Short-term psychotherapy for depression

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General introduction

Introduction

This thesis concerns the efficacy of short-term psychotherapy for depression. It consists of a collection of studies that were conducted in an effort to further broaden this field of research by adding research findings to current and important issues in order to improve clinical practice. In this first chapter, a general background is provided, relevant concepts are described, and the aims of this thesis are stated.

Depression

Depression is a mental disorder characterized by depressed mood and markedly diminished interest or pleasure in (almost) all activities. Other symptoms include significant weight loss/gain or decreased/increased appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, indecisiveness or diminished ability to think or concentrate, and recurrent thoughts of death. One speaks of a depressive episode when five or more of the beforementioned symptoms, at least one of which is depressed mood or loss of interest or pleasure, are present for (nearly) every day during the same two-week period. Furthermore, the symptoms present have to cause clinically significant distress or impairment in important areas of functioning (American Psychiatric Association [APA], 2000a). One speaks of major depressive disorder when at least one depressive episode is present that is not better accounted for by or not is superimposed on schizophrenia or another psychotic disorder, and no (hypo)manic episodes have occurred (APA, 2000a). Major depressive disorder is a unipolar depression type and can be distinguished from the bipolar depression type, which is commonly known as manic depression and also (or exclusively) involves episodes of hypomania or mania. Hypomanic or manic episodes are in many ways the opposite of depressive episodes and are characterized by euphoria or irritability, sleeplessness, feelings of grandiosity, and uncontrollable impulses.

The lifetime prevalence of major depressive disorder has been estimated at 16.2%, with rates being nearly twice as high under women as under men (Kessler et al., 2003), making it one of the most common psychiatric disorders. More than 150 million people around the world are suffering from a depression (World Health Organization, 2003). As 87% of all patients who recover from one major depressive episode will experience at least one more (Keller, 2001), depression is increasingly thought of as a chronic recurrent disorder. Major depressive disorder carries a tremendous burden for the patient, as it is associated with substantial symptom severity and role impairment, high comorbidity rates, and high risks for suicide (Kessler et al., 2003). In addition, depressive disorders constitute a major financial health problem in today's society. Depressive disorders constitute the fourth leading cause of disease burden worldwide and are expected to rank first in high-income countries by the year 2030 (Mathers & Loncar, 2006).

Treatment of depression

Given the tremendous burden of disease, there is a high need for effective treatment of depression. Pharmacological treatment by means of antidepressant medications and different psychological treatments constitute the predominant treatments for depressive disorders (Marcus & Olfson, 2010) and will be described here.

Pharmacological treatments of depression include monoamine oxidase inhibitors (MAOIs) that work by inhibiting the enzyme monoamine oxidase that degrades biogenic amines, and 'classic' tricyclic antidepressants (TCAs), which are assumed to work by means of influencing different neurotransmitters in the brain. Pharmacological treatments of depression also include the 'modern' antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) or serotonin-noradrenalin reuptake inhibitors (SNRIs) have assumed working mechanisms that involve blocking the reuptake of respectively serotonin and serotonin/noradrenalin in brain structures, thereby prolonging the effects of these neurotransmitters. Comparisons with pill-placebo have shown different antidepressants to be efficacious in the treatment of major depression (Mulrow et al., 1999). However, recent studies indicate that antidepressants might have clinically significant effects only for severe depression (Khan, Leventhal, Kahn, & Brown, 2002; Kirsch et al., 2008; Fournier et al., 2010) and that antidepressants might not be as efficacious as has been previously suggested due to selective publication of positive outcomes (Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008).

Psychological treatments of depression encompass a large variety of different therapies based on different theoretical models. Two of the most widely available and practiced methods are psychodynamic therapies, including short-term psychodynamic supportive psychotherapy, and cognitive behavioral therapy. These methods will be described in more detail here, because of their relevance to the subject of this thesis.

Psychodynamic therapy for depression

Psychodynamic therapies for depression refer to a family of treatments, which are based on psychoanalytic models that have been developed since the early 20th century to explain the etiology and persistence of depressive symptoms and to form a rationale for depression treatment. These models generally agree that vulnerability to depression is created by individual biological and temperamental factors, early attachment relations and significant experiences in early childhood, which influence a person's perception of himself and others.

