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Improving long-term outcome of major depression in primary care

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Chapter 7

Improving long-term outcome of depression

in primary care:

a review of randomized controlled trials

with psychological and supportive interventions

Annet Smit, Bea Tiemens, Johan Ormel

Abstract

Background and objective: Depression is often a recurrent or persistent disorder, associated with high levels of disability. Since the majority of depressed patients are treated in primary care, it is clear that to attain more favorable long-term outcomes more effective treatments in this setting are needed. The goal of this study was to review the strategies used for improvement of routine treatment in terms of their effects on patient outcome.

Methods: We conducted a systematic literature search to identify improvement strategies. Randomized controlled trials conducted in primary care, reporting at least six months effects on depression course and outcome of psychological treatments and supportive interventions for major depression in adults were included. The search strategy was expanded to include literature on patient outcome of educational programs and targeted approaches used in other settings. Results are presented in the form of a narrative review.

Results : Four strategies were identified: (1) training primary care physicians (PCPs) – this appears ineffective; (2) supporting PCPs management of depressed patients by other professionals, which includes collaborative care models– this may result in better short term outcomes but does not prevent recurrence ; (3) quality improvement, by adressing both the contents of treatment as well as the broader care context in which treatment is delivered- this shows improved outcomes at 6 months, and there is some evidence of longer term effectiveness; and (4) integration of recurrence and chronicity prevention strategies into treatment from the start - these have not been shown to be effective.

Conclusions: Findings show that effects of the reviewed strategies generally do not seem to persist over time. Moreover, with the exception of some US-based studies, no clear superiority over usual care has been demonstrated. We conclude that for improving long-term outcome of major depression in primary care new directions are needed.

Introduction

Depression is a common 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; Kessler *et al.* 2003). Increasingly, it has become clear that the concept of depression as a transient, acute and self-limiting disorder is incorrect. Longitudinal research has shown high rates of relapse, recurrence and chronicity (Judd, 1997; Mueller *et al.* 1999; Lin *et al.* 1999; Simon 2000; Solomon *et al.* 2000; Brink *et al.* 2001; Spijker *et al.* 2002). For many patients, depression is a recurrent and potentially persistent disorder, associated with levels of social and vocational disability comparable to rates found in chronic somatic illnesses (Ormel *et al.* 1994, 2004; Wells & Sherbourne 1999).

Primary care physicians (PCPs) are the most important initial health care contact for nearly all patients with mental health or psychosocial problems and depression is no exception. Since the majority of depressed patients continue to be treated in primary care (Spijker *et al.* 2001) , this can be considered to be the de facto mental health care setting for depression (Regier *et al.* 1998). However, the appropriateness of this situation has been questioned. PCP's have been found to under recognize and under treat a substantial number of depressive patients (Űstűn & Sartorius 1995 ; Tiemens *et al.* 1996; Hirschfeld *et al.* 1997; Schulberg *et al.* 1997; Goldberg *et al.* 1998; Os *et al.* 1999). Although more recent findings indicate that recognition of depression in general practice has improved, providing effective treatment remains an issue (Davidson & Meltzer-Brody 1999; *Andrews et al.* 2000). Moreover, especially from a long-term perspective, not all treatment is effective (Von Korff & Goldberg 2001).

Evidence-based, standardized management guidelines for the treatment of depression in primary care have been available since the 1990's (Paykel & Priest 1992; AHCPR 1993, Schulberg *et al.* 1998; Ellis & Smith 2002; Marwijk *et al.* 1994, 2003; NICE 2004). Summarized, these recommend a combination of antidepressant medication and brief, supportive counselling and include criteria for patient referral to specialized mental health care. Outcome studies have found that about half of depressed primary care patients

recover or improve significantly within a few months. Howver, many do not recover, or only partially, while about a fifth of these patients has episodes lasting more than a year and the relapse rate is high, in particular in those patients who achieve only partial remission (Brilman *et al.* 1992; Ormel *et al.* 1993; Lin *et al.* 1998; Tiemens 1999; Simon 2000; Brink *et al.* 2002; Os *et al.* 2006). In sum, the need for more effective treatment of patients with major depression in primary care is clear. However, it is less evident how this improvement can be realized: which interventions or strategies should be used in order to attain better long-term patient outcomes in this setting ?

In the present paper, we critically review a number of approaches that have been designed and tested to improve routine care for depression in primary care. The leading question is: is this method effective in improving long-term (beyond six months) depression outcomes in primary care patients? We explicitly searched the literature for clues as to which intervention succeeds in achieving recovery and in maintaining this over time, as shown by reduced rates of depression relapse, recurrence and persistence. We identified four approaches, which will be briefly introduced here.

1: The first and historically oldest strategy focuses on education and training of PCPs (paragraph 3.1). This is based on the assumption that education will change PCP behavior, improve skills in patient care and thereby also enhance clinical outcomes.

2: A second strategy explores ways in which PCPs can be supported in their diagnosis and management of depressed patients (par. 3.2). This includes brief psychological interventions by other primary care providers such as counsellors and collaborative care models where patient care is shared (through feedback and consultation) with mental health professionals such as psychiatrists and psychologists.

3: The third and most recent strategy not only addresses the contents of depression care itself but also the broader care context in which this treatment is usually delivered (par. 3.3). This has involved explorations of potentially more effective ways of organizing and delivering support to PCPs and includes studies in which nurses or case managers are employed to provide services such as patient education and monitoring of patients' progress

and treatment adherence, and comprehensive quality improvement programs which not only include training packages for PCPs and other qualified staff members, but also offer regular patient follow-up monitoring contacts and improved access to specialist care, if necessary.

4: Also of recent date is the fourth strategy, characterized by the integration of depression relapse- and recurrence prevention strategies into treatment from the start (par. 3.4) . Given the high risks of depression becoming a recurrent or persistent disorder even despite recognition and treatment, further targeting of treatment to individual patients seems a rational way to improve long-term patient outcomes, but studies evaluating these interventions for patients considered to be prone to relapse and recurrence are still rare. The few studies that have been conducted will be looked at in more detail.

In the final section of this paper (par. 3.5) we will look outside of the primary care setting to examine approaches used in outpatient and convenience patient samples and inspect these on their potential for improving long-term outcome of depression.

2   Methods

2.1   Search procedure

We conducted a systematic literature search. First, we searched in major electronic bibliographical databases, i.e. Medline, Pubmed, PsycLIT, PsycINFO, Current Contents and the Cochrane Library, to identify studies on depression treatment in primary care settings. Central search terms were major depression / depressive episode; primary care treatment; and randomized controlled (clinical) trial. These were coupled separately with the following terms: course; outcome; chronicity (persistence) ; recurrence; relapse; remission; recovery; long-term management; psychotherapy; antidepressant medication; relapse prevention; intervention. Secondly, we collected the available professional Guidelines and major meta-analyses and reviews published on the subject. By means of the 'snowball-effect' (i.e. using references in the published articles) we retrieved additional publications that were examined for possible inclusion. Finally, in the third part of the literature study we expanded the search

strategy to include literature on patient outcomes of PCP educational programs and of targeted approaches used in other care settings (outpatient, convenience samples) to improve long-term depression outcomes.

