General practitioners' perceptions of the tolerability of antidepressant drugs: a comparison of selective serotonin reuptake inhibitors and tricyclic antidepressants

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Abstract

Objective: To examine inceptions and discontinuations of antidepressants in general practice.
Design: An observational study analysing data from an ongoing cross sectional postal survey. Every three months a representative sample of 250 doctors recorded prescribing activity for four weeks. This provided 4000 general practitioner weeks of recording per year.
Setting: A representative panel of general practitioners in England, Wales, and Scotland.
Subjects: Patients who began a new course of an antidepressant or had their treatment stopped or changed by the general practitioner between 1 July 1990 and 30 June 1995.
Main outcome measures: Numbers of patients prescribed a new course of antidepressant; numbers discontinuing treatment; the ratio of antidepressant discontinuations to antidepressant inceptions; reasons for discontinuation; proportion of switches to another antidepressant.
Results: There were 13 619 inceptions and 3934 discontinuations of selective serotonin reuptake inhibitors and tricyclic antidepressants during the study. The number of newly prescribed courses of antidepressants increased by 116%, mostly due to an increase in prescribing of serotonin reuptake inhibitors. The ratio of total discontinuations to inceptions was significantly lower for serotonin reuptake inhibitors (22%) than for tricyclic antidepressants (33%). Differences persisted when controlled for age and sex of patients and severity of depression. However, there was more switching away from selective serotonin reuptake inhibitors when they failed (72%) than from tricyclic antidepressants (58%).
Conclusions: Selective serotonin reuptake inhibitors are less likely than tricyclic antidepressants to be discontinued. A prospective study is needed in general practice to assess the implications of differences in discontinuation rates and switches on clinical and economic outcomes.

Introduction

Prescribing of selective serotonin reuptake inhibitors in general practice has recently increased rapidly,[1] but their routine first line use is controversial.[2-4] Though they are as effective as tricyclic antidepressants,[5] they are comparatively expensive and potentially a huge burden on the NHS drugs budget.[6] Justifying their first line status requires evidence of greater tolerability and safety.

Drop out rates may be a useful proxy for tolerability.[7] Meta-analyses of clinical trials comparing tricyclic antidepressants with selective serotonin inhibitors have given conflicting results.[8 9] Song *et al* found no difference in total drop out rates between patients taking serotonin reuptake inhibitors and those taking tricyclic antidepressants (32.3% *v* 33.2%)[8] but may have underestimated the difference by grouping comparatively well tolerated non-tricyclic antidepressants in the tricyclic comparator group.[10] Anderson and Tomenson found a significantly lower total drop out rate with serotonin reuptake inhibitors than with tricyclic antidepressants (30.8% *v* 33.4%),[9] but the small difference may not be clinically important. In their study drop out rates due to side effects were 14.4% for serotonin reuptake inhibitors and 18.8% for tricyclics[9]; by contrast, Song *et al* found no significant difference (15.4% *v* 18.8%).[8] Inefficacy rates were around 7% in both studies.

Evidence from these trials, however, may not be generalisable to primary care,[11] as in these settings patients may have different degrees of severity and different symptom profiles[12 13] and prescribing patterns may differ.[14 15] We examined general practitioners' perceptions of the tolerability of selective serotonin reuptake inhibitors compared with tricyclic antidepressants by assessing inception rates, discontinuation rates, switches, and reasons for changing treatment.

Subjects and methods

We examined data from the "new and change therapy enquiry," an ongoing survey of drug inceptions and discontinuations in general practice in England, Wales, and Scotland since 1987,[16 17] administered by an independent research organisation (CompuFile Ltd). Patients were those diagnosed as depressed who were prescribed a new course of a tricyclic antidepressant

(*British National Formulary*, section 4.3.1[18]; but excluding non-tricyclics, which may be better tolerated)[9] or a selective serotonin reuptake inhibitor and those who had their treatment changed or discontinued by the general practitioner between 1 July 1990 and 30 June 1995. A new course of treatment was defined as (*a*) first ever antidepressant treatment, (*b*) a switch to new treatment, (*c*) a restart of the same drug prescribed in the past ("restart renew"), (*d*) a restart of another drug after relapse ("restart new"), and (*e*) a new antidepressant added to existing antidepressant treatment. Discontinuation was withdrawal of a drug or change in treatment by the general practitioner.

