Improving long-term outcome of major depression in primary care

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Chapter 4

Short-term effects of enhanced treatment for depression in primary care: results from a randomized controlled trial

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Abstract

Background: Depression is a highly prevalent, often recurring or persistent disorder. The majority of patients are initially seen and treated in primary care. Effective treatments are available, but possibilities for providing adequate follow-up care are often limited in this setting. This study assesses the effectiveness of primary-care-based enhanced treatment modalities on short-term patient outcomes.

Methods: In a randomized controlled trial we evaluated a psycho-educational self-management intervention. We included 267 adult patients meeting criteria for a DSM-IV diagnosis of major depressive disorder, assessed by a structured psychiatric interview. Patients were randomly assigned to: the Depression Recurrence Prevention (DRP) program (*n* = 112); a combination of the DRP Program with psychiatric consultation (PC+DRP, *n* = 39); a combination with brief cognitive behavior therapy (CBT+DRP; *n* = 44); and care as usual (CAU, *n* = 72). Follow-up assessments were made at three months (response: 90%) and six months (85%).

Results: Patient acceptance of enhanced care was good. The mean duration of the index episode was 11 weeks (s.d. = 9.78) and similar in CAU and enhanced care. Recovery rate after six months was 67% overall; 17% of all participants remained depressed for the entire 6-month period.

Conclusion : Enhanced care did not result in better short-term outcomes. We found no evidence that the DRP program was more effective than CAU and no indications for added beneficial effects of either the psychiatric evaluation or the CBT treatment to the basic format of the DRP program. Observed depression treatment rates in CAU were high.

Introduction

Major depression is not only a serious and highly prevalent disorder, its typical course is recurrent or chronic (Ormel *et al*. 1990; Judd, 1997; Lin *et al.* 1999; Mueller *et al*. 1999; Simon, 2000; Solomon *et al.* 2000; van den Brink *et al*. 2001; Spijker *et al.* 2002). It has been estimated that more than 50% of clinically depressed patients will have another episode within ten years and that those who have experienced two episodes have an almost 90% chance of experiencing a third. Once the disorder becomes recurrent, rates of relapse may be as high as 40 % within four months after recovery (Keller,1994). In around 20% of cases depression becomes a chronic disorder (Spijker *et al.* 2000, 2002; van den Brink *et al.* 2001).

In the Netherlands, the majority of depressed individuals are initially seen by their primary care physician (PCP) and most of them continue to be treated in primary care (Spijker *et al*. 2001; Meijer *et al.* 2003; Linden *et al*. 2004). Characteristic of the Dutch healthcare system is the open and unlimited access to a PCP, the longitudinal continuity of the patient – PCP relationship and the gatekeeper role of the PCP, who controls access to specialist healthcare for somatic as well as psychiatric conditions. Effective treatments for depression, including pharmacological, psychotherapeutic and supportive approaches, are available in primary care (Marwijk *et al*. 1994, 2003; Os *et al*. 1999). However, given the often recurrent course of depression, the limited possibilities for providing adequate follow-up care and maintenance treatment in the primary care setting give reason for concern (Tiemens *et al*. 1999; Ludman *et al.* 2003).

In the present paper, we report results on short-term effectiveness of enhanced treatment in primary care on: duration of the index episode, time to remission, recovery rates and the percentages of patients free of any depressive symptoms after six months. Core elements of the Depression Recurrence Prevention (DRP) program (Tiemens et al. 1998) include patient education, three visits with a prevention specialist and provider-initiated follow-up care, consisting of monitoring of depressive symptoms and treatment adherence by telephone and mail. Effects of this enhanced care on the course of depression and healthcare use

(including the use of antidepressant medication) are compared with effects of the care usually provided for depression. Moreover, we evaluate whether the addition of a psychiatric consultation or brief cognitive behavior therapy to the basic format of the DRP program, has any surplus effects.

Method

The DRP program was tested in a pragmatic type randomized trial contrasting four conditions: (1) care as usual (CAU), (2) the DRP program, (3) the DRP program plus psychiatric consultation (PC+DRP), (4) the DRP program plus brief cognitive behavioral therapy (CBT+DRP).

Setting

The settings for this study were PCP practices in and around the city of Groningen, in the northern part of the Netherlands. The selection of PCPs was primarily guided by pragmatic principles and circumstances, such as availability, the location of the practice, the number of physicians sharing a practice and participation in earlier studies by the department. No formal criteria applied for the inclusion. Participating PCPs were invited to attend a 2-hour booster session about guidelines for the treatment of depression in general practice (Marwijk et al. 1994; Jenner et al. 1995; Schulberg et al. 1998). During these group meetings the risk of depression turning into a recurrent or chronic illness was emphasized and implications for management in primary care were discussed.