2.2. Selection criteria

We included studies if they were randomized controlled trials (RCTs) conducted in primary care and reporting at least six months patient outcome data of psychological treatments or supportive interventions for major depression (MD; DSM, APA 1994) or depressive episode (ICD-10; WHO 1992). Studies comparing effectiveness of psychotherapy and pharmacotherapy with care as usual (CAU) by the primary care physician were included, but not studies that examined effects of antidepressants (AD) only. Several good quality reviews and meta-analyses on this latter subject are available (e.g. Mulrow *et al.* 2000; Simon 2002; MacGillivray *et al.* 2003; *Arroll et al.* 2005). Furthermore, studies had to be conducted in the adult population (≥ 18 years) and we excluded studies limited to selected patient groups such as the elderly. Finally, publications had to be available in English.

The quality of the trials was assessed as follows. Depression diagnosis had to have been established by a standardized measure, preferably a structured interview. In the absence of a research diagnosis, symptoms assessed by reliable and valid (self-report) questionnaires had to be reported. We required that all interventions, the study design, randomization procedure and treatment assignment, as well as patient recruitment and attrition were described adequately. Also, the main outcome analyses should have covered all patients initially included in the research, hence on an intention-to-treat basis.

2.3 Presentation

We present the results in the form of a narrative review, which we consider to be more informative on the interventions than a meta-analysis or a systematic review, and thus better suited for our purposes. All study reports were summarized with regard to size and composition of the research population, patient selection, setting, outcome variables,

measuring instruments, contents and format of the intervention, and the actual depression outcomes observed at the follow-up assessments, if available. This information will be presented in the next section (paragraphs 3.1 - 3.4) that includes three tables outlining the main study characteristics, format and contents of the interventions and key results on depression outcome.

3. Improving long-term outcome of depression in primary care

We identified four approaches.

3.1 Training primary care physicians

Historically, the oldest wave of efforts to improve depression outcomes in primary care focuses on education and training of PCPs. Developing and disseminating evidence-based, standardized management guidelines are essential in this approach. Several strategies to promote guideline concordant behaviour can be distinguished, ranging from simply distributing these guidelines to all registered practicing PCPs to comprehensive postgraduate training and implementation programs (Thompson *et al.* 2000; Baker *et al.* 2001). However, evidence for the underlying assumption that educating physicians will by definition improve depression outcomes of their patients has long remained inconclusive because many studies mainly addressed physician behavior and other process outcomes (Kroenke *et al.* 2000; Hodges *et al.* 2001; Gilbody *et al.* 2003). It is now clear that studies that have evaluated clinical effectiveness, generally show that these programs are well received but fail to achieve substantial or enduring improvements in depression outcomes (Lin *et al.* 1997; Tiemens *et al.* 1999; Worrall *et al.* 1999; Brown *et al.* 2000; Thompson *et al.* 2000; Os *et al.* 1999). For that, more elaborate strategies seem warranted.

3.2   Supporting the PCP : Enhanced treatment and collaborative care

Key characteristic of the second strategy to improve treatment of depression in primary care is the involvement of other (mental health) professionals. Enhanced treatments include brief psychological interventions by other primary care providers such as social workers and counsellors, and collaborative care models, in which psychologists deliver (brief) psychotherapy, psychiatrists provide consultation on diagnosis and medication management, and nurses educate patients in problem-solving skills or monitor adherence to antidepressant medication. We identified eight studies about this approach that fitted our criteria: 1 on consultation liaison psychiatry, 4 studies on counselling and 3 studies on psychotherapy. These studies will be described in this section; main characteristics and findings are summarized in Table 1.

Legend of abbreviations

General:
FU = follow-up; sx = symptoms

Treatment:
GP = general practioner; PCP= primary care physician; MD=Major Depression;
PN = Practice Nurse; UC = usual care ; AD=antidepressant medication; COUN=Counselling; CBT= Cognitive Behavioral Therapy; CT = Cognitive therapy; CLP = Consultation Liaison Psychiatry ; CM= care management ;DRP= Depression Recurrence prevention ;
FB= feedback; FCM= Feedback & Care Management ; GC = generic counselling ;
IPT= Interpersonal therapy; NDC = non-directive counselling; NTC = Nurse Telehealth Care ; PC= Psychiatric Consultation; PST= Problem Solving treatment ; SWC= Social Work Counselling; PDC = Psychodynamic counselling; QEC =Quest Enhanced Care;
QI = Quality improvement ; QI-M= Quality improvement – focus on medication; QI-T= Quality improvement with focus on Therapy

Outcome measures:
BDI= Beck Depression Inventory; CES-D= Center for epidemiologic studies–Depression scale ; CIDI= Composite Diagnostic Interview Schedule; SCID= Structured Clinical Interview; CIS=Clinical Interview Schedule; HAD = Hospital Anxiety and Depression scale; HRSD=Hamilton Rating Scale for Depression; HAM-D = Hamilton depression scale ;
IDS = Inventory of Depressive Symptomatology; PSE= Present State Examination; RDC=Research Diagnostic Criteria; SCL-90: Symptom Checklist.

Author(s) , year, country	Conditions	Treatment number & duration	Patient selection; inclusion criteria	Patient sample	Depression outcome measures & criteria
CONSULTATION	*LIAISON PSYCHIATRY*	*(CLP)*			
Katon et al, 1995 & Lin et al, 1998, 1999 **USA**	1: CLP ; n = 108 2: UC ; n = 109	Acute phase: 8 weeks Continuation phase: 3 - 7 mths	By PCP Depressed, willing to use AD	N = 217 78% ♀, mean age: 47	Diagnosis: MD according to IDS Improvement : ≥ 50% change in IDS ≥ 50% improvement in SCL-90 depression
COUNSELLING					
Corney, 1984 ; 1987 **UK**	1: Social Work Counselling (SWC); n = 41 2: UC ; n = 39	Max. 6 months; actual number not clear	Identification by GP: women 18-45 presenting with depression (symptoms either appeared or intensified in previous 3 months) Inclusion by psychiatrist : CIS depressive symptoms + clinical severity rating ≥ 2	N = 80 100 % ♀ , mean age: 29	CIS Severity rating , range 1 – 5 Improvement : Follow-up CIS severity rating ≤ 1
Ward et al, 2000; & King et al, 2000; UK	1:Non-Directive Counseling (NDC) 2: Cognitive Behavioural Therapy (CBT) 3: UC Randomised between all treatments: n= 197; NDC: 67, CBT: 63, UC: 67 Randomised between 2 treatments: n = 130 ; NDC : 59, CBT: 71 Preference: n = 137; NDC: 54, CBT: 81, UC: 2	NDC: mean 6.4 sessions CBT : mean 5 sessions UC: mean 9.1 contacts	Identification by GP: diagnosis of depression or mixed depression/anxiety & psychological intervention indicated. BDI score ≥ 14 No current AD use No psychological therapy in past 6 months	N = 464 77 % ♀, mean age : 37 62 % MD (including 24% mixed anx / dep)	Diagnosis ICD-10 ; CIS BDI Improvement : positive change in mean BDI scores