Pocket sized booklets were sent to each doctor, who completed one page for every drug withdrawal or change (appendix 1) and another for each new prescription issued for one of a range of specified conditions, including depression (appendix 2). The records included demographic details, all current diagnoses, and a clinical assessment by the general practitioner of the severity of the condition for which treatment was initiated or changed.

Selection of general practitioners

General practitioners were mailed and invited to participate in prescribing research. Token remuneration was offered. Mailing was continued until a sampling frame of around 1000 doctors was achieved, from which a panel representative of unrestricted general practitioners by age and region was obtained each year (table 1).[19 20] Every three months 250 randomly selected doctors recorded for four weeks, giving a total of 4000 prescribing weeks a year. Each participant recorded a maximum of once in any six month period. The actual numbers reporting up to the end of June each year from 1991 to 1995 were 641, 664, 694, 773, and 791. Thus in any one year some doctors were sampled again in the next six month period to complete the quota of 250 doctors each quarter. However, of those sampled in successive six month periods in one year, fewer than 10% reported twice the next year.

As each doctor recorded for a short period, the data provided a cross sectional picture of the number of new courses that were prescribed and, independently, the number of withdrawals that were made. The study design did not allow follow up of each new course of treatment.

Analysis of data

Replies from open ended questions were coded from a defined coding frame to permit descriptive analysis of the data. Logistic regression analysis of trend was used to analyse changes in prescribing by year for each class of antidepressant. The proportion of patients stopping treatment with selective serotonin reuptake inhibitors (number of discontinuations divided by number of newly started courses) was compared with those stopping tricyclic antidepressants to give the relative risk of discontinuing treatment. This allowed comparisons of one treatment with the other by using the cross sectional nature of the data. In order to test for confounding due to differences in prescribing by age, sex, and severity of depression the Mantel-Haenszel summary χ^2 value and weighted relative risk ratio were used.

Table 1 Percentage of unrestricted general practitioners in each of five geographic areas and three age bands in England, Wales, and Scotland† as at 1 October 1993[19 20] compared with those in the new and change therapy enquiry panel (1993-4)

	Percentage of general practitioners in England, Wales, and Scotland† (n=31 466)	Percentage of general practitioners in panel‡ (n=1000)
Region§		
A: Northern and Scotland	16.5	17.3
B: Yorkshire, Trent, East Anglia	18.1	17.4
C: West Midlands, Merseyside, North Western	19.4	18.4
D: Wessex, Oxford, South Western, Wales	21.7	21.6
E: North West Thames, North East Thames, South West and South East Thames	24.3	25.3
Total	100.0	100.0
Age band (years)†		
< 40	38.9	38.0
40-54	45.4	46.0
⩾ 55	15.7	16.0
Total	100.0	100.0

† Age data for Scotland—personal communication, Scottish Office.
‡ Includes general practitioners who reported twice in that year.
§ Each broad area is broken down into its composition by regional health authority area (before 1 April 1994) for comparison with available statistics. In addition, area A includes Scotland and area D includes Wales.

Results

In the study period 5275 new courses of selective serotonin reuptake inhibitors and 8344 new courses of tricyclic antidepressants were prescribed. Thirty one per cent of serotonin reuptake inhibitors were prescribed to men compared with 29% of tricyclic antidepressants ($P = 0.027$). A greater proportion of serotonin reuptake inhibitors (46%) were prescribed to patients between 26 and 45 years of age compared with tricyclic antidepressants (39%).

Overall, antidepressant inceptions increased by 116% between 1990 and 1995 (table 2) and serotonin reuptake inhibitor inceptions rose by 732%. In 1995 fluoxetine had the highest share of new prescriptions for antidepressants (24%) whereas the market share for "newer" tricyclic antidepressants (lofepramine and dothiepin) had decreased by 39% from 1990 levels.

