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Research paper

The ten-year course of depression in primary care and long-term effects of psychoeducation, psychiatric consultation and cognitive behavioral therapy

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ABSTRACT

Background: While the majority of depressed patients are treated in primary care, long-term follow-up data on the naturalistic course of depression and treatment effectiveness in this setting are scarce. This study examined the ten-year course of depression in primary care patients who had participated in a randomized clinical trial aiming at enhancement of depression outcomes.

Methods: Of the original sample (n=267), 166 patients participated in the ten-year follow-up; missingness was random. Four treatments were compared: (1) Care As Usual (CAU; n=51); (2) a Psychoeducational Prevention program (PEP; n=68); (3) Psychiatric Consultation followed by PEP (PC+PEP; n=21); and (4) brief Cognitive Behavioral Therapy followed by PEP (CBT+PEP; n=26). During the first three years interviews based on the Composite International Diagnostic Interview (CIDI) were three-monthly applied, the seven years thereafter were assessed with a once applied CIDI and a face-to-face life chart-based interview.

Results: During the ten-year follow-up 76.5% of the patients developed a new depressive episode, 83.4% used antidepressants (median usage 3.1 years), median depression diagnosis-free time was 9.0 years, and median residual symptom-free time 3.8 years. Treatments did not significantly differ on these outcomes, only trends appeared for lower depression severity for CBT+PEP, and, along with PEP, a higher proportion of symptom-free time.

Limitations: Assessment with the once applied life chart interview (a valid and reliable instrument) is less precise than the three-monthly assessments during the first three years.

Conclusions: The long-term course of depression in primary care is unfavorable, whereas treatment effects over time seem absent or small.

1. Introduction

Depression is a very common disorder, as is marked by its lifetime prevalence of 16.6% (Kessler et al., 2012). The unfavorable long-term course of depression is characterized by very high relapse rates (Mueller, 1999; Solomon, 2000; Simon, 2000), substantial residual symptomatology (ESEMeD/MHEDEA 2000 consortium, 2004a), serious impairment, and high health care costs (Kessler, 2005). Moreover, about 10–20% of all cases run a chronic course (Eaton et al., 2008).

Most naturalistic long-term studies concern either community (e.g. Spijker et al., 2001) or psychiatric samples (e.g. Keller et al., 1992). Examining the long-term naturalistic course of depression in primary care, however, is of particular interest because most depressed patients are treated in this setting (ESEMeD/MHEDEA 2000, 2004b). Nevertheless, such studies are rare and have limitations, including relative short follow-up periods, i.e. 18 months (Vuorilehto et al., 2009) to three years (Stegenga et al., 2012). The studies that covered long-term follow-up, e.g. five to 23 years, were comprised because of the method applied, i.e. historical case record examination that did not allow for the assessment of continuous depression outcomes and yielded uncertain diagnosis rates (Van Weel-Baumgarten et al., 1998; Wilson et al., 2003), or, although applying DSM diagnostic criteria using a life chart interview, examined a small sample (Yiend et al., 2009).

The knowledge that is available about the unfavorable short- and medium-term course of depression in primary care (Vuorilehto et al., 2009; Stegenga et al., 2012) underscores the need for effective treatment. Antidepressant medication, the most widely applied treatment strategy, has proven effective in both the acute phase (Cipriani et al., 2009), and at long-term follow-up when applied as maintenance treatment (Geddes et al., 2003). Discontinuation of antidepressants, however, is associated with a return of the risk of relapse (Dobson

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et al., 2008; Huijbers et al., 2016), which is problematic, since long-term compliance may not be realistic. A low-intensity alternative to pharmacological interventions is disease management consisting of psychoeducation and motivational techniques. A meta-analysis (Cuijpers et al., 2009) revealed small effects of such low-intensity treatments on depression severity. Cognitive Behavioral Therapy (CBT) shows more favorable outcomes than psychoeducation, with moderate to large effect sizes, which is comparable to other psychotherapies or pharmacotherapy (Cuijpers et al., 2013).

Problematic, however, is that most of the mentioned treatment effectiveness studies are confined to acute phase treatment or at best medium-term follow-up effects of up to two years. A meta-analysis by Steinert et al. (2014) on longer-term treatment effects identified 11 randomized clinical trials (RCTs) with an average follow-up duration of 4.4 years, including the original RCT on which the current long-term follow-up study is based (Conradi et al., 2007). It was found that psychotherapy (mainly CBT), resulted in significantly less relapse than non-psychotherapeutic treatments (mainly care as usual, medication and psychoeducation), i.e. 53.1% vs. 71.3% respectively. Primary care-based long-term treatment studies, however, are absent.

The fact that only 11 longer-term treatment studies were identified is due to high costs associated with conducting such trials, but also with methodological problems like increasing attrition rates and the mounting effect of potential confounders as additional care seeking and medication use. This makes it harder to unravel the effect of the treatment to which patients were originally randomized and that of additional care. To complicate matters further, the treatment to which the patients were originally randomized may also affect the degree to which they consume additional care thereafter.

