

Factors associated with duration of new antidepressant treatment:

analysis of a large primary care database

Abstract

Background

It is not known how much the duration of newly prescribed antidepressant treatment is influenced by patient characteristics or practice variation.

Aim

To describe the relationship between patient characteristics and the duration of new antidepressant treatment by general practices.

Design and setting

Large primary care database cohort study of all patients with a newly initiated course of eligible antidepressant treatment during 1 year, from a database of 237 Scottish practices.

Method

Detailed prescription data were used to estimate the duration of new antidepressant treatment for each patient. Cox proportional hazards regression was used to estimate the influence of patient characteristics on continuation of treatment and, by multilevel modelling, the variation between practices.

Results

A total of 28 027 (2.2%) patients commenced antidepressant treatment during the year; 75% continued beyond 30 days, 56% beyond 90 days, and 40% beyond 180 days. Treatment was less likely to be continued in patients from areas of high socioeconomic deprivation: hazard ratio 1.22 [95% confidence interval (CI) = 1.16 to 1.29]; in patients under 35 years, 1.33 [95% CI = 1.28 to 1.37]; and in those for whom the GP recorded no relevant diagnostic code, 1.16 [95% CI = 1.13 to 1.18]. Models accounted for between 2.2% and 3.9% of the variation in treatment duration.

Conclusion

Patient demographic characteristics account for relatively little variation in the duration of new antidepressant treatment, though treatment was shorter in younger patients and those with greater socioeconomic deprivation. There is variation in treatment duration between practices and according to whether patients have a depression diagnosis coded in their records.

Keywords

antidepressive agents; clinical practice variation; depressive disorder; primary care.

INTRODUCTION

Evidence-based guidelines for the drug treatment of depression, such as guidelines from the British Association for Psychopharmacology,¹ recommend continuation of antidepressant treatment for up to 6 months after the resolution of symptoms of depression, with longer continuation after multiple episodes. In practice, the duration of treatment is commonly shorter than this,²⁻⁴ and critics of antidepressant treatment have suggested that GPs may initiate treatment in response to patient distress,^{5,6} but with little commitment to treatment follow-up.

The prevalence of antidepressant prescribing varies greatly across general medical practices and is associated with socioeconomic deprivation and the prevalence of chronic illness,⁷ which may in turn reflect the prevalence of depression in need of treatment. The duration of treatment appears to be increasing over time,⁸ and is influenced by personal attitudes of patients — such as willingness to take medicine for psychological problems³⁻⁹ — and of their GPs.¹⁰ It is not known whether the duration of newly initiated antidepressant treatment varies systematically, either between general practices, or with patient demographic characteristics such as age, sex, and socioeconomic deprivation.

As part of the Mental Health Collaborative, a Scottish Government initiative to improve mental health care

including antidepressant prescribing, this study used a large database of anonymised routine primary care data to examine variation in the duration of new antidepressant prescribing. The study aim was to determine whether the duration of new courses of antidepressant treatment varies with characteristics of patients (age, sex, socioeconomic deprivation, physical comorbidity) or their treatment (whether there had been previous antidepressant treatment or coding of depressive episodes in the clinical record).

METHOD

Setting

Data were used from the Primary Care Clinical Informatics Unit Research (PCCIUR) database held by the University of Aberdeen. The PCCIUR database comprises anonymised extracts from the General Practice Administration System for Scotland — including all prescriptions, clinical codes, and demographic data — from a large sample of Scottish practices that are representative of the Scottish population.¹¹

Patients

All patients receiving a new course of antidepressant treatment in the study period between 1 April 2007 and 31 March 2008 were identified in two stages. The first stage identified all patients who were registered with the same GP practice throughout the study period and who received one or more

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How this fits in

Guidelines recommend that new courses of antidepressants last at least 6 months, but many courses are shorter than this. Little is known about how much or why this varies between practices and individuals. In this large database study of newly started antidepressant treatment, differences were found in the duration of antidepressant treatment with patient age and deprivation, but not with sex or physical comorbidity. Meaningful variation between practices was also found, with treatment continuing for longer in patients for whom GPs recorded a relevant diagnosis.

prescriptions for an eligible antidepressant. Eligible antidepressants comprised serotonin-specific reuptake inhibitors and serotonin noradrenaline reuptake inhibitors (SNRIs), and the tricyclic-related drugs lofepramine and trazodone.

