three key time points: 30 days (indicating that a second prescription had been issued), 90 days (indicating three consecutive months of treatment; less time than guidelines recommend, but suggestive of meaningful engagement in treatment), and 180 days (indicating the potential to be compliant with guidelines). These time points were chosen because they are suitable time points for individual practice audit of treatment duration and because proportions of patients continuing treatment beyond these points is an easier concept to convey to clinicians than the hazard ratios generated by survival analysis. For analysis of treatment at each time point, cases were only included that could have reached that given time point, for example, a patient who began treatment 120 days before the end of the study period would only be included in the analysis of 30 and 90 day continuation. The choice of practice characteristics was based on previous patient-level findings and the literature regarding diagnosis and treatment rates. Specifically, factors examined might be associated with patient-centredness (such as small practice and more female doctors), workload (such as area deprivation and practice antidepressant prescribing rate), and protocol-centredness (such as patient coding rate).

The patient-level variables were entered separately into a multilevel logistic regression model (clustered by practice) for each of the three individual time points. The practice variables were then added and tested for change in model fitting by comparison of the Akaike information

Table 1. Characteristics of practices (n = 237)

Characteristics	Median	Interquartile range
Practice list size	4720	2920–7410
Number of GPs	5	3–7
Proportion of female GPs	50	37.5–66.7
Patients prescribed eligible AD, per 1000	76.6	63–89.9
Patients starting eligible AD, per 1000	20.3	16.2–24.7

AD = antidepressant.

criterion (AIC). As two of the variables (deprivation category and diagnostic coding) were present at both the individual patient level and the practice level, both measures of each variable were initially included in the model. The patient-level measure of these two variables was then removed to examine the effects of these variables at practice level alone.

In the case of coding with a depressive disorder diagnosis — which may have been a function of the severity of the patient's depression and of practice behaviour — two additional tests were conducted. First, the distribution of coding rates and prescribing rate adjusting for practice size were plotted, expecting that if practice coding was related to (random) patient variation in severity,

then values should scatter around a mean, with larger practices closer to the mean.

Second, the analysis was repeated, restricting it to patients who were prescribed only one antidepressant drug, on the grounds that changing drug is more common in patients with more severe or treatment resistant depression,¹² who may be more likely to be coded. Analyses were carried out in R (version 3.01), with multilevel logistic regression using maximum likelihood fitting with the glmer function from the lme4 package.

RESULTS

The total population from which the sample was drawn comprised 1 280 840 patients. These patients were registered with 237 general practices containing 1245 GPs. A total of 28 027 patients (2.2%) met the criteria for new treatment, of whom 26 122 had no gaps in treatment of greater than 60 days. Seventy-five per cent of treatment courses continued beyond 30 days: 56% lasted more than 90 days, and 40% lasted more than 180 days after allowing for treatment continuing beyond the study period.

Practice characteristics

Characteristics of included practices are shown in Table 1. The mean practice incidence of new antidepressant treatment prescriptions during the year was 20.3/1000 patients (range 3.4–49.9). The mean proportion of patients beginning a course of treatment who received a diagnostic code for depression was 29% (range 0–80%).

Practice variation in rates of antidepressant prescribing and depression coding

Figure 1 shows the relationship between the practice new antidepressant prescribing rate (expressed as patients/1000) and the proportion of episodes of new antidepressant treatment which received a diagnostic code. There was no correlation between these measures (Pearson's $r = 0.03$ [95% confidence intervals {CIs} = -0.1 to 0.16]), suggesting that whether episodes of depression were coded or not was unrelated to how many patients were prescribed treatment for depression. This plot uses circle size as an indicator of practice size, such that if variation was due to random factors such as case-mix, one would expect the larger practices to lie closer to the mean and smaller ones to be more scattered. The plot indicates that this central tendency was seen for the new antidepressant prescribing rate, but not for the proportion of antidepressant episodes coded.

Figure 1. Bubble plot comparing practice prescribing rate for new antidepressants with practice depression coding rate. Size of circles represents relative size of individual practices.

