Managing depression as a chronic disease: a randomised trial of ongoing treatment in primary care

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Abstract

Objectives To evaluate the long term effect of ongoing intervention to improve treatment of depression in primary care.
Design Randomised controlled trial.
Setting Twelve primary care practices across the United States.
Participants 211 adults beginning a new treatment episode for major depression; 94% of patients assigned to ongoing intervention participated.
Intervention Practices assigned to ongoing intervention encouraged participating patients to engage in active treatment, using practice nurses to provide care management over 24 months.
Main outcome measures Patients' report of remission and functioning.
Results Ongoing intervention significantly improved both symptoms and functioning at 24 months, increasing remission by 33 percentage points (95% confidence interval 7% to 46%), improving emotional functioning by 24 points (11 to 38) and physical functioning by 17 points (6 to 28). By 24 months, 74% of patients in enhanced care reported remission, with emotional functioning exceeding 90% of population norms and physical functioning approaching 75% of population norms.
Conclusions Ongoing intervention increased remission rates and improved indicators of emotional and physical functioning. Studies are needed to compare the cost effectiveness of ongoing depression management with other chronic disease treatment routinely undertaken by primary care.

Introduction

Depression is increasingly viewed as a chronic illness,[1 2] as depressed individuals experience high rates of symptom recurrence[3–6] and sustained functional impairment.[7] In recognition of the chronicity of the condition, most trials of depression treatment incorporate principles of chronic disease management into the interventions tested.[8–10] However, these interventions have generally been tested for only brief periods, six months or less.[11–30] Results from studies examining how brief intervention affects depression symptoms and functioning one year after termination[31–34] have led investigators to quip that "no intervention has much impact longer than two months after it ends." This lack of sustained effect is not surprising given that many primary care patients whose depression recurs after brief intervention ends fail to get high quality care.[35]

To evaluate whether applying principles of chronic disease management in the long term can achieve sizeable and sustained improvements in symptoms and functioning, we tested an intervention to improve depression treatment on an ongoing basis. We hypothesised that ongoing intervention would increase remission and improve functioning over 24 months in patients starting a new treatment episode for major depression.

Methods

Assignment

Our methods are described in detail elsewhere.[36] After approval of the study by the Human Research Advisory Committee of the University of Arkansas for Medical Sciences and the Colorado Multi-Institutional Review Board, we conducted the study in 12 community primary care practices across the United States (eight in metropolitan areas, four in non-metropolitan areas), none of which employed onsite mental health professionals to treat depression. We randomised the 12 practices to enhanced or usual care using the following procedure. First, participating doctors in the 12 practices completed logs that allowed one of the authors (JS) to estimate the proportion of patients with diagnosed depression who were receiving care in accordance with guidelines.[37 38] Proportions for the eight metropolitan practices, identified by numerical code only, were forwarded to the first author (KR), who matched the practices into four blocks by pairing practices with similar proportions. The first practice in each block was randomly assigned to enhanced or usual care by coin toss, with the remaining practice in the block assigned to the other form of care. The same method was used to randomise the four non-metropolitan practices.

Patient eligibility criteria

Patients presenting for routine visits at the selected practices between April 1996 and September 1997 completed a two stage screening questionnaire, which identified patients reporting five or more of the nine criteria for major depression listed in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition revised (DSM-III-R) in the past two weeks. We excluded

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patients who met criteria for bereavement, mania, alcohol dependence, pregnancy or the postpartum period, or life threatening physical illness; patients who did not intend to use the clinic as their usual source of care during the year after the index visit; patients who did not have telephone access; patients who were illiterate in English; and patients who were cognitively impaired. To reflect the results from previous intervention studies,[11–15 17 19 20 22 24 25] we excluded patients from analysis who were identified at baseline with treatment resistant depression (depressed despite current treatment with antidepressants or recent specialty care), since such depression seems to require more complex treatment than primary care settings can readily provide.[39–42]

Intervention protocols

Enhanced care

Before patient enrolment, we provided brief training[36] to the participating doctors, nurses, and office staff in the practices randomised to enhanced care. The goal of the training was to encourage the practice staff to provide patients presenting with major depression with two years of high quality treatment in accordance with guidelines from the Agency for Health Care Policy and Research.[37 38] This ongoing intervention consisted of initial intervention (baseline to six months) and continuing intervention (seven to 24 months).

