

Antidepressant drugs and generic counselling for treatment of major depression in primary care: randomised trial with patient preference arms

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Abstract

Objectives To compare the efficacy of antidepressant drugs and generic counselling for treating mild to moderate depression in general practice. To determine whether the outcomes were similar for patients with randomly allocated treatment and those expressing a treatment preference.

Design Randomised controlled trial, with patient preference arms. Follow up at 8 weeks and 12 months and abstraction of GP case notes.

Setting 31 general practices in Trent region.

Participants Patients aged 18-70 who met research diagnostic criteria for major depression; 103 patients were randomised and 220 patients were recruited to the preference arms.

Main outcome measures Difference in mean Beck depression inventory score; time to remission; global outcome assessed by a psychiatrist using all data sources; and research diagnostic criteria.

Results At 12 months there was no difference between the mean Beck scores in the randomised arms.

Combining the randomised and patient preference groups, the difference in Beck scores was 0.4 (95% confidence interval -2.7 to 3.5). Patients choosing counselling did better than those randomised to it (mean difference in Beck score 4.6, 0.0 to 9.2). There was no difference in the psychiatrist's overall assessment of outcome between any of the groups. 221/265 (83%) of participants with a known outcome had a remission. Median time to remission was shorter in the group randomised to antidepressants than the other three groups (2 months *v* 3 months). 33/221 (15%) patients had a relapse.

Conclusions Generic counselling seems to be as effective as antidepressant treatment for mild to moderate depressive illness, although patients receiving antidepressants may recover more quickly. General practitioners should allow patients to have their preferred treatment.

Introduction

Both antidepressants and psychological interventions have been shown to be effective in patients with major

depression.^{1 2} The counselling and antidepressants in primary care study was set up to compare the efficacy and cost effectiveness of antidepressant drugs and generic counselling in a naturalistic general practice setting. The short term outcomes from this study (at eight weeks) have been published.³ We report here the outcomes at 12 months.

Participants and methods

Recruitment and treatment

Full details of the methods have been published.³ Briefly, we invited a random sample of 410 general practices in the Trent health region to enter patients into the trial. General practitioners recruited participants and obtained informed consent. Eligible patients were those aged 18-70 years who met the research diagnostic criteria (assessed by the general practitioner using a checklist) for major depression.⁴ We excluded patients with psychosis, suicidal tendencies, postnatal depression, a recent bereavement, or drug or alcohol misuse. The study was approved by 12 local research ethics committees.

For patients who agreed to randomisation, treatment was allocated by telephone with a randomisation strategy using blocks of four stratified by practice. Patients who refused randomisation but agreed to participate in the patient preference trial were given their choice of treatment. Treatment and follow up were identical in the randomised and patient preference groups.

We provided general practitioners with written guidelines on routine drug treatment of depression. Patients in the counselling arms were given six sessions by experienced counsellors, who adopted the counselling approach that they believed to be most suitable.

Data collection and follow up

All patients completed the Beck depression inventory⁵ and SF-36 questionnaire at enrolment.^{6 7} At the follow up visits eight weeks and 12 months after enrolment, the general practitioner completed a form that included the research diagnostic criteria and the patient was asked to complete a form including the Beck depression inventory and SF-36. Patients who did

not keep their follow up appointments were asked to complete the forms at home.

Outcome measures

The main outcome measures at 12 months were Beck depression inventory score, time to remission,^{8,9} global outcome (classified as good, moderate, poor, or unknown), and research diagnostic criteria. Remission was defined as a score of less than 4 on the research diagnostic criteria, a Beck score of less than 10, or clear documentation in the general practitioner's notes that the patient was well. Relapse was defined as deterioration within six months of remission, and recurrence as deterioration after six months of remission.

Global outcome was assessed by a psychiatrist (NB) blind to treatment allocation using the research diagnostic criteria, Beck score, and general practitioners' notes. If the research diagnostic criteria and Beck scores were not available, global outcome was estimated from the case notes. The outcome was considered good if the patient responded to treatment within eight weeks and then remained well; moderate if the patient was slow to respond but then remained well or was well initially and then became unwell; and poor if the patient remained depressed throughout. The criteria for being well were the same as the criteria for remission.