Patients

Main inclusion criterion was a current (i.e. present in the past two to twelve weeks) diagnosis of major depression according to DSM-IV criteria. We excluded patients younger than 17 and older than 70 years of age, patients suffering from a life-threatening medical condition, a psychotic disorder, dementia, and those with a primary addiction to alcohol or psychotropic drugs. In addition, women who were pregnant or nursing and patients already receiving

treatment for depression elsewhere (i.e. by a psychiatrist, psychologist or social worker) were excluded.

Inclusion of patients was by a three stage-procedure. First, participating PCPs were asked to refer any patient whom they considered to be depressed. Referral was based on the PCP's assessment on a brief symptom checklist on which the DSM-IV criteria for major depression were summarized; the checklist was provided by the project. In the second stage research assistants contacted the patients by telephone to establish study eligibility. For confirmation of the PCP depression diagnosis we used a brief screening instrument, containing the stem items for major depression and dysthymia from the Composite International Diagnostic Interview (CIDI; WHO, 1997). Patients fulfilling study entry criteria were provided with detailed information on the study, verbally and in writing, in order to obtain their consent. Patients agreeing to enter the third step in the inclusion procedure – thereby stating their willingness to be randomized- were interviewed face to face with the computerized life time version of the CIDI. With this interview the final diagnosis leading to inclusion or exclusion was reached. If the diagnosis was positive for depression the patient entered the randomization procedure.

Randomization procedure and treatment assignment

Randomization took place immediately at the baseline appointment. We used a randomized design stratified for use of antidepressants (AD: yes/no) at baseline. Within each stratum, patients were assigned to one of four conditions by means of a computer-generated random allocation list.

Once the diagnosis of major depression was confirmed by CIDI, the interviewer contacted a research assistant by telephone. This assistant, who had had no prior personal contact with the patient, opened the first sealed opaque envelope from the appropriate set, representing the AD+ or AD- stratum, and passed the information on treatment allocation on to the interviewer.

For patients assigned to one of the experimental conditions time and place of the first session with the appropriate specialist were scheduled. Patients assigned to the DRP program received the educational materials (book and videotape) that are an integral part of the program. PCPs were informed about study inclusion and the outcome of randomization within one week of the baseline assessment.

Measures

All patients were followed up prospectively for three years. Research assessments were made at baseline and every three months thereafter. Follow-up interviews were conducted by telephone by trained research assistants using a laptop computer. Each follow-up included a core set of questions concerning the presence of depressive symptoms and their course over time, the use of antidepressant medication, contacts with healthcare providers and competence in daily functioning. The interviews were combined with several self-report questionnaires every six months.

Depression status

At the baseline assessment, the full depression and anxiety sections of the lifetime version of the computerized CIDI (CIDI-auto, WHO, 1997; Dutch version by Smitten *et al*. 1998) were included. The CIDI is a structured diagnostic interview, with good reliability and validity (Wittchen, 1994, Andrews & Peters, 1998) and suitability for use in primary care populations (Űstűn & Sartorius, 1995). We added questions on the presence of (any residual) depressive symptoms in the past four weeks to obtain a full symptom profile. To systematically record onset and recency of depressive symptoms in the follow-up interviews, we developed a brief, structured and computerized interview measure based on the CIDI. We examined treatment effects on duration of the index episode, time to remission, recovery rates and the percentages of patients free of any depressive symptoms after six months. In accordance with the consensus-paper of Frank *et al*. (1991) and DSM-IV criteria, remission is defined as at least two consecutive weeks without depression and recovery as at least eight

consecutive weeks without depression.

The Beck Depression Inventory (BDI; Beck *et al*. 1961) is included in each follow-up to monitor depression severity. BDI-scores < 9 are generally seen to indicate normal, non-depressed mood states, whereas BDI-scores ≥ 15 indicate a fully symptomatic depression (Beck *et al.* 1988; Frank *et al.* 1991). The BDI has good psychometric characteristics (e.g. Hammen, 1997) and is also sensitive to change over time (Richter *et al*. 1998*).*

Use of antidepressants, contacts with PCP and other care utilization

Number of visits with the PCP and use of antidepressant (AD) medication were recorded at each follow-up. In addition, we asked patients whether they had received help from other (mental) health providers, including ambulatory mental health care and freely established psychologists and psychiatrists in private practices.