Non-eligible antidepressants included the tricyclic antidepressants amitriptyline, imipramine, dosulepin, and nortriptyline (as they are rarely used for the treatment of depression but are commonly used for chronic pain), and the SNRI duloxetine, as it is licensed for other medical conditions as well as depression. Liquid preparations of antidepressants were also excluded, as these are rarely used in routine primary care.

The second stage restricted inclusion to those patients identified in the first stage who had no prescriptions for an antidepressant in the 12 months prior to the study period. Patients with an eligible antidepressant prescription were included, whether or not they had a diagnostic code for a depressive or anxiety disorder in their records. Each patient was only entered once in the database, starting from the date of their first antidepressant prescription in the study period.

Patient characteristics

Patient variables comprised age, sex, socioeconomic deprivation, physical comorbidity, whether there was a history of antidepressant treatment prior to 1 April 2006, and whether the new prescription of antidepressant was accompanied by a relevant diagnostic code. Deprivation was measured using the Scottish Index of Multiple Deprivation,¹² and patients were categorised by quintiles of this measure. Physical comorbidity was recorded as present if the records included a diagnostic code at any time for coronary heart disease, diabetes, or cancer. Relevant diagnostic

codes for antidepressant treatment comprised those for depression or anxiety disorders, including diagnoses (for example, 'depressive episode') and symptoms (for example, 'depressed mood'); details of Read Codes are given in Appendix 1.

Extraction of prescription data

For each antidepressant prescription, the drug name, preparation (including strength), dosing instructions, and quantity were extracted. As prescription details were stored as free text (including abbreviations), these were converted to structured data, using lookup tables specifically for the study, and translated into defined daily doses.¹³ For each prescription, the intended duration of treatment was estimated from the dosing instructions and the quantity prescribed; where doses were expressed flexibly (for instance, 'one or two tablets daily'), the maximum daily dose was used, which provided the shortest intended duration of treatment. Individual prescription data were pooled for each patient, including multiple drugs prescribed either in sequence or concurrently.

Treatment duration was estimated in two ways: from the prescription issue dates and from the total intended duration of treatment. Treatment duration from prescription dates was calculated as the difference between the first and last prescription dates plus the intended duration of the last prescription. Treatment duration from the total intended duration of treatment was calculated by summing the intended duration of treatment for each prescription received by the patient. For each patient, the shorter of these two was selected. In addition, the maximum gap between the expected end of one prescription and the beginning of the next was calculated for each patient, and patients were excluded where this was greater than 60 days, as it was considered they may have stopped and restarted treatment later rather than having one continuous course.

Treatment duration thresholds

Three thresholds of treatment duration were set at 30, 90, and 180 days of treatment. These were based on the following assumptions:

- treatment lasting up to 30 days indicates very short treatment. It suggests either self-limiting distress, inadequate follow-up by the GP, or a mismatch in treatment preference between the patient and the GP;²