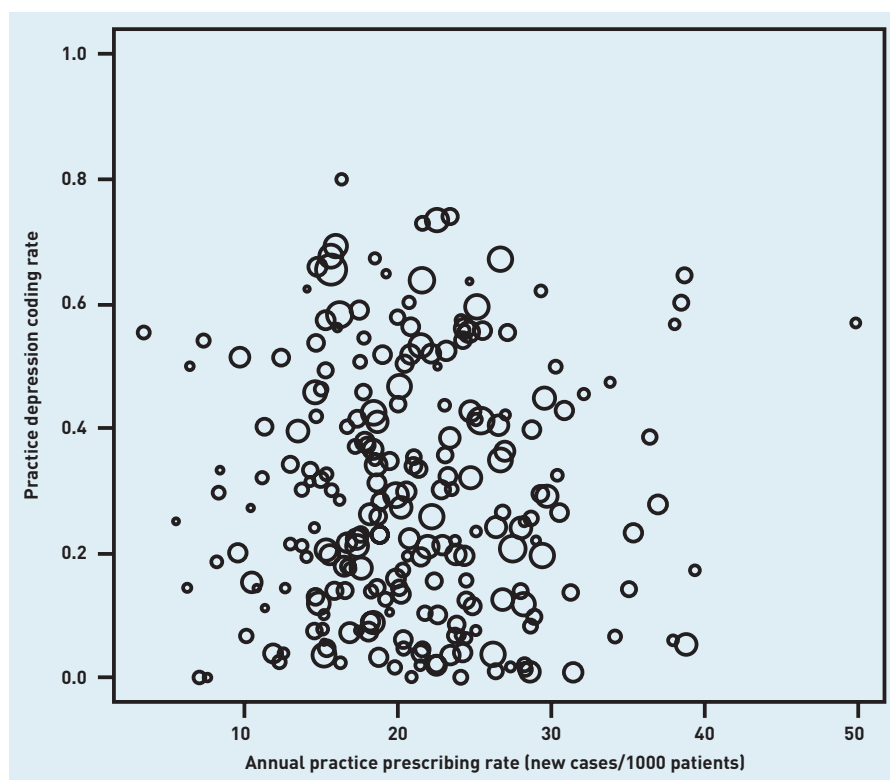


Table 2. Odds of continuing treatment beyond 30, 90, and 180 days by patient and practice level variables. Full model with overlapping patient and practice variables

	Continuation beyond 30 days			Continuation beyond 90 days			Continuation beyond 180 days		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Patient variables									
Male	1.00	0.94 to 1.06	0.95	0.92	0.87 to 0.98	0.01	0.92	0.86 to 1.00	0.04
Deprivation ^a	0.98	0.95 to 1.01	0.18	0.96	0.93 to 0.99	0.007	0.97	0.93 to 1.00	0.07
Age 35–64 years	1.25	1.18 to 1.34	<0.001	1.40	1.32 to 1.50	<0.001	1.53	1.41 to 1.66	<0.001
Age ≥65 years	1.13	1.04 to 1.23	0.006	1.39	1.27 to 1.52	<0.001	1.83	1.64 to 2.05	<0.001
Episode coded ^b	1.99	1.85 to 2.14	<0.001	1.70	1.59 to 1.83	<0.001	1.56	1.44 to 1.70	<0.001
Practice variables									
Female GPs ^c	1.23	1.00 to 1.50	0.04	1.19	0.98 to 1.45	0.09	1.34	1.06 to 1.68	0.01
Deprivation ^d	0.97	0.93 to 1.01	0.11	0.98	0.94 to 1.02	0.31	1.00	0.95 to 1.04	0.90
Practice list size ^e	1.00	0.99 to 1.02	0.67	1.00	0.99 to 1.01	0.99	1.00	1.00 to 1.00	0.63
Episodes coded ^f	0.81	0.63 to 1.03	0.08	0.81	0.64 to 1.02	0.08	0.90	0.69 to 1.18	0.46
Prescribing rate ^g	1.00	0.99 to 1.00	0.22	1.00	0.99 to 1.01	0.64	0.99	0.98 to 1.00	0.14

Model fit described using Akaike Information Criterion. Values for 30 days = 28 043; 90 days = 26 170, and 180 days = 17 618. ^aPer category of the 7 category DepCat measure.