Busch, Rudden and Shapiro (2004) have extracted five core dynamics from the existing psychoanalytical models that are considered to predispose a person to depression in the context of a larger diathesis-stress model: narcissistic vulnerability (the tendency to react to mistakes and disappointments with a significant loss of self-esteem), reactive anger (anger to the person causing the narcissistic injury, which is regarded as destructive and thereby turned toward the self), a severe superego (causing feelings of guilt and self-punishing behaviors), idealization and devaluation (of the self and others), and defense mechanisms (e.g., denial, projection, passive

aggression, and identification with the aggressor). Busch et al. (2004) combine these central dynamics into two dynamic interaction cycles that can result in depression. In the first cycle, the narcissistic vulnerability results in sensitivity to perceived rejection by others. This perceived rejection triggers anger toward the person causing the narcissistic injury, which is experienced as destructive, causing guilt and self-directed anger. This guilt and self-directed anger lowers self-esteem, thereby increasing the narcissistic vulnerability and extending a vicious cycle that can eventually result in depression. The second cycle includes the individual's attempt to deal with the low self-esteem by a compensatory idealization of the self or others, which leads to disappointment when the self-set high standards are not met. This disappointment results in devaluation of the self and others, which decreases self-esteem further, resulting in a vicious cycle that can cause depression.

Psychodynamic therapy is distinguished from other psychotherapy methods by its emphasis on the importance of early experiences related to the vulnerability to depression and by the exploration of unconscious feelings, motivations, or desires. Psychodynamic treatment can be time-limited and brief as well as open-ended and of longer duration. Brief psychodynamic therapies, also referred to as short-term psychodynamic psychotherapies (STPPs), are focused, and in the case of depression, primarily aimed at the relief of depressive symptoms. The purpose of treatment is to gradually link the depressive symptoms to the core dynamics, thereby reducing the negative consequences of the latter (Busch et al., 2004). Longer psychodynamic psychotherapy is primarily aimed at changing personality features, thereby reducing vulnerability to depression recurrence.

Since the second half of the 20th century, several different types of STPPs have been developed, such as Malan's (1963) brief psychoanalytic therapy, Mann's (1973) limited psychotherapy, Sifneos' (1979) short-term (anxiety provoking) dynamic psychotherapy, Davanloo's (1980) intensive short-term dynamic psychotherapy, Strupp and Binder's (1984) time-limited dynamic psychotherapy, Luborsky's (1984) supportive-expressive psychoanalytic psychotherapy, and Pollack and Horner's (1985) brief adaptation-oriented psychotherapy. Techniques in these brief psychodynamic treatments include clarification (pointing out thought or behavior patterns related to the depression), confrontation (strong-worded clarifications of self-destructive or aggressive behavior), interpretation (linking observations of behavior or thought patterns to dynamic factors), transference interpretation (linking observations of behavior or thoughts in the therapeutic relation to dynamic factors), working with countertransference (the reactions of the clinician to strong affects the patient feels toward the therapist), and working with free associations, dreams, and slips of the tongue.

With regard to the techniques used, various STPP types can be placed on a continuum from a purely 'expressive' to a purely 'supportive' pole (Luborsky, 1984). The more expressive therapies define the therapeutic relationship by its transference aspects, rely heavily on interpreting conflicts concerning drives (e.g., sexuality and aggression) or defenses that the patient uses, emphasize insight as being curative, and consider personality restructuring to be paramount. The more supportive therapies

define the therapeutic relationship by its interpersonal aspects, rely heavily on a strong therapeutic alliance that is consciously experienced by the patient, consider growth through the relationship as curative, and consider personality building to be paramount. It must be emphasized, however, that this distinction is a continuum and not a dichotomy. Most STPPs include both expressive and supportive interventions and vary the implementation of these interventions from patient to patient. However, the relative weight they place on either one of the poles merits the division into supportive and expressive therapy modes.