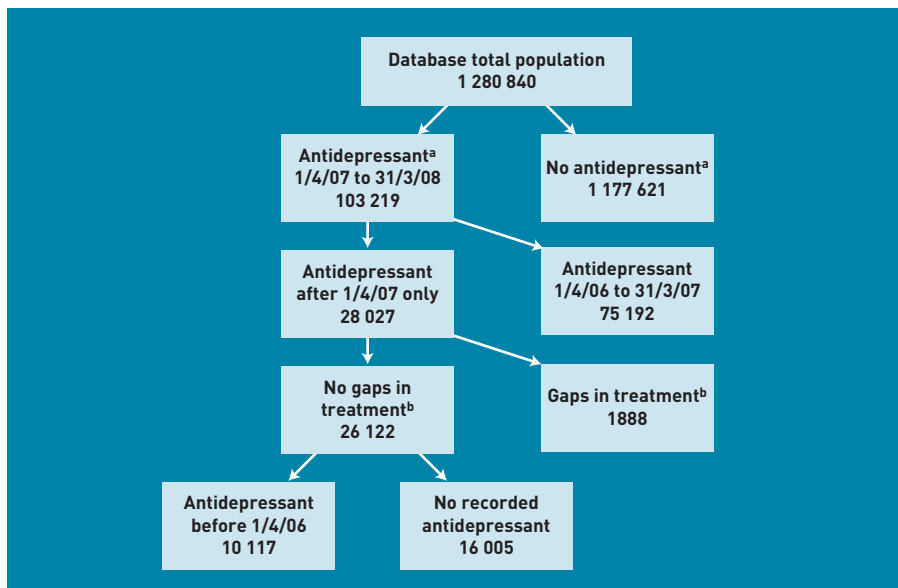


Figure 1. Flowchart showing eligibility for inclusion in the study. ^aEligible antidepressants all commonly used except amitriptyline, nortriptyline, imipramine, and duloxetine. ^bInterval between expected end of last prescription and issue of next >60 days.

Table 1. Characteristics of patients starting antidepressant treatment

Characteristic	n	%
Sex		
Female	17 456	67
Male	8666	33
Age, years		
<35	8453	32
36–65	13 725	53
>65	3944	15
Deprivation quintile^a		
1 Low	3395	13
2	4273	16
3	6399	25
4	6502	25
5 High	5553	21
Comorbidity^b		
No	19 546	75
Yes	6576	25
Diagnosis coding^c		
None	17 122	65
Symptom	3567	14
Diagnosis	5433	21
Previous treatment^d		
No	16 005	61
Yes	10 117	39
Total	26 122	

^aScottish Index of Multiple Deprivation. ^bCoronary heart disease, diabetes, or cancer coded in patient record. ^cPresence of a clinical code relating to depression in the current year; details of codes are given in Appendix 1. ^dHistory of treatment with eligible antidepressant.

- treatment between 31 and 90 days indicates early discontinuation of treatment by either the patient or GP;
- treatment between 91 and 180 days indicates a fair trial of treatment. While less than recommended in guidelines, this may represent a trade-off between medical recommendation and patient preference; and
- treatment beyond 180 days suggests compliance with guidelines, which recommend at least 6 months of treatment.¹

Because the study was carried out using data collected over a 12-month period and patients started treatment at any stage within the study period, not all patients were eligible for assessment of treatment at each stage.

Statistical analysis

Kaplan–Meier survival models were used to estimate the proportion (with 95% confidence intervals) of patients continuing treatment beyond the three time thresholds of 30, 90, and 180 days, and survival curves were plotted. Survival analysis was chosen to take into account censoring — where patients were still continuing treatment at the end of the study period. The analysis was performed by subgroups to make comparisons. Hazard ratios were estimated by Cox proportional hazards regression for each variable in turn, and by multifactorial analysis. Data were then adjusted for practice effects by carrying out multilevel Cox proportional hazards modelling using penalised likelihood methods. The proportion of variation explained by these

models was estimated by deriving a generalised coefficient of determination from the log likelihood values of the respective models.¹⁴

Analyses were carried out using the R-2.11.0 statistical approach with the survival and coxme packages for Cox proportional hazards models. Because of the potential for large datasets to yield very small *P*-values for clinically unimportant effects, a clinically important difference was set as a 5% absolute difference in continuation rates between any two groups at a given time point.

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.

Prevalence of new and continued antidepressant treatment

During the study year, 103 219 (8.0%) patients were prescribed at least one eligible antidepressant; in total, 651 707 antidepressant prescriptions were issued. Of the patients prescribed an antidepressant, 28 027 (27.2%) met the study criteria for new treatment, of whom 26 122 had no gaps in treatment of greater than 60 days (Figure 1). Thus 2.2% of the total population received a new course of antidepressant treatment in the year. They received 107 613 prescriptions, which accounted for 16.5% of the total prescriptions for antidepressants in the practices in that year. Characteristics of the patients included in the study are listed in Table 1. Mean practice incidence of new antidepressant treatment prescriptions was 20.3/1000 patients (range 3.4/1000 to 49.9/1000).