The objective of initial intervention was to increase the proportion of patients who received pharmacotherapy or psychotherapy for major depression. Although we presented both treatments as equally effective, we expected the initial intervention to increase pharmacotherapy more than psychotherapy because none of the practices had onsite mental health professionals. After training, office staff systematically screened patients before they saw a doctor. When the doctors concurred with a screening derived diagnosis of depression, they asked the patients to make a return visit the next week. Immediately before this return visit, an office nurse trained to provide care management reassessed the patient's depressive symptoms, provided education about treatment options, asked the patient to complete "homework" assignments to increase his or her readiness to engage in active treatment, and arranged subsequent follow up contacts.

The objective of continuing intervention was to sustain or increase improvement. Designed to be started at six months, when initial intervention ended, continuing intervention actually began an average of nine months after the index visit, when funding for its implementation became available. In telephone calls averaging 12 minutes in length nurse care managers monitored depression symptoms, encouraged patients whose symptoms were resolving to adhere to treatment recommendations, and suggested to patients whose symptoms had not resolved that they raise this problem with their primary care doctor at their next visit. Patients reporting three or more of the nine criteria for depression were called again the next month, whereas patients reporting fewer than three depression criteria were called again in three months. Primary care doctors reviewed monthly summaries of patient symptoms and current treatment prepared by nurse care managers, along with reminders to adjust treatment for symptomatic patients according to guidelines reviewed by psychiatrist.

Usual care

Depressed patients in usual care practices received no regular contacts from nurse care managers during the initial or continuing phase of the intervention. Doctors in these practices were not systematically informed when patients screened positive for depression.

Participant flow and follow up

As described earlier, 16% (1722/11 006) of patients failed to complete the two stage screening to determine initial eligibility, and 27% (174/653) of the patients meeting initial eligibility criteria failed to complete the baseline interview to determine eligibility for this analysis.[36] The staff in enhanced care practices used all available methods to encourage patients to participate in ongoing intervention but did not require them to undertake treatment. Nurse care managers reached 94% (108/115) of patients in enhanced care practices during the initial intervention, providing an average of 5.0 contacts per patient, and reached 83% (95/115) of patients during the continuing intervention (all but two of whom had participated in initial intervention), providing an average of 6.9 contacts per patient. The 82% participation rate in the continuing intervention reflected the fact that only 88% of patients reported that their practice at the index visit remained their primary source of health care 12 months later. In concordance with an intention to treat design, we interviewed patients who had left their practice even though they could not participate in continuing intervention. Follow up interviews conducted at six, 12, 18, and 24 months between October 1996 and September 1999 achieved response rates of 90%, 82%, 73%, and 67% respectively (fig 1).

Data collection and masking

Data were collected by telephone using structured instruments administered by an independent member of the research team blinded to patients' intervention status, except for three patients, for whom primary care

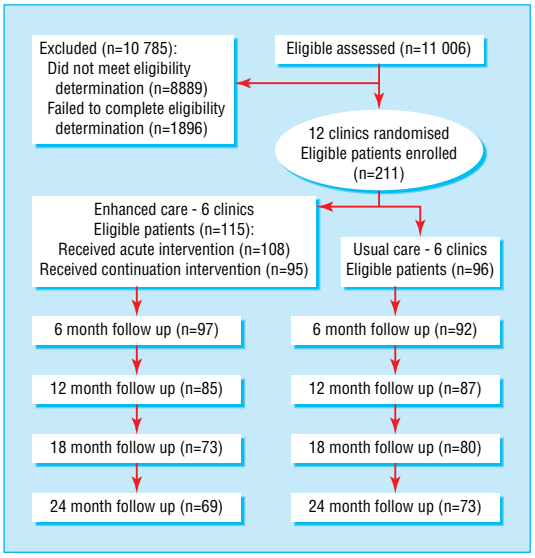


Fig 1 Flowchart of patient recruitment and participation

practices had to be contacted to request updated contact information.

