Improving long-term outcome of major depression in primary care

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Chapter 2

The course of depression in primary care:

design and implementation

of a randomized controlled trial

on the prevention of relapse and recurrence

Introduction

Major depression is a common and disabling mental disorder, with a life time prevalence of up to 15% for men and around 24% for women in the general population (Bijl *et al.* 1998). Increasingly, it has become clear that the concept of depression as a transient, acute and self-limiting disorder is inaccurate. Longitudinal research has shown that major depression is often a recurrent or persistent disorder from which many patients do not fully recover (Keller *et al.* 1992; Keller 1994; Ormel *et al.* 1993; Paykel 1994; Judd 1997; Mueller *et al.* 1999; Simon 2000; Spijker *et al.* 2000, 2002; Solomon *et al.* 2000) .

In the Netherlands, primary care physicians (PCPs) are the most important health care contact for nearly all patients with mental health or psychosocial problems. For many patients with a depressive disorder, primary care is the defacto mental health treatment setting (Regier *et al.* 1993; Tiemens *et al.* 1995; Spijker *et al.* 2001; Meijer *et al.* 2003; Linden *et al.* 2004). In the past, PCPs have been found to under recognize and under treat a substantial number of depressive patients (Rost *et al.* 1998; Tiemens *et al.* 1996; Os *et al.* 1999), and there have been many efforts to improve detection and treatment of depression in this setting. The most common strategies were educational and included the dissemination of specific depression management guidelines, which recommend a combination of antidepressant medication and brief, supportive counseling by the PCP (Marwijk *et al.* 1994, 2003; *Os et al.* 1999).

The main goal of our study was to explore the potential of a long-term depression management strategy aimed at the prevention of depression relapse and persistence, and the possibilities of incorporating such an approach in the primary care setting. In this chapter we describe the design of the trial, give an overview of the contents and format of the experimental interventions and outline the procedures and methods used. The main intervention consisted of a psycho-educational Depression Recurrence Prevention (DRP-) Program, which included innovative components such as provider-initiated follow-up care, in which depression self-management and patients' adherence to a treatment - and depression

prevention plan were monitored and reinforced on a regular basis. Main objective of the trial was to compare the treatment effects of this DRP-Program on depression severity, course and outcome over a three year period with effects of the care that is usually provided for depression in primary care. Furthermore, to evaluate whether there were additional effects of psychiatric consultation (PC) or brief Cognitive Behavioral Therapy (CBT) to the basic format of the DRP-Program. The focus of the study was on determining the longer-term benefits of the different treatment strategies. The central question to be answered was: which treatment protects best against relapse, recurrence and persistence of major depression ?

Methods

Design

The study was designed as an effectiveness trial, meant to measure the benefit the treatments produced in routine clinical practice (Kluiter & Wiersma 1996 ; Roland & Torgerson 1998). Randomization took place at the patient level and was stratified for use of antidepressant medication (AD) at the baseline assessment. We used a computer-generated random allocation list for the treatment assignment per stratum (AD+ , AD -) .

Patients who met inclusion criteria were assigned to one of four treatment conditions, including treatment as usual (control group). The three experimental interventions are: the Depression Recurrence Prevention (DRP-) Program; psychiatric consultation plus the DRP-Program; brief cognitive behavioral therapy, followed by the DRP-Program.

All included patients were followed up longitudinally for a total of three years, with repeated assessments conducted by telephone interview every three months. In addition, patients were asked to fill out and return a comprehensive set of questionnaires every six months.

Primary care setting

The primary care physician (PCP) has a crucial role in the Dutch health care system. He / she is the gatekeeper, controlling access to for specialist healthcare for somatic as well as

psychiatric conditions. Characteristic of the healthcare system in the Netherlands is the open and unlimited access to a PCP, the person-centered orientation and the longitudinal continuity of the relationship between patient and PCP.