Statistical analyses

Sample sizes were determined by power analysis. We originally hypothesized the following gradient of outcome success, expressed in percentages of patients being recovered at six months: in CAU 60%, in DRP 70%, in PC+DRP 80% and in CBT+DRP 90%. With 62 patients in CAU, 96 in DRP, 32 in PC+DRP and 36 in CBT+DRP these outcomes would yield a Cramer's ϕ' of 0.223, corresponding with a satisfactory power of 81 %.

To analyze differences between groups, we used chi-square tests for dichotomous variables and t-tests or non-parametric tests (Mann-Whitney, Kruskal-Wallis) for continuous variables, depending on their distribution. Change over time in continuous outcome variables between the treatment groups was tested by means of repeated measures ANOVAs. Where appropriate, full comparisons were supplemented with pair wise comparisons. Survival analysis, including the log rank test, was applied in comparing the treatment groups as to the time to recovery.

All analyses were based on intention to treat. In addition, completer analyses were applied where judged to be informative. We used SPSS version 12 (SPSS Inc., Chicago, USA).

Interventions

Depression Recurrence Prevention program

The DRP program is a structured psycho-educational intervention, based on an ongoing relationship between the patient, a prevention specialist and the PCP. The primary goal is to reduce depression recurrence. The intervention is aimed at increasing patients' self-efficacy with regard to coping with depressive symptoms, extending the potential of pro-active measures and stress-management strategies and skills to identify relapse or recurrence early on. The focus is on improving patients' resilience and self-management skills (Smit et al. 2005).

The program consists of three individual face-to-face sessions with a trained prevention specialist, followed by four telephone monitoring contacts per year for a 3-year period. Prior to the first session, patients receive a book and corresponding videotape on depression, treatment options, relapse prevention and self-management strategies. At the last face-to-face session, depression specialist and patient prepare a patient-tailored depression prevention plan, with the following topics: regular self-registration of early warning signs; stress reduction strategies; an 'emergency plan'; and a medication plan, for patients using antidepressants. A copy of this plan is sent to the PCP. Main goals of the standardised three-monthly follow-up contacts are to systematically monitor depressive symptoms, review patient progress and to provide feedback and support. Motivational interviewing (Miller & Rollnick 2002) is used to enhance confidence in the patient's ability to succeed, to support self-efficacy and strengthen commitment to the program over time.

One psychiatric nurse and two psychologists, all females, were trained by two experts from the Seattle project to deliver the enhanced treatment program. Adherence to the DRP

protocol was monitored in regular supervision sessions with a psychiatrist who had also attended the training. The prevention specialists used standardized forms for each patient contact. During the first phase, they provided the PCP with written feedback of each session, and in the follow-up phase they kept a record of all patient contacts.

The intervention was developed by Katon and co-workers at the Center for Health Studies of the University of Washington in Seattle, USA (Katon et al.1996; Ludman et al. 2000) and adapted for use in the Netherlands by Tiemens and colleagues (Tiemens et al.1998). For a more detailed description we refer to Smit et al (2005).

Psychiatric Consultation plus DRP program

Patients in the PC+DRP group were offered one 1-hour visit with one of two available psychiatrists, prior to the DRP-Program. The PCP provided the psychiatrist with information about the patients' health and treatment status. Afterwards, the psychiatrist reported his diagnostic findings and treatment advice to the PCP. A copy of this written report was also made available to the prevention specialist. The main purpose of the psychiatric consultation was to make more specific psychiatric expertise on diagnosis and pharmacological treatment of depression available for use in primary care practice.

Cognitive behavioral therapy plus DRP program

The CBT+DRP group was offered 10 – 12 individual weekly one-hour sessions of CBT treatment, tailored to primary care by Boelens (1997). The DRP-Program started after the final CBT session. The CBT-therapist informed the prevention specialist about the main themes that the CBT had addressed and the progress achieved.

Three qualified CBT therapists were employed. To reinforce concepts and CBT techniques and to monitor their adherence to the protocol, regular supervision sessions were held. The acting supervisor was the regional CBT expert who developed the treatment protocol.

The main purpose of including CBT was that this has been found to be an effective treatment for depression and there are indications that CBT may reduce relapse rates (Fava *et al*. 1998; Paykel *et al.* 1999; Scott *et al.* 2000). However, studies on CBT in primary care patients are scarce and results are not consistent (see: Scott *et al.* 1997; Ward *et al.* 2000).