Operational definition of major constructs

Treatment

We evaluated how the intervention affected treatment with antidepressants or counselling from a series of questions that patients completed at each follow up interview. Antidepressant use was defined as the number of months in the previous six months that patients reported taking antidepressants at doses in accordance with guidelines. Counselling was defined as patient report of any counselling from a mental health professional in the previous six months. It was not possible to estimate intervention effects on drug management by a psychiatrist or number of counselling sessions with a mental health professional because too few patients received these types of care.

Outcomes

Because functional improvement has been reported to lag behind symptom improvement,[43] we analysed separate measures of symptoms and functioning rather than summary scales which combine both symptoms and functioning.[44 45] As was done in previous effectiveness trials,[34] we measured probable remission by determining whether patients reported depressive symptoms on the modified Center for Epidemiological Studies—depression (CES-D) scale equivalent to a score of < 16, the cut-off point widely used to identify individuals at risk of depression.[46] We measured role functioning with two 100 point subscales of SF-36[47] that examine perceived limitations in usual daily activities in the previous month because of physical or emotional problems (higher scores indicating better outcomes).

Covariates

We collected patients' sociodemographic and clinical covariates at baseline. Sociodemographic covariates in analyses of remission and functioning included age, sex, ethnic minority status, education, paid employment, marital status, insurance status, annual income adjusted by family size, geographical region, and acceptability of treatment with antidepressants or mental health counselling (4 point Likert scales). Clinical covariates in remission analyses included physical comorbidity, dysthymia in the previous year, and functioning. Clinical covariates in treatment and functioning analyses included physical comorbidity, dysthymia in the previous year, and depressive symptoms.

Data analysis

We conducted intention to treat analyses for all patients using weighted multilevel models in SAS 8.0 PROC MIX and GLIMMIX (to approximate the logistic regression model for dichotomous outcomes) in which repeated measures were nested within patients, patients were nested within doctors, and doctors were nested within practices.[48] We modelled time as a random effect and simplified the model structure when no clustering of patients within doctors or doctors within practices was observed.

We evaluated the effects of intervention on treatment using mixed effects time-trend (growth curve) models, starting with the six month follow up because no patient had depression treatment at baseline by design. We obtained a conservative estimate of total antidepressant use over two years by summing patient reports of number of months when such drugs were taken in the previous six months, after assigning all patients who failed to complete a follow up interview a value of 0 months for the six month period.

To evaluate the effects of intervention on outcomes we used mixed effects time-trend (growth curve) models. We used preplanned linear contrasts to compare patients from enhanced and usual care practices at specific times in the presence of a significant interaction between intervention and time (intervention*time). Lastly, to explore any variation in the intervention's effect, we repeated these analyses within blocks, recognising that the limited sample size in each block reduced our power to find differences.

Power analyses indicated that our final sample size gave us 80% power to detect a 23% difference in remission in unclustered models (28% difference in clustered models) using a χ^2 test for proportional outcomes with α set at 0.05 and assuming 40% of patients in usual care would meet criteria for remission. We used recruitment weightings in all analyses to increase the representativeness of participating patients to all eligible patients. We created these weightings by comparing the sociodemographic and clinical characteristics of eligible patients who did and did not complete screening or enrol in the study, and weighted patients who enrolled in the study to the distribution of all eligible patients. We also used attrition weightings in all analyses to increase the representativeness of patients who completed follow up to patients who enrolled in the study. We created attrition weightings by comparing the sociodemographic and clinical characteristics of enrolled patients who did and did not complete follow up and weighted patients who completed a given follow up to patients who should have completed follow up, allowing us to address potential biases introduced when patients who did not complete a given follow up interview had to be excluded in estimates of intervention effect.

