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Improving long-term outcome of depression in primary care: a review of RCTs with psychological and supportive interventions

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ABSTRACT – *Background and objectives:* Depression is often a recurrent or persistent disorder. Since the majority of depressed patients are treated in primary care, it is clear that to improve 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 tested in randomized controlled trials in primary care, reporting at least six months effects on depression course and outcome.

Results: Four strategies were identified: (1) training primary care physicians (PCPs) – this appears ineffective (2) supporting PCPs by other professionals – this produces better short term outcomes but does not prevent recurrence (3) organisational quality improvement – this shows improved outcomes at 6 months, and there is some evidence of longer term effectiveness; and (4) recurrence – and chronicity prevention strategies – these have not been shown to be effective.

Conclusion: Since effects of the reviewed strategies generally do not seem to persist over time and no clear superiority over usual care has been demonstrated, we conclude that for improving long-term outcome of depression in primary care new directions or even a novel paradigm is needed.

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Introduction

The majority of depressed patients are treated in primary care[1], but the appropriateness of this situation has been questioned. Especially from a long-term perspective, not all treatment is effective[2].

Evidence-based, standardized management guidelines for the treatment of depression in primary care have been available since the 1990's[3,4]. 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. However, many patients do not recover or only partially, while about a fifth has episodes lasting more than a year and the relapse rate is high, in particular in those patients who achieve only partial remission[5-7]. In sum, the need for more effective treatment for patients who do not recover within a few months is clear.

In the present paper, we critically review approaches to improve routine care for depression and ask whether it succeeds in improving long-term outcome (≥ six months) in primary care patients?

Methods

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. Central search terms were major depression / depressive episode; primary care treatment; and randomized controlled (clinical) trial. The following terms were added to each of these central 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. Finally, we used reference lists from selected publications.

Selection criteria

Studies were included if they were:

- randomized controlled trials (RCTs)
- conducted in primary care
- reporting at least six months patient outcome data
- comparing psychological treatments or supportive interventions
- with care as usual (CAU) by the primary care physician
- for adult patients (≥ 18 years),
- with major depression (DSM-IV) or depressive episode (ICD-10).

Studies comparing effectiveness of psychotherapy and pharmacotherapy with CAU 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[8,9]. Furthermore, we excluded studies limited to selected patient groups such as the elderly. Finally, publications had to be available in English.

Depression diagnosis had 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 study, hence on an intention-to-treat basis.

Results

We identified four approaches.

Training primary care physicians

Historically, the oldest wave of efforts to improve depression outcomes in primary care focused on education and training of primary care physicians (PCPs). However, studies that have evaluated clinical effectiveness of these programs generally show that they are well received but fail to achieve substantial or enduring improvements in depression outcomes[10-15]. For that, more elaborate strategies seem warranted.

Supporting the PCP by other professionals

Key characteristic of the second strategy to improve treatment of depression in primary care is the involvement of other (mental health) professionals such as psychiatrists, social workers, counsellors, psychologists, and nurses. We identified eight studies about this approach that fitted our criteria: 1 on consultation liaison psychiatry; 4 studies on counselling and 3 on psychotherapy (see Table I).

Consultation Liaison Psychiatry (CLP)

Patients in the CLP condition in the study of Katon et al.[16] had alternating visits with the PCP and a psychiatrist, receiving education and antidepressant monitoring. PCPs in the CLP–arm were also offered education and case by case consultation. Forty-two percent of included patients were diagnosed with MD. After seven months, more of the patients receiving CLP (75%) had improved than usual care patients (44%). However, at 19 months no such difference was left[17,18].

Counselling

All four counselling studies were from the United Kingdom (UK). Counsellors came from diverse professional backgrounds and used a variety of models and techniques, from "reflective listening to enable the patient to resolve their own difficulties"[19], to psychotherapeutic techniques, more directive advise and the provision of practical help.

Only in the study of Simpson et al.[20], counselling was more effective than usual care; 52% patients recovered in the counselling condition and 36% in the usual care condition. Compared to the other three studies, this study included only patients with chronic depression and the intervention was psychodynamic counselling, where the other studies offered more general forms of counselling, called social work counselling[21,22], non-directive counselling[23,24] and generic counselling[25].

Two of these counselling studies incorporated patient preference arms in the design, but in neither did this choice of treatment confer additional benefit on outcome.

Psychotherapy

We selected four psychotherapy studies, including the counselling study of Ward et al.[23]; two were carried out in the UK and two in the United States of America (USA).

Table I
Enhanced treatment and collaborative care programs.