Probability of continued treatment

One-quarter of treatment courses lasted 30 days or less. Thus 75% of courses continued beyond 30 days: 56% of all courses lasted more than 90 days, and 40% lasted more than 180 days. Figure 2 shows the survival curves with comparisons for each predictor variable, and Table 2 shows the proportion of patients in each subgroup continuing treatment beyond the prespecified time points of 30, 90, and 180 days. Differences between groups for age, deprivation, and coding of diagnosis met the study criteria for a clinically important difference (absolute difference ≥5%): younger patients, those in the higher quintiles of socioeconomic deprivation, and those for whom no diagnostic code was entered were more likely to discontinue

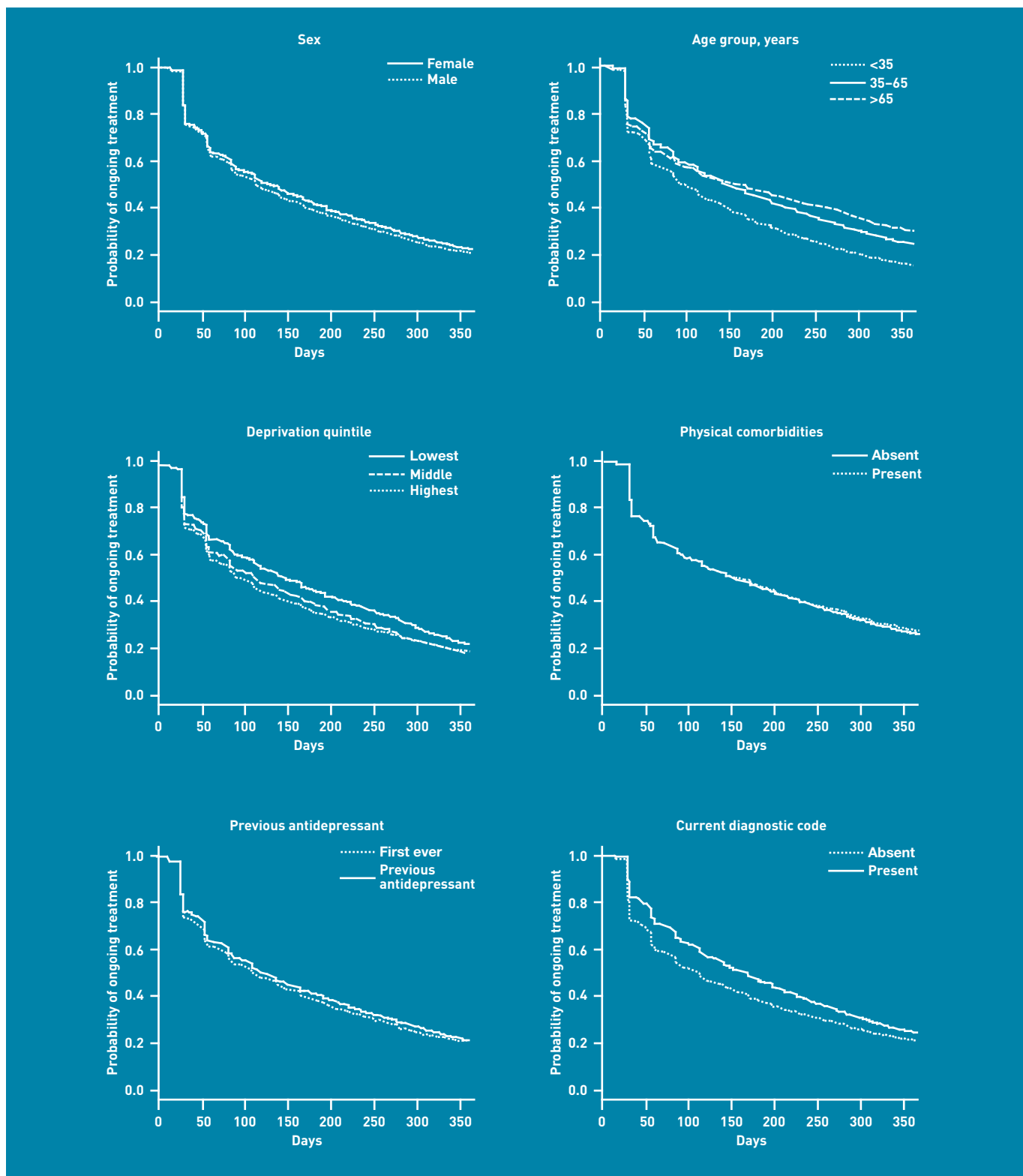


Figure 2. Kaplan-Meier plots of treatment duration for newly initiated antidepressant. Deprivation quintile = Scottish Index of Multiple Deprivation (2nd and 4th quintiles omitted for clarity). Physical comorbidities = code present for coronary heart disease, diabetes, or cancer. Current diagnostic code = code for depressive diagnosis recorded in the current year.