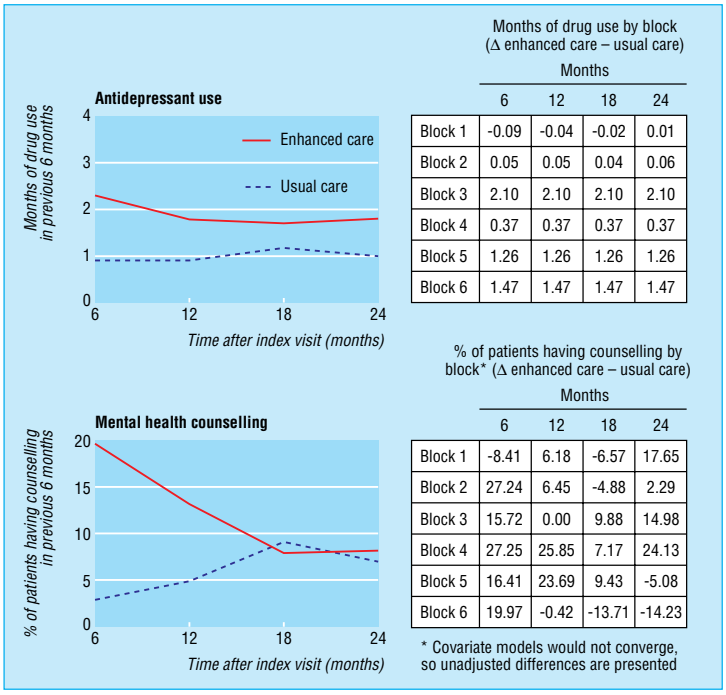
Results

Patients

At baseline, the 211 subjects participating in the study had a mean age of 43 years (SD 15), 84% were women, 16% were of an ethnic minority, 47% were currently married, 79% had been educated at least to high school level, 62% were employed full or part time, 83% had health insurance, and had a mean of 2.1 physical comorbidities. They reported an average of 6.4 of the DSM-III-R criteria for depression in the previous two weeks, 10% met criteria for dysthymia in the previous year, and 73% reported a previous episode of depression. The 96 patients in usual care practices were similar to the 115 patients in the enhanced care practices in all sociodemographic and clinical variables except that they were older (47 years *v* 40 years, P=0.002) and had more physical comorbidities (2.5 *v* 1.7, P=0.001).

Intervention effects on treatment

Antidepressant use—Enhanced care significantly increased patients' use of antidepressants over the two



Months of drug use by block (Δ enhanced care – usual care)

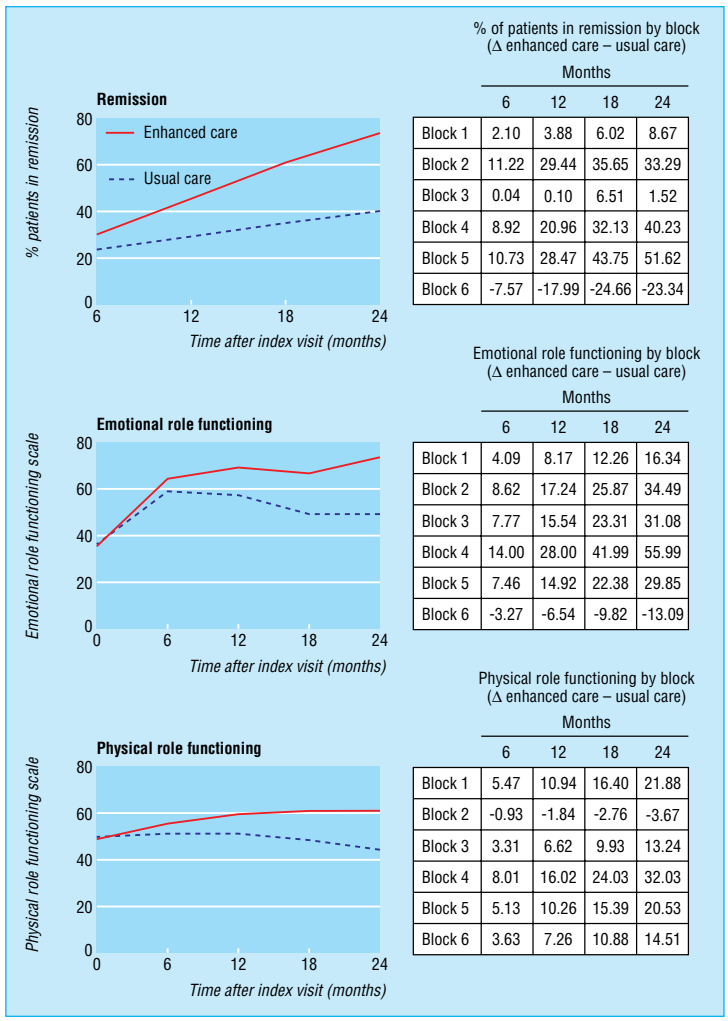
	Months 6	12	18	24
Block 1	-0.09	-0.04	-0.02	0.01
Block 2	0.05	0.05	0.04	0.06
Block 3	2.10	2.10	2.10	2.10
Block 4	0.37	0.37	0.37	0.37
Block 5	1.26	1.26	1.26	1.26
Block 6	1.47	1.47	1.47	1.47