Taken together, more insight into the long-term course of depression and treatment effects in primary care is needed. In the current study we covered a follow-up of ten years after a randomized treatment phase of several months, and studied the course of depression during this ten-year period in terms of medication use, health care utilization, relapse/recurrence rates, duration of depression diagnosis-free time and symptom-free time, and severity of depression. We examined:

(1) as the main objective of the study the naturalistic long-term course of primary care depression by assessing the course of the outcomes in all available participants;

(2) and as a secondary more explorative study aim the potential differential long-term treatment effectiveness by comparing the outcomes across the four treatments to which patients were originally randomized, i.e. Care as Usual (CAU) by the general practitioner (GP), the Psychoeducation Prevention program (PEP), Psychiatric Consultation followed by PEP (PC+PEP), and CBT followed by PEP (CBT+PEP). The original study revealed no differences in the medium-term on most outcome measures except for PC+PEP and CBT+PEP showing lower severity of depression over the three-years follow-up (Conradi et al., 2007). Based on this finding and previous research showing favorable outcomes of CBT (Cuijpers et al., 2013) we anticipated CBT+PEP to have the most favorable long-term course. Although PC+PEP also showed lower depression severity at the three-year follow-up, prior research shows that favorable outcomes of antidepressants only hold when applied as maintenance treatment (Geddes et al., 2003). Because compliance during the ten-years period we studied, however, may not be realistic, this inevitably will result in an increase of the risk of relapse (Dobson et al., 2008; Huijbers et al., 2016). Therefore we anticipated a less favorable outcome with PC+PEP.

2. Methods

2.1. Patients and procedure

We sought to contact all patients who were included in the original RCT (INSTEL), conducted in primary care between January 1998 and June 2003 (for details see Conradi et al., 2007). Inclusion criterion for INSTEL was meeting criteria for a current or recent Major Depressive Episode (MDE) treated by the GP. Exclusion criteria were suffering from a life-threatening somatic disease, meeting criteria for bipolar disorder, psychosis, substance abuse or dependency, dementia, being pregnant, or being already in psychotherapy for depression. Originally, 267 patients were randomized to one of four treatments: CAU (n=72), PEP (n=112), PC+PEP (n=39) or CBT+PEP (n=44). Because CBT+PEP and PC+PEP were expected to have greater positive effects than PEP-only in comparison to CAU, fewer patients were randomized to these two treatments. CAU consisted of brief supportive counseling, possible antidepressant prescription, and/or referral according to clinical guidelines. PEP was a low-intensity psychoeducation-based program consisting of three face-to-face sessions and short quarterly telephone contacts in the three years thereafter. In the PC+PEP condition one session with a psychiatrist, mainly focusing on antidepressant medication, preceded PEP, and in the CBT+PEP arm on average 10 sessions of CBT were provided prior to PEP. Patients in the INSTEL study were followed-up for up to three years (average 2.75 years; SD=0.48). The INSTEL study was approved by the Medical Ethics Committee of the University Medical Center Groningen (MEC96/02/028c).

The present Long-Term INSTEL (LTI) follow-up study took place between October 2010 and June 2012. After consent from their GP, patients were contacted by mail and subsequently by telephone. After reading the information brochure 166 patients signed the informed consent; CAU (n=51), PEP (n=68), PC+PEP (n=21) and CBT+PEP (n=26). Next, they were face-to-face interviewed by an experienced research assistant for about two hours. The procedure was approved by the Medical Ethics Committee of the University Medical Center Groningen (METc2009.319). Patients received a 15 euro coupon for participation.

2.2. Instruments

Outcomes during the three-year follow-up of the INSTEL study were assessed with the Composite International Diagnostic Interview (CIDI Auto 2.1; WHO, 1997; Ter Smitten et al., 1998) a valid and reliable structured interview (Wittchen, 1994). The lifetime CIDI was administered face-to-face at baseline and the end of follow-up concerning the previous three years. In-between a slightly adapted version of the CIDI was administered three-monthly by telephone. The adapted version contained additional questions probing onset and remission of each of the DSM-IV symptoms, subsequently allowing determination of diagnosis, duration of depressive episodes, depression-free time and symptom-free time. Questions with respect to medication and health care utilization were added.

Outcomes concerning the seven years after the end of the INSTEL study, i.e. the LTI follow-up, were covered by two face-to-face interviews at the patient's home in a single two hour session. First, as in INSTEL, the lifetime CIDI was administered. The CIDI contained extra questions with which month and year of onset and remission of the identified MDEs were established and subsequently duration of depression-free time. Second, a version of the Longitudinal Interval Follow-up Evaluation (LIFE) life-chart based interview as used by Yiend and colleagues (2009) was administered to measure month-by-month severity of depression and proportion of symptom-free time during the follow-up. The LIFE has shown good to excellent ICCs (Keller et al., 1987). Research has shown that retrospective long-term recall is a valid method when accompanied with proper anchoring of major events (Wells and Horwood, 2004). Therefore we provided patients with three types of anchor points. First, interviewers and patients spent approximately one hour to identify key personal and historical events that were used as aids for retrieval of severity of depressive complaints. These events were: relationships (start, crises and breakup), education and work (exams and change of jobs of self, partner and children), housing (moves), birth, diseases and death (self