Author(s) Country	Conditions	Patient Sample	Depression outcome measure	Last follow-up + attrition	Results
Consultation liaison psychiatry					
Katon et al.[16] Lin et al.[17,18] USA	Consultation Liaison Psychiatry (CLP); 8 weeks, continuations phase, 3-7 months Usual care	N = 217 CLP; n = 108 Usual care; n = 109 78% ♀; mean age: 47	Inventory of Depressive Symptomatology	19 months response: ?	7 months: More improvement in CLP condition 19 months: no difference
Counselling					
Corney[21,22] UK	Counselling; max. 6 months Usual care	N = 80 Counselling; n = 41 Usual care; n = 39 100% ♀; mean age: 29	Clinical Interview Schedule	6 months response: 100%	No difference
Ward et al.[23] King et al.[24] UK	Counselling; mean 6.4 sessions Cognitive behavioural therapy (CBT); mean 5 sessions Usual care; mean 9.1 contacts	N = 464 Counselling; n = 181 CBT; n = 214 Usual Care; n = 69 (preference; n = 137) 77% ♀; mean age: 37	Diagnosis ICD-10 Clinical Interview Schedule Beck Depression Inventory	12 months response: 81%	No difference
Chilvers et al.[25] UK	Counselling; 6 sessions Antidepressants by own PCP	N = 323 Counselling; n = 192 Antidepressants; n = 131 (preference; n = 220) 75% ♀; mean age: 37	Research Diagnostic Criteria Beck Depression Inventory	12 months response: 64%	No difference
Simpson et al.[20] UK	Psychodynamic counselling; 6-12 sessions Usual care; mean 5 contacts	N = 145 Psychodynamic counselling; n = 73 Usual Care; n = 72 80 % ♀; mean age: 43	Beck Depression Inventory	12 months response: 80%	More recovery in counselling condition

Table I (continue)

Author(s) Country	Conditions	Patient Sample	Depression outcome measure	Last follow-up + attrition	Results
Psychotherapy					
Schulberg et al.[27] US	Interpersonal therapy (IPT) acute (16 sessions 1/ wk) + continuation (4 sessions 1/mth) Antidepressants (AD) acute (bi- weekly visits during 16 wks) + continuation (4 visists / 1 month) Usual care	N = 276 IPT acute + continuation; n = 93 AD acute + continuation; n = 91 Usual care; n = 92 83 % ♀; mean age: 38	Diagnosis: DSM-III-R Hamilton Rating Scale for Depression	8 months response = ?	IPT and AD more effective than usual care. No difference between IPT and AD
Scott et al.[29] UK	Brief cognitive therapy (BCT); mean 7 sessions Usual care; n = 24	N = 48 BCT; n = 24 Usual care; n = 24 67% ♀; mean age: 41	Diagnosis: DSM-III-R Beck Depression Inventory Hamilton Rating Scale for Depression	58 weeks response: 50%	No difference
Katon et al.[30] Lin et al.[17,18] USA	Brief cognitive behavioural therapy (BCBT); 4-6 sessions, monitoring to 24 weeks Usual care; n = 76	N = 153 BCBT; n = 77 Usual care; n = 76 74 % ♀; mean age: 47	Symptom Checklist (SCL-90) depression scale Inventory of Depressive Symptomatology	19 months response: 77%	7 months: More improvement in BCBT condition 19 months: no difference

Therapies that were tested are: interpersonal therapy (IPT; 1 study), cognitive therapy (CT; 1 study) & cognitive behavioural therapy (CBT; 2 studies).

IPT is aimed at improving interpersonal skills and learning more effective strategies for dealing with the stressors associated with depression[26]. The study carried out in the USA by Schulberg et al.[27,28] compared IPT with antidepressants and usual care by the PCP. At eight months follow-up significantly more patients in both the IPT (46%) condition and the antidepressants (48%) condition had recovered than in the usual care (18%) condition.

CT and CBT aim at modifying negative thoughts and beliefs and thereby also change behaviour that might be dysfunctional and contributing to (maintenance of) depression. Ward et al.[23] found similar 1-year outcomes for CBT, counselling and usual care. Another British study by Scott and colleagues[29] demonstrated better outcomes in the CT condition over usual care on the short-term, but not after a year.

In the USA, Katon and co-workers[30] developed a structured program in which PCPs cooperated with psychologists who provided brief CBT (including a video and book) and monitored antidepressant adherence. 43% of the patients met criteria for MD. After 7 months more MD-patients in the CBT condition had improved compared to usual care (70% vs. 42%). At 19 months, no differences in outcome were left and 37% of all patients had experienced a relapse[17,18].

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[31,32]. These approaches not only address the contents of depression treatment, but also the context and organization in which this treatment is delivered (see Table II).

Practice support by nurses or care managers

We found four studies in which nurses or care managers actively follow the patients, mainly by telephone, to support patients in adhering to their antidepressant medication, monitor their symptoms, and give feedback to their PCP. Generally, these studies showed that more patients in the experimental conditions improved (varying from 55% to 60%) than in the usual care condition (varying from 38% to 47%). However, in all four studies follow-up time was limited to 6 months.

Some aspects need further attention. In the Nurse Telehealth Care (NTC) study of Hunkeler et al.[33], additional peer support by trained volunteers was offered in a third condition, but no additional effects were found. In their first study, Simon and colleagues[34] found that a feedback and care management program (FCM) was more effective than written feedback alone or usual care. However, in their second study[35], no additional beneficial effects of FCM over usual care were found. Interestingly, patients receiving an FCM version that included brief CBT by telephone, improved more than patients in both other conditions.

Comprehensive practice-level quality improvement strategies

Two studies in the United States report about elaborate practice-level strategies to improve depression management.

In the "Quality Enhancement by Strategic Teaming" ('Quest') strategy[36-38] the roles of all members of community primary care

Table II
Quality Improvement of Depression care.

Author(s) country	Conditions	Patient sample	Depression outcome measure	Last follow-up + attrition	Results
Practice support by nurses or care managers					
Hunkeler et al.[33] USA	Nurse Telehealth Care (NTC); mean 10 calls NTC + peer support; 6 months Usual care	N = 302 NTC; n = 117 NTC + peer support ; n = 62 Usual care; n = 123 69% ♀; mean age: 55	Hamilton Rating Scale for Depression Beck Depression Inventory	6 months response: 85%	More improvement in NTC conditions. No additional effect of peer support.
Simon et al.[34] USA	Written feedback (WF) after 8 and 16 weeks Feedback and care management (FCM) by telephone at inclusion, 8 and 16 weeks Usual care	N = 613 WF; n = 221 FCM; n = 196 Usual care; n = 196 72% ♀; mean age: 47	Structured Clinical Interview –Depression module	6 months, response: 94%	More improvement in FCM condition compared to WF and usual care. WF not more effective than usual care.
Simon et al.[35] USA	Feedback and care management (FCM) by 3 calls + personalized mailed feedback FCM + telephone brief CBT; about 4 sessions Usual care	N = 600 FCM ; n = 207 FCM + telephone brief CBT; n = 198 Usual care; n = 195 75% ♀; mean age: 44	Symptom Checklist depression scale Patient rated global improvement	6 months, response: 89%	More improvement in FCM +CBT condition compared to FCM and usual care. No difference between FCM and usual care.
Dietrich et al.[52] USA	Care management (CM); 6 months, monthly and as needed Usual Care	N = 405 CM; n = 224 Usual Care; n = 181 80% ♀; mean age: 42	Diagnosis: DSM-IV HSCL-20	6 months response: 80%	More improvement in CM condition
Comprehensive practice-level quality improvement strategies					
Rost et al.[36,38] USA	Quality Enhancement by Strategic Teaming (QUEST); mean contacts 5,2 Usual care	N = 479 QUEST; n = 239 Usual care; n = 240 84% ♀; mean age: 43	Center for epidemiologic tudies-Depression scale DSM-IV	6 months response: 90%	More improvement in QUEST condition
Wells et al.[39,40] + Sherbourne et al.[41] USA	Quality Improvement Medication support (QI-M); 6-12 months Quality Improvement Therapy (QI-T); 4 (brief) or12-16 sessions (group) Usual care; n = 443	N = 1356 QI-M; n = 424 QI-T; n = 489 Usual care; n = 443 71% ♀; mean age: 44	Composite Diagnostic Interview Schedule Center for epidemiologic studies-Depression scale	57 months response: 73%	6 and 12 months: more improvement in QI-M and QI-T condition 24 and 57 months: more improvement in QI-T condition only

practice teams were redefined: administrative staff was trained to screen and recruit patients meeting criteria for major depression; nurses were trained to be able to provide education and monitor adherence to treatment and progress; and PCPs received a brief training in guideline concordant treatment. At six months follow-up, patients in the QUEST-practices showed more improvement in depressive symptoms than patients treated in usual care settings. However, this was only the case for patients that had started with a new treatment; patients with persistent symptoms despite recent treatment did not benefit.

The quality improvement (QI) program in the Partners in Care study[39-41] included: a 2-day basic depression management training package to primary care providers, nurses and therapists; enhanced resources for antidepressant treatment (QI-M; with support of a nurse care manager) or (individual or group) CBT (QI-T). 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 major depression and/ or dysthymia. At the 2- and 5-year follow-up the therapy version of QI (i.e.: CBT) was found to have more sustained benefits than both other conditions. However, interpretation of these results is complicated. By design, this study did not randomly assign patients to specific treatments but rather randomized opportunities for getting appropriate depression care[42], so that actual treatment that patients received may not have been that different across conditions.

Interventions aimed at reduction of relapse, recurrence and persistence of depression

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 strategy. The studies are summarized in Table III.

Katon and co-workers[43-45] conducted two studies. One was targeted at patients with persistent symptoms of depression, who received CLP as described in 3.2. While this strategy was more effective than usual care on the short run, no differences were present after two years. The other intervention was aimed at patients who were recovered but considered to be at high risk for relapse. They received a Relapse Prevention Program (RPP) that focused on the continued use of antidepressants, systematic monitoring of symptoms and the development of a personal relapse prevention plan[46]. Similar relapse rates (35%) over 1 year show that the RPP did not result in improved outcome over usual care.

In the Netherlands, Smit and colleagues[47,48] replicated the RPP study of Katon et al. with an adapted version (the Depression Recurrence Prevention (DRP) Program[49]) aimed at 'new' as well as chronic patients. This enhanced care did not lead to better 6-months outcomes compared to usual care. Furthermore, there were no indications for any surplus effects of addition of a psychiatric consultation or CBT to the DRP.

Finally, Rost et al.[50] evaluated effects of enhanced care (EC) targeted at patients still reporting many depressive symptoms after being treated for 6 months. The 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 the practice. By 24 months, more EC than usual care patients (74% vs. 41%) met criteria for remission.

Table III
Primary care interventions aimed at reducing risk of relapse, recurrence, chronicity.

Author(s), Country	Conditions	Patient sample	Depression outcome measures	Last follow-up & attrition	Results
Katon et al.[43,45] USA	Consultation Liaison Psychiatry (CLP): 2-4 visits Usual care	n = 228 CLP; n = 114 Usual care; n = 114 74% ♀; mean age: 47	Structured Clinical Interview-depression module Symptom Checklist, 20 item version	28 months, response: 75%	6 months: more recovery in CLP condition 28 months: no difference (only moderate severe depressed patients in CLP improved more)
Katon et al.[44] USA	Relapse Prevention Program (RPP): 1 year Usual care	N = 368 RPP: n = 194 Usual care; n = 192 74% ♀; mean age: 46	Structured Clinical Interview-depression module Symptom Checklist, 20 item version LIFE interview	12 months response: 85%	No difference
Rost et al.[50] USA	Enhanced care with continuation phase (EC); 6 months plus max. 2 year continuation; mean contacts: 5 Usual care	N = 211 (EC) n = 115 Usual care; n = 96 84% ♀; mean age: 43	Modified Center for epidemiologic studies-Depression Scale	24 months response: 67%	More remission in EC condition
Smit et al.[48] The Netherlands	Depression Recurrence Prevention Program (DRP); max 36 months Psychiatric consultation (PC)+DRP Cognitive Behavioural Therapy (CBT) +DRP; Usual care	N = 267 DRP; n = 112 PC+DRP; n = 39 CBT +DRP; n = 44 Usual care; n = 72 63% ♀; mean age: 43	Composite Diagnostic Interview Schedule	6 months response: 85%	No difference

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 does not achieve improvements in long-term depression outcome.

2. Enhanced and collaborative care may result in improved short-term outcomes, but do not appear to prevent recurrence.

3. Quality improvement strategies do show improved outcomes at 6 months, and there is some evidence of longer term effectiveness.

4. It is as yet inconclusive whether tailored interventions aimed at prevention of relapse, recurrence and chronicity succeed in improved long-term depression outcome.

Unfortunately, we did not find a clear answer. Most studies have not demonstrated success in the prevention of chronicity. Maybe new directions are needed to resolve the problems. Parker[51] has stated that the present concept of major depression had led to sterility in depression research and clinical practice. For instance, it has become the convention to neglect all differentiations which exist among patients. However, findings in this review illustrate how often different results are found for different subgroups of patients in terms of severity and duration. Diversity goes further than that and also exists in the way patients (and their loved ones) deal with their depression and if and where they seek help for their problems. Therefore, we conclude that to improve the long-term outcome of depression in primary care, we should not persist in doing 'more of the same', but instead search for new directions or even a novel paradigm.

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