Care as usual

Patients assigned to the usual care group were referred back to their own PCP and received the care that this PCP deemed appropriate. In most cases, this included a combination of antidepressant medication and counseling during regular visits (Os *et al*.1999). As in current practice PCPs were free to refer patients to any service normally available, such as social workers, private practice psychiatrists or psychologists, or specialized mental health agencies.

Results

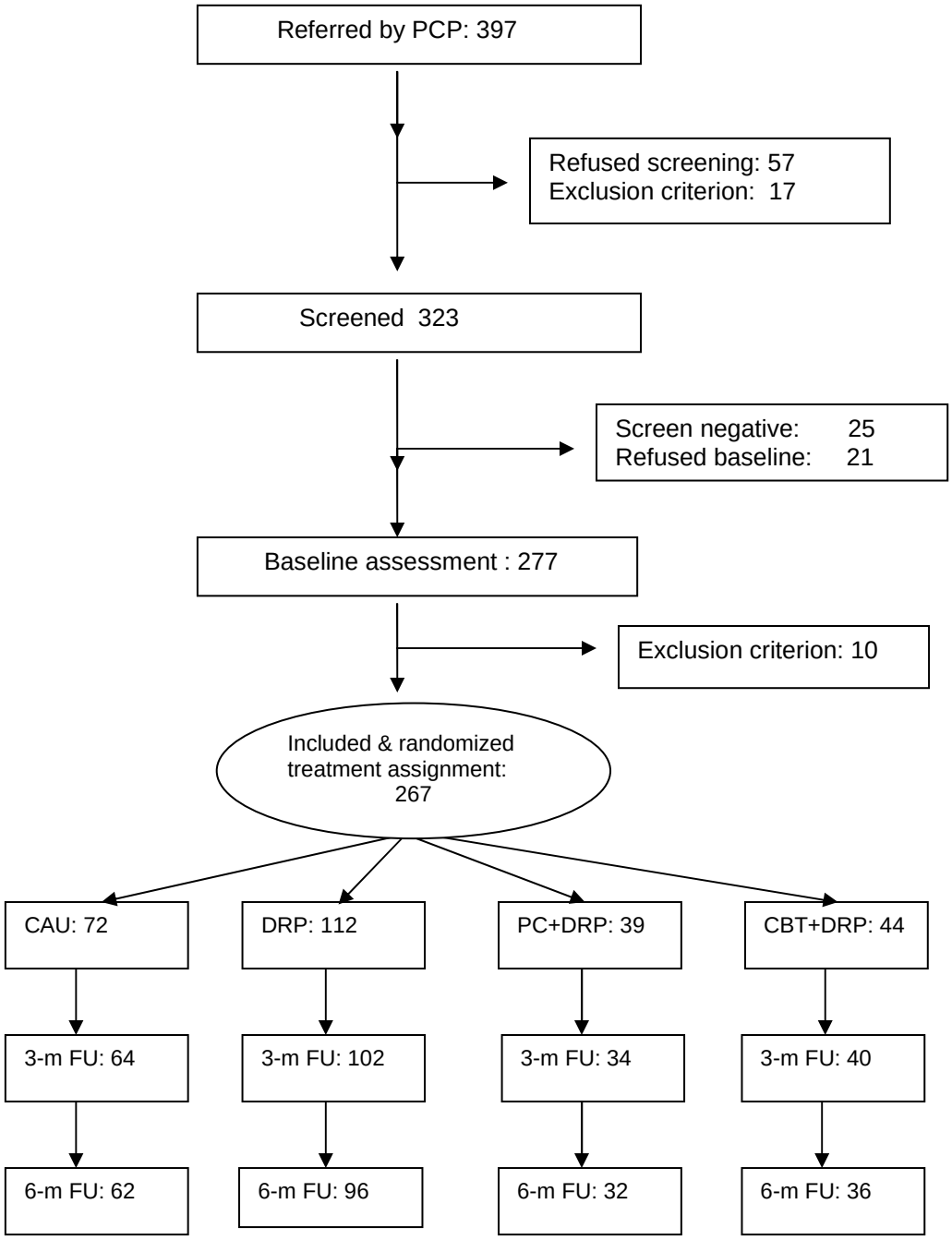
Primary care physicians

A total of 55 PCPs in the northern part of the Netherlands agreed to participate. The mean number of patient referrals per PCP was 7.2, but there were considerable differences between PCPs in this respect (range: 1 – 43); 13 PCPs (24%) referred 10 or more patients. The mean number of included patients per PCP was 5.5 (range: 1 - 35); of eight PCPs, 10 or more patients were included. The final study group consists of 267 patients from 49 PCPs.