^bEntry during the treatment period of a Read Code for a depression or anxiety disorder. ^cProportion of GPs in the practice who were female not adjusted for part-time working. ^dPer DepCat category of the practice main address. ^eList size in thousands. ^fProportion of cases with one or more Read Codes indicative of depression or anxiety during the treatment period. ^gPatients prescribed new antidepressant treatment per thousand registered patients.

Practice factors associated with treatment duration

At each time point, adding practice level data reduced (improved) the AIC for the model, by between 108 (30 days) and 41 (90 days), indicating a better fitting model. Table 2 shows the results of the multilevel logistic regression for continuing treatment beyond 30, 90, and 180 days. Of the practice-level variables, none had a consistently significant effect when patient-level variables for deprivation and coding of treatment episodes were included in the model.

Table 3 shows the effect of removing these two variables at the patient level

to test for effects at the practice level. Although the model fit is not as good when individual patient data are removed, both coding and deprivation become consistently significant when entered at the practice level only. When the analysis was limited to patients who only received one antidepressant drug (that is, those who were more treatment resistant, or possibly had more severe depression), the results were not substantially changed; for the practice proportion of episodes coded, odds ratios were 1.52 [95% CI = 1.19 to 1.94] beyond 30 days, 1.41 [95% CI = 1.11 to 1.80] beyond 90 days, and 1.52 [95% CI = 1.15 to 2.01] beyond 180 days.

Table 3. Odds of continuing treatment beyond 30, 90, and 180 days by patient and practice level variables. Restricted model with only practice level measures of deprivation and coding

	Continuation beyond 30 days			Continuation beyond 90 days			Continuation beyond 180 days		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Patient variables									
Male	0.99	0.94 to 1.06	0.85	0.92	0.87 to 0.98	0.009	0.92	0.86 to 0.99	0.04
Age 35–64 years	1.25	1.17 to 1.33	<0.001	1.40	1.32 to 1.50	<0.001	1.53	1.41 to 1.65	<0.001
Age ≥65 years	1.06	0.97 to 1.15	0.21	1.32	1.20 to 1.44	<0.001	1.74	1.56 to 1.95	<0.001
Practice variables									
Female GPs ^a	1.24	1.01 to 1.51	0.04	1.20	0.98 to 1.26	0.09	1.36	1.08 to 1.70	0.01
Deprivation ^b	0.96	0.92 to 0.99	0.02	0.96	0.92 to 0.99	0.01	0.98	0.94 to 1.02	0.26
Practice list size ^c	1.00	0.99 to 1.02	0.65	1.00	0.99 to 1.01	0.97	1.00	0.98 to 1.01	0.71
Episodes coded ^d	1.54	1.22 to 1.94	<0.001	1.37	1.09 to 1.71	0.006	1.41	1.10 to 1.82	0.007
Prescribing rate ^e	0.99	0.99 to 1.00	0.17	1.00	0.99 to 1.00	0.41	0.99	0.98 to 1.00	0.09

Model fit described using Akaike Information Criterion. Values for 30 days = 28 401; 90 days = 26 394, and 180 days = 17 725. ^aProportion of GPs in the practice who were female not adjusted for part-time working. ^bPer DepCat category of the practice main address. ^cList size in thousands. ^dProportion of cases with one or more Read Codes indicative of depression or anxiety during the treatment period. ^ePatients prescribed new antidepressant treatment per thousand registered patients.

DISCUSSION

Summary

Despite the fact that most prescriptions for antidepressants are managed by GPs, this is the first study to look at the influence of GP practice on treatment duration. The study found that of a number of plausible factors, the one most strongly associated with treatment duration was the proportion of patients beginning antidepressant treatment who received a coded diagnosis. Although the number of female doctors in a practice has previously been shown to be associated with the amount of antidepressant prescribing,¹³ this study found only a small effect, of borderline statistical significance, of female GPs on treatment continuation.