treatment early. In relative terms, patients in the highest deprivation quintile were 7.5% more likely to discontinue antidepressant treatment before 30 days than patients in the lowest deprivation quintile, and 20% more likely to discontinue before 180 days.

Differences in continuation of treatment due to sex, physical comorbidity, and prior antidepressant treatment were small and, while statistically significant, they failed to meet the study criteria for a clinically important difference.

Table 2. Rates of continuation of antidepressant beyond specified time points by patient characteristics

Characteristic	30 days		90 days		180 days	
	%	95% CI	%	95% CI	%	95% CI
All patients	75.4	74.9 to 75.9	55.5	54.9 to 56.1	40.1	39.4 to 40.8
Sex						
Female	75.6	75.0 to 76.2	56.2	55.5 to 57.0	41.0	40.2 to 41.8
Male	75.0	74.1 to 75.9	54.0	52.9 to 55.1	38.3	37.2 to 39.5
Age, years						
<35	71.7	70.7 to 72.7	49.3	48.2 to 50.4	32.1	31.0 to 33.2
36–65	77.9	77.2 to 78.6	58.7	57.9 to 59.6	43.3	42.3 to 44.2
>65	74.7	73.3 to 76.1	57.3	55.8 to 59.0	46.1	44.4 to 47.8
Deprivation quintile^a						
1 Low	78.8	77.4 to 80.2	61.4	59.7 to 63.1	45.8	43.9 to 47.7
2	76.7	75.5 to 78.0	57.4	55.9 to 59.0	41.9	40.2 to 43.6
3	74.9	73.8 to 76.0	54.9	53.6 to 56.2	39.9	38.6 to 41.3
4	75.4	74.4 to 76.5	54.8	53.5 to 56.0	38.9	37.6 to 40.3
5 High	72.9	71.7 to 74.1	51.9	50.6 to 53.3	36.9	35.5 to 38.3
Comorbidity^b						
No	76.7	75.5 to 77.9	59.0	57.6 to 60.4	45.6	44.1 to 47.1
Yes	76.9	75.7 to 78.1	59.4	57.9 to 60.9	46.3	44.7 to 47.9
Diagnosis coded^c						
No	72.0	71.4 to 72.7	51.7	50.9 to 52.5	37.1	36.3 to 37.9
Yes	81.8	81.0 to 82.6	62.7	61.6 to 63.7	45.8	44.6 to 46.9
Previous treatment^d						
No	74.3	73.7 to 75.0	54.5	53.7 to 55.3	39.2	38.3 to 40.0
Yes	77.1	76.2 to 77.9	57.0	56.0 to 58.0	41.6	40.5 to 42.6

^aScottish Index of Multiple Deprivation. ^bCoronary heart disease, diabetes, or cancer coded in patient record.

^cPresence of a clinical code relating to depression in the current year; details of codes are given in Appendix 1.

^dHistory of treatment with eligible antidepressant.

Table 3. Cox proportional hazards regression for the effect of patient predictors on the probability of discontinuing antidepressant treatment