Patients

Of 397 patients who were identified as depressed by their PCP and referred to the study, 323 (81.4 %) agreed to the screening procedure. The majority (*n* = 277; 85.8%) was eligible and willing to take part in the study (see Fig.1).

Figure 1: Flowchart



On the baseline assessment 10 patients were excluded because they did not fulfill study entry criteria. Thus, a total of 267 patients, comprising 67% of all initially referred patients and 83% of those who could be contacted and screened, met the inclusion criteria and were randomly assigned to one of the four treatment conditions. 72 patients (27%) were assigned

to care as usual (CAU) and 195 patients were assigned to the enhanced care program: 112 patients (57 %) were offered the DRP program only, 39 patients (20%) were assigned to PC plus DRP and another 44 patients (23%) were assigned to the brief CBT followed by DRP.

The percentages of respondents at the follow-up were 90% after 3 months and 85% after 6 months. These rates were similar between treatment groups.

Baseline characteristics

In Table 1, socio-demographic and clinical characteristics of the baseline sample are summarized. Randomization proved to be successful; there were no significant differences on any of these characteristics between patients in the four treatment groups.

Table 1: Baseline demographic and clinical characteristics

	CAU n = 72	***DRP n = 112***	***PC + DRP n = 39***	***CBT + DRP n = 44***
% female	65	65	69	54
Age *mean (sd)*	44.2 (11.3)	42.5 (10.6)	41 (13.0)	42.8 (11.6)
Marital status: %				
- Married / Cohabiting	68	69	67	48
- Single	13	18	18	34
- Divorced	15	10	15	14
- Widowed	4	4	-	5
Primary role: %				
- Employed	56	65	59	57
- Homemaker	25	17	21	14
- Student	4	5	8	7
- Unemployed	7	6	5	14
- Disabled	6	6	3	9
- Retired /other	3	1	5	-

	CAU n = 72	*DRP n = 112*	*PC + DRP n = 39*	*CBT + DRP n = 44*
Educational attainment: %				
- Low	49	42	46	39
- Medium	29	41	33	39
- High	22	17	21	23
Severity rating current MDD:				
- **mild**	28	32	36	23
- **moderate**	24	38	28	32
- **severe**	49	30	36	39
Recurrent DSM-IV MD %	74	64	64	68
If recurrent: % > 3 episodes	57	51	56	60
Age at first onset *Mean,sd*	32.4 (14.3)	30.9 (11.8)	30.6 (15.4)	31.1 (13.2)
Suicide attempt, ever %	13	8	10	12
BDI, *mean,sd*	18.9 (9.49)	20.6 (9.32)	20.3 (9.84)	20.3 (9.25)
% Comorbid, current * :				
- Dysthymic disorder	3	12	10	8
- Panic disorder	13	13	15	11
- Agoraphobia	8	6	13	9
- Social phobia	14	17	15	14

* Current : present in past month.
No statistically significant differences ($p < 0.05$).

Patient acceptance of treatment assignment

Overall, 92 % of the intervention patients attended all three individual face-to-face sessions with a depression prevention specialist; 94 % attended at least one. Participation in this phase was highest among patients randomized to the DRP program only (96 %) and in those assigned to PC+DRP (97 %), but lower in the group where DRP followed after CBT (75 %; $x^2 = 23.97$; df = 2; $p < 0.0001$).

In the 6 months after the last session, prevention specialists remained in contact with the vast majority of the patients, with 98 % returning their mail and responding to both of the telephone calls.

With regard to the additional treatments by mental health specialists, all 39 patients randomized to PC+DRP agreed to the visit with the psychiatrist. In comparison, compliance with CBT was lower: 33 of the 44 patients assigned to CBT completed this treatment (75 %), while three patients refused and eight dropped out prematurely (after a mean of four sessions).

Depression outcome

As shown in Table 2, we found no evidence that enhanced care was more effective than CAU in the short term. After 27 weeks the recovery rate was 66% and similar among CAU and enhanced care patients. A total of 17% of study participants remained depressed during this entire period.