According to general practitioner responses a total of 1146 courses of selective serotonin reuptake inhibi-

Table 2 Trends in prescribing by class and type of antidepressant. Figures in parentheses are total percentage yearly market share of each drug

Drug	July 1990 to June 1991	July 1991 to June 1992	July 1992 to June 1993	July 1993 to June 1994	July 1994 to June 1995
Selective serotonin reuptake inhibitors	226 (12)	654 (28)	1123 (38)	1391 (42)	1881 (47)†
Fluoxetine	187 (10)	371 (16)	507 (17)	765 (23)	959 (24)
Paroxetine	2 (0.1)	129 (6)	361 (12)	383 (12)	581 (15)
Sertraline	15 (1)	111 (5)	184 (6)	198 (6)	288 (7)
Fluvoxamine	22 (1)	43 (2)	71 (2)	45 (1)	53 (1)
Tricyclic antidepressants	1485 (81)	1576 (67)	1668 (57)	1734 (52)	1881 (47)
Dothiepin	629 (34)	633 (27)	796 (27)	780 (24)	890 (22)
Lofepramine	340 (18)	350 (15)	347 (12)	381 (12)	385 (10)
Amitriptyline	234 (13)	302 (13)	248 (8)	288 (9)	355 (9)
Clomipramine	69 (4)	77 (3)	70 (2)	99 (3)	79 (2)
Trimipramine	90 (5)	86 (4)	82 (3)	67 (2)	54 (1)
Imipramine	69 (4)	66 (3)	67 (2)	79 (2)	63 (2)
Other	54 (3)	62 (3)	58 (2)	40 (1)	55 (1)
Other classes	130 (7)	120 (5)	133 (5)	181 (5)	206 (5)
Total	1841 (100)	2350 (100)	2924 (100)	3306 (100)	3968 (100)

† Logistic regression analysis of differences in trend between selective serotonin reuptake inhibitors and tricyclic antidepressants: P< 0.0005.

Table 3 Discontinued treatment compared with new prescriptions for selective serotonin reuptake inhibitors and tricyclic antidepressants, July 1990 to June 1995. Relative risk gives likelihood of discontinuation of serotonin reuptake inhibitors when compared with tricyclic antidepressants

	Selective serotonin reuptake inhibitors	Tricyclic antidepressants
Total No of new courses	5275	8344
Total No (%) discontinued	1146 (22)	2788 (33)
Relative risk of discontinuation (95% confidence interval)	0.65 (0.61 to 0.69)**	
Corrected for age	0.66 (0.62 to 0.70)**	
Corrected for sex	0.65 (0.61 to 0.69)**	
Corrected for severity†	0.66 (0.59 to 0.74)**	
Total No (%) discontinued because of side effects	560 (11)	1218 (15)
Relative risk of discontinuation because of side effects (95% confidence interval)	0.73 (0.66 to 0.80)**	
Corrected for age	0.75 (0.68 to 0.82)**	
Corrected for sex	0.73 (0.66 to 0.80)**	
Corrected for severity†	0.78 (0.66 to 0.93)*	
Total No (%) discontinued because of poor efficacy	398 (8)	1221 (15)
Relative risk of discontinuation because of poor efficacy (95% confidence interval)	0.52 (0.46 to 0.57)**	
Corrected for age	0.52 (0.47 to 0.58)**	
Corrected for sex	0.51 (0.47 to 0.58)**	
Corrected for severity†	0.50 (0.41 to 0.61)**	

* P=0.005. ** P< 0.0001.
† Based on general practitioner's own clinical assessment of severity as mild, moderate, or severe. Assessment of severity was obtained for 1536 (29.1%) inceptions of selective serotonin reuptake inhibitors and 325 (28.4%) discontinuations compared with severity recorded for 2603 (31.2%) inceptions and 800 (28.7%) discontinuations of tricyclic antidepressants.

tors and 2788 courses of tricyclic antidepressants were discontinued (table 3). The ratio of total discontinuations to inceptions was significantly lower for selective serotonin reuptake inhibitors (22%) than for tricyclic antidepressants (33%) (relative risk 0.65; 95% confidence interval 0.61 to 0.69). The discontinuation ratios for side effects (relative risk 0.73; 0.66 to 0.80) and poor efficacy (0.52; 0.46 to 0.57) were also significantly lower for selective serotonin inhibitors than for tricyclic antidepressants. Risk ratios were not altered when corrected for age and sex. Withdrawal due to improvement was recorded in 90 patients taking serotonin reuptake inhibitors and 138 patients taking tricyclic antidepressants.