Statistical analysis

We investigated differences in baseline characteristics and outcome measures between the groups using descriptive statistics, unpaired *t* tests, χ^2 tests, and Fisher's exact test. The analyses stratified by randomised or patient preference status used Mantel-Haenszel techniques. The time to remission was analysed by the Kaplan-Meier method, and differences were tested with the logrank test.^{10,11}

Based on a clinically important difference between the groups in mean Beck scores of 5 points, and assuming a standard deviation of 8.3 with two sided significance of 0.05, we required 44 patients per arm for power of 80% and 60 per arm for power of 90%.

Results

Response rates

The figure shows the numbers of patients recruited and followed up. Sixty five (63%) patients in the randomised trial completed the Beck depression inventory and SF-36 at 12 months compared with 142 (65%) in the patient preference trial. The proportions of patients in each group who kept their 12 month appointment differed ($P=0.01$), with attendance ranging between 25% for patients choosing antidepressants and 53% for those randomised to antidepressants.

We abstracted the general practitioner's notes for 96% (99/103) of patients in the randomised trial and 96% (212/220) in the patient preference. There was sufficient information to carry out the psychiatrist's overall assessment on 79% (81/103) of patients in the randomised trial and 74% (163/220) in the patient preference trial.

Patient characteristics at entry

The characteristics of randomised patients were comparable at baseline (table 1). Patients preferring

counselling were less severely depressed than the randomised patients or those preferring antidepressants.³

Beck inventory scores at 12 months

Mean Beck scores did not differ significantly between the two groups in the randomised controlled trial ($P=0.49$, table 2). There was no evidence for an interaction between treatment and preference ($P=0.6$) so we combined the randomised and patient preference groups. Mean Beck scores were similar in counselled patients and those receiving antidepressants.

Global outcome and time to remission

We found no differences in global outcome between the randomised or patient preference trials when outcome was split into good or moderate versus poor (table 3). Stratification by randomised or patient preference status gave similar outcomes for antidepressants and counselling (Mantel Haenszel $P=0.63$).

Research diagnostic criteria scores

Of the randomised patients who kept their 12 month follow up, nine (47%) in the counselling group were no longer depressed compared with 21 (78%) in the antidepressant group ($P=0.07$). When we assumed that all those failing to attend had recovered, then 81% in the counselling group and 88% in the antidepressant group were no longer depressed. The figures when we assumed that patients failing to attend were treatment failures were 17% and 41% respectively ($P=0.01$).

In the patient preference trial, 48 (80%) patients choosing counselling and 17 (85%) choosing antidepressants had recovered at 12 months ($P=0.87$). If missed appointments were assumed to be treatment successes the outcomes were similar, but if all missed appointments were treatment failures, patients choosing counselling would do better than those choosing antidepressants.

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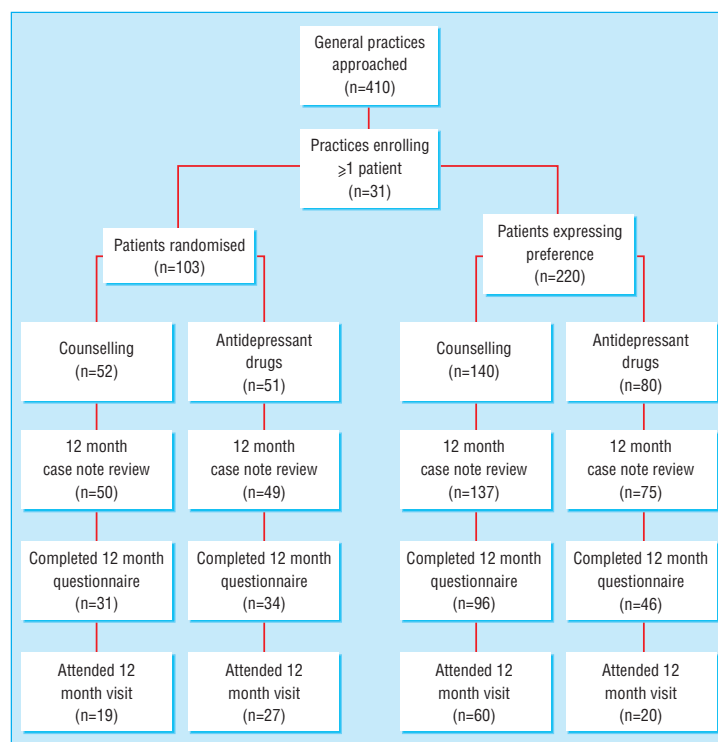
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Recruitment and follow up of patients

Table 1 Summary of baseline characteristics. Values are numbers (percentages) unless stated otherwise

Characteristic	Randomised			Patient preference			P value for comparison of 4 groups
	Counselling (n=52)	Antidepressants (n=51)	P value	Counselling (n=140)	Antidepressants (n=80)	P value	
Men	16 (31)	8 (16)	0.12	36 (26)	21 (26)	1.00	0.34
Mean (SD) age	37.3 (11.2)	38.4 (11.8)	0.60	36.4 (10.1)	38.1 (12.7)	0.27	0.60
Married*	17/35 (49)	23/36 (64)	0.29	58/101 (57)	25/45 (56)	1.00	0.63
Living alone*	7/35 (20)	2/36 (6)	0.14	11/101 (11)	5/45 (11)	1.00	0.29
Family history of depression*	15/34 (44)	19/36 (53)	0.47	51/94 (54)	21/43 (49)	0.56	0.76
Mean (SD) age at onset*	33.3 (24.2)	35.6 (18.6)	0.65	35.1 (20.7)	34.1 (20.6)	0.79	0.96
Social class*:							
I or II	6/30 (20)	12/31 (39)	0.24	38/91 (42)	12/41 (29)	0.28	0.30
III non-manual or manual	12/30 (40)	11/31 (35)		34/91 (37)	16/41 (39)		
IV or V	12/30 (40)	8/31 (26)		19/91 (21)	13/41 (32)		
Beck inventory score:							
Mean (SD)	27.1 (8.0)	27.0 (8.0)	0.97	25.8 (7.7)	25.4 (9.5)	0.78	0.57
Not known	2	2		6	8		
Research diagnostic criteria score:							
4 or 5	19 (37)	14 (27)	0.44	59 (42)	22 (28)	0.04	0.10
6-8	32 (62)	36 (71)		81 (58)	58 (73)		
Not known	1 (2)	1 (2)		0	0		
General practitioner's rating:							
Mild	12 (24)	10 (19)	0.29	45 (32)	10 (13)	0.001	0.004
Moderate	33 (66)	31 (61)		87 (62)	62 (78)		
Severe	3 (6)	8 (16)		5 (4)	8 (10)		
Not known	2 (4)†	2 (4)		3 (2)	0		

*Some patients did not have the telephone interview immediately after recruitment. †Data were not completed by the general practitioner for two further patients.

Discussion

The data from our randomised controlled trial suggest that at 12 months follow up generic counselling and antidepressants are equally effective in patients with mild to moderate depression; remission rates are impressive with both treatments. Patients treated with antidepressants recovered more quickly than those receiving counselling. Choice of treatment seemed to be beneficial, but this applied only to counselling. This finding should be treated with caution as the power of the study to detect interactions was low.

The larger numbers of patients choosing counselling in this trial suggests that patients prefer

counselling to antidepressants.³ A survey of people attending general practice had similar findings.¹²

Several caveats must be taken into account when interpreting these data. Firstly, we had difficulty recruiting patients into the randomised controlled trial. The patient preference arms, although increasing the power of the study, tend to make our findings less robust. Secondly, the counselling offered in the study was of a high standard; patients were referred within two weeks, and all the counsellors were experienced. Thirdly, although we found some benefit associated with choice, we did not investigate the effect of giving an alternative treatment to those with a specific preference.

Table 2 Scores on Beck depression inventory scale at 12 months

	Counselling		Antidepressants		Difference (95% CI)	P value
	No of patients	Mean (SD) score	No of patients	Mean (SD) score		
Randomised patients	31	16.7 (11.5)	34	14.6 (13.1)	2.1 (-4.0 to 8.2)	0.49
All patients*	127	13.2 (11.3)	80	12.8 (10.7)	0.4 (-2.7 to 3.5)	0.81

*Score adjusted for patient preference or randomised group and baseline score for research diagnostic criteria: P=0.34.