Short psychodynamic supportive psychotherapy

Short psychodynamic supportive psychotherapy (SPSP) is a variant in the family of STPPs and was developed as a relatively structured psychodynamic treatment approach for depressed outpatients in the early '90s of the previous century by de Jonghe (de Jonghe, Rijnierse, & Janssen, 1994; de Jonghe, 2005). SPSP is rooted in six psychoanalytical theories, which together assume six innate, basic social needs: sexuality, aggression, the need to engage in relationships, and the needs to be protected, loved, and esteemed. If these needs are inadequately met in early infancy, they persist in adults as ongoing malignant aspects of internal relationships. Internal relationships can be thought of as (internalized) representations of early relationships with significant others in the form of unconscious images, memories, expectation of others or emotions experienced in a relation. These internal relationships can act as moulds on new external relationships in the present.

SPSP considers gratification of the abovementioned basic needs to be particularly relevant in the treatment of depressed patients. The therapeutic action of SPSP consists in experiencing 'relational dissonance' or friction between two contradictory relationships simultaneously felt in the therapeutic situation. One is determined by moulds resulting from the past relationships, the other by the present relationship with the therapist, in which the patient will experience adequate gratification of his unmet early infantile need. The proper gratification of unmet developmental needs forms the psychoanalytical definition of 'support', which is considered the most important curative factor in SPSP. SPSP can be regarded as situated within the supportive half of the expressive-supportive continuum (de Jonghe et al., 1994; de Jonghe, 2005).

Specific to SPSP is the distinction of nine different levels of discourse within the discussion of the problem area that serve to structure and foster the therapeutic process. Treatment starts with levels one and two, in which the patient's physical and psychological symptoms and complaints are discussed as well as the influence of life circumstances on the depressive symptoms. Interventions at these levels are mainly supportive and include encouraging adaptive coping mechanisms, supporting guilt-reducing thoughts, and giving praise or advice, while in the higher levels the therapist may use more interventions to facilitate insight, such as clarification or confrontation.

At the third level, the focus shifts from discussing the influence of life circumstances to discussing the influence of external interpersonal relationships (e.g., current relational problems) on the depressive symptoms. At the fourth level, one or more

relational patterns in the patient's life are discussed that may contribute to the depression onset or maintenance. At the fifth level, the focus proceeds to the patient's own contribution to the ongoing existence of these patterns. The sixth level concerns how past relationships persist in the patient's current life, and the seventh level regards the intrapersonal relationship the patient maintains with himself or herself as a consequence of identification with these past relationships. At the eighth and ninth levels, the focus shifts to how the problems discussed at the previous levels manifest themselves in the relationship with the therapist. These transference manifestations are recognized and if necessary adapted to improve the therapeutic process, but they are not interpreted in SPSP (de Jonghe, 2005).

The levels of discourse can vary considerably during the course of treatment (de Jonghe, 2005). SPSP usually starts at level one and in many cases proceeds to level five, while levels six and seven are reached considerably less often. Thus, the levels merely aim to structure the steps that can be taken during the therapeutic process, rather than implying to signify that the highest level should be reached with every patient.

Cognitive behavioral therapy

Cognitive behavioral therapy (CBT) was developed in the early '60s of the previous century by Beck (1964, 1970, 1976) and is founded in cognitive theory, which states that information in the human brain is organized in certain patterns, or schemata, that contain general knowledge about the world and the person itself. These schemata are used to select, reduce, and interpret information. According to the cognitive theory, mental disorders are caused and maintained by dysfunctional thought schemata. These schemata can be thought of as diatheses in a diathesis-stress model, such that they by themselves are not sufficient to cause a disorder, but can do so in combination with stressors such as current life events. Dysfunctional schemata express themselves in logical errors and dysfunctional automatic thoughts and give rise to all sorts of emotional and behavioral problems.

Beck asserts that with depressive disorders, thinking in general is preoccupied with loss and hopelessness. The so-called depressive schemata are characterized by thoughts about one's own worthlessness and guilt, the world's cold-heartedness and injustice, and the future's desperateness. The cognitive part of CBT aims at locating and correcting the negative automatic thoughts and logical errors, thereby alleviating the depressive symptoms. The cognitive part of CBT also aims at correcting the underlying schemata, which is considered to be relevant to the prevention of subsequent symptom return.