Controlling for the general practitioner's own clinical assessment of severity for patients in whom this was recorded did not alter our risk estimates (table 3). Though severity of depression was recorded for only about one third of inceptions and discontinuations, recording rates were similar for selective serotonin reuptake inhibitors and tricyclic antidepressants and adjusted relative risk estimates were similar to unadjusted risk estimates.

Table 4 Prescribing of initial courses of antidepressants by past prescribing history of patient between July 1990 and June 1995†

	Selective serotonin reuptake inhibitors (%)	Tricyclic antidepressants (%)
Total No of new courses	5275	8344
No known past antidepressant treatment	2211 (41.9)	3580 (42.9)
Added treatment	189 (3.6)	366 (4.4)
Switched to stated agent	1315 (24.9)	1377 (16.5)
Restarted treatment	1560 (29.6)	3021 (36.2)
Restart renew (% of total restarted courses)	819 (52.5)	2187 (72.4)
Restart new (% of total restarted courses)	741 (47.5)	834 (27.6)

† See methods for definitions of categories.

The newer tricyclic antidepressants (dothiepin and lofepramine), which may have greater tolerability, were also analysed separately. Their discontinuation ratio was 31.4% compared with 39.0% for older tricyclic antidepressants ($P<0.001$). They also had lower discontinuation ratios for side effects compared with older tricyclics (12.9% *v* 18.0%; $P<0.0001$) but there was no difference for poor efficacy (14.3% *v* 15.3%; $P=0.20$). However, all discontinuation ratios for the newer tricyclics were significantly higher than those for serotonin reuptake inhibitors ($P<0.001$).

Serotonin reuptake inhibitors (41.9%) were as likely as tricyclics (42.9%) to be prescribed as a first ever course of antidepressant (table 4), but more tricyclics were given when restarting treatment (36.2% *v* 29.6%). When restarting treatment a greater proportion of tricyclic antidepressants were the same drugs as previously used (72.4% *v* 52.5%) and a greater proportion of serotonin reuptake inhibitors were new drugs (47.5% *v* 27.6%). Fewer tricyclic antidepressant inceptions were a result of a switch in antidepressant.

Stimulatory adverse effects accounted for 30.0% of withdrawals of fluoxetine compared with 14.8% for other serotonin reuptake inhibitors (table 5). More withdrawals of fluvoxamine (70.7%) were due to gastrointestinal adverse effects compared with other serotonin reuptake inhibitors (38.9%). Lethargy accounted for 18.5% of lofepramine withdrawals compared with 12.1% for serotonin reuptake inhibitors and 52.0% for other tricyclic antidepressants. Stimulatory (13.3%) and gastrointestinal adverse effects (25.0%) were more common with lofepramine than with other tricyclics (6.2% and 9.7% respectively).

Table 6 shows that when antidepressant treatment was stopped 63% of serotonin reuptake inhibitors and 73% of tricyclic antidepressants were switched to another antidepressant. A total of 63% of serotonin reuptake inhibitor switches were to a tricyclic antidepressant but 42% of tricyclic antidepressant switches were within the same class.

Discussion

We found that antidepressant inception rates—especially for serotonin reuptake inhibitors—rose rapidly in England, Scotland, and Wales, as occurred in the United States a decade ago.[21] The active marketing of serotonin reuptake inhibitors is an important factor in their widespread adoption. The "defeat depression" campaign aimed at raising awareness,[22] though the trend probably existed before the campaign became high profile.