% of patients having counselling by block* (Δ enhanced care – usual care)

	Months 6	12	18	24
Block 1	-8.41	6.18	-6.57	17.65
Block 2	27.24	6.45	-4.88	2.29
Block 3	15.72	0.00	9.88	14.98
Block 4	27.25	25.85	7.17	24.13
Block 5	16.41	23.69	9.43	-5.08
Block 6	19.97	-0.42	-13.71	-14.23

* Covariate models would not converge, so unadjusted differences are presented

Fig 2 Effect of ongoing intervention in primary care on treatment of patients with depression



% of patients in remission by block (Δ enhanced care – usual care)

	Months 6	12	18	24
Block 1	2.10	3.88	6.02	8.67
Block 2	11.22	29.44	35.65	33.29
Block 3	0.04	0.10	6.51	1.52
Block 4	8.92	20.96	32.13	40.23
Block 5	10.73	28.47	43.75	51.62
Block 6	-7.57	-17.99	-24.66	-23.34

Emotional role functioning by block (Δ enhanced care – usual care)

	Months 6	12	18	24
Block 1	4.09	8.17	12.26	16.34
Block 2	8.62	17.24	25.87	34.49
Block 3	7.77	15.54	23.31	31.08
Block 4	14.00	28.00	41.99	55.99
Block 5	7.46	14.92	22.38	29.85
Block 6	-3.27	-6.54	-9.82	-13.09

Physical role functioning by block (Δ enhanced care – usual care)

	Months 6	12	18	24
Block 1	5.47	10.94	16.40	21.88
Block 2	-0.93	-1.84	-2.76	-3.67
Block 3	3.31	6.62	9.93	13.24
Block 4	8.01	16.02	24.03	32.03
Block 5	5.13	10.26	15.39	20.53
Block 6	3.63	7.26	10.88	14.51

Fig 3 Effect of ongoing intervention in primary care on outcomes among patients with depression

years of the study (intervention: t=5.41, P<0.0001, df=174) (fig 2). Estimated conservatively, enhanced care patients reported taking antidepressants for 6.5 months during the 24 months, whereas usual care patients reported 3.4 months of drug use.

Counselling from a mental health professional—Enhanced care also significantly increased patients' use of counselling (intervention: t=5.87, P<0.0001, df=175, and intervention*time: t=−2.50, P=0.01, df=461), though the increase occurred only at six months (21% *v* 4%, P<0.0001) and 12 months (8% *v* 3%, P=0.01) (fig 2).

The examination of intervention effect within blocks (see fig 2) indicated that enhanced care patients reported more use of antidepressants over time than patients in usual care practices in five out of six blocks, and more counselling over time in four of six blocks.

Intervention effects on outcomes

Enhanced care significantly increased remission (intervention*time: t=2.27, P=0.02, df=654), emotional role functioning (intervention*time: t=3.13, P=0.002, df=651), and physical role functioning (intervention*time: t=2.80, P=0.005, df=652) over two years (fig 3). At 24 months, enhanced care had increased remission by 33 percentage points (95% confidence interval 7% to 46%) compared with usual care (74% remission *v* 41%), improved emotional functioning by 24 points (11 to 38) compared with usual care (73 points *v* 49), and improved physical functioning by 17 points (6 to 28) compared with usual care (61 points *v* 44). The 24 point improvement in emotional functioning represents a 67% (24/36) improvement over baseline functioning (36 points) that is attributable to the intervention. The 17 point improvement in physical functioning represents a 35% (17/49) improvement over baseline that is attributable to the intervention. No adverse events attributable to the intervention were reported by patients in enhanced care practices.