Predictor	Unifactorial model, unadjusted for practice			Multifactorial model, adjusted for practice		
	HR ^a	95% CI	P-value	HR	95% CI	P-value
Sex						
Female	—			—		
Male	1.07	1.03 to 1.1	<0.001	1.06	1.02 to 1.09	0.001
Age, years						
<35 ^b	—			—		
36–65	0.76	0.73 to 0.78	<0.001	0.77	0.74 to 0.79	<0.001
>65	0.73	0.69 to 0.77	<0.001	0.71	0.67 to 0.74	<0.001
Deprivation quintile						
1 Low	—			—		
2	1.09	1.03 to 1.16	0.006	1.07	1.00 to 1.14	0.043
3	1.18	1.12 to 1.25	<0.001	1.12	1.05 to 1.19	<0.001
4	1.19	1.12 to 1.25	<0.001	1.17	1.09 to 1.24	<0.001
5 High	1.27	1.2 to 1.34	<0.001	1.18	1.10 to 1.26	<0.001
Comorbidity^c						
No	—			—		
Yes	0.99	0.94 to 1.04	0.66	— ^d		
Diagnosis coded						
No	—			—		
Yes	0.88	0.86 to 0.9	<0.001	0.86	0.85 to 0.88	<0.001
Previous treatment						
No	—			—		
Yes	0.94 ^e	0.91 to 0.97	<0.001	0.92	0.89 to 0.95	<0.001

^aHazard ratio (HR) = note that HR greater than one indicates a greater risk of discontinuing treatment at any given time point. ^bWhen age <35 years compared to all other patients, hazard ratio = 1.33 [95% CI = 1.28 to 1.37].

^cComorbidity includes diabetes, coronary heart disease, and cancer; analysis was restricted to patients aged over 45 years. ^dComorbidity was omitted from the multifactorial model as unifactorial analysis was restricted to patients aged over 45 years. ^eWhen restricted to patients aged over 35 years, hazard ratio = 0.98 [95% CI = 0.94 to 1.02], P-value = 0.4.

Cox proportional hazards regression

Results of the Cox proportional hazards regression are summarised in Table 3 which includes both unifactorial analysis unadjusted for practice, and the multilevel multifactorial analysis with practice as a random effect. While highly statistically significant, none of the models explained a large proportion of the variation in duration: the best fit was for the random-effects multifactorial analysis, which had a Nagelkerke R^2 of 0.039. This was higher than for the unadjusted multifactorial analysis (0.023), suggesting that 41% of explained variation was due to practice variation rather than patient characteristics.

DISCUSSION

Summary

This is the first UK large database study of duration of antidepressant treatment to include all patients with a new course of antidepressants and to examine factors associated with continuation of treatment. These patients comprised 2.2% of the total population. Seventy-five per cent were treated for more than 30 days, 56% for more than 90 days, and 40% for more than 180 days. Patient demographic factors such as age, sex, and socioeconomic deprivation, which are frequently associated with treatment inequalities, had little influence on continuation of newly initiated antidepressant treatment. Patients who had been recently coded with depression by a GP were more likely to continue antidepressant treatment. There was detectable variation between practices in the continuation of antidepressant treatment after adjusting for patient characteristics.

Strengths and limitations

This study used a comprehensive and representative database of routine care across a broad range of practices. By using detailed individual prescription data, the information available was increased over that from conventional summary prescribing data. While it was not possible to tell how many prescriptions were issued but not dispensed or taken, it was assumed that as patients commonly stop treatment themselves,⁹ relatively few would repeatedly attend their GP for prescriptions that they did not take. Conservative criteria were chosen for estimating treatment duration, and patients who may have finished one course and started another later in the study period were excluded. However, the study did include patients who switched from one drug to another, provided that the

gap between prescriptions was shorter than 60 days.

Because the study excluded prescriptions for older tricyclic antidepressants, such as amitriptyline, which are mostly used as treatment for chronic pain, it may have missed some new prescriptions for these drugs in patients with depression who had benefited from them in the past. The study was unable to include a measure of depression severity, as even where this was recorded as having been carried out, there was no reliable way of accessing the result. This lack of any severity measure may be one reason why the analysis only accounted for around 4% of the variance in treatment duration.

By reporting rates of continuation of treatment at three separate time thresholds, in addition to a series of Cox proportional hazards models, it was possible to highlight the absolute difference between categories and relate this to the clinically important difference of 5% in the proportion of patients continuing treatment beyond meaningful time thresholds.