Strengths and limitations

This study used a large NHS primary care database, providing confidence that the findings may be generalised beyond the sample. It is important to consider the quality of data recorded: as shown, the behaviours for entering data varied in completeness of diagnostic coding, however, prescription data are recorded in the Primary Care Clinical Informatics Unit Research (PCCIUR) database with a high level of accuracy.¹⁴

This study was designed after the original database queries that examined individual patient variation, however, the practice-level data supplied by PCCIUR included an appropriate range of measures for analysis. The dataset was not restricted to treatment of individuals with a coded diagnosis of depression, as others have,^{2,15} or to a depression-indicative Quality and Outcomes Framework (QOF) depression severity measure score.¹⁵ As such, this study may be more broadly representative of individuals receiving antidepressant prescriptions. For example, only 29% of patients in the current study had a depression diagnostic code recorded. Using the General Practice Research Database, Davé *et al*¹⁵ found that 16% of individuals identified with a first-time SSRI prescription within their study period had either a major depressive disorder Read Code entry or a depression indicative score on a validated measure. By excluding individuals without a diagnostic code or depression score, such samples may be unrepresentative of individuals receiving antidepressants for depression in primary care. This study excluded prescriptions for those antidepressants that are licensed, or commonly used, for non-psychiatric disorders, so reduced the chances of including patients who had no mental

distress. Instead, it is assumed that most non-coded instances of SSRI prescribing are for depressive or anxiety complaints that have not been coded. Coding of anxiety disorders by GPs is uncommon and it is possible that a substantial proportion of patients prescribed SSRIs in primary care would meet the criteria for an anxiety disorder.

Furthermore, anxiety and depressive disorders clearly overlap and one recent classification for primary care suggests combining them.¹⁶ Antidepressant prescribing is sometimes seen as a 'coalface option' by GPs faced with distressed patients,¹⁷ and the elements of performance-related pay for depression care in the QOF may have acted as a further barrier to coding. Finally, a high rate of non-coded prescribing of SSRIs is not restricted to the UK.¹⁸ While further information may have been possible if analysis of free text data in the clinical record was available, this was not the case.

It may be possible that the association of coding with prolonged treatment was due to both being indicators of severity, as has been observed in relation to recognition of depression.^{19–21} Sihvo *et al*²² observed severity to be a predictor of continuation of treatment, while others have found fewer consistent associations.^{23,24} While it was not possible to use estimates of severity, particularly where patients had not been coded, a sensitivity analysis was conducted restricted to patients who only received one antidepressant drug in their course of treatment on the grounds that more severely affected patients are more likely to change or have additional treatment. This single-agent analysis showed that coding remained a significant predictor at practice level at all three follow-up times. This study looked for evidence that variation in coding rates was due to differences between practices in depression severity but concluded there was no strong evidence of this.

Comparison with existing literature

It has previously been demonstrated that patient demographic characteristics (age and socioeconomic status) account for only a small part of the variation in the duration of antidepressant treatment.⁹ The current study found that independently of patient characteristics, practice characteristics meaningfully impact on duration of antidepressant treatment. This is in keeping with a Danish study,⁸ which observed a systematic difference between practices in the proportion of patients who only collected

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Ethical approval

As this study involved secondary analysis of anonymised data, independent ethical review was not required.

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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one prescription. It found no associations between duration of treatment and prescriber characteristics such as age, sex, workload, and years of experience in primary care. However, early discontinuation was associated with practices with generally high rates of antidepressant prescribing. The authors concluded that efforts to reduce early discontinuation of antidepressants would be served by focusing on high prescribers of antidepressant drugs. The current study found that the proportion of treated patients who received a diagnostic code was the factor with the strongest association with treatment duration and that prescribing rates had no effect.

Implications for practice

This study highlights wide inter-practice variation in coding for depression but indicates that higher coding rates are associated with longer duration of prescribed treatment. This appears to be

independent of depression severity. The depression performance indicators in the QOF specifically required GPs who coded a new diagnosis of depression to conduct a structured assessment of depression at two time points. Practices which elected to code a higher proportion of patients with depression are likely to have engaged in more assertive follow up of patients to complete these and it is possible that this led to continued treatment. While these indicators have recently been withdrawn because of a lack of evidence of effectiveness,²⁵ the results of this study suggest that incentivising assertive follow-up alone may have improved treatment for patients with depression.

Therefore encouraging coding and structured follow-up at the onset of treatment of depression is likely to reduce early discontinuation of antidepressant treatment and improve outcomes.

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