Besides this cognitive element CBT contains a behavioral part. The inclusion of this behavioral part is based on the notion that depression is partly caused or maintained by a lack of pleasant or satisfactory activities (Lewinsohn, Biglan, & Zeiss, 1976). In CBT patients are therefore encouraged to identify activities that affect their mood positively and engage in these more often. Another important reason for this encouragement is that engaging in certain activities can provide a powerful test of the patient's beliefs. Interventions in which planned activities are undertaken by patients

to test existing beliefs or to help test more adaptive beliefs are called 'behavioral experiments'. CBT is further characterized by a limited time span, a structured approach, and the use of homework assignments.

Current issues the field of psychotherapy for depression efficacy research

Since the early '60s of the previous century, investigators have examined the effectiveness of psychotherapy methods for depression (e.g., Daneman, 1961; Covi, Lipman, Derogatis, Smith, & Pattison, 1974; Klerman, DiMascio, Weissman, Prusoff, & Paykel, 1974). This has led to 315 randomized controlled trials (RCTs) studying the effects of different psychological treatments for depression to date (Cuijpers, van Straten, Warmerdam, & Andersson, 2008). In general, psychological treatments have been found to be efficacious relative to control conditions (Cuijpers, van Straten, Warmerdam, & Smit, 2007) and no clinically meaningful differences in acute response have been found when psychotherapy is compared to antidepressant medication among nonpsychotic patients (Cuijpers, van Straten, van Oppen, & Andersson, 2008). Furthermore, minimal treatment differences have been found in acute response when comparing different psychotherapy methods (e.g., Cuijpers, van Straten, Andersson, & van Oppen, 2008), which led Luborsky, Singer, and Luborsky (1975) to reconfirm Rosenzweig's (1936) 'dodo bird-verdict' ("everybody has won and all must have prizes").

Although major advances have been made in the field of psychological treatment for depression outcome research since the publication of the first psychotherapy outcome trial, the field still is an evolving one with numerous issues unresolved and major research questions remaining to be answered. In this thesis, five of such issues are discussed, which represent current and important topics that can help improving clinical practice. The main objective of this thesis is to broaden the field of psychological treatment for depression efficacy research by adding research findings to these five issues, which relate partly to the efficacy of short-term psychotherapy for depression in general and moderators of this efficacy, and more specifically to the efficacy of STPP and its moderators, as STPP is less extensively studied than other psychotherapies.

Psychotherapy for depression in general

A. It is unclear whether depression severity moderates efficacy

Recent studies have suggested that the efficacy of antidepressant medication is moderated by depression severity, with antidepressants having clinically significant effects only for patients with more severe depressions (Khan, Leventhal, Kahn, & Brown, 2002; Kirsch et al., 2008; Fournier et al., 2010). With regard to psychological treatment of depression, it also is believed that efficacy is moderated by depression severity, but in the opposite direction, such that psychological treatment has little

effect on more severely depressed patients. This is reflected in treatment guidelines which suggest that although psychotherapy may be sufficient for patients with less severe depressions, antidepressant medications or electroconvulsive therapy (ECT) is necessary for more severely depressed patients (APA, 2010). However, the relation between pre-treatment depression severity and psychological treatment outcomes has not yet been studied in depth systematically. The aim of this thesis is to conduct a study that systematically assesses whether pre-treatment severity is related to the outcome of psychological treatment relative to control conditions by means of different meta-analytic techniques (Chapter 2).

