Blended Care Psychodynamic Therapy or Cognitive Behavioral Therapy versus Face-to-Face Psychotherapy for Depression: A pragmatic multicentre randomized controlled non-inferiority trial

Blended Care vs. Face-to-Face Therapy for Depression (BLENDED)

Study Protocol Synopsis

Version 1.1

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Depression is a highly prevalent disorder with a lifetime prevalence of 15-25%, and is associated with high psychosocial and economic costs (e.g, suicide, absenteeism, long-term disability). Epidemiological research shows that depression is underrecognized and underdiagnosed in Belgium, resulting in very high unmet needs, with more than 50% of patients not seeking professional help in the first year after onset and often taking patients up to 10 years and more to effectively seek professional help (Bruffaerts et al., 2007, 2008). The current lack of capacity of mental health services in Belgium is a major obstacle in attempts to increase access to effective psychotherapy for depression. Centers for Mental Health Care ('Centra Geestelijke Gezondheidszorg', CGGs) in particular are faced with a growing number of patients (+3% per year). Despite their efforts (e.g., by offering more group-based psychotherapy and interventions), CGGs in Belgium are faced with increasingly longer waiting lists. There is therefore an urgent need for (cost-)effective, time-saving interventions in the mental health care system in Belgium.

Both pharmacotherapy and psychotherapy alone or in combination have been shown to be effective in the treatment of depression, and meta-analyses have shown no substantial differences in the efficacy of two of the empirically most validated types of brief face-to-face (FTF) psychotherapy in major depression, i.e., Cognitive Behavioral Therapy (CBT) and Psychodynamic Therapy (PDT) (Cuijpers et al., 2013; Cuijpers, Van Straten, Van Oppen, & Andersson, 2008; Driessen et al., 2015; Luyten & Blatt, 2012; Munder et al., 2018). Moreover, meta-analyses and qualitative reviews converge to suggest that internet-based interventions, particularly offered as blended care (combining face-to-face sessions with internet-based modules), may be equally effective as FTF psychotherapy and pharmacotherapy in major depression both at treatment termination and at follow-up in the medium to long-term, suggesting non-inferiority (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). Extant research in this domain also suggests that both CBT and PDT delivered through the internet may be effective in depression. Moreover, the available evidence suggests that internet-based psychotherapy if combined with therapist support may be more cost-effective as it typically reduces the number of face-to-face contacts, without compromising the effectiveness of psychotherapy (Andersson, Titov, Dear, Rozental, & Carlbring, 2019). Hence, the implementation of blended care may lead to increased availability of psychotherapy for depression and a more effective use of resources in mental health care, at least for a subsample of depressed patients.

The primary objective of this study is therefore to investigate the non-inferiority (defined as a small-sized difference in effect size (Cohen's *d*= .20) of blended PDT and CBT for depression compared to FTF PDT and CBT in adults diagnosed with major depressive disorder (n=504) in the context of a pragmatic, multicenter randomized controlled trial. Patients will be randomized to one of four conditions (i.e., blended PDT, blended CBT, FTF PDT, or FTF CBT). The primary outcome is changes in the severity of depression as measured by the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996) at 6 months follow-up (approximately 12 months after the start of treatment).

In addition, this study will investigate the comparative efficacy of blended care versus FTF psychotherapy on the following secondary outcomes: severity of depression as measured with the BDI-II at treatment termination, and at 6-month, and one- and two-year follow-up; recovery from depression as assessed with the Structured Clinical Interview for DSM 5 disorders – Clinical Trials Version (SCID-5-CT; American Psychiatric Association) and the Patient Health Questionnaire-9 (PHQ-9) at treatment termination, and at 6-month, and one- and two-year follow-up; and quality of life as measured with the EuroQol-5D-5L (EQ-5D-5L; Herdman et al., 2011) at treatment termination, and at 6-month, and one- and two-year follow-up.

Furthermore, this study will also examine possible predictors of treatment response in blended care versus FTF therapy, such as severity of depression (BDI-II, PHQ-9), psychiatric co-morbidity (SCID-5-CT), and patients' experience of both types of treatment as assessed with the Credibility and Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000). In addition, the feasibility of implementing blended care in mental health care centers in Flanders, Belgium, will be investigated. To this end, we will record recruitment rate, retention in treatment, treatment adherence, and adherence to the research protocol. Acceptability will be indicated by the number of sessions attended, including the number of individuals who refuse treatment, and feasibility by the number of patients failing to comply with the full clinical and

research protocol. Patients will also complete very brief measures of credibility of the treatments and satisfaction with the treatments. Treatment integrity of therapists will be assessed on the basis of independent ratings of audio or video recorded psychotherapy sessions, applying a treatment integrity instrument developed in the UK specifically for the treatments used in this study (Lemma, Target, & Fonagy, 2011).

Finally, provided blended care is non-inferior to FTF therapy, the cost-effectiveness of blended care versus FTF psychotherapy will be investigated from a societal perspective, i.e., taking all relevant costs and effects into account (intervention costs, direct and indirect medical costs, as well as productivity losses and costs made elsewhere in the health care system). To this end, patients will complete the Trimbos and Institute for Medical Technology Assessment (iMTA) Questionnaire on Costs Associated with Psychiatric Illness (TIC-P; Bouwmans et al., 2013). Moreover, health care use data for all patients will be provided by the Rijksinstituut voor Ziekte- en Invaliditeitsverzekering (RIZIV).

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