Author(s) , year, country	Conditions	Treatment number & duration	Patient selection; inclusion criteria	Patient sample	Depression outcome measures & criteria
Chilvers et al, 2001 **UK**	1: Generic Counselling (GC) - randomised: n = 52 - preference: n = 140 2: AD by own GP - randomised: n = 51 - preference: n = 80	GC: 6 sessions actual number not clear	Identification by GP (checklist) ; mild to moderate MD	N = 323 75 % ♀, mean age: 37 GP rating of severity: mild: 24% moderate: 66% severe: 7 %	Diagnosis: RDC criteria ; BDI; GP casenotes Time to remission; Remission : BDI < 10, RDC ≤ 4 or clear documentation in GP notes that patient was well; Relapse: deterioration within 6 m of remission Global outcome rating by psychiatrist using all data sources: good = response to treatment within 8 wks& staying well; moderate = slow response to treatment but remained well or well initially but became unwell later; poor =remained depressed
Simpson et al, 2003 **UK**	1: Psychodynamic Counselling (PDC); n= 73; 2: UC: n=72	PDC: 6 -12 sessions mean: 5 sessions; 88% at least 1 ; 74% ≥ 4	Initially referral by GP but changed to screening because of slow referral rates chronic depression: BDI ≥ 14 ; Duration ≥ 6 months but < 5 years *Exclusion of difficult or hard to treat patients (?)*	N = 145 80 % ♀, mean age: 43 Note: mean BDI higher in PDC at inclusion	BDI Chronic MD: BDI ≥ 14 mild to moderate depression: BDI 14 - 23; severe: BDI ≥ 24

Author(s) , year, country	Conditions	Treatment number & duration	Patient selection; inclusion criteria	Patient sample	Depression outcome measures & criteria
PSYCHOTHERAPY					
Schulberg et al, 1996 **USA**	1: IPT acute (16 sessions 1/ wk) + continuation (4 sessions 1/mth) ; n = 93 2: AD acute (bi- weekly visits during 16 wks) + continuation (4 visists / 1 month) ; n = 91 3: UC; n= 92	8 months IPT: 51 % completed acute phase; of those , 83% completed contin. AD: 55 % acute phase, of those 60% completed continuation	3 phase assessment: screening; interview; final selection by psychiatrist MD & HRSD > 12	N = 276 83 % ♀ , mean age: 38	Diagnosis: DSM-III-r MD + HRSD Recovery: HRSD < 8 Partial recovery: HRSD > 8 < 13 No recovery: HRSD > 12
Scott et al, 1997; **UK**	1: brief Cognitive Therapy ; n =24 2: UC; n = 24	6 weeks CT mean number of sessions : 7	Referral by GP; Eligibility determined by psychiatrist: MD & BDI > 19	N = 48 67% ♀, mean age: 41 mean duration: 8.6 months; 60% recurrent	Diagnosis: DSM-III-r Improvement : changes in BDI, HRSD Relapse: authors refer to NIMH criteria but provide no clear definition
Katon et al, 1996 & Lin et al 1998, 1999 **USA**	1: brief CBT ; n= 77 2: UC ; n = 76	CBT: 6 wks, 4 - 6 sessions FU monitoring : up to 24 wks after last session	By PCP Depressed, willing to use AD	N = 153 74 % ♀, mean age: 47 MD : 43 %	SCL-90 depression scale: ≥ 50% improvement IDS symptom severity: ≥ 50% improvement

Table 1: Enhanced treatment and collaborative care programs continued, part B

Author/s	last FU assessment + attrition	Results: Depression Outcome	Conclusions
CONSULTATION LIAISON PSYCHIATRY (CLP)			
Katon et al, 1995 & Lin et al, 1998, 1999	19 months response ?	7 months (MD patients only): Improved ≥ 50% on SCL depression scale: CLP : 75 % , UC: 44 % At 19 months : no differences in relapse rates and depressive symptoms	At 7 months, more improvement in CLP patients At 19 months: no differences
COUNSELLING			
Corney	6 months 100% , n = 80	Improvement : SWC: 68 % , UC: 62 % Link with duration: 72% of SWC-patients whose sx had intensified benefited vs. 45 % of SWC with new depression	SWC no more effective than UC overall (improvement rate 65 %) ; SWC more effective than UC for more chronic depression
Ward et al & King et al	12 months response : 81 % , n =	Faster resolution of depressive sx by both NDC & CBT at 4 months; At 12 months: no differences	NDC and CBT equally effective and superior to UC at 4 months Neither NDC nor CBT more effective than UC in symptom reduction over 12 months Treatment preference not related to clinical outcome
Chilvers et al, 2001	12 months response: 64 % (n= 207) for questionnaires, 96 % (n=311) for GPcase note reviews	Remission: 68 % - similar in each group Time to remission (median) : 3 months; for AD: 2 mths Relapse: 15 % Global outcome rating by psychiatrist: good : 33 %, moderate: 31 %, poor: 37 %	GC and AD equally effective, time to remission slightly shorter with AD No remission in 32 % and of those remitted, 15% relapsed within 1 year No difference in psychiatrist's overall outcome assessment between any of the groups Treatment preference not related to clinical outcome

Author/s	last FU assessment + attrition	Results: Depression Outcome	Conclusions
Simpson et al, 2003	12 months 80% , n = 115	Not recovered (still a case): all patients: PDC: 48 % , UC : 64 % depression of mild-moderate severity: 32 % vs 57 %; depression of higher severity: 20 % in both PDC + UC Improvement in mean BDI scores: PDC: 6.7 (22 -> 15.3) ; UC: 4.7 (19.7 -> 15)	More recovery with PDC No differences in improvement of depressive symptoms
PSYCHOTHER	*APY*		
Schulberg et al, 1996	8 months n = ?	Recovery: Partial recovery: No recovery: IPT: 46 % 35 % 19 % AD: 48 % 27 % 25 % UC: 18 % 34 % 48 %	IPT and AD more effective than usual care No significant outcome differences at any time point between IPT and AD
Scott et al , 1997	58 weeks 50% CT: n = 16 (33% drop out) UC: n = 8 (66 % drop out)	Recovered at 7 wks : CT: 63 %, UC: 34 % Relapse: CT: 7 % , UC: 50 % Mean HRSD score at w 58 lower in CT patients	CT patients recovered earlier trend towards fewer relapses and greater symptom reduction over FU with CT But: small numbers and high , differential dropout
Katon et al, 1996 & Lin et al, 1998, 1999	19 months n = ? (7 months: 77 % , n = 117)	At 4 months (MD patients only) : MD diagnosis : CBT: 7 % , UC : 23 % At 7 months: Improved ≥ 50% SCL depression scale: CBT: 70 %, UC: 42 % 19 months : similar relapse rates and symptoms	7 months: greater improvement with CBT 19 months: no differences

Consultation Liaison Psychiatry (CLP)

We found one study examining the potential value of CLP for depression treatment in primary care. Katon and coworkers (1995) report results of a collaborative care RCT which included a comparison of co-management by a psychiatrist and a PCP, with depressed patients alternating visits in combination with psycho education and AD monitoring by the psychiatrist with usual care. PCPs in the CLP–arm were also offered education and case by case consultation. Forty-two percent of included patients were classified as having MD. Seven months later, CLP-patients with MD showed greater improvement in depressive symptoms overall than those randomized to usual care. No data is provided on recovery or persistence of MD.

Counselling

Four counselling studies fitted our inclusion criteria; two of them incorporated patient preference arms in the design. All four were from the United Kingdom (UK), reflecting the fact that counselling has become commonplace in primary care in this country. General practioners use the assistance of counsellors for a range of psychosocial and psychological problems, including depression (Churchill *et al.* 1999; Bower *et al.* 2000, 2002). Counsellors come from diverse professional backgrounds and use a variety of models and techniques. Next to the key element of "reflective listening to enable the patient to resolve their own difficulties" (from the formal counselling definition used for the Cochrane review by Bower and coworkers, 2002: p.5), counselling as developed within the context of the UK healthcare system may also include the use of psychotherapeutic techniques, more directive advise and the provision of practical help to address the patients' problems.

The social work counselling (SWC) in the trial by Corney (1981, 1984, 1987) was provided by social workers already attached to the health centers involved. No specific guidelines were given. Counsellors were instructed to see their clients on a regular basis and to use a flexible, broad approach, tailored to the needs of the patients. After six months,

SWC was found no more effective than usual care (UC), but women with more chronic depression benefited more from the input of SWC than from UC, while for women with a more recent onset of depression the reverse was true. Thus, there were indications that differential outcome was linked to the chronicity of the patient's depression.

Ward and co-workers (2000; King *et al.* 2000) compared effectiveness of non-directive counselling (NDC) relative to effects of cognitive behavioral therapy (CBT) or usual care. Eligible patients who refused random assignment were given a choice between the treatments; most preferred CBT. After 12 months, no meaningful differences in outcome were found between the treatment groups.

Chilvers and associates (2001) compared generic counselling (GC) with antidepressants (AD). Again, there was no specific treatment protocol: counsellors could use whichever approach they believed was most suitable for their patients, given the diagnosis of depression. In this trial only one third of the participants agreed to the randomized treatment assignment; the majority of those in the preference arm chose counselling over AD. Main results were that after one year there were no significant differences between treatment groups and also that receiving the treatment of preference was not related to depression outcome.

Finally, the trial by Simpson and co-workers (2000, 2003) evaluated effectiveness of psychodynamic counselling (PDC) and usual care for patients with chronic depression. As far as we can establish, the PDC was not specifically provided to address the persistent nature of depression. Rather, these patients were chosen because of the constant workload they present for GPs, in terms of time spent in consultation and as high consumers of psychotropic drugs. After one year, more PDC than UC patients had recovered. Thus, this is the only study that showed counselling to be more effective than usual care.

Psychotherapy

Four studies fitted our inclusion criteria, among them the study by Ward and colleagues that was also presented under the heading of counselling. Two of the therapy studies were

carried out in the UK and two in the United States of America (USA). Therapies that were tested are: interpersonal therapy (IPT; 1 study), cognitive therapy (CT) and cognitive behavioral therapy (CBT; 2 studies).

IPT was developed by Klerman and colleagues (1984) as a therapy for improvement of interpersonal skills and coping. The purpose of IPT for depression is to alleviate symptoms and improve interpersonal functioning by clarifying the problem areas associated with onset of depression, followed by refocusing and choosing alternative, more effective strategies for dealing with these stressors (Weissman & Markowitz, 1994).

The RCT carried out in the USA by Schulberg and coworkers (1996, 1998) compared effectiveness of IPT for depression treatment in primary care with antidepressants and usual care by the PCP. The IPT consisted of manual-based acute phase and continuation therapy over eight months. At the end of treatment, significantly more patients in both the IPT and AD arms of the trial had recovered, compared to those receiving UC. IPT was equally effective as AD at any time point in these 8 months. However, compliance with IPT was low, with only 42 % of the patients actually following the full IPT protocol.

CT and CBT aim at modifying negative thoughts and beliefs and thereby also change behavior that might be dysfunctional and contributing to (maintenance of) depression. CBT is intended to be time-limited, relatively brief, active, directive, focused on current problems and dysfunctional thinking (Hammen 1997). Key ingredients are 'thought-catching' (identify automatic negative thoughts and challenge these) and behavioral activation.

Among the included studies is the trial of Ward and colleagues that found similar 1-year outcomes for CBT, NDC and UC. The study by Scott and colleagues (1997) examined whether brief CT had excess benefits over UC. On the short-term this proved to be the case, and there was also a trend towards lower subsequent relapse rates over the next year. However, findings from this study should be treated cautiously since it suffered from small numbers and high treatment drop-out rates.

In the USA , Katon and co-workers (1996) developed a structured program in which PCPs cooperated with psychologists who provided brief CBT. Additional components of this collaborative care approach were patient education (including a video and book) and monitoring of AD adherence ; patients were only included if they were willing to use AD. Of the total sample, 43% met criteria for a baseline MD diagnosis. Main findings of a follow-up after 7 months show that for these patients the CBT/co-management intervention resulted in greater symptom improvement than UC. No information is available on recovery or on the proportion of patients still meeting MD criteria at this point.

Long-term effects of collaborative care with CBT or CLP (combined cohorts)

Additional information on long-term outcome of patients with MD who participated in the Katon et al trials evaluating effectiveness of co-management by either a psychologist or a psychiatrist , is provided in two papers by Lin and others. In the first (Lin *et al.* 1998) , relapse rates are presented for patients that did not satisfy DSM criteria for MD at 7 months (n=251). Relapse was defined as satisfying DSM-criteria at the 19-months assessment or reporting an interval episode in the interval between 7 and 19 months. 37% of all patients in this combined cohort had experienced a relapse and this proportion was similar in the collaborative and usual care patients. Also, relapse rates did not differ between patients from the original CBT or CLP treatments. Retrospectively, patients who relapsed had had significantly more persistence of depressive symptoms at 7 months. In the second paper (Lin *et al.* 1999) the focus is on outcomes for a sample consisting of patients that had a diagnosis of MD at study entry (n = 116). Findings show that there were no differences in depressive symptomatology at 19 months FU between the patients who had received the enhanced treatment (i.e.: with CBT or CLP) and those that had received usual care. Since short-term outcomes had been better in the collaborative care patients, the conclusion is that these failed to persist.

Conclusion

While enhanced treatment and collaborative care often resulted in improved short-term outcomes, this did not seem to prevent major depression from becoming a persistent disorder – whether by lack of remission, or by relapse or recurrence following initial recovery. None of the studies provide solid evidence for improved long-term effectiveness over usual care.

Two of the included studies incorporated patient preference arms in the design, to allow potential participants with a strong treatment preference to be allocated to their treatment of choice. This was done in an attempt to overcome difficulties in recruitment and selective treatment drop-out, problems often encountered in the implementation of randomized treatment trials (Fairhurst & Dowrick 1996; Hunt *et al.* 2001). Results showed that in neither of these studies choice of treatment conferred additional benefit on outcome.

3. 3   Organizational quality improvement

The need for better coordinated care and for more systematic, active patient follow up to monitor progress over time, can be identified as central themes in recent approaches to improve long-term depression outcomes (Badamgarav *et al.* 2003; Gensichen *et al.* 2006). In recognition of the potentially recurrent or persistent nature of MD, principles of chronic illness management (Tiemens 1999; Andrews 2001; VonKorff *et al.* 2002) have become more integrated in acute phase treatment. Strategies have been developed and evaluated which not only address the contents of depression treatment, but also the context and organization in which this treatment is delivered. Several potentially more effective ways of delivering depression care within the primary care setting have been examined. Six studies, all from the USA, fitted our criteria and will be presented in this section (see table 2).

Table 2 : Quality Improvement of Depression care

Author(s) , year country	Interventions , control conditions	Treatment Duration, number	Patient selection; Inclusion criteria	Patient sample	Outcome measures & criteria
Hunkeler et al, 2000 **USA**	1 : NTC ; n = 117 2: NTC + peer support ; n = 62 3: UC; n = 123	NTC: 16 weeks mean number of calls per patient: 10 Peer support: (at least) 6 months; 68% had at least 1 contact with volunteer	Referral by PCP or nurse practioner PCP diagnosis of MD or dysthymia Willing to start AD treatment	N = 302 69% female, mean age: 55	Improvement : 50% improvement on mean HRSD and / or BDI
Simon et al, 2000 **USA**	1: FB ; n = 221 2: FCM; n = 196 3: UC; n = 196	16 weeks 1: reports after 8 and 16 wks ; 2: as 1) + 3 telephone calls (at inclusion and after 8 + 16 wks); 93% completed	Selected from pharmacy records by researchers Diagnosed with depression and starting new AD treatment (i.e. no AD in previous 120 days)	N = 613 72 % female, mean age: 47	MD: SCID –Depression module Improvement: ≥ 50% in SCL-20
Simon et al, 2004 **USA**	1: FCM ; n = 207 2: FCM + telephone brief CBT; n = 198 3: UC; n=195	20 weeks FCM: 3 calls + personalised mailed feedback ; 85% completed all 3 calls FCM+CBT: 84 % completed ≥ 4 CBT sessions	Selected from pharmacy records and visit registration; Current depressive sx of moderate severity , 2-4 wks after starting new AD treatment	N = 600 75% female, mean age: 44	SCL depression scale Patient rated global improvement at least 50% improvement in SCL-depression score rating of (very) much improved
Dietrich et al, 2004 **USA**	1: CM; n = 224 2: UC; n = 181	6 months monthly and as needed telephone support calls from caremanagers 64% ≥ 1 FU call in first 3 m; 59% ≥ 1 FU call between 4-6m	MD and/or dysthymia Starting or changing depression treatment	N = 405 80 % ♀; mean age: 42 MD: 79 % MD & Dysthymia: 20 %	Diagnosis: DSM-IV Severity of symptoms : HSCL-20 Response to treatment: ≥50 decrease in HSCL-score; Remission: HSCL score < 0.5

Author(s) , year country	Interventions , control conditions	Treatment Duration, number	Patient selection; Inclusion criteria	Patient sample	Outcome measures & criteria
QUEST **Rost et al 2001** **USA**	1: QEC ; n = 239 2: UC ; n= 240	93 % at least 1 session with nurse; mean number of contacts in the 8 wks after index visit: 5.2	Screening MD	N = 479 84% female, mean age: 43 New treatment : n =189 ; recently treated: n= 243	CES-D (modified) DSM-IV Improvement : decrease in mean CES-D
Partners in Care **Wells et al 2000, 2004; + Sherbourne et al 2001;** **USA**	1: QI-M; n = 424 2: QI-T ; n = 489 3: UC ; n = 443	12 months QI- M: 6 - 12 months QI-T: 12-16 sessions of CBT; most used open group CBT brief CBT (4 sessions) offered for minor depression	Screening screen positive = probable MD	N = 1356 71 % ♀; mean age: 44 MD: 41 % MD & Dysthymia: 11 %	Screen : CIDI stem questions (≥ 2 wks of depressed mood or loss of interest during last year or persistent depression over the year plus at least 1 week in past month) Diagnosis: CIDI (baseline & 24 m FU) probable MD (other FU's) : modified screener i.e.: referring to prior 6 months and without dysthymia item ; Depressive symptoms : CES-D

Table 2 : Quality improvement continued, part B

Authors	F-U last assessment + attrition	RESULTS: Depression outcome	Conclusions
Hunkeler et al, 2000	6 months 85% (n = 256)	≥ 50% improvement HRSD: BDI: NTC * : 57 % 48 % UC : 38 % 37 % * Both NTC interventions combined in main analyses	NTC superior to UC in symptom reduction measured by HRSD but of marginal benefit in BDI-scores; No additional effects of peer support to NTC

Simon et al , 2000	6 months,
	
	94% (n = 575)
		≥ 50% improvement in SCL:
		FB: 43 % ; CM: 55 %; UC: 40 %
		
		Probability of persistent MD at 6 m :
		FB: 15 % ; FCM: 8 % ; UC: 15 %
			FCM more effective than FB only and than UC :
			  - more improvement in depressive sx
			  - lower probability of persistent MD 6 months after start of AD treatment
			
			FB only: no more effective than CAU

Simon et al, 2004	6 months, 89% (n= 532)	≥ 50% improvement in SCL: FCM: 51 %; FCM+CBT: 58 % ; UC: 43 % Patient rated improvement: FCM: 66 %; FCM+CBT: 80 % ; UC: 55 %	FCM with brief CBT more effective than FCM on itself FCM with brief CBT more effective than UC FCM and UC equally effective
Dietrich et al, 2004	6 months 80% (n= 325)	Response to treatment: CM: 60 % , UC: 47 % Remission: CM: 37 % , UC: 27 %	Outcome effects modest but better for patients in CM practices

Authors	F-U last assessment + attrition	RESULTS: Depression outcome	Conclusions
Rost et al , 2001	6 months 90% (n= 432)	Mean reduction in CES-D scores : QEC: from 56 -> 37.9 =18.1 ; UC: from 55 -> 42.8 = 12.2 Decrease in CES-D in patients with new treatment episode : QEC : 21.7 vs. UC: 13.5 Decrease in CES-D in recently treated patients: QEC: 14.5 vs. UC: 11	More improvement in depressive symptoms in QEC patients But : no effects in patient already receiving treatment at inclusion, who remained depressed
Partners in Care 2000, 2001, 2004	57 months 73% (n = 991)	6 m FU probable disorder : QI : 40 % , UC 50 % 12 m FU probable disorder : QI : 42 % , UC 52 % 24 m FU current MD : QI-M: 39 % ; QI-T : 31 % , UC: 34 % 57m FU , probable disorder: QI-M: 38 % ; QI-T : 36 % , UC: 44 %	6 and 12 m FU : both QI approaches similarly improved clinical outcomes relative to UC 24 m FU: - more sustained benefit of QI-T - no differences between rates of MD among QI-M and UC 57 m FU: - QI-T significantly lowered rate of probable disorder relative to UC - difference between rates of probable disorder in QI-M and UC not significant

Practice support by nurses or care managers

Nurses played a central role in an intervention program called Nurse Telehealth Care (NTC), that was evaluated by Hunkeler and associates (2000) in the USA. In this intervention, nurses supported patients in adhering to their AD treatment and informed PCPs about the progress these patients made. Key element were regular telephone calls with the patients, scheduled in advance. There were two versions of NTC, with one also offering additional peer support by trained volunteers. No additional effects for peer support were found and both NTC versions were combined for the outcome analyses. At six-month follow-up NTC patients showed greater improvement in depressive symptoms than those randomized to UC. No data is provided on recovery or persistence of MD.

Simon and collegues (2000) found that a feedback and care management (FCM) program that included (written) feedback of computerized data on treatment, practice support by a care manager, and regular monitoring and follow-up of patients by telephone, of which PCPs received detailed reports, significantly improved six month patient outcomes over usual care. This approach was found to be more effective than (written) feedback to PCPs of computerized data from pharmacy and visits, which included algorithm based recommendations for treatment, on itself ; the latter did not yield any benefits at all over usual care. Probability of persistent major depression at 6 months follow-up was 15% for FCM patients, compared with 8% in both routine care and the feedback only group.

More recently, the same research group reported results of another RCT (Simon *et al.* 2004) in which effectiveness of a similar, updated version of the FCM intervention was compared with a version that included brief structured CBT, delivered by telephone. Six months FU findings showed that patients assigned to the care management plus CBT condition were significantly more likely to experience substantial improvement in depressive symptoms and greater self reported improvement than patients in both other conditions (FCM and usual care). However, in contrast to findings of the first study, no additional beneficial effects were demonstrated for the FCM over usual care .

Dietrich et al (2004) report 6-month outcomes of a large RCT with randomization taking place at practice level. The intervention practices implemented a systematic approach to the assessment and management of depression (including dysthymia). Key elements included telephone follow-up of patients by a care manager (with background in primary care or mental health nursing) , support of this care manager and the PCP by a psychiatrist and increased attention to patient education and goal setting by the PCP. Brief training was provided to all involved parties; PCPs in the control practices were offered a 1 hour-course. Six months after inclusion, more patients in the care management practices were in remission (37% versus 27% of patients in UC practices). Interestingly , hardly any differences were found in the actual treatment patients had received during this period : of all patients about 80% had used an AD and around 25% were provided with some form of (unspecified) counselling. This suggests that the improved outcome could be contributed to the specific FU-monitoring elements of the intervention.

Comprehensive practice-level quality improvement strategies

Two studies in the United States developed and used elaborate practice-level strategies to improve detection and depression management.

In the "Quality Enhancement by Strategic Teaming" ('Quest') intervention (Rost *et al.* 2000; 2001 a+b) the roles of all members of community primary care practice teams in the care process were redefined. Administrative staff was trained to screen and recruit patients meeting criteria for MD. Nurses were trained to be able to provide clinical services, like assessing depressive symptoms, providing education, stimulating adherence to treatment and monitor progress over time. PCPs received a brief training in which they were encouraged to select the type of guideline concordant treatment (pharmacotherapy and/or psychotherapy) the patient preferred. Effects of this intervention were studied in a RCT with randomization taking place at the practice level. Twelve practices participated ; in each intervention practice two PCP's, one nurse and one administrative staff member were trained. At six months FU, patients in I-practices showed more improvement in depressive

symptoms than patients treated in UC settings. However, this improvement was only found in the subgroup of patients that had started with a new treatment i.e. no AD in the past month or any specialty visits in the past six months). Moreover, the intervention did not have any effect on the outcome in patients with persistent symptoms, of whom almost 73% had used AD in the month before study inclusion. These patients (estimated by the authors to constitute approximately 56% of the sample) remained depressed: depressive symptoms in these patients declined less than 20%, even though the majority of them (82%) seemed to receive appropriate, guideline-concordant care.

The Partners in Care study (Wells *et al.* 2000, 2004; Sherbourne *et al* 2001) is , as far as we are presently aware, the first quality improvement (QI) program at practice level to report on five year impact of the QI intervention relative to usual care. In the literature this study is described as a combination of expert intervention, local managed care organization involvement (mainly with organizing resources and finances) and provider behavior change strategies. Training of local staff of primary care clinics was used as a means to increase the percentage of depressed patients who would receive appropriate care. Partners in Care (PIC) offered a 2-day basic depression management training package to primary care providers, nurses and therapists. Moreover, PIC provided enhanced resources for either AD treatment, with access to a nurse care manager for six to twelve months of follow-up medication adherence support (QI-M) or to (individual or group) CBT by a study-trained therapist (QI-T). Control practices received copies of the guidelines, but no extra training or resources. All participating practices continued to have access to commonly available (primary care or specialist) mental health treatments. PCPs and patients were free to choose among treatments or to choose no treatment. The effects of both strategies were compared with those of usual care in a RCT, with randomization taking place at the practice level. Forty-two percent of the included patients had a baseline MD diagnosis, another 11% suffered from MD and dysthymia. After one year, both QI interventions had reduced depression more than usual care: 42% of QI-patients compared with 52% of UC-patients

(still) suffered from MD and/ or dysthymia. At the 2-year FU the therapy version of QI (i.e.: CBT) was found to have more sustained benefits than both other conditions when comparing rates of current MD (see table 2) . At the last reported FU five years after the study started , QI-T patients again had the lowest rates for probable depressive disorder.

However, interpretation of these results is complicated. By design, this study did not randomly assign patients to specific treatments but rather randomized opportunities for receiving appropriate care (Roth & Fonagy 2004). Actual treatment that patients received may not have been that different across conditions. In fact, all QI patients had access to CBT and service use data show that next to about 40% of QI-T patients, 30% of QI-M patients actually received at least 4 (group) CBT sessions in the first year, which was the period of active depression treatment. The researchers themselves state that there is no clear answer to the question why there were more long-term benefits of QI-T, compared with QI-M and usual care (Wells *et al.* 2004, p. 384) .

Conclusion

The QI strategies reviewed in this section primarily involve implementation of evidence based care on the level of primary care practices. They mostly include education for PCPs and other staff, and additionally provide either direct patient support or offer improved access to (AD or CBT) treatment. Findings show that the aid of these supportive services, and possibly also the involvement of other mental health specialists, may result in more favorable depression outcomes. However, of the six included studies only one provides outcome data beyond six months and only three present outcome findings in terms of remission or recovery; not one study reports on relapse or recurrence. Thus, at present there is only limited evidence for long-term effectiveness. Furthermore, interpretation of the findings is complicated by the great diversity and exact contents of the actual treatment that patients received.

Two studies deserve special attention. First, the study of Dietrich and coworkers, because results strongly suggest beneficial effects of the specific FU-monitoring elements of

the intervention, given that this was probably the only element which was truly different between treatments. Second, the PIC study , which is unique for it's long follow-up and is very informative in demonstrating the course of MD over 5 years.

3. 4 Interventions aimed at reduction of relapse, recurrence and persistence of depression

In evaluating depression outcomes, the central question to be answered should be which treatment not only alleviates the current episode but also protects best against relapse and recurrence. Sustained recovery should be an important goal of depression treatment, irrespective of the care setting in which the patient is seen (Keller 2003) . Therefore, indicated or selective preventive interventions, specifically targeted at those considered to be at high risk, may be necessary. Risk-reduction strategies usually focus on factors directly associated with the disorder (such as residual depressive symptoms) or at enhancing protective aspects or circumstances, including self-management and coping. We found four studies, three from the USA , testing this approach in primary care. These will be presented in more detail in this paragraph. The studies are summarized in table 3.

Katon and coworkers (1999, 2002) evaluated an intervention targeted at patients with persistent symptoms of depression, despite their being treated with antidepressants for 6 to 8 weeks (stepped collaborative care). Patients in the intervention group received psycho-education and increased frequency of visits by a psychiatrist collaborating with the PCP (CLP as described in 3.2) . After six months, 44 % of I-patients and 31% of UC controls had recovered. However, only patients with moderate symptom severity at study entry (65 % of the sample; Walker et al 2000) were found to benefit from this shared care, while there were no effects for patients initially suffering from more severe symptoms. Sustained improvement during the next 2 years was found only in the CLP-patients with depression of moderate severity. No data on relapse or recovery is presented.

Table 3: Primary care interventions aimed at reducing risk of relapse, recurrence, chronicity

Author(s) , year	Conditions	Treatment duration	Patient Selection	Inclusion Criterion	Patient sample	Outcome measures & criteria
Katon et al, 1999; 2002	1: CLP : 2-4 visits with liaison psychiatrist; pharmacotherapy; monitoring of follow-up visits and AD-adherence; patient education; n = 114 2: UC; n = 114	2 – 4 mths of shared care and as-needed consultation available for PCP mean number of patient visits : 2.75	By research team, based on automated registration, pharmacy and visit data	Persistent symptoms after 6-8 weeks of AD; ≥ 4 DSM-IV MD symptoms + SCL-20 mean score ≥ 1	n = 228 74 % ♀ , mean age 47 recurrent MD: 80%; dysthymia: 55%	SCID SCL-20 Severe depression: SCL > 2 Moderate depression : SCL ≤ 2 Recovery : 0 -1 DSM-IV MD sx
Katon et al, 2001	1: Relapse Prevention Program (RPP) by depression specialist: n = 194 2: UC; n = 192	1 year	by research team, based on automated registration, pharmacy and visit data	Recovered but at high risk for relapse after 6-8 weeks of AD: < 4 DSM –IV MD sx + ≥ 3 prior episodes of MD or dysthymia; OR 4 residual sx, SCL-20 mean score < 1 and history of MD or dysthymia	N = 368 74% ♀, mean age: 46 recurrent MD: 75%; dysthymia: %	SCID LIFE interview SCL- 20 Relapse/recurrence: meeting criteria for MD Recovery: Not meeting criteria MD
Smit et al , 2006	1: DRP; n = 112 2: PC+DRP; n = 39 3: CBT +DRP; n = 44 4: UC; n = 72	Max. 36 months; 92% of all 3 DRP patients attended 3 sessions with prevention specialist; 94% at least one	3 stage procedure: referral by PCP, followed by screening and interview by researchworker	Current MD (ipresent in last 2-12 weeks)	N = 267 63 % female, mean age 43 comorbid dystymia: 8%	Diagnosis : CIDI Recovery: no MD diagnosis

Author(s), year	Conditions	Treatment duration	Patient Selection	Inclusion Criterion	Patient sample	Outcome measures & criteria
Rost et al, 2002	1: Enhanced care with continuation phase (EC); n = 115 2: UC ; n = 96	6 months plus max. 2 year continuation 94 % at least 1 contact during initial 6-m EC; mean number of contacts: 5; 83 % at least 1 contact during continuation phase; mean: 7	Screening	DSM-IV MD new treatment episode at study entry persitent symptoms after 6 months of treatment	N = 211 84% female Mean age: 43 (EC patients sign younger: 40 vs. 47) 73% recurrent MD; 10% dysthymia in previous year	Modified CES-Depression scale Remission : CES-D < 16

Table 3: Primary care interventions aimed at reducing risk of relapse, recurrence, chronicit, continued part B:

Author/s	Last F-U & attrition	RESULTS: Depression Outcome	Conclusions
Katon et al, 1999; 2002	28 months, 75 % (n = 171)	Recovery after 6 months : CC: 44 % vs. UC: 31 % Depression severity (mean SCL-20 score) at 28 m: Overall: I: 1.16, C: 1.19 moderate severity : 1.23 vs 0.88 high severity: 1.16 vs 1.19	At 6 months: - significantly more intervention patients recovered ; I-patients recovered faster At 28-months: - continued improvement in I-patients in the moderate severity group - no outcome differences in the high severity group
Katon et al, 2001	12 months 85% (n =) (RPP 90% , UC 79%)	Relapse / recurrence rates: RPP: 35 % vs. UC: 35 % Depressive symptoms: SCL-20 scores of RPP-patients on average 0.08 points below those of UC patients	- no differences in overall rates of relapse / recurrence of MD over 1 year - modest intervention effect on depressive symptoms
Smit et al, 2006	6 months 85% (n = 226)	Recovered : overall 67% DRP: 61%, PC+DRP: 79%; CBT+DRP: 70% ; UC: 68% Depressed full 27 weeks: DRP: 20%, PC+DRP: 6%; CBT+DRP: 15 % ; UC: 17%	DRP did not result in better 6-month outcomes over UC No evidence for added beneficial effects of additional CBT and PC over DRP only
Rost et al , 2002	24 months 67% (n = 142)	Remission over 2 years: EC: 74 % , UC: 41 %	Over 2 years, continued enhanced care significantly increased remission compared with UC

In a related trial (Katon et al. 2001), an intervention targeted at patients who were recovered but considered to be at high risk for relapse because of their depression history (recurrent episodes or dysthymia) was studied. This Relapse Prevention Program (RPP) focused on the continued use of antidepressants, the timely recognition of relapse/recurrence through systematic monitoring of symptoms and the development of a personal relapse prevention plan (Ludman et al. 2000). Patients in the intervention group were offered two primary care visits with a depression specialist (a psychologist, social worker or nurse practioner), followed by three telephone contacts over a one-year period. Twelve month FU assessments showed that , although RPP-patients experienced less depressive symptoms across FU, they did not experience fewer episodes of depression. Overall relapse rates over 1 year were similar (35%), showing that the RPP did not improve outcome over usual care.

The RPP study of Katon and coworkers was replicated with a modified version of the intervention in the Netherlands by Smit and colleagues (Smit et al. 2006, 2005). In this trial , aimed at 'new' as well as chronic MD patients, effectiveness of enhanced care with a continuation-phase was evaluated. Primary intervention was the Depression Recurrence Prevention (DRP) Program (Tiemens et al. 1998) that focused on improving patients' resilience and self-management skills and was based on an ongoing relationship between patient, prevention specialist and PCP. Six-month follow up findings showed that 67% of all patients had recovered, while 17% remained depressed. Enhanced care did not result in improved outcomes over usual care. Furthermore, there were no indications for any surplus effects of addition of a psychiatric consultation or CBT to the basic format of the DRP. Presently, a publication on 3-year effects is underway (Conradi et al., in preparation).

Finally, Rost et al (2002) evaluated effects of a chronic illness approach to depression management. Key element was continued care management by practice nurses, which was targeted more specifically at patients still reporting high numbers of depressive symptoms after being treated for 6 months. All patients had had a new episode of MD at study inclusion. The ongoing intervention was matched to the persistence of depression, with patients reporting more symptoms contacted more frequently by care managers monitoring symptoms

and antidepressant use and providing feedback to the PCPs. Patients whose symptoms persisted were encouraged to visit their PCP. By 24 months, 74% of enhanced and 41% of usual care patients met criteria for remission, so that the continuation of care management resulted in significantly higher remission rates.

Conclusion

Further targeting of treatment to individual patients considered to be at risk seems a rational way to improve long-term patient outcomes. Results of the 4 studies that incorporated recurrence and chronicity prevention strategies to test this hypothesis in primary care populations varied. The only study to report 1-year relapse rates found no evidence for additional protective effects of RPP over usual care. Only one study did clearly demonstrate superiority of this approach.

3.5   Relapse / recurrence prevention in other care settings

Since there is a lack of studies performed in primary care, we looked elsewhere for information on potentially more effective relapse/recurrence prevention strategies to improve long-term depression outcome. We performed a new search of the depression literature , now focusing on research conducted in non-primary care settings (outpatient care, community settings) with treatment targeted specifically at high-risk factors. The main findings of this additional search will be described briefly in this section.

    In the outpatient setting, issues concerning the long-term outcome of MD and consequences for it's treatment have already been evident longer. Several longitudinal studies had shown depression as a disorder characterized by high risks of relapse and recurrence, despite treatment (Keller 1994; Mueller et al. 1999). Much research in this setting focused on the potentially protective effects of continued AD use in those considered to be at high risk, which is now generally defined as three or more previous episodes (see guidelines). Evidence shows that this is effective in reducing relapse/recurrence rates (Melfi

et al. 1998; Geddes et al. 2003) although still not much information is available on necessary length of AD treatment, and compliance remains an issue.

In comparison, psychological interventions specifically aimed at improving long-term outcome were only developed and evaluated fairly recently. Although IPT was the first psychotherapy to be examined for its benefits as a maintenance therapy in outpatients (Frank et al. 1990;1991), the field seems to be dominated by studies investigating the effectiveness of various versions of CBT , either targeted at persistent or residual symptoms after treatment with AD (Fava et al. 1996, 1998a , Paykel et al. 1999; Scott et al. 2000) or at patients with recurrent depression (Fava et al. 1998b, 2004; Jarrett et al. 2001). Also, new therapies have been developed that often integrate elements of other therapies , such as the cognitive behavioral-analysis system of psychotherapy (CBASP; McCullough, 2000) and mindfulness-based cognitive therapy (MBCT; Segal et al. 2002).