The increased use of serotonin reuptake inhibitors in general practice could be due to the perception that they are better tolerated than tricyclic antidepressants. Like Anderson and Tomenson,[9] we found that total discontinuations and discontinuations for side effects were significantly fewer with serotonin reuptake inhibitors. Antidepressants may affect quality of life but not be withdrawn, and non-compliance may not be reported.[23] However, the discontinuation ratios reported in this study reflect intolerability resulting in a medical decision to discontinue and are useful for comparing antidepressants.[7]

Table 5 Main adverse effects resulting in discontinuation of treatment for selective serotonin reuptake inhibitors and tricyclic antidepressants (percentages in parentheses)

		Adverse effects†				
Drug	Total stopped	Stimulation‡	Gastrointestinal‡	Headache	Lethargy	Other central nervous system‡
Selective serotonin reuptake inhibitors	560	126 (23)	231 (41)	41 (7)	68 (12)	140 (25)
Fluoxetine	283	85 (30)	104 (37)	21 (7)	28 (10)	64 (23)
Paroxetine	161	26 (16)	75 (47)	8 (5)	26 (16)	45 (28)
Sertraline	75	13 (17)	23 (31)	7 (9)	9 (12)	20 (27)
Fluvoxamine	41	2 (5)	29 (71)	5 (12)	5 (12)	11 (27)
P value§		P=0.0001	P=0.0001	P=0.318	P=0.288	P=0.617
Tricyclic antidepressants	1218	93 (8)	156 (13)	23 (2)	551 (45)	355 (29)
Dothiepin	465	28 (6)	38 (8)	8 (2)	267 (57)	105 (23)
Lofepramine	248	33 (13)	62 (25)	10 (4)	46 (19)	87 (35)
Amitriptyline	332	18 (5)	28 (8)	2 (1)	167 (50)	103 (31)
Other	173	14 (8)	28 (16)	3 (2)	71 (41)	60 (35)
P value§		P=0.015	P< 0.0001	P=0.032¶	P< 0.0001	P=0.0007

† Proportions of adverse effects exceeded 100%, as some were recorded more than once per treatment change.
‡ "Stimulation" was agitation, anxiety, panic attacks, hallucinations, insomnia, and nightmares. "Gastrointestinal" included symptoms of nausea, vomiting, diarrhoea, stomach upset, abdominal pain, heartburn, and bloating. "Other central nervous system" included dizziness, tremor, shakes, and wooziness.
§ Within each drug class each symptom column was separately tested for significant differences by χ^2 test and P values presented (df=3).
¶ Fisher's exact test.

Table 6 Switches in antidepressant treatment by class of drug

		Total switched to another antidepressant (% of total discontinued)	New drug (% of total number of switches)		
Former drug	Total discontinued		Selective serotonin reuptake inhibitor	Tricyclic antidepressant	Other
Selective serotonin reuptake inhibitor	1146	719 (63)	199 (28)	456 (63)	64 (9)
Tricyclic antidepressant	2788	2033 (73)	1065 (52)	848 (42)	120 (6)
Other	239	153 (64)	51 (33)	73 (48)	29 (19)

Overall χ^2=166.4, df=4, P<0.0001.

Definition of discontinuation ratio

The denominator for the discontinuation ratio was the number of patients starting the drug rather than the total number of patients currently taking the drug. As the use of serotonin inhibitors increased steeply during the study the numbers of patients starting these drugs in any week compared with the numbers starting a tricyclic would be greater than the equivalent ratio based on all patients currently taking the two drug classes. This will bias downwards the apparent discontinuation ratio for serotonin inhibitors. However, the median period for which patients continue with an antidepressant (which influences the total number at any one time) is only a small proportion of the study period.[14 24] Therefore, the ratio of those currently taking the two drug classes is likely to be similar to the ratio of new prescriptions over the five year study period, and the bias is unlikely to affect our conclusions.