Table 2: Clinical outcomes at 27 weeks

	CAU	*DRP*	*PC+DRP*	*CBT+DRP*	**TOTAL**
% recovered	68	61	79	70	67
duration index episode, in weeks *mean (sd)*	10.7 (9.9)	11.8 (10.0)	9.3 (8.2)	11.2 (10.6)	11.0 (9.8)
% patients remitted at least once	25	28	15	18	21
% depressed full 27 weeks	17	20	6	15	17
% with neither remission or recovery *	20	23	12	20	20

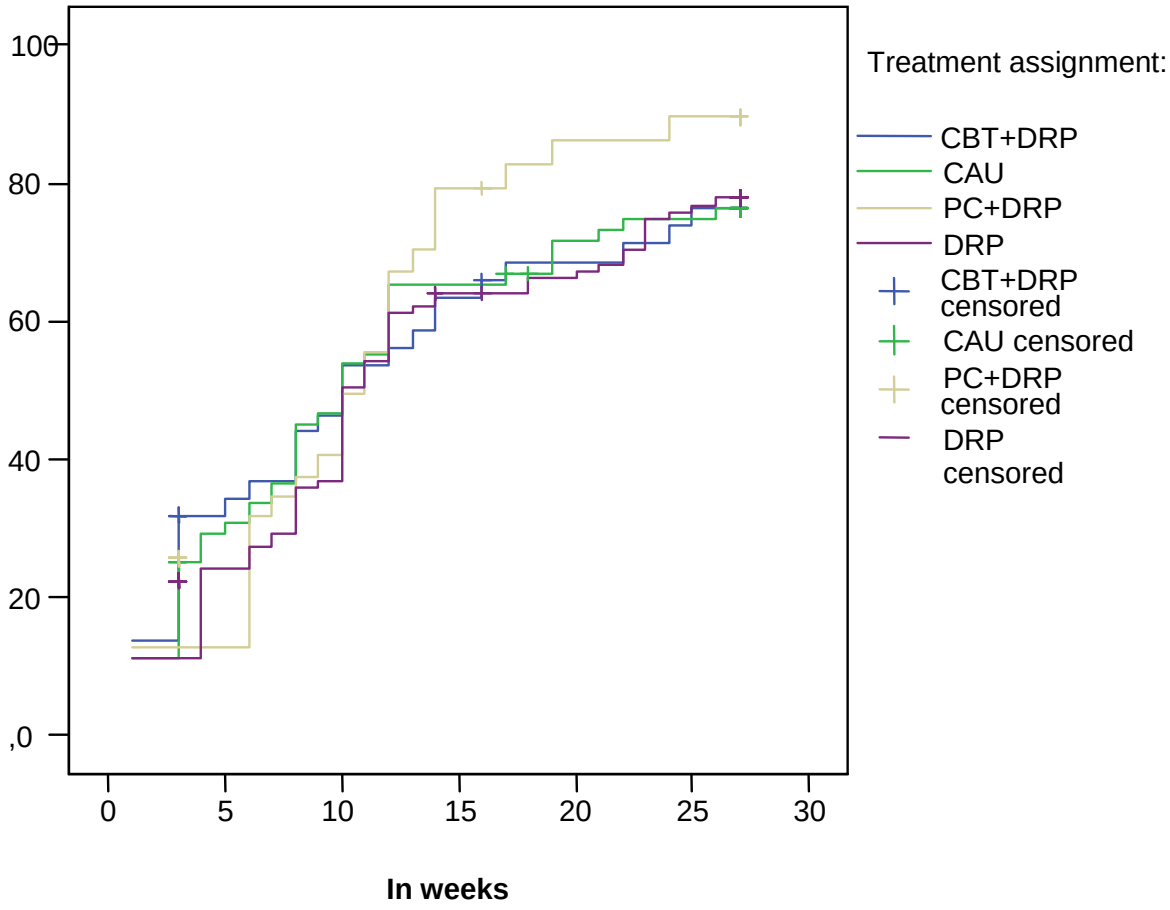
* Recovery: no diagnosis for at least 8 weeks; Remission: no diagnosis, lasting 2 – 7 weeks.
No statistically significant differences ($p < 0.05$). [1]

[1] We also performed additional pairwise comparisons (no statistically significant differences; results available on request).

Time to recovery

The mean duration of the index depressive episode was 11 weeks (s.d. = 9.78) and similar in CAU and enhanced care patients (see Fig. 2).

Figure 2: Time to recovery (Kaplan-Meier curve)



Numbers censored: CAU: 19; DRP: 31; PC+DRP: 8; CBT+DRP: 12.
Log rank: 1.74; df = 3; p = 0.63.