B. Efficacy might be overestimated due to publication bias

It has been shown that the efficacy of antidepressant medications for depression has been overestimated due to selective publication of positive outcomes (Turner et al., 2008), also referred to as publication bias. The question can be raised as to whether the effects of psychological treatments for depression also might be overestimated due to publication bias. Cuijpers, Smit, Bohlmeijer, Hollon, & Andersson (2010) examined this question in 117 published trials by means of statistical procedures and found strong indications of publication bias, implying that psychological treatments may not be as efficacious relative to controls as the published literature would suggest. However, Cuijpers et al. (2010) were forced to infer the presence of publication bias by means of statistical procedures that rely on the assumption that a nonsymmetrical relationship between sample size and effect size necessarily stems from a failure to publish small studies with weak effects. As small studies may show disproportionately large effects for other reasons (Borenstein, Hedges, Higgins, & Rothstein, 2009), the findings of Cuijpers et al. (2010) may be the consequence of reasons other than publication bias. Given that "the only true test for study publication bias is to compare the effect in the published studies formally with effects in the unpublished studies" (Borenstein et al., 2009, p. 280), it is currently unclear to what extent the efficacy of psychological treatment for depression is overestimated due to publication bias.

This thesis aims to do such a 'true' test for study publication bias with regard to the efficacy of psychological treatment for depression by identifying a cohort of studies and directly ascertaining the frequency with which studies conducted were not published. Moreover, this thesis aims to provide an estimate of the efficacy of psychological treatment for depression adjusted for study publication bias by adding the unpublished findings to the published data (Chapter 3).

C. Equal efficacy is based on superiority trials rather than equivalence trials

Since Luborsky et al. (1975) reconfirmed Rosenzweig's (1936) 'dodo bird-verdict' ("everybody has won and all must have prizes"), different psychotherapy methods for depression have been considered by many as equally efficacious. This notion has been reinforced by meta-analytic findings that generally failed to find significant differences among psychotherapies (e.g., Cuijpers, van Straten, Andersson, van Oppen, 2008). At the same time, the psychotherapy efficacy literature is dominated by superiority trials,

which are designed to show the superiority of one treatment over another. These trials are based on a null hypothesis of equal efficacy and an alternative hypothesis of efficacy differences between the treatments. As the null hypothesis by definition can only be rejected and never 'proven', equal efficacy of two treatments can not be concluded from a superiority trial (Blackwelder, 1982).

In contrast, an equivalence trial is designed to show therapeutic equivalence of two methods (Piaggio, Elbourne, Altman, Pocock, & Evans, 2006). In these trails, efficacy differences are assumed under the null hypothesis and equal efficacy constitutes the alternative hypothesis. As any comparison between treatments will result in differences, some of which might be too small to consider clinically relevant, equivalence intervals need to be set in order to define the boundaries for which differences found are no longer clinically relevant. If the differences between the treatments are completely within the pre-defined equivalence intervals, two treatments can be shown equivalent in terms of efficacy in an equivalence trial (Piaggio et al., 2006). A non-inferiority trial refers to a study with a similar design that can be used to demonstrate that the experimental treatment is not worse than an active control by more than the equivalence margin.

Although different psychotherapies for depression are generally considered equally efficacious, this notion is based on superiority trials and meta-analytic findings summarizing the findings of superiority trials, rather than on equivalence or non-inferiority trials. This thesis aims to add to the field of psychological treatment for depression outcome research by means of comparing cognitive behavioral therapy and psychodynamic therapy in the outpatient treatment of depression in a randomized clinical trial employing a non-inferiority design (Chapter 7).

STPP for depression

D. STPP has a limited evidence-base

Although widely practiced, STPPs for depression are less extensively studied than other psychotherapies such as CBT (Cuijpers, van Straten, Andersson, & van Oppen, 2008). Existing findings suggest equivalence to other psychological treatments, but a lack of good-quality trials makes it difficult to draw conclusions regarding the efficacy of psychodynamic therapy for depression (Roth & Fonagy, 2005; Abbass, Hancock, Henderson, & Kisely, 2006).

Connolly-Gibbons, Crits-Christoph, and Hearon (2008), for example, have argued that STPP for depression currently does not meet the criteria for empirically supported psychological treatments formulated by Chambless and Hollon (1998). These criteria require demonstration of superiority of an intervention over no-treatment, placebo control, or alternative treatment, or demonstration of equal efficacy to an alternative evidence-based treatment by at least two independent research groups using adequate research methods (e.g., RCT-design, the use of treatment manuals, appropriate data-analytic procedures). