The effects of detection and treatment on the outcome of major depression in primary care: a naturalistic study in 15 cities

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SUMMARY

Background. *This study reports the responses of patients with confirmed depressive illnesses to different treatments in the WHO Mental Disorders in General Health Care study, conducted in 15 cities around the world.*

Aim. *To discover how depressions recognized by the doctor compare with unrecognized depressions, both in terms of the initial illnesses and their outcomes, and to compare the outcomes of those depressions treated with antidepressants with those treated with daytime sedatives.*

Method. *The design of the study was naturalistic, in that physicians were free to treat patients however they wished. Patients with confirmed depressive illnesses were assigned to four groups: treatment with an antidepressant; treatment with a daytime sedative (usually a benzodiazepine); patients recognized as having depression by the physician but were not offered drug treatment; and patients unrecognized as having depression by their physician.*

Results. *Both groups receiving drugs had illnesses of equal severity, were demographically similar to one another, and had similar previous histories of depression. Those receiving antidepressants had significantly fewer overall symptoms and fewer suicidal thoughts than those treated with sedatives. By the end of one year, differences between the groups had disappeared: patients not given drugs had milder illnesses but did significantly better than those receiving drugs, both in terms of symptoms lost and their diagnostic status. Unrecognized depressions were less severe than recognized depressions, and had a similar course over the year.*

Conclusions. *Patients receiving antidepressants were better in terms of overall symptoms and suicidal thoughts than those treated with sedatives at three months, but this advantage does not persist. Depression emerges as a chronic disorder at one-year follow-up — about 60% of those treated with drugs, and 50% of the milder depressions, still meet criteria for caseness. The study does not support the view that failure to recognize depression has serious adverse consequences, but, in view of the poor prognosis of depression, measures to improve compliance with treatment would appear to be indicated.*

Keywords: depression; primary care; illness recognition; naturalistic study.

Introduction

THIS paper examines the effects of interventions by general practitioners (GPs) in confirmed cases of depressive illness, in the 15 cities participating in the WHO Study of Mental Disorders in General Health Care. GPs have been criticized for failing to recognize depression,[1] and, having recognized it, for failing to treat it energetically enough.[2] However, the significance of unrecognized depression in primary care is equivocal, and studies at single centres[3,4] have failed to find an association between recognition and outcome, perhaps because recognition does not imply optimal treatment. One US study[5] randomized depressed patients to 'usual care' or enhanced or 'multi-faceted care' (MC). The latter involved greater frequency of visits, two with a psychiatrist. In those with major depression, MC produced greater compliance and greater satisfaction with treatment, with patients rating antidepressants as more helpful and resulting in greater symptom reduction. However, in minor depression, MC produced better compliance but not better outcomes or satisfaction.

The present paper studies the natural history of confirmed depressions that were undetected by the doctor, as well as contrasting the course of those episodes of depression treated using antidepressants with those treated using sedatives. The study was naturalistic, in that doctors were free to treat patients however they wished. The design ensured that the depressive illnesses seen were representative of those occurring in general practice, and doctors did not know whether or not a patient they had seen had been identified by the research interview as a case of depressive illness. In spite of evidence of efficacy in controlled clinical trials,[6-8] there is lack of information on efficiency; the question being whether, under routine clinical treatment conditions, antidepressants can be shown to influence the course of these disorders. Some recent studies have failed to show a difference between antidepressants and placebos,[9,10] while others have shown equal effects with benzodiazepines,[11-13] and others still have shown that psychological treatments are equally effective.[14,15] Controlled studies, therefore, need to be supplemented by epidemiological studies on the provision and outcome of treatment. In the present study, GPs frequently reported counselling as one of the treatments given to the patients either on its own or in combination with drug treatment, but the investigators had no control over what was meant by this term. Those patients who did not receive a prescription were therefore called 'no drugs', whether or not they were also reported as having received counselling.

The aim of the present study was to discover how depressions recognized by the doctor compare with unrecognized depressions, both in terms of the initial illnesses and their outcomes, and to compare the outcomes of those depressions treated with antidepressants with those treated with daytime sedatives. The

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initial hypotheses were:

- Depressions treated with drugs would be more severe than those not so treated, and that depressions recognized by the doctor would be more severe than unrecognized depression;
- Those treated with antidepressants would do better than those treated with daytime sedatives; and
- Unrecognized depressions would have a poorer outcome than recognized depressions.

This paper extends earlier work by examining the effects of recognition and treatment on outcome in a large primary care sample.

Method

The study involved 15 centres around the world, in which a total of 11 languages were spoken.[16] Consecutive patients attending clinics at participating centres were approached, providing that they were over 17 years old, were not too ill to participate, were able to communicate, and had a fixed address. The latter requirement was necessary, as the study used a longitudinal design. Consecutive patients eligible for the study completed the 12-item General Health Questionnaire (GHQ),[17] and subjects were selected for the second interview stage using a stratified sampling procedure, such that all patients with the highest scores were selected. Half of those in an intermediate range and 10% of those in the lowest range were interviewed by a research assistant using the primary care version of Composite International Diagnostic Interview (CIDI-PC)[18] and the Groningen Disability Schedule[19] shortly after their appointment in the clinic. Patients were interviewed three months later with a brief set of measures, including the GHQ-28 and the Brief WHO Disability Questionnaire[20] and questions relating to compliance with any treatment prescribed, and were interviewed at length with a full set of measures at 12 months. All instruments were translated and back-translated in each of the 11 languages.

The CIDI-PC can generate diagnoses using either the International Classification of Disease (10th edition[21]), or the Diagnostic & Statistical Manual of the American Psychiatric Association (4th edition[22]). For the purposes of the present study, 'lifetime' diagnoses were ignored, and only current mental status was considered. It was projected that 1500 patients needed to be screened in each centre in order to detect 60 current cases of depression and to have adequate numbers to allow a centre to compare the course of depression relative to other disorders that were common at that centre. The present study a reports data on all patients who satisfied diagnostic criteria for current major depressive episode on the CIDI, and who were seen on at least one occasion for follow-up assessment.

Four sources of information were used in the present study:

1. The Physician's Encounter Form provided information about recognition of depression and treatment offered.
2. The first interview with the patient provided the diagnosis of depression from the CIDI, a baseline GHQ-28 score, and indicated whether they were taking the tablets prescribed.
3. The three-month follow-up provided measures of symptoms experienced, disability, and how long they had taken any tablets prescribed.
4. The one-year follow-up provided a full range of outcome measures.

It must be emphasized that these were not first onset depressions; indeed, just over a third had previous episodes of depression, and the episode could have been at any stage at the time of the initial interview. The detailed methodology is described elsewhere.[16]

Patients satisfying these entry criteria were assigned to one of four groups depending upon whether the GP had recognized them as a psychiatric 'case' and, if recognized, whether a drug had been prescribed. If the patient was prescribed a drug, we checked with the CIDI to ensure that the patient told the researcher that the drug was being taken. All those prescribed an antidepressant, who said that they were taking it, plus a few additional patients who were already on antidepressants, were entered into group 1: 'antidepressants'. All those taking benzodiazepines and other anxiolytics, but not taking antidepressants, plus a few additional patients who were already on these drugs, were entered in group 2: 'daytime sedatives'. All those whose mental disorder was recognized by their doctor, but who were not receiving any psychoactive drug, were entered in group 3: 'no drug'. The remaining depressed patients, whose doctor had rated them as non-cases, were entered into group 4: 'unrecognized depression'. Although data was collected on non-pharmacological treatments: these are not presented here, as it was found that there were not only large centre differences, but also large differences between one physician and another in what was meant by these treatments.

Comparisons between baseline and three months were made for all patients for whom three-month data were available; however, at one-year follow-up we were limited by the number of patients available for interview at that time. In order to study the extent to which patients reported suicidal ideas, a score for the four items on the GHQ dealing with such ideas was computed: feeling that life is not worth living; wishing that one was dead and away from it all; thinking of the possibility of suicide; and having repeated suicidal thoughts. These items were scored using Likert scoring, producing a score that varied between 0 and 12 for each subject.

Results

Baseline status

It can be seen from Table 1 that there were no significant differences between the two drug groups for age, sex, marital status, times since first onset of symptoms, or the proportion with a previous episode of depressive symptoms. In terms of the severity of the depressive illnesses at baseline, the number of depressive symptoms on the CIDI, the baseline GHQ scores, and associated disability were the same for both groups receiving drugs (Tables 2 and 3).

In contrast, patients who were recognized as depressive, but not prescribed for, were younger and more likely to be male, as well as having had their symptoms for a shorter period of time. They also had less severe illnesses, with fewer depressive symptoms on the CIDI, and fewer symptoms on the GHQ.

Length of previous episode was the same for all recognized patients (over 90% of the recognized groups reported previous episodes lasting longer than one month), but was less for unrecognized patients (significantly fewer [83.5%; $\chi^2 = 22.8$; d.f. = 2; $P = 0.00$] had such episodes). Unrecognized patients were also younger and had their symptoms for less time than recognized patients. They also had less severe illnesses than recognized patients with fewer CIDI symptoms (Table 2), lower GHQ scores (Table 3), lower scores relating to suicide (Table 5), and lower disability scores at baseline (7.7 versus 9.6; $t = 2.1$; $P = 0.035$). Patients said they took the drugs for widely varying lengths of time: for antidepressants, 21 (25.3%) took them for less than one month, and the mean length of time was 10.7 weeks; and for

Table 1. Baseline characteristics of five groups of depressed patients, compared using chi-squared and Student's *t*-test. (NS = not significant.)

Group	Mean age	Male (%)	Married (%)	Time since first onset (years)	Proportion with previous episode (%)
Antidepressants (n = 85)	42.6	20.0	48.2	12.4	49.2
Sedatives (n = 71)	43.2	16.9	54.9	13.1	39.2
No pschoactive drugs (n = 161)	39.3	29.2	56.8	8.4	36.9
Unrecognized depression (n = 323)	38.1	24.8	58.5	7.8	38.3
Antidepressants versus sedatives (1 versus 2)	NS	NS	NS	NS	NS
Drug versus no drug (1+2 versus 3)	t = 2.8[a] P = 0.006[b]	c^2 = 4.9 P = 0.035[a]	NS	t = 3.3 P = 0.001[b]	NS
Recognized versus unrecognized (1+2+3 versus 4)	t = 2.9[a] P = 0.004[b]	NS	NS	t = 3.0 P<0.003[b]	NS

[a]Significant beyond the 5% level; [b]significant beyond the 1% level.

Table 2. Number of symptoms on the CIDI at baseline and one-year follow-up. The baseline values are compared with t-tests; the ACOVAs for one-year outcome used sex, age, and initial CIDI depressive symptoms at baseline as covariates. (NS = not significant.)

Group	Number of CIDI symptoms	
	Baseline severity	Severity at one year
Antidepressants (n = 64)	11.9	6.6
Sedatives (n = 49)	11.8	7.5
No psychoactive drugs (n = 120)	9.4	3.7
Unrecognized depression (n = 241)	8.8	3.7
Antidepressants versus sedatives (1 versus 2)	t = –0.62; NS	ACOVA NS
Drug versus no drug (1+2 versus 3)	t = 3.5; P = 0.000[a]	F = 7.5; P = 0.007[a]
Recognized versus unrecognized (1+2+3 versus 4)	t = 4.6; P = 0.000[a]	ACOVA NS

[a]Significant beyond the 1% level.

Table 3. Scores on the GHQ-28 at baseline, at three months, and at the one-year follow-up. The covariates for the ACOVAs were sex, age, and initial GHQ score. (NS = not significant.)

Group	Baseline	Three months	One year
Antidepressants (*n* = 85; 64 at one year)	17.1	10.1[a]	9.6
Sedatives (*n* = 71; 49 at one year)	18.2	13.3	11.0
No psychoactive drugs (*n* = 161; 120 at one year)	15.9	10.4	6.6
Unrecognized depression (*n* = 323; 240 at one year)	13.9	8.8	5.5
Antidepressants versus sedatives (1 versus 2)	t = 1.1; NS	F = 4.6; P = 0.034[a]	ACOVA NS
Drug versus no drug (1+2 versus 3)	t = 2.5; *P* = 0.014[a]	ACOVA NS	*F* = 6.3; *P* = 0.013[a]
Recognized versus unrecognized (1+2+3 versus 4)	t = 5.8; *P* = 0.000[b]	ACOVA NS	*F* = 3.6; *P* = 0.058

[a]Significant beyond the 5% level; [b]significant beyond the 1% level.

sedatives, 23 (32.6%) took them for less than one month, and the mean length of time on medication was 9.15 weeks. Of the patients who were not prescribed a psychoactive drug, 54% received a prescription for a tonic, placebo, vitamin, or herbal remedy: these substances were taken for shorter periods of time, 70% for less than a month, and the mean time was only 5.6 weeks for those given these substances.

Participation in the follow-up

Eighty per cent of the patients with major depression at the baseline assessment completed at least one of the follow-up assessments. Follow-up participation did vary significantly among centres, but was not significantly related to baseline GHQ-28 score, number of depressive symptoms at baseline, or baseline disability as rated by the SDS or BDQ. There were considerable centre differences in the way in which depression was treated, with some centres treating the majority of recognized depressions with antidepressants, while others hardly used these drugs at all. A test of the interaction between centre and management showed that the effects of management were not significantly different between centres, so that the relationship between management and outcome of depression was not found to vary between centres. However, this is not a very powerful test. It was also found that exclusion of subjects with co-morbid disorders produced essentially similar results to those reported here.[23]

Progress at three months

The rate of loss of symptoms over time was tested using analysis of covariance, with initial symptom counts as a covariate, as well as sex and age. The GHQ scores at three months show that there is a significant advantage for those receiving antidepressants over those receiving sedatives (Table 3), and this difference is also seen in the items dealing with suicidal ideas (Table 4). However, there was no difference between the two classes of drug in disability, as measured by the Brief Disability Questionnaire (8.1 versus 9.5; NS)

Table 4. Suicide scores on GHQ at baseline, three months, and one-year-follow-up. (NS = not significant.)

Group	Baseline	Three months	One year
Antidepressants (n = 84; 64 at one year)	4.7	2.5	2.7
Sedatives (n = 70; 48 at one year)	5.0	3.7	3.1
No psychoactive drugs (n = 160; 120 at one year)	3.5	2.5	1.7
Unrecognized depression (n = 321; 239 at one year)	2.71	1.76	1.6
Antidepressants versus sedatives (1 versus 2)	NS	F = 4.6; P = 0.033[a]	ACOVA NS
Drug versus no drug (1+2 versus 3)	NS	ACOVA NS	ACOVA NS
Recognized versus unrecognized (1+2+3 versus 4)	t = 1.8; P = 0.07	ACOVA NS	ACOVA NS

[a]Significant beyond the 5% level.

Table 5. Diagnostic status of the four groups at one-year follow-up assessment. (NS = not significant.)

Group	Well	Sub-threshold	Another diagnosis	Continuing case of depression
Antidepressants (*n* = 64)	20 (31.3%)	4 (6.3%)	7 (10.9%)	33 (51.6%)
Sedatives (*n* = 49)	12 (24.5%)	8 (16.3%)	7 (14.3%)	22 (44.9%)
No drug (*n* = 240)	47 (39.5%)	13 (10.9%)	29 (24.4%)	30 (25.2%)
Unrecognized (*n* = 240)	100 (41.7%)	24 (10.0%)	48 (20.0%)	68 (28.3%)
Antidepressants versus sedatives	NS	NS	–	–
Drug versus no drug	$c^2 = 15.3$	P = 0.002[a]	–	–
Recognized versus unrecognized	NS	NS	–	–

[a]Significant beyond the 5% level.

Patients who were not prescribed drugs lost their symptoms to the same extent at three months, had similar scores on suicide, and were equal in terms of disability reduction. Patients with unrecognized depressions also lost symptoms on both the CIDI and GHQ and had similar reductions in disability as patients with recognized depression.

Outcome at one year

For the two classes of drug, all differences had disappeared a year later, and the loss of depressive symptoms on the CIDI were also similar, confirming the findings with the GHQ. Table 5 shows the diagnostic status of patients at one-year follow up: it can be seen that about 60% of both groups receiving drugs were still 'cases' of mental disorder one year later, and that the difference between the two groups was not significant. Those patients not receiving drugs did better on both CIDI and GHQ, even after adjustment for initial scores on each instrument, but were similar to the drug group in terms of their disability scores.

Patients with depressions that were unrecognized by the doctor lost their symptoms on the CIDI at a similar rate to recognized depressions, but the results on the GHQ were equivocal (significantly better at the 10% level). They were similar to the recognized patients, both in terms of disability scores at one year and diagnostic status, with 48.3% still regarded as 'cases'.

Discussion

This is a naturalistic study, with all its strengths and weaknesses. It cannot document the efficacy of antidepressants, nor can we know whether the drugs were prescribed in therapeutic doses, or indeed whether the patients who said they were taking drugs really were doing so. Furthermore, not all the patients were available at the one-year follow-up — although those not followed up were in no way different from those whose results we report here. Finally, there were large centre differences in the drugs prescribed for depression. In some centres, antidepressants were hardly ever used, while in others, daytime sedatives were avoided.

Against these shortcomings, there are some undoubted strengths. The data presented here allow a much more complete picture to emerge of the effects of drug use, as no depressed patients are excluded from the trial by the researchers, or refused to collaborate with a therapeutic trial. Those patients given drugs can be viewed in the context of others with depression but not given drugs and those not even recognized by the physician. The longitudinal design lasting a year, and the wide variety of cultural settings, is also an advantage. We were able to make a comparison between antidepressants and daytime sedatives, as use of the latter was so widespread in some of the centres that comparable groups in terms of severity and baseline characteristics were available. Finally, all cases of depression were confirmed by independent interview.

Conclusions

Recognized versus unrecognized depression

Unrecognized cases of depression in primary care have, as a group, less severe illnesses in a number of important respects: they have fewer symptoms of depression, they experienced their first symptoms of depression more recently, and their previous episodes of depression lasted for shorter periods of time. Our failure to show that non-recognition of depression has serious measurable effects does not, of course, mean that there were not depressives in that group who would have benefited from treatment; however, such patients may possibly be hidden by detected patients who did not benefit from treatment, and who therefore contributed to a worse outcome for the treated group. It is unlikely that a purely statistical adjustment can fully allow for all the respects in which the groups differed. However, the group as a whole does better than the recognized cases, and, one year on, it is not more likely to still be suffering from depression. The fact that almost half of the unrecognized cases (48.3%) were still either cases of depression or cases of another mental disorder, suggests that efforts to improve the ability of doctors to detect depressive illness are worthwhile, although the generally good outcome for the whole group suggests that this cannot be thought a major problem.

Drugs versus no drugs

Depressive patients who were not treated with drugs had lower GHQ scores and fewer depressive symptoms reported on the CIDI than those given drugs. They also had similar numbers of disability days. However, over the following year the changes in the groups were similar, and the analyses of covariance failed to show that those without drugs were at any disadvantage. This in no way means that drugs are unnecessary, but we have seen that they appear to be being given to patients with the most severe illnesses, both in terms of their current status and their previous experience of illness. The finding that patients with less severe illnesses had a better outcome should cause no surprise, the more important point is that there appeared to be no long-term penalties for failing to prescribe psychotropics for those with less severe illnesses.

Antidepressants versus daytime sedatives

The data indicate that those depressions treated with antidepressants had fewer general psychiatric symptoms, and scored less on items dealing with suicidal ideas at three months follow-up, when compared with those treated with sedatives. At one year, differences between patients treated with the two classes of drug were no longer significant. However, our findings need to be considered in the context of the study design — we identified patients on an 'intention to treat' basis, and confined our analyses to those patients who started out on their assigned drug; however, we have no way of knowing the extent to which dosage was adequate, or that tablets were actually taken. Antidepressants appeared to be offered to those who were more severely depressed, and this is appropriate in view of the better outlook of the milder illnesses being managed without psychoactive drugs. The generally very poor outcome for the treated groups at one-year follow-up — about 60% were still psychiatric cases — may reflect the generally poor outcome of more severe illnesses, or failure to ensure that depressed patients continued to receive antidepressants.

It is known from other studies[24] that chronic depression is associated with severe social and interpersonal problems, and such illnesses are unlikely to resolve completely unless there is some improvement in the patient's personal circumstances.

Antidepressants were often taken for relatively short periods of time in this naturalistic study. While the results do not support using drugs more widely, those more severe depressions treated with antidepressant drugs may benefit from longer periods of treatment. The findings suggest that a future trial of efficacy might address the advantages of ways of improving compliance with treatment protocols over the longer term.

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