Median survival time: CAU: 10 ; DRP: 10 ; CBT+DRP: 11 ; PC+DRP:10

Depression severity (BDI)

BDI scores improved the most in the first 3 months (on average 6.81 points), and the percentage of patients scoring above the threshold (BDI ≥ 15) fell from 69% to 38% overall at the 6-month follow-up. We found no statistically significant differences in the comparisons between treatment groups.

Treatment: antidepressant medication and additional healthcare use

At the 3-month follow-up, antidepressant use was significantly lower in patients assigned to CBT+DRP, compared with CAU and both other DRP groups (Table 3). At the 6-month follow-up, AD use in CBT patients remained significantly lower compared with that of PC+DRP patients. The majority of patients remained in touch with their PCP during the first 6 months, but this proportion was lowest in the CBT+ DRP group. Additional mental healthcare use was different for CAU and enhanced care patients, with CAU patients receiving more specialist mental health care by freely established psychologists, ambulatory mental health care or social workers. In the period between the 3- and 6-month follow-up, when most enhanced care patients finished the first phase of the DRP program, the number of DRP patients receiving other mental health care also rose.

Table 3: Treatment : Antidepressant use and healthcare utilization

	CAU	*DRP*	*PC + DRP*	*CBT + DRP*
AD-use at baseline % *(n = 267)*	76	74	72	73
AD-use at 3 m FU % [1] *(n = 240)*	72	70	74	50
AD-use at 6 m FU % [2] *(n = 226)*	60	59	69	42
Between baseline and 3 m FU :				
Visited PCP at least once [3]	94	85	79	58
number of visits (mean)	2.9	3.3	3.8	3.2
additional mental health care [4]	39	19	24	10
Between 3 and 6 month FU:				
Visited PCP at least once [5]	66	78	69	61
Number of visits (sd)	2.4	2.2	2.5	1.8
Additional mental health care [6]	34	31	19	11

[1] CBT+DRP versus CAU: $x^2 = 5.08$, df = 1, p = 0.02; CBT+DRP versus DRP: $x^2 = 4.80$, df = 1, p = 0.03; CBT+DRP versus PC+DRP: $x^2 = 4.27$, df = 1, p = 0.04
[2] CBT+ DRP versus PC+DRP: $x^2 = 5.01$, df = 1, p = 0.03
[3] $x^2 = 23.24$, df = 3, p< 0.001
[4] $x^2 = 14.09$, df = 3; p = 0.003.
[5] CBT+DRP vs DRP: $x^2=3.89$; df=1; p = 0.05
[6] $x^2= 8.08$; df=3 ; p = 0.04 ; CAU versus CBT+DRP: $x^2 = 6.21$; df = 1; p = 0.01

Discussion

The DRP program aims at integrating treatment for the acute episode and the prevention of depression relapse and recurrences. Patients included in this trial suffered from recurrent depression. The short term outcome data presented in this paper reflect initial response to treatment and show hardly any contrasts between the CAU and enhanced care patients. Several explanations should be considered for this lack of difference.

Foremost of course, the DRP program and its combinations with either a psychiatric consultation or brief CBT may not have been capable or powerful enough to add to the effects already achieved by usual care. We saw high depression treatment rates in CAU,

especially in the interval between study inclusion and the 3-month follow-up, which may mean that most patients already received optimal and guideline-concordant treatment from their PCP.

At baseline, AD use was almost 75% overall. At follow-up, medication adherence rates in the CAU, DRP and PC+DRP patients were higher than anticipated. Although poor compliance with drug treatment is frequently reported as a problem (Pampallona *et al*. 2002), especially in primary care (Lawrenson *et al.* 2000), this did not seem to be the case in the present study. Thus, with the exception of CBT+DRP (there was no specific focus on medication compliance in the CBT protocol) , rates of both initial AD use as well as adherence are higher than found in previous primary care studies. This may be explained in several ways. First, relevance of medication adherence was a subject dealt with explicitly in the DRP program. Second, because of the experience of multiple episodes, patients may have been more willing to accept AD continuation treatment for their present episode. Third, AD treatment seems to have become more routine practice in Dutch primary care settings. Data from national studies show that PCPs are responsible for the majority (78%) of prescriptions for antidepressants in The Netherlands and that the number of these prescriptions has increased substantially year by year (Marwijk *et al*. 2001; CVZ 2003). Laurant and colleagues (2004) report that in 68% of PCP-diagnosed depressive episodes an AD was prescribed. Furthermore, the majority of patients in our study visited their PCP regularly. Data on PCP prescribing behavior demonstrates that the increase in AD prescriptions occurred mainly during repeat consultations (Marwijk *et al.* 2001; Os *et al.* 2002). In addition, recent findings confirm that AD-adherence among primary care patients seems to have become less problematic. Brook and coworkers (2005) studied the effects of a pharmacy-based program on improving adherence to AD treatment in primary care and found 6-month adherence rates of 73 % in CAU (and 76% in the experimental group).