The majority of patients suffering from depressive disorders receive treatment primarily from their primary care physician. This is a consistent finding in community surveys conducted in the USA (ECA: Regier *et al.* 1993) , the UK (Bebbington *et al.* 2000) and the Netherlands (Nemesis: Spijker *et al.* 2001; Linden *et al.* 2004). Recognition and treatment of depression have been found to be associated with the severity of the disorder (Tiemens *et al* 1996; Simon & Von Korff 1995) and its consequences in terms of for example impaired functioning (Ormel *et al.* 1994; Buist-Bouwman *et al.* 2006) .

Primary care physicians

The settings for this study were mainly PCP-practices in and around the city of Groningen in the northern part of the Netherlands. Selection of primary care physicians was primarily guided by pragmatic principles and circumstances, such as availability, the location of the practice and the number of physicians sharing a practice. PCP's with whom we were already familiar because of their participation in previous primary care studies undertaken by the department were also asked to participate. We applied no formal criteria for the PCP selection.

Initial contact with the PCP's was made by the research-PCP who was part of the research group. Interested PCP's received written information about aims and design of the trial and were visited in their practices for further discussion about study procedures and implications of participation. They were also invited to attend a 2-hour booster session in which the Clinical Guidelines for treatment of depression in general practice (Marwijk *et al.* 1994, 2003) and the Depression Module of the INSTEL postgraduate training program for primary care physicians (Jenner *et al.* 1995) were summarized. Both guidelines recommend the prescription of antidepressants as the first choice of treatment, combined with psycho-education and supportive counseling to improve medication adherence. During these group

meetings the risk of depression turning into a recurrent or chronic disorder was emphasized and implications for management were discussed.

Patients

The primary inclusion criterion for the study was the presence of a current (i.e. present in the past 2 - 12 weeks) DSM-IV diagnosis of major depressive episode, according to the primary care physician and confirmed by a structured psychiatric interview.

Patients could not be referred by their primary care physician if they were older than 70, suffered from a life-threatening medical condition, a psychotic disorder, dementia, alcohol- or drug abuse. In addition, women who were pregnant or nursing, and patients already receiving mental health treatment for depression elsewhere (by a psychiatrist, psychologist or social worker) were excluded.

Recruitment and selection procedure

Inclusion of patients was by a three stage procedure. Since we aimed to include depressed patients typically seen and treated in primary care, an enrollment procedure was chosen in which PCPs would make the initial decision to refer a patient to the study. For this purpose, participating PCPs were provided with a brief symptom checklist on which the DSM-IV criteria for major depression (i.e. : at least 5 symptoms, including either depressed mood and / or loss of interest ; symptoms present for a minimum of two weeks and for 50 % of the time or more) were summarized. They were asked to refer any patient whom they considered to be depressed, fitted the selection profile described and who consented to being contacted by the researchers to determine study eligibility.

In the next step, consenting patients were contacted by telephone for a brief screening interview with a research-assistant. The main aims were confirmation of the depression diagnosis made by the PCP and obtaining consent for further study participation. We used a brief screening instrument , containing the stem items for major depression and dysthymia from the full Composite International Diagnostic Interview (CIDI; WHO 1997) to

assess whether, in the past 12 months, the patient experienced a 2-week period of daily sadness or loss of interest, co-occurring with the presence of other depressive symptoms. Also, whether the patient had had a two year period of daily depressed mood, extending in the past 12 months. To be invited for the next step, patients had to meet criteria for a current depressive disorder (last episode in the past 12 weeks); patients with comorbid dysthymia were also selected. Screen-positive patients were given more detailed information on the study, the interventions and the randomized treatment assignment procedure and were asked to sign the "Informed Consent form".

The third and last step in the inclusion procedure consisted of a face to face interview by a trained interviewer, in which eligibility was determined with the computerized lifetime version of the Composite International Diagnostic Interview (CIDI-auto 2.1; Smitten *et al.* 1998). If this interview resulted in a diagnosis of depression, the patients entered the randomization procedure, which took place immediately at this baseline assessment. The CIDI interviews, which mostly took place in the patients' homes , were conducted by trained lay interviewers; some of them were already familiar with the 'paper-and-pencil' version of the CIDI.

Randomization and treatment assignment

After eligibility was decided, the interviewer contacted a research assistant who had had no personal contact with the patient by telephone. This assistant had two sets of consecutively numbered and sealed opaque envelopes, one set for each stratum (based on current use of antidepressant medication). Within each stratum, patients were assigned to one of four conditions by means of a computer-generated random allocation list. After being informed about the correct stratum the research-assistant opened the next envelope from the appropriate set. Treatment allocation was then passed on to the interviewer, who informed the patient.

We considered minimal delay between treatment assignment and first contact with the assigned caregiver to be relevant. Time and place of the first meeting with the

appropriate specialist were scheduled immediately by the interviewer for patients randomized to one of the experimental interventions. If possible, all face to face sessions were to take place in the primary care practice where the patient was registered. Patients assigned to the DRP-Program also received the educational materials (book and videotape) that are an integral part of the DRP-Program. Patients randomized to treatment as usual were referred back to their PCP and were encouraged to schedule an appointment to discuss diagnosis and further treatment.

Within one week of the baseline assessment, referring physicians were notified about study inclusion and treatment assignment of their patients.

Follow-up assessments

Included patients were followed up for a total of three years, with repeated assessments conducted by telephone every three months. All FU-interviews included detailed assessments of depressive symptoms and questions on socio-demographic circumstances, employment and disability issues, treatment adherence, health care use (medication, physical treatment, psychological treatment, other service utilization) and satisfaction with the care received for depression. In addition, patients received a set of self-report questionnaires at each 6-m FU; these addressed topics such as life events and health related quality of life.

Interventions

Choice of treatments

At the time of the designing of the study in the mid-nineties, (long-term) use of antidepressant medication and brief, structured psychotherapies like cognitive behavioral or interpersonal therapy had emerged as feasible and potentially effective strategies to prevent the unfavorable course often seen in depressive disorders. However, most research evaluating these treatments had been conducted in specialty settings was limited to short-term-outcomes and the prevention of relapse and recurrences was typically not evaluated (Ormel & Tiemens 1995; Brown & Schulberg 1995). Around the same time, educational

approaches aimed at improving self-efficacy in symptom management and treatment adherence, were used successfully in programs for several chronic somatic illnesses (Lorig 1993; Wagner *et al.* 1996) . Whether the same sort of approach would be applicable and effective in the management of psychiatric disorders in a primary care setting was unknown.

The Depression Recurrence Prevention Program

The Depression Recurrence Prevention (DRP-) Program is best characterized as a structured psycho-educational self-management intervention, with a continuation phase based on an ongoing relationship between the patient, a prevention specialist and the PCP. The primary goal of the DRP is to reduce depression relapse and recurrence, by increasing the patients' self-efficacy, enhancing and maintaining positive mood states and extending the patients' potential of pro-active steps in response to early warning signs of depression relapse or recurrence. The intervention is aimed at reducing the chances of unfavorable course and outcome of major depression by raising awareness of prodromal symptoms and by teaching patients a diversity of skills and coping strategies to obtain greater control over depressive symptoms.

Self-management behavior is a priority in the DRP Program (Ludman *et al.* 2000). To motivate and encourage patients, the Motivational Interviewing strategy (Miller & Rollnick 1991; 2002) was used. This is described as '*a client-centered, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence'* (Miller & Rollnick 2002, p.25). The prevention specialists were trained in the use of this empathic, flexible and reflective counseling style, and learned to tailor this to individual patients. The motivational interviewing strategy was used throughout the DRP-Program to enhance confidence in one's own abilities to succeed , to support self-efficacy and to strengthen commitment to the Prevention Plan over time.

The basic format and contents of the intervention are derived from the Relapse Prevention Program developed by Katon et al (1996) from the University of Washington,

Seattle. This program was originally designed to address primary care maintenance treatment for recovered patients at high risk for relapse (Ludman *et al.* 2000).

In order to ensure suitability for a Dutch depressed primary care population, some modifications in contents and format of the original Program were made. The main change was in the focus of the intervention, which is more on activation and self management behavior (changes in lifestyle) and less on (long-term) use of antidepressant medication in our DRP-Program; at the start of the study , the expectation was that acceptability of pharmacological treatment would be lower in Dutch patients compared to their counterparts in the United States.

Format

The DRP-Program consisted of three individual face-to-face sessions with a trained prevention specialist, followed by four telephone contacts per year for a three-year period (figure 1). Central elements of all contacts were mood registration, behavioral activation and, if applicable, monitoring of anti-depressant medication use. Stressors and early precursors of recurrence were identified, as well as ways to cope with them.

First phase: face to face sessions with prevention specialist

Prior to the first session, patients had received a book and corresponding videotape on depression, various treatment options, relapse prevention and self-management strategies, and a 2-page instruction booklet to prepare for the first session. In this session the prevention specialist gave an overview of the DRP-Program, her own role and the collaboration with the patients' PCP. She collected information on current episode, past episodes, treatment history, personal situation and (current and past) use of antidepressant medication by the patient . The potential benefits of self-monitoring of depressive symptoms and various stress reduction strategies were then introduced and discussed. In the second session preparations were made for the personal Recurrence Prevention Plan, with special attention to self care and what could be learned from earlier episodes experienced by the

patient. At the third and final session, depression specialist and patient drew up the final Prevention Plan, with the following topics: personal warning signs; stress reduction strategies; an “Emergency-plan”, with the steps that the patient is planning to take once s/he fears a relapse or recurrence; and a medication plan for patients currently using antidepressants. Socializing and the scheduling of pleasant activities were encouraged. It was stressed that regularly planning sports or other leisure activities and undertaking these jointly with a friend or family member, could help in unwinding and at the same time maintaining a social network.

Follow-up phase: structured telephone contacts

Two weeks before the first scheduled follow-up telephone contact , patients received a “Follow-up Patient Monitoring Form’, which included a 2-page copy of their original Prevention Plan, a graph representing their score on the Beck Depression Inventory (BDI; Beck *et al.* 1961, 1988) at the last visit and the 13-item BDI.

The Monitoring Form included:

- Current Rating of Mood
- Checklist of early warning signs (‘present in past 2 weeks?’)
- Adherence to the Prevention Program on a scale from 0 to 10
- Activity Rating
- If applicable: Compliance with antidepressants.

Patients were requested to return the Monitoring Forms to the prevention specialist. This written information provided the basic material for the follow-up calls.

The DRP-program follow-up contacts were scheduled to take place four times a year, irrespective of the patients’ current symptoms. Main goals were to systematically review progress by monitoring depression status and to provide ongoing feedback and support. Patients were encouraged to adhere to their Depression Recurrence Prevention Plan in

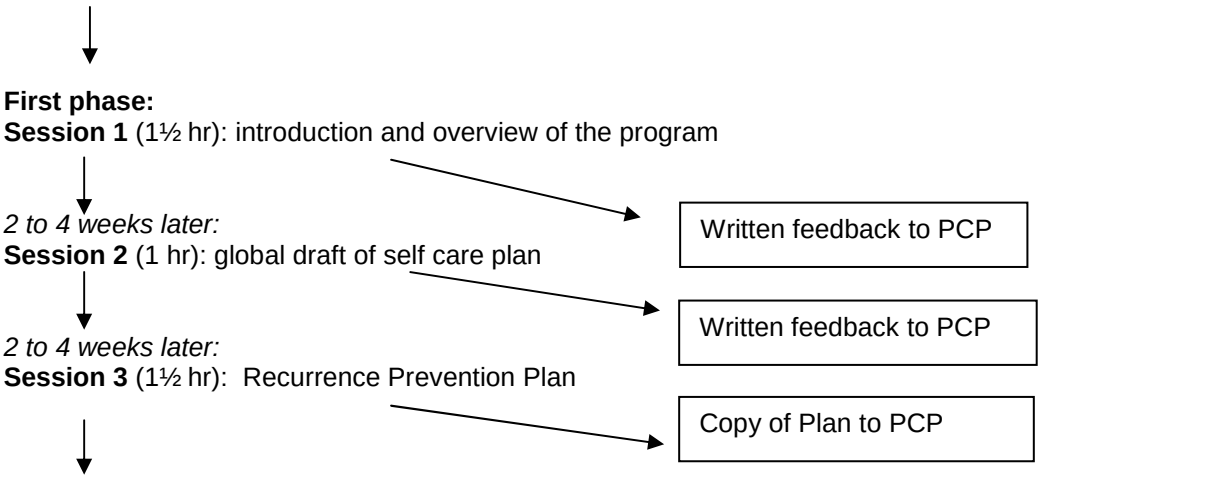
'good and in bad times' and the prevention specialists boosted motivation and reinforced confidence in self-management skills by giving positive feedback.

Continuous feedback to PCP

In the first phase of the DRP-Program, the PCP regularly received written feedback about patient cooperation and progress, and about medication use including side-effects. After the last session, a copy of the patients' Prevention Plan was sent to the PCP with an accompanying letter in which specific elements of the plan were highlighted.

In the follow-up phase, contacts between prevention specialist and PCP were less regular and more on a shared 'need to know' base. For example, suicide threats were always reported back to the patient's PCP. During the entire 3-year follow-up period the PCP remained in charge of treatment and was responsible for the prescription and delivery of antidepressants in adequate dosage and duration.

Figure 1: Outline of the Depression Recurrence Prevention Program



Prevention specialists

One experienced psychiatric nurse and two psychologists, all females, carried out the intervention. They were trained initially during four days by two experts from the Seattle project (Terry Bush & Stephanie Wahab); training included the use of motivational interviewing skills. The psychiatrist who acted as supervisor and monitored adherence to the DRP-Program in regular supervision sessions throughout the study also attended the training. Halfway through the study, a booster session with a Dutch expert was organized to reinforce (confidence in) the use of motivational interviewing with patients in various stages of the follow-up phase of the DRP-Program.

Psychiatric consultation and DRP- Program

Patients in this treatment group had one visit with one of two study psychiatrists before they started with the DRP. Prior to seeing the patient, the psychiatrist received information about diagnosis, current treatment and any comorbid somatic and/or psychiatric disorders from the referring primary care physician. After the appointment with the patient, the psychiatrist reported his findings back to the PCP. In general, the focus in the psychiatric report was on pharmacological treatment of the depression, i.e. type , dose, and duration of prescribed antidepressant medication. A copy of the psychiatric report was made available to the prevention specialist.

In general, the main functions of a psychiatric consultation in general practice are diagnostic evaluation and management advise. Consultations offer the possibility to exchange information between a PCP, who often has unique knowledge of the patients personal situation, and a psychiatrist with specialist knowledge of mental disorders. Different models of involving psychiatrists in the care for primary care patients with mental health problems exist. In short, the main difference between these models is whether the patient is actually seen by the psychiatrist or not. A meta-analysis published at the time of designing

the study concluded that a consultation liaison-model in which patient and psychiatrist meet, could improve treatment of depression (Katon and Gonzales 1994).

brief Cognitive Behavioral Therapy and DRP-Program

Patients assigned to this intervention received twelve individual one-hour sessions of standardized brief Cognitive Behavioral Therapy (CBT) by a clinical psychologist. The CBT was tailored to use in a primary care population, time-limited (maximum duration: 16 weeks) and manual guided (Boelens 1997). After the final CBT session both the referring PCP and the prevention specialist were informed by the CBT-therapist about treatment progress and results of the cognitive behavioral approach. The therapist also informed the prevention specialist on main themes that had been addressed in treatment. The patient then continued treatment with the DRP Program.

In CBT the focus is on identifying and challenging maladaptive thoughts and negative beliefs, which are thought to play a major role in the origins and maintenance of depression. The main purpose of including CBT was that at the time of designing the study, several clinical trials in specialty settings had suggested that improvement of long-term prognosis for depression was possible with CBT, which resulted in reduced relapse rates (Evans *et al.* 1992 ; Kupfer *et al.* 1992; Fava *et al.* 1996). However, results from the scarce CBT studies conducted in primary care were inconsistent (Blackburn *et al.* 1986; Scott & Freeman 1992; Scott *et al.* 1997) .

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. Acting supervisor was the regional CBT expert who developed the treatment protocol.

Treatment as usual ; control condition

Patients assigned to ‘care as usual’ were referred back to their own practitioner for further treatment. This could include whatever treatment option the PCP deemed appropriate, such

as anti-depressant medication, counseling by the PCP or referral to psychiatric services for psychotherapeutic interventions or other specialist mental health care. As described earlier, all participating physicians had been invited to a booster session on the Dutch guidelines for treatment of depression in general practice, which are routinely disseminated amongst all PCPs. In addition, a number of participating PCPs had been involved in a previous study in which a comprehensive training program, that sought to improve their ability to detect, diagnose and manage depression, was evaluated (Tiemens *et al.* 1999; Os *et al.* 1999).

Role of PCP

All patients included in the study continued to be managed by their own PCP. DRP-patients were encouraged to keep regular contact with their PCP. We asked the participating physicians to refrain from referring patients in one of the experimental conditions to (other) primary care or mental health professionals during the time in which the face-to-face sessions with the prevention specialist or the CBT-therapist took place, but PCPs were free to act upon this request. Treatment decisions concerning use of antidepressant medication, including those with respect to the duration of use, remained in the hands of the PCPs throughout the entire study period. PCPs received more specific advice on pharmacotherapy only for those patients assigned to the PC+DRP condition, but whether or not to follow the advice of the psychiatrist was to be decided by the PCP and the patient.

Main outcome variables and measures

1: Treatment effectiveness : Depression course and outcome

Two characteristics define depression outcome: severity and duration of symptoms (Frank 1991). In designing the trial, the main differential treatment effects we meant to study were effects on the duration of the index-depressive episode (or time to recovery) and the number,

severity and duration of any subsequent recurrence. All definitions of outcome were based on the DSM-IV system.

Definitions of used concepts:

Depressive episode	2 consecutive weeks of depression
Remission	2 to 7 consecutive weeks without depression
Relapse	2 consecutive weeks of depression started within remission
Recovery	8 consecutive weeks without depression
Recurrence	2 consecutive weeks of depression started within recovery

Thus, relapse was defined as the return of major depression before recovery (individuals get worse within less than 2 months of staying well), while recurrence is the start of a new episode of major depression, following a period of recovery which lasted at least 2 months.
In addition, we considered the depression to be persistent if the disorder was still present after one year in which there was no depression free period, i.e. a period in which depressive symptoms were either fully absent or sub threshold, e.g. fall below criteria for a diagnosis .

Depression measures

Diagnosis

Definite study eligibility was determined with the computerized version of the Composite International Diagnostic Interview (CIDI-auto 2.1; WHO 1997, Dutch version by Smitten *et al.* 1998). The CIDI is a structured and standardized psychiatric interview, developed by the World Health Organization and designed to be used by trained interviewers, who are not clinicians. The CIDI-auto uses computerized algorithms to map the symptoms elicited during the interview onto ICD-10 (WHO 1992) and DSM-IV (APA 1994) diagnostic criteria and reports whether these are met. Although some differences exist in the definition of depression and dysthymic disorder, the two diagnostic systems are largely comparable with high cross-system diagnostic concordance (Andrews & Slade 1998). Field trials of the CIDI

have documented good test-retest reliability and high interrater reliability for mood disorder diagnoses (Wittchen 1994; Andrews & Peters 1998) and suitability for use in primary care populations (Üstün & Sartorius 1995).

In the baseline assessment the full mood disorders-section of the CIDI-Auto 2.1 was used to determine life-time occurrence of the following disorders:

- DSM-IV : Major Depression (296.2x single episode; 296.3x recurrent episode); Dysthymia (300.04); Bipolar disorder (296.x); Generalized Anxiety Disorder (300.02); Panic Disorder (300.01, 300.21), Agoraphobia (300.22) and Social Phobia (300.23).
- ICD-10 : Single and Recurrent Depressive Episode (F32, F33); Dysthymia (F34); Bipolar Affective disorder (F31) ; Generalized Anxiety Disorder (F41.1), Panic Disorder (F41.00, F41.01), Agoraphobia (F40), and Social Phobia (F40.1).

To get a full symptom profile, we added questions on the presence of depressive symptoms in the past four weeks.

Severity

The Beck Depression Inventory (BDI, Beck *et al.* 1961) was used to asses depressive symptoms by self-report. The focus in the BDI is on establishing depression severity, defined by the combination of number, frequency, duration and intensity of symptoms in the past week (including today). The BDI consists of 21 items selected to represent the affective, cognitive, motivational and physiological symptoms of depression. For each symptom question there is a graded series of four alternative statements, ranging from neutral to a maximum level of severity. The BDI is scored by summing the rating given for each of the items and the BDI total score provides an estimate of the overall depression severity. Scores below nine are generally seen to indicate normal, non-depressed mood states whereas scores greater than 29 represent more severe levels of depression (Hammen 1997; Beck *et al.* 1988).

Psychometric properties of the BDI are reported as good, high internal consistency and high test-retest reliability in both clinical and non-clinical populations have been shown (e.g. Hammen, 1997). The BDI is also sensitive to change over time (Richter *et al.* 1998).

Follow-up assessments

All 3-month follow-up telephone interviews consisted of detailed assessments of depressive symptoms, to establish current status and to monitor the course in the interval between interviews. For these repeated assessments we developed a brief, structured and computerized interview based on the CIDI, in which current depressive symptoms were systematically checked and compared with those present and absent at the interview three months earlier. Onset and recency of symptoms was dated and recorded. In addition, the BDI was included at each FU to monitor depression severity.

The computerized nature of the interview was meant to ensure that protocol was followed by each interviewer. In order to maintain uniformity in scoring, regular group booster-sessions and individual supervision were scheduled throughout the study.

Other psychological

At all 6–month FU's , participants were also asked to fill in the SCL-90 (Arrindell & Ettema 1986). This is a multidimensional self-report inventory, designed to assess a broad range of psychological problems and well-being. Each of the 90 items is scored on a 5-point Likert scale of distress, ranging from 'not at all' to 'extremely'. Subsequently the answer codes are combined in nine primary dimensions / subscales, these are: depression, anxiety, agoraphobia, somatic complaints, sleeping problems, cognitive problems, interpersonal sensitivity, and hostility. The SCL-90 sum score can be seen as an overall measure of psychological state.

2: Treatment effectiveness : functional improvement (disability, wellbeing)

Next to clinical outcome, the concept of treatment effectiveness also includes functional status, wellbeing and more overall health related quality of life. Depression has an impact on

many areas of daily life and can impair functioning to levels that are comparable with or worse than chronic medical conditions such as diabetes or asthma (Wells *et al.* 1989). High levels of disability, poor role functioning and impaired health-related quality of life have been reported (Broadhead *et al.* 1990; Ormel *et al.* 1994; Hays *et al.* 1995; Olfson *et al.* 1997).

All assessments included questions on employment, days missed from work due to health problems, role limitations and other performance issues in the preceding month. In addition, we assessed functional status and health related quality of life at baseline and each 6-m FU by the Medical Outcomes Study 36-item Short Form Health Survey (SF-36*;* Ware & Sherbourne 1992; in Dutch: van der Zee & Sandeman 1993), a self-report questionnaire assessing mental, social and physical aspects of health-related quality of life, including impaired role performance (perceived limitations in usual daily activities because of emotional or physical problems). Timeframe is the previous month. Good reliability and validity of the SF-36 has been reported (McHorney *et al*. 1993, 1994; Burke *et al.* 1995) and the questionnaire has been found to be suitable for use in primary care populations (Brazier *et al.* 1992; Weissman *et al.* 2001).

We also asked the patients to fill in the visual analogue scale of the EuroQol on self perceived health status (range from 0 to 100); the latter data will be used primarily in a separate cost effectiveness analysis (Stant *et al.,* submitted) .

3: Other treatment effects (secondary outcome measures) :

Perceived self-efficacy for managing depression

The DRP-program was expected to improve self-confidence in controlling depressive symptoms and in preventing future episodes. Questions concerning confidence in coping with depression were included in the baseline interview, the 3-, 12 , 24 and final interview at the 36–month FU. We used the 6-item Depression Self-Efficacy Scale (DSES; developed by Bush and colleagues in Seattle) , which is a brief self-report scale containing items concerning confidence in ability to overcome or control a new episode of depression, prevent

depression from returning, recognize symptoms early on and take effective actions to deal with these. Answers were rated on a ten-point scale, with '0' indicating 'not at all confident 'and '10' indicating 'extremely confident'. Good internal consistency of this new scale has been reported (alpha=.79; Bush *et al.* 2001).

4: Feasibility and patient evaluation of treatment

Patients' acceptance of different treatment strategies and their opinion about, and satisfaction with the information and care they received for depression was another topic we planned to examine. For this, we looked at participation rates and compliance with the DRP-Program in the different treatment groups. Compliance with treatment data was gathered from specific registration forms, that needed to be filled in by the prevention specialists, the psychiatrists and the CBT therapists.

At several follow-ups data on the participants opinion and satisfaction regarding various aspects of the treatment received was collected, using questions with a 4-point response format ranging from "not at all' to 'helped a great deal'. Patients also rated their satisfaction with the PCP and the prevention specialist on a 10-point scale.

5: Response prediction

Next to nothing is known about indication criteria for the selected treatments: which patients will benefit (most) from which treatment, what will work for whom? (Roth & Fonagy 2004). In the study several (psychosocial) variables that have been found to be associated with response to treatment, such as neuroticism, selfesteem, familial psychiatric history and poor physical health, were explored. Also, data was gathered on several putative risk factors for depression relapse and recurrence, such as loneliness, perceived lack of social support, threatening life events and long-term difficulties.

This data was gathered with questionnaires and by interviews. The structured and computerized interview included questions on a variety of socio-demographic data including

marital status, living arrangements, educational level, employment and income. Furthermore, data was gathered about the presence of chronic somatic conditions and family history of depressive disorders.

Conclusion

The purpose of this paper was to describe the design and implementation of a randomized controlled trial on primary care based enhanced treatment for depression with a continuation phase. The INSTEL Depression Research project aimed at investigating effectiveness of the Depression Recurrence Prevention (DRP-) Program, an experimental intervention for depression management in primary care which takes the often chronic and recurring course of depressive disorders into account, by focusing on psycho-education, promoting self management and pro-activity and providing long-term low-intensity follow-up care. Effects of the DRP- program on the course and outcome of depression were evaluated in a randomized clinical trial, the first to study effects of primary care based interventions on course and outcome of depressive disorders over a 3-year period in the Netherlands. This trial was set up as an effectiveness trial, meant to measure the benefit treatments produce in routine primary care practice. Ultimately, the goal is to improve long-term course and outcome of depressive disorders by evaluating this preventive, pro-active strategy to sustain recovery in ‘real life’ settings and patients.