Comparisons with other studies

Our results are consistent with those of a prospective study of initial antidepressant choice in primary care in Seattle, which found that patients given fluoxetine reported fewer adverse effects and were more likely to continue with the drug than those given tricyclics.[25] Discontinuation ratios for side effects were similar to results from meta-analyses.[8 9 26] However, despite consistent evidence of equal efficacy[8 9 26 27] serotonin reuptake inhibitors were less likely to be discontinued for poor efficacy in our study. This finding may partly be explained by the use of subtherapeutic doses of tricyclic antidepressants reported in general practice.[28]

Antidepressants are discontinued for several reasons,[23] and attributional bias whereby stating side effects or poor efficacy provides medical legitimacy may have selectively affected our estimates.[29] This was more likely to occur with reported poor efficacy, which was subjective in our study but measured objectively in clinical trials. Nevertheless, total discontinuation rates, which are important in assessing overall acceptability,[9] should not have altered. Discontinuations because of improvement were few compared with the findings of Maddox *et al*; in their study 35% of patients stopped because they felt better.[23] The difference was probably because improvers are not routinely identified in general practice and our study was not designed to assess this. However, reporting of improvement was similar in both drug groups and did not influence our conclusions.

Cost effectiveness considerations

This observational study may be more likely to reflect what is actually occurring in general practice than results from clinical trials, in which both patients and physicians are motivated to continue treatment.[30] Acceptability may have greater impact on cost effectiveness than the actual costs of treatment.[31] However, calculations of cost effectiveness have relied on results from clinical trials and make several assumptions about pathways of treatment.[32] Another factor in treatment costs is drug switches. More patients switched away from serotonin inhibitors when they failed than from tricyclic antidepressants. Given the apparent differences in tolerability this is perhaps unexpected but may be because there are drugs with a different side effect profile within the class of tricyclics or may indicate loyalty by tricyclic antidepressant prescribers.

Adverse effects as reasons for discontinuation

Adverse effects resulting in drug discontinuation differed between the individual serotonin reuptake inhibitors. Stimulation occurred with fluoxetine, and fluvoxamine was associated with gastrointestinal adverse effects, also found in a prescription event monitoring study.[33] This suggests that patients who are intolerant of one serotonin inhibitor may tolerate another.[34]

Potential confounding factors

The possibility that systematic biases may explain some of the differences needs to be explored. Selective prescribing for patients with different severity of depression[35] and prescribing history could affect discontinuation rates. There was no evidence of confounding by age, sex, or (from available data) severity. The rate for first ever prescribing was equally distributed between classes but there were differences in past prescribing history when people had previous antidepressant treatment. A greater proportion of people restarting a tricyclic agent were given the same drug as before whereas more people were given a selective serotonin inhibitor for the first time. We do not know whether people restarting the same tricyclic were more or less likely to discontinue than patients restarting a new selective serotonin inhibitor. The effect of this potentially important confounder is unclear from our study and needs to be explored in a prospective cohort study.

Doctors who agreed to participate may have been atypical prescribers, but the survey included many conditions and there is no reason to suspect idiosyncratic antidepressant prescribing behaviour. In any one year some doctors may have reported in two successive six month periods. However, few reported twice the next year, thus levelling reporting frequency and avoiding any weighting of experience or behaviour. The study used self reported data and was limited by lack of information on their validity. Nevertheless, the study had face validity, as suggested by inception rates which mirrored data from the Prescription Pricing Authority[1] and the study by Donoghue *et al*.[36] The adverse effect profiles were similar to those in other studies.[37]

Key messages

- The number of new prescriptions for antidepressants increased by 116% between 1990 and 1995, mostly due to increased prescribing of selective serotonin reuptake inhibitors
- In an observational study in general practice the ratio of antidepressant discontinuations to antidepressant inceptions was lower for selective serotonin reuptake inhibitors than for tricyclic antidepressants
- Data suggest that selective serotonin reuptake inhibitors are tolerated better in the general practice setting than tricyclic antidepressants
- However, there may be more switching away from selective serotonin reuptake inhibitors when they fail (72% in this series) than from tricyclic antidepressants (58%)
- Prospective studies are required in general practice to evaluate the implications of differences in discontinuation rates and switching on clinical and economic outcomes

Conclusions

Selective serotonin reuptake inhibitors seemed to be better tolerated than tricyclic antidepressants in this general practice observational study. Despite methodological limitations of the study the results may have important implications for cost effectiveness. A prospective cohort study to examine the clinical andeconomic consequences of differences in discontinuation rates and switches is required.