The referral rates to specialized mental health care also deserve attention. The fact that during the first six months more than one third of CAU patients received some form of specialist care may have been an side-effect of the study, in two ways: (1) a number of PCPs

may have ‘used’ the selection procedure primarily for diagnostic purposes, i.e. to get their suspicions confirmed; once this happened they may have seen referral of the patient as the most appropriate reaction; (2) patients assigned to usual care may have been disappointed by this randomized assignment and sought treatment elsewhere, whether or not by formal referral. However, these figures may also reflect the growing tendency in The Netherlands for PCPs to refer patients with a psychological diagnosis to more specialized mental health agencies, including private practice psychologists (Verhaak *et al*. 2000; Meijer *et al*. 2003).

After finishing the first phase of the DRP program, the number of enhanced care patients receiving specialized mental health care also rose. This could have been due to the same shift described above, with more patients being referred. Patient preferences may also be of importance, since available studies show that many patients prefer psychotherapy in the treatment of depressive disorders (Schaik *et al*. 2004). Furthermore, given that most patients had already experienced more episodes, lack of confidence in their own abilities to successfully overcome depression and prevent future episodes may also explain this helpseeking behavior. We found indications for a persistent lack of self-confidence in dealing with depression in 3-month follow-up scores on a self-efficacy questionnaire (DSES: Bush *et al.* 2001), where scores remained low overall and there was no evidence that enhanced care patients benefited more from their treatment than patients receiving CAU (Smit *et al.* 2005).

Strengths and limitations

Our study has several strengths. Since the aim is to find information on effectiveness of the intervention, patient inclusion criteria were not very stringent. This permitted the majority (83%) of patients who where screened after being referred by their PCP to enter the trial. Also, more than 50 PCPs were willing to participate. Several researchers (Fairhurst & Dowrick 1996; Hunt *et al*. 2001) have found this kind of participation hard to achieve. Randomization was successful, with similar demographic and clinical characteristics in all four arms of the study. Acceptance of the interventions was high. CBT and PC are common referral options for depression treatment, which increases the relevance of our findings for

primary care practice. Our method of establishing depression status at each follow-up enabled us to systematically record current symptoms week by week, follow the course of existing symptoms and trace the onset of 'new' ones. Last but certainly not least, follow-up response rates were good.

By definition, conducting a pragmatic trial implies that several factors are beyond the control of the researchers. Participating PCPs were free to manage the CAU and enhanced care patients as they saw fit. We did not influence or determine their treatment decisions. Referral rates for CAU patients seemed high, although we now find that they may also reflect current primary care practice. Selection of the PCPs was not random, and participating PCPs may have been more interested in the subject of depression treatment and relapse prevention than the average PCP. Patient recruitment was slower than anticipated and we needed more time than originally planned to enroll enough patients. During this recruitment period, lasting 3,5 years in total, the observed changes in referral behavior and the prescription of antidepressants may have become more routine practice for depression management by PCPs. Another limitation is that, while the study had sufficient power to test the gradient of outcome-success hypothesis, pairwise comparisons of the PC and CBT arms with CAU or DRP are probably underpowered. There appeared to be a trend towards more positive outcomes in the PC+ DRP group, but on the other hand, observed differences were small and it can be questioned whether they are clinically relevant. Finally, it was not possible to blind interviewers from treatment status of the participants.

Conclusion

Although well-received and appreciated by patients and PCPs, we found no evidence that the DRP program was more effective than CAU in the short term. Three and six months into the trial period, we found similar depression rates in enhanced care and CAU patients, but it should be noted that depression treatment rates in CAU were high. In addition, we found hardly any indications for added beneficial effects of either the psychiatric evaluation or the

CBT treatment to the basic format of the DRP-Program. Thus, enhanced care did not result in better depression outcomes on the short term. However, given that the follow-up care provided in the context of the DRP program continues for three years, it might be that benefits of this enhanced care over CAU will only become clear after a more prolonged period.