Table 3 Global outcome, remission, and relapse in randomised and patient preference groups. Values are numbers (percentages) of patients. Totals exclude missing data but include patients in whom outcome was uncertain

	Randomised patients			Patient preference			P value for Mantel Haenszel χ^2 test
	Counselling (n=52)	Antidepressants (n=51)	P value	Counselling (n=140)	Antidepressants (n=80)	P value	
Global outcome:							
Good or moderate	29 (56)	33 (65)	0.854*	90 (64)	54 (68)	0.803*	0.626
Good	13 (25)	21 (41)	0.196*	50 (36)	22 (28)	0.191*	0.868
Ever remitted	33/48 (69)	39/50 (78)	0.633*	95/129 (74)	54/78 (69)	0.872*	0.739 (yes v no)
Ever relapsed	5/33 (15)	4/39 (10)	0.820†	18/95 (19)	6/54 (11)	0.615*	0.455
Outpatient psychiatric referral	2 (4)	0	0.505†	10 (7)	5 (6)	0.927*	0.668
Inpatient treatment for depression	1‡ (2)	2 (4)	0.970†	2 (1)	0	0.849†	§
Other inpatient treatment	6 (12)	8 (16)	0.711*	22 (16)	14 (18)	0.706*	0.498

* χ^2 test. †Fisher's exact test. ‡One patient attended twice. §Invalid because of small numbers.

What is already known on this topic

Antidepressants and specific psychological interventions are effective in major depression.

Generic counselling has not previously been compared with antidepressants in primary care

What this study adds

12 months after starting treatment, generic counselling is as effective as antidepressants

Patients treated with antidepressants may recover more quickly

Given a choice, more patients opt for counselling

Patients who choose counselling may benefit more than those with no strong preference

What conclusions should commissioners and general practitioners draw from this study? Firstly, that both counselling and antidepressant drugs are effective, but antidepressants may result in more rapid recovery. Secondly, that given the choice more patients with depression will choose counselling and those who choose antidepressants are likely to be more severely depressed. We recommend that general practitioners should allow patients to have their choice of treatment. However, if the patient does not have a preference, antidepressant drugs should be prescribed because counselling is a scarce resource that is best reserved for those patients who express a preference for it.

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Contributors: CC, MD, CD, KF, GH, AL, DW, and IW developed the study protocol. RC, VG, DW, and IW recruited the practices. VG carried out the fieldwork with clinical support from RC. NB, CD, and AL reviewed the case notes and global outcomes. BP, MD, and PM carried out the data analysis. CC wrote the paper, and all authors commented on the drafts. CC and CD are the guarantors.

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A memorable patient

A case of mistaken diagnosis

It was around May or June 1977. I had started my house job in psychiatry in India a couple of months before. Psychiatry was a brand new subject for me.

I was attending an outpatient clinic daily. The clinic was extremely busy. There were no set appointments (most of the patients did not have telephones at home), no distinct catchment area, and a referral letter from the general practitioner was not required. It was not surprising that a big crowd gathered in the clinic every morning seeking treatment. It was probably only the stigma of mental illness, which was more prevalent in those days, that prevented the clinic getting busier, and we were expected not to return anybody without providing treatment.

It was a Monday morning, traditionally the busiest day of the week. A male patient was making too much noise in the waiting area, and his relatives made vain attempts to quieten him. My consultant called for the attendant, who told us that this man was an employee of the port trust. He had had problems with his supervisor in the past. He had been involved in a minor accident at work a few days ago and had been behaving strangely ever since. My consultant jokingly said that the patient probably had compensation neurosis. He asked me to see this man ahead of his turn so that peace could return to the waiting area.

When I interviewed the patient in the company of his relatives I could not elicit any relevant stressors. The patient, and his relatives, played down the importance of work related problems. The patient was rather dramatic in his presentation. He complained of disturbed sleep and difficulty in swallowing which

had coincided with the injury he sustained at work the previous week. Though he was incoherent and loud, at times my impression was that he was not psychotic or manic. My boss agreed with me. The patient was given the diagnosis of hysterical conversion, which was not uncommon among our patients. The patient and his family were reassured, a prescription for benzodiazepine was given, and the patient was advised to report back a week later.

I did not take much notice when the patient failed to attend. Another fortnight passed, and a relative made a courtesy call to inform me that the patient had died four days after seeing me. He had become more incoherent and also refused to drink. He was taken to the infectious diseases hospital three days later. He was diagnosed with rabies and died soon after. His family recalled that he had mentioned being bitten on his leg by a stray dog a couple of months ago. He thought that the bite was superficial and did not bother to see a doctor.

I opened *Brain's Diseases of the Nervous System* and read that rabies could have a long incubation period, up to 64 days. I felt guilty for this missed diagnosis and the ease with which we were fooled. The only consolation was that once the disease manifests itself death is almost certain, meaning that a correct diagnosis was not likely to have impacted on the final outcome at all.

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