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The clinical effectiveness of concise cognitive behavioral therapy with or without pharmacotherapy for depressive and anxiety disorders; a pragmatic randomized controlled equivalence trial in clinical practice

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ABSTRACT

Background: Depressive and anxiety disorders contribute to a high disease burden. This paper investigates whether concise formats of cognitive behavioral- and/or pharmacotherapy are equivalent with longer standard care in the treatment of depressive and/or anxiety disorders in secondary mental health care.
Methods: A pragmatic randomized controlled equivalence trial was conducted at five Dutch outpatient Mental Healthcare Centers (MHCs) of the Regional Mental Health Provider (RMHP) 'Rivierduinen'. Patients (aged 18–65 years) with a mild to moderate anxiety and/or depressive disorder, were randomly allocated to concise or standard care. Data were collected at baseline, 3, 6 and 12 months by Routine Outcome Monitoring (ROM). Primary outcomes were the Brief Symptom Inventory (BSI) and the Web Screening Questionnaire (WSQ). We used Generalized Estimating Equations (GEE) to assess outcomes.
Results: Between March 2010 and December 2012, 182 patients, were enrolled ($n = 89$ standard care; $n = 93$ concise care). Both intention-to-treat and per-protocol analyses demonstrated equivalence of concise care and standard care at all time points. Severity of illness reduced, and both treatments improved patient's general health status and subdomains of quality of life. Moreover, in concise care, the beneficial effects started earlier.
Discussion: Concise care has the potential to be a feasible and promising alternative to longer standard secondary mental health care in the treatment of outpatients with a mild to moderate depressive and/or anxiety disorder. For future research, we recommend adhering more strictly to the concise treatment protocols to further explore the beneficial effects of the concise treatment.
The study is registered in the Netherlands Trial Register, number NTR2590. Clinicaltrials.gov identifier: NCT01643642.

1. Introduction

Depression and anxiety disorders are highly prevalent, cause great suffering and disability, and have a large impact on society [4,23–25,40]. Fortunately, several effective psycho- and pharmacotherapeutic treatments are widely applied for these disorders [7]. However, they place a high demand on healthcare services [15,27,32]. Offering these treatments in a more concise form without compromising effectiveness might mitigate this problem [5]. In this paper, we report the clinical results of a pragmatic, randomized controlled equivalence trial. This entails comparing concise and standard care. We tested the hypothesis that concise care is 'as effective as' standard care delivered in a secondary outpatient setting. We focused on patients with mild to moderate illness severity because we assumed that since in most cases their illness is less complicated, they would react more favorable to a concise approach. In both conditions, patients are treated with psycho- and/or pharmacotherapy delivered in routine practice. However, in concise care the treatments are limited in time and in number of (weekly) sessions (maximum 7) and offered as first (brief) step in a stepped-care model [8,17]. Standard care is not confined to a maximum number of sessions or limited time-period [37]. Patient characteristics and treatment effectiveness are assessed with Routine Outcome Monitoring (ROM; [9]), a standard monitoring procedure already in use in the participating outpatient clinics. We hypothesized that concise care is equally effective as (equivalent to) standard care 3, 6 and 12 months after baseline assessment.

2. Methods

The methods were published previously [21] and are summarized briefly here. The Medical Ethics Committee (MEC) of the Leiden University Medical Center (LUMC) approved the study. It involved a

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comprehensive protocol (titled "Psychiatric Academic Registration Leiden database") which safeguarded the anonymity of patients and participants and ensured proper handling of the data. We followed consolidated standards for reporting randomized controlled equivalence trials [18,22,28]. All participants provided written informed consent before study entry.

2.1. Study design and participants

A two-armed pragmatic randomized controlled equivalence trial was conducted at five outpatient Mental Health Clinics (MHCs). These clinics were part of Rivierduinen (RD), a secondary Regional Mental Health Provider (RHMP) in the province of South-Holland, the Netherlands. Eligible participants were patients referred to the MHCs by their general practitioners (GP), aged 18–65 years, and meeting the DSM IV-TR criteria for a primary current diagnosis of anxiety disorder and/or depression, established using the Mini-International Neuropsychiatric Interview-Plus, version 5.0.0 (MINI-Plus; [31,36]). For a list of included diagnoses see Appendix A, Table I. Excluded were patients with suicidal or homicidal risk, severe social dysfunction, delusions, hallucinations and/or suffering from bipolar or psychotic disorders. Other co-morbidity with psychiatric disorders was allowed. The inclusion (and exclusion) criteria for enrolling subjects in this study induced a study sample of patients suffering from mild to moderate anxiety and/or depressive disorders [2]. Insufficient mastery of Dutch was a reason for exclusion. Experienced psychiatrists at the MHCs determined study eligibility [21]. Eligible participants were randomly assigned to concise or standard care and assessed by ROM at baseline (T_1), 3 (T_2), 6 (T_3) and 12 (T_4) months thereafter.

2.2. Randomization and masking

A block randomization scheme, stratified by MHC ($n = 5$) and gender was used. Randomization was carried out by one of the researchers (D.M.). Patients and therapists were informed about the outcome; the psychiatric test nurses responsible for the ROM assessments were not [21].

2.3. Treatment

The treatment protocols in both conditions followed the Dutch and international guidelines for the evidence-based treatment of depressive and anxiety disorders. In both concise and standard care, a choice could be made between pharmacotherapy with a selective serotonin reuptake inhibitor (SSRI; [16], Cognitive Behavioral Therapy (CBT; [3,6]) and, in case of a posttraumatic stress disorder, Eye Movement Desensitization and Reprocessing- therapy (EMDR; [30]). A combination of pharmaco- and psychotherapy was also possible. In *standard care* the number of sessions, start and duration of treatment is variable and treatment could continue during the entire study period of 1 year. On average, psychotherapy is provided in 3–6 months on a weekly basis, but in practice once every 2 to 3 weeks, pharmacotherapy for 1 year or longer [37]. In contrast, *concise care* started within one week after the baseline measurement and had to be given within 7 weeks thereafter. Concise care was initially described as 4 to maximum 7 individual 45-min psychotherapy sessions, depending on the treatment protocol (see also [21]). The pharmacotherapy protocol for depressive and/anxiety disorders in concise care was confined to a maximum of 4 sessions within 7 weeks. Moreover, therapists' treatment choice in both standard and concise care followed the principles of shared decision-making [42,43]. Contrary to standard care, treatment goals and procedures in concise care are clearly established and mutually agreed on, prior to initiating treatment. In addition, treatment success of concise care was evaluated at the end of treatment. When either the patient or therapist is convinced that the clinical effects are insufficient or patients are insufficiently helped by the initial treatments in concise care, 'stepping up' or continuation of (additional) standard treatment, in line with stepped-care principles, was possible [8,17]. Pharmacotherapy in concise care was also evaluated after 7 weeks, and continued when necessary according to the (inter) national clinical guidelines. After implementation changes to the treatment protocols were made at the recommendation of the MHCs; these included extending the treatment duration of concise care to a maximum of 7 sessions in 7–9 weeks. This was to allow treatment continuation of concise care in case of cancelled or missed sessions by therapists or patients.

Therapists providing concise care received a 2 h instruction in the core elements of the intensified psychotherapy and/or pharmacotherapy, as described in the protocols. Therapists in the standard condition did not get additional training [21]. The same therapists were responsible for delivering standard and concise care. All sessions in concise care were audiotaped for post-hoc assessment of treatment fidelity. Sufficient treatment protocol-adherence (>75%) was demonstrated in a random sample of 20 patients with a satisfactory overall agreement between two independent raters (Cohen's Kappa: 0.74).

3. Measures

3.1. Routine Outcome Monitoring (ROM)

ROM is a computer-based system to routinely assess symptom severity and functioning with an extensive battery of psychometric instruments. ROM is administered as part of the intake procedure (at baseline) and repeatedly during and after treatment (de Beurs et al. [9]. In the present trial, measures of participants characteristics were collected at baseline, while symptom measures were administered at each time point (see also [21]). An overview of ROM instruments at the different time-points, is given in Appendix A, Table 2.

3.2. Outcomes

The Brief Symptom Inventory (BSI; [10] and the Web Screening Questionnaire (WSQ [12] constituted the primary outcome measures in this study. The secondary measures used were the Clinical Global Impression (CGI [16] and the Short- Form-36 Health Survey (SF-36; [1,38]. Additionally, patients' satisfaction with their care was explored by The Dutch Mental Healthcare Thermometer of Appreciation by Clients ([20].

3.2.1. Primary outcomes

Brief Symptom Inventory (BSI; [10]. This patient-rated, 53 item questionnaire which is based on the Symptom Checklist (SCL-90 [11] assesses psychopathological symptom severity on a 5-point Likert scale (from 0 'not at all' to 4 'extremely'). The BSI total score, most indicative of general psychopathology, was computed as the mean score of all individual items (range 0–4).

Web Screening Questionnaire (WSQ; [12]. This is a self-rated, 15 item questionnaire which is based on the screening questionnaire (SQ) of Marks and colleagues. It is used as a quick tool to screen patients for most common mental disorders [14]. The WSQ has 8 'yes' or 'no' answers, the other 7 are Likert-type scales. Response was defined as a score above the pre-specified threshold for being diagnosed with any particular WSQ diagnosis [12].

3.2.2. Secondary outcomes

Clinical Global Impression (CGI; [16] This is a clinician rated scale that assesses illness severity. The main item 'severity of illness' measured on a 7-point Likert scale (from 1 'normal, not at all ill' to 7 'among the most extremely ill patients') is used in the present analyses.

The Short Form-36 Health Survey (SF-36; [1,38]. This self-report questionnaire assesses current general health status and quality of life in eight domains (36 items). Measurement scales vary per subscale, ranging from yes/no to answers on 3-, 5-, or 6-point Likert scale. All raw