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Conflict of interest: None.

Appendix 1

PATIENT SEX _____ AGE _____	**DIAGNOSIS** Please indicate **severity and concomitant conditions**
THERAPY CHANGE Please include **all items** and specify **form, strength, and dosage** PLEASE WRITE " + " TO INDICATE ADDED DRUGS	
FROM	**TO**
Please tick if this change was advised by hospital or consultant	REASONS FOR CHANGE. Please give details of **side effects, contraindications, special precautions**

Appendix 2

PATIENT SEX _____ AGE _____	**DIAGNOSIS** Please indicate **severity and concomitant conditions**
NEW or RESUMED THERAPY	Please include **all items** and specify **form, strength, and dosage**
Has the patient EVER been treated before for this condition? YES NO DON'T KNOW	IF YES: Is the resumed therapy the SAME as before or DIFFERENT? Same/Different How long since LAST treatment **STOPPED?** By whom last treated? Self/Partner/Other general practitioner/Hospital
Please tick if this choice was advised by hospital or consultant	**REASONS FOR CHOICE** Please give details of **contraindications, special precautions**

Clinical conditions for which a page was completed: cardiovascular, hyperlipidaemia, musculoskeletal, upper gastrointestinal, asthma, other chronic respiratory conditions, anxiety, insomnia, neurological, contraception, hormone replacement therapy, dermatological and migraine, depression.