The examination of intervention effect within blocks (see fig 3) indicated that patients in enhanced care practices reported better outcomes over time than patients in usual care practices in five of the six blocks.

Discussion

After brief training, primary care practices encouraged patients starting a new treatment episode for major depression to participate in active treatment and monitored their response over 24 months. The ongoing intervention increased the average duration of antidepressant use to well within the recommendations for depressed patients not requiring maintenance therapy[38] and increased rates of mental health counselling during the first year. In terms of outcomes, the intervention improved both symptoms and role functioning so that, by 24 months, 74% of patients in enhanced care practices met criteria for remission, with emotional role functioning exceeding 90% of population norms and physical role functioning approaching 75% of population norms.[47]

The intervention provided combined care management and feedback over 24 months, rather than four months as previous interventions have done.[20] Interventions lasting up to six months have no observ-

able impact on depression remission after 18 months,[31–34] in contrast to the 33 percentage point increase in remission we observed with enhanced care at 24 months. Interventions lasting up to six months also have no observable impact on role functioning at 24 months,[34] in contrast to the 17-24 point improvement associated with enhanced care. We suspect that we achieved these effects because the intervention led to (*a*) more patients taking antidepressants over longer periods, (*b*) more patients learning skills in counselling to prevent relapse,[34 49 50] and (*c*) more patients talking with their primary care doctors about treatment adjustment.

Strengths and limitations of study

The internal validity of our results are strengthened by the use of a randomised block design to evaluate the intervention's ability to improve care with an intention to treat analysis that included all patients even if they did not receive ongoing intervention. As with many quality improvement efforts, our study design did not allow us to draw definitive conclusions about which components of the intervention were responsible for the differences observed. Use of a more sophisticated randomisation procedure could have increased confidence that the process was not open to any bias.

The generalisability of our findings is strengthened by three factors. Firstly, we tested the intervention on sociodemographically diverse patients in organisationally diverse practices. Although we were not able to follow every participant over two years, our sample loss was smaller than in most studies of this kind, and we tried to reduce the impact of sample loss by using attrition weighting and modelling techniques that allowed us to project trends when patients did not complete all follow up interviews. Secondly, the intervention was implemented by primary care practices, rather than by the research team or its employees, under normal practice conditions in which doctors and patients were free to select the treatments they preferred. Thirdly, analyses within blocks qualitatively showed that five of the six enhanced care practices consistently achieved better outcomes than their usual care counterparts. Our results relate to patients starting a new treatment episode. Interventions to improve primary care management of treatment resistant depression may need to test models that increase specialist management of drug treatments[11] and on site problem solving therapy.[12 17 29]

Conclusions

When interpreted in the context of previous studies,[31–34] our findings provide empirical support for the view that ongoing initiatives of modest but continuing cost are needed to achieve and sustain substantial improvements in the health of patients with depression. While brief interventions play an important role early in the dissemination of new models of care, their benefits are not sustained. Given the sizeable and sustained benefits of the intervention we tested, cost effectiveness analyses are needed to compare the value of the intervention with the value of interventions for other chronic diseases that primary care practices routinely provide. If these cost effectiveness analyses support the widespread adoption of quality improvement initiatives for depression treatment, health services should be encouraged to make small but continuing investment in their depressed populations to reduce the substantial disability they bear,[51] matching the duration of the intervention to the chronicity of the condition.

What is already known on this topic

Most trials of depression treatment incorporate principles of chronic disease management into the interventions tested in recognition of the chronicity of the condition

Research shows that brief implementation of these interventions has little or no impact on depressive symptoms and functioning a year after the intervention ends

What this study adds

Ongoing efforts to improve depression management yield ongoing benefits for patients starting a new treatment episode for depression

These results encourage health services to make a small but continuing investment in their depressed populations to reduce the substantial disability they bear, matching the duration of the intervention to the chronicity of the condition

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Contributors: KR and PN initiated and designed the study, analysed and interpreted data, drafted and revised the paper, and approved the final version of the paper. JLS contributed to the study design; collected, analysed, and interpreted data; drafted and revised the paper; and approved the final version of the paper. CEE and MD manipulated, analysed, and interpreted data; drafted and revised the paper; and approved the final version of the paper. KR is guarantor for the paper.

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