Comparison with existing literature

There have been reports of suboptimal adherence to antidepressants in primary care for almost 20 years, but over that time there has been a steady increase in the proportion of patients continuing treatment.⁸ Data from the present study suggest better adherence to treatment than in three recent reports using comparable routine care data from England,² Spain,¹⁵ and the US.¹⁶ In contrast to at least one of these studies,¹⁵ the present study found no clinically important difference in duration of treatment between males and females, and little difference between first-ever and subsequent treatment, suggesting a consistent approach to prescribing by GPs. By looking at population rather than individual case characteristics, it was not possible to ascertain what personal features, such as attitudes and beliefs, are associated with continuation, although these have been examined elsewhere.^{2,3}

Data in this study related to all prescriptions for antidepressants commonly used to treat depression in primary care. Unlike the findings of Moore *et al*,⁸ this research did not limit the study to patients with a computer-coded diagnosis of depression; thus the sample includes those issued an antidepressant for an anxiety disorder and those without a formally coded diagnosis.

The lack of formal diagnoses is a potential problem in research of this type

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Provenance

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Competing interests

The authors have declared no competing interests.

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and, as there was no way of inferring this from the data, the following contextual evidence was considered: first there is no contractual requirement for GPs to enter a diagnostic code before treating a patient for depression; by introducing a structured assessment for depression with penalties for non-completion, the General Medical Services contract at the time of the study may have disincentivised GPs from coding some patients. Second, GPs commonly report feeling pressured into prescribing an antidepressant with questionable indications,⁶ and the researchers in the present study wished to capture these cases which may be less likely to receive a diagnostic code. In view of these contextual factors, it was decided to include in the primary analysis all patients prescribed a new course of an eligible antidepressant.

To test whether the effects of other variables were similar in patients with and without diagnostic codes, a post-hoc subgroup analysis of the effects of other variables on treatment duration was carried out; this showed no qualitative difference between patients with and without a diagnostic code.

Studies of the relationship between socioeconomic deprivation and the treatment of depression have shown conflicting results.^{7,17,18} However, as it appears that deprivation has a greater effect on the duration of depression than on its incidence,^{19,20} the study finding of shorter durations of treatment in patients from the highest deprivation quintile suggests a mechanism whereby health inequalities are maintained for patients with depression.

Implications for practice and research

The findings of this study suggest that, in general, patients receive antidepressant treatment which, once initiated, is not greatly influenced by patient demographics. Nonetheless, patients in the most deprived areas were more likely to discontinue treatment early and it may be that this group warrants specific attention to increase adherence to treatment.³ The finding that where GPs commit to a firm diagnosis of depression (within the UK Quality and Outcomes Framework this also places them under obligation to perform additional tasks), patients are more likely to receive treatment of longer duration. This aspect of practice may be amenable to quality-improvement measures: as meaningful variation between practices were found, the authors suggest that the proportion of new courses of antidepressant treatment continuing beyond set thresholds, or the proportion of new courses of treatment that receive a validated diagnosis, should be considered as possible future quality metrics.

The duration of new courses of antidepressant treatment, though better than previously reported, still falls short of guidelines. Patients living in areas of greater socioeconomic deprivation, those aged under 35 years, and those with no concurrently recorded diagnosis were less likely to continue with treatment. Variation between practices accounted for almost as much variation as individual patient characteristics.

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Appendix 1. List of Read Codes used in the analysis

1.1. Depression diagnosis codes

E0013 – PS dementia with depression
E0021 – Senile dementia with depression
E112. – Major Dep Episode (1st)
E113. – MDE (recurrent)
E118. – SAD
E11y2 – atypical depression
E11z2 – masked depression
E130. – reactive depressive psychosis
E135. – agitated depression
E2003 – anxiety with depression
E291. – prolonged depressive reaction
E2B.. – depressive disorder NOS
E2B1. – chronic depression
Eu204 – post schizophrenia depression
Eu251 – schizoaffective depression
Eu32. – depressive episode
Eu33. – recurrent depressive episode
Eu341 – Dysthymia
Eu412 – Mixed anxiety & depression

1.2. Depressive symptoms codes

1B17. – feeling depressed
1B1U. – symptoms of depression
1BT.. – depressed mood
1465. – H/O Depression
2257. – O/E Depressed
62T1. – puerperal depression

1.3. Physical comorbidity

B.... – Cancer
C10.. – Diabetes
G3... – Coronary Heart Disease

The search strategy identified patients with the specific codes listed and all sub-codes.