1 Prescription Pricing Authority. *Depression and antidepressants. PACT report.* Newcastle upon Tyne: PPA, 1995.
2 Edwards J. Selective serotonin reuptake inhibitors: a modest though welcome advance in the treatment of depression. *BMJ* 1992;304:1644-6.
3 Harrison G. New or old antidepressants? New is better. *BMJ* 1994;309:1280-1.
4 Owens D. New or old antidepressants? Benefits of new drugs are exaggerated. *BMJ* 1994;309:1281-2.
5 British Association for Psychopharmacology. Guidelines for treating depressive illness with antidepressants. *J Psychopharmacol* 1993;7:19-23
6 Effective Health Care. *The treatment of depression in primary care.* Leeds: University of Leeds, 1993.
7 Lader M. Fluoxetine efficacy vs comparative drugs: an overview. *Br J Psychiatry* 1988:153(suppl 3):51-8.
8 Song F, Freemantle N, Sheldon TA, House A, Watson P, Long A, *et al.* Selective serotonin reuptake inhibitors in depression: a meta-analysis of efficacy and acceptability. *BMJ* 1993;306:683-7.
9 Anderson IM, Tomenson BM. Treatment discontinuation with selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis. *BMJ* 1995;310:1433-8.
10 Effective and acceptable treatment for depression. *BMJ* 1993;306:1124-7.(Correspondence.)
11 Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutic trials. *J Chronic Dis* 1967;20:637-48.
12 Sireling LI, Paykel ES, Freeling P, Rao BM, Patel SP. Depression in general practice: clinical features and comparison with out-patients. *Br J Psychiatry* 1985;147:119-26.
13 Sireling LI, Paykel ES, Freeling P, Rao BM, Patel SP. Depression in general practice: case thresholds and diagnosis. *Br J Psychiatry* 1985;147:113-8.
14 Johnson DAW. Treatment of depression in general practice. *BMJ* 1973;2:18-20.
15 Thompson C, Thompson CM. The prescribing of antidepressants in general practice: 1: a critical review. *Hum Psychopharmacol* 1989;4:91-102.
16 Burgess I. The incidence and treatment of NSAID induced GI symptoms. *Horizons* 1990;4:433-6.
17 Martin R, Hilton S, Kerry S. Review of prescribed treatment for children with asthma—more recent data suggest guidelines are being adhered to. *BMJ* 1995;311:1645.
18 Joint Formulary Committee. *British national formulary.* No 29. London: British Medical Association and Royal Pharmaceutical Society of Great Britain, 1995:165-8.
19 Central Statistical Office. *Regional trends.* No 30. London: HMSO, 1995.
20 General Medical Services Committee. *Basic statistics. England and Wales national and regional tables.* Leeds: Department of Health NHS Executive Headquarters, 1993.
21 Olfson M, Klerman GL. Trends in the prescription of antidepressants by office-based psychiatrists. *Am J Psychiatry* 1993;150:571-7.
22 Paykel ES, Priest RG. Recognition and management of depression in general practice: consensus statement. *BMJ* 1992;305:1198-202.
23 Maddox JC, Levi M, Thompson C. The compliance with antidepressants in general practice. *J Psychopharmacol* 1994;8:48-53.
24 MacDonald TM, McMahon AD, Reid IC, Fenton GW, McDevitt DG. Antidepressant drug use in primary care: a record linkage study in Tayside, Scotland. *BMJ* 1996;313:860-1.
25 Simon GE, VonKorff M, Heiligenstein JH, Revicki DA, Grothaus L, Katon W, *et al.* Initial antidepressant choice in primary care: effectiveness and cost of fluoxetine vs tricyclic antidepressants. *JAMA* 1996;275:1897-902.
26 Montgomery SA, Henry J, McDonald G, Dinan T, Lader M, Hindmarch I, *et al.* Selective serotonin reuptake inhibitors: meta-analysis of discontinuation rates. *Int Clin Psychopharmacol* 1994;9:47-53.
27 Anderson IM, Tomenson BM. The efficacy of selective serotonin reuptake inhibitors in depression: a meta-analysis of studies against tricyclic antidepressants. *J Psychopharmacol* 1994;8:238-49.
28 Donoghue JM, Tylee A. The treatment of depression: prescribing patterns of antidepressants in primary care in the UK. *Br J Psychiatry* 1996;168:164-8.
29 Ramchandani P, Webb V. Acceptability of side effects as reason for stopping may bias results. *BMJ* 1995;311:751.
30 Andrade SE, Walker AM, Gottlieb LK, Hollenberg NK, Testa MA, Saperia GM, *et al.* Discontinuation of antihyperlipidemic drugs—do rates reported in clinical trials reflect rates in primary care settings? *N Engl J Med* 1995;332:1125-31.
31 Jonsson B, Bebbington PE. What price depression? The cost of depression and the cost effectiveness of pharmacological treatment. *Br J Psychiatry* 1994;164:665-73.
32 O'Brien JT. Cost-effectiveness of antidepressants. *Br J Psychiatry* 1994;165:411-2.
33 Edwards JG, Inman WH, Wilton L, Pearce GL. Prescription-event monitoring of 10 401 patients treated with fluvoxamine. *Br J Psychiatry* 1994;164:387-95.
34 Brown WA, Harrison W. Are patients who are intolerant to one serotonin selective reuptake inhibitor intolerant to another? *J Clin Psychiatry* 1995;56:30-4.
35 Isacsson G, Redfors I, Wasserman D, Bergman U. Choice of antidepressants: questionnaire survey of psychiatrists and general practitioners in two areas in Sweden. *BMJ* 1994;309:1546-9.
36 Donoghue J, Tylee A, Wildgust H. Cross sectional database analysis of antidepressant prescribing in general practice in the United Kingdom, 1993-5. *BMJ* 1996;313:861-2.
37 Cohn CK, Shrivastava R, Mendels J, Cohn JB, Fabre LF, Claghorn JL, *et al.* Double-blind, multicenter comparison of sertraline and amitriptyline in elderly depressed patients. *J Clin Psychiatry* 1990;51:28-33.

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Correction

Prevalence of potentially inappropriate long term prescribing in general practice in the United Kingdom, 1980-95: a systematic literature review

A production error occurred in this paper by Stephen A Buetow and colleagues (30 November, pp 1371-4). In the reference list the numbers of the references from 109 on should be increased by one. The numbering of the references immediately before these has been changed on the *BMJ*'s web site.