Promising findings from these studies add to the evidence that this targeted strategy is effective with outpatients. For example, Paykel and Scott found lower relapse rates in outpatients who had previously recovered with AD but continued to suffer from residual symptoms, for which they then received CBT (n = 80). Over a period of 17 months , fewer CBT than UC patients suffered a relapse (23 % of CBT and 35 % of usual care patients respectively). Recently, results of an extended follow-up of this patient sample were published (Paykel et al. 2005). Findings indicated that CBT delayed recurrences, that were spread more evenly for CBT than for UC patients over a 6 year-period. Nevertheless, although protective effects of CBT had seemed to persist for some time, no significant differences in total recurrence rates were present and 60 to 65% of all patients had experienced at least one recurrence in this period.

In the study by Jarrett and associates (2001) the hypothesis that continuation-phase cognitive therapy (C-CT) would reduce relapse rates more than acute phase CT only in outpatients with a history of recurrent MD tested. Patients who had responded to acute CT (n = 84) were subsequently randomized to either 8 months of C-CT (10 additional sessions) or to a control group (assessment only). The C-CT explicitly focused on residual symptoms,

maintaining skills to prevent relapse / recurrence and the (further) development of coping strategies to face identified personal vulnerabilities. After these 8 months, 10% of C-CT patients versus 31% of the controls had experienced a relapse, demonstrating that the addition of specific continuation CT was more effective.

CBASP was developed specifically for the treatment of chronic and recurrent MD. This manualized therapy combines elements from behavioral, cognitive, psychodynamic and interpersonal techniques to achieve more effective coping and improvement of interpersonal social skills (Keller et al. 2000). In the literature CBASP is described as being more structured and directive than IPT and as different from CBT by focusing primarily on interpersonal interactions. Klein and associates (2004) report on 1 year effects of CBASP in remitted outpatients (n = 82) who were assigned to monthly maintenance CBASP-sessions or to assessment only, without any formal treatment. Recurrence rates were significantly lower in the CBASP-patients (11% versus 32% in the other participants), demonstrating that sustained remission can be achieved through low-intensive continuation of the therapy to which patients had responded in an earlier stage.

Effectiveness of relapse and recurrence prevention strategies have in recent years also been studied in convenience samples . Again, CBT in most cases is the treatment of choice. Ma and Teasdale (2004) conducted a RCT to examine 1-year protective effects of a novel form of group therapy, MBCT. This is described as a manualized skills-training program, based on an integration of aspects of traditional CBT for MD and components of a stress reduction program (Teasdale *et al.* 2000). Effects were evaluated in a sample (n=75) of individuals with a history of recurrent MD who were recruited from primary care practices and through media advertisements. Over a period of 14 months, 39% of the MBCT patients versus 62% of the control patients experienced a relapse or recurrence (these are not presented separately). Protective effects of MBCT were strongest in those with at least 3 previous episodes , constituting roughly 75% of the sample. Although promising, the benefit of MBCT in this study might be somewhat exaggerated given that the control condition could also

include no treatment at all. Service use data show that about 65 % of control patients had no depression-related visits with their GP during the study period, fewer than 30% received a form of professional mental health support and around 35% used AD for at least part of the time.

Finally, a recent study in the Netherlands by Bockting and coworkers (2005) also focused on protective effects of group CT in individuals with recurrent MD, who were in remission at study entry. Patients included in this RCT were recruited through media announcements (69%) and at outpatient psychiatric centers (31%). Patients were randomized to either group CT or assessment only and followed up for 2 years. Main findings show that group CT was effective in reducing relapse/recurrence, but only in patients with five or more previous episodes (41% of the total sample). Of special interest is that this difference in relapse/recurrence rates was achieved in the first 3 months and remained stable over FU. No significant differences were found in AD use and psychological treatment, either in treatment of the last episode before study entry (when about 60% received a combination of psychotherapy/counselling with AD) or during the 2 year study period (41 % treated with combination of 'pills and talk'). Thus, effect of 8 weeks of group CT seemed not to be moderated by various other treatments.

Conclusion

Risk factors for unfavorable long-term outcome that are the target for specific continuation- or maintenance-therapy , are mainly incomplete recovery (residual symptoms) and recurrent major depression, with growing evidence that the number of previous episodes is also of relevance. Study findings demonstrate the growing evidence base for effectiveness of this targeted approach in reducing relapse /recurrence rates over time. The mechanism behind this success is probably that patients learn to integrate certain protective skills in their daily life and behavior, while the additional provision of regular monitoring contacts acts as a kind of booster. Nevertheless, these findings also underscore the persistent nature of MD since in many cases relapse and recurrence continued to be the rule, rather than the exception.

4   General conclusions

Given that major depression often follows a chronic course, with few people having only one isolated episode and primary care in many cases being the main treatment setting, the core question we wanted to answer with this systematic literature search was: what is an effective method to improve long-term outcome for depression in primary care?   Summing up the results of the reviewed studies, we can conclude that :

1: Training of PCPs, which has long been thought of as the major vehicle for improving depression outcomes, has not fulfilled its promise. On its own, this appears ineffective in achieving better long-term outcome.

2: Supporting PCPs by enhanced treatment and collaborative care may result in improved short-term outcomes, but does not seem to prevent recurrence. No solid evidence is available that supports claims of increased effectiveness over usual care. Thus, beneficial effects of adding psychiatric consultation , counselling or psychotherapy (CBT, IPT) to usual care do not appear to persist over time.

3: Quality improvement strategies, adressing both the contents of treatment as well as the broader care context in which treatment is delivered , show improved outcomes at 6 months though at present there is still limited evidence for it's effectiveness over usual care. There is some evidence of longer term effectiveness. Interpretation of QI-findings is complicated by the great diversity and exact contents of the treatment that patients across conditions actually received.

4: It as as yet inconclusive whether the approach in which tailored interventions aimed at prevention of relapse, recurrence and chronicity or targeted at specific high-risk patients succeed in improving long-term course and outcome of depression.

5: Studies involving targeted approaches in outpatient or convenience samples, show that psychotherapy (especially -individual or group- CBT) can have protective effects on the longer run. These findings challenge the assumption of continued use of antidepressants as the only tool to prevent relapse and recurrence.

Implications

Improving the detection and accuracy of diagnosing and treating depressive disorders in primary care has always received much attention. However, the idea that improved recognition would automatically result in more adequate treatment and hence, a better prognosis, has proven to be too optimistic. Active and sustained follow-up of patients to monitor depression course and outcome, including persistence of residual symptoms and early signs of relapse/recurrence, and to support patients' self-care skills where possible, may be required. Assigning such care management tasks to nurses or (other) professionals cooperating with PCPs is mostly well-received and feasible, but as main findings of this review show, effectiveness on the longer run is as yet undecided. Although certainly progess has been made, most studies have not demonstrated succes in the prevention of recurrence and chronicity of major depresion and moreover, with some exceptions, no excess benefit over usual care was demonstrated; the exceptions concern US-based studies , which might point at differences in the nature and quality of usual care between the US and Europe. Unfortunately, we did not find a clear answer to our question. We conclude that for improving the long-term outcome of major depression in primary care new directions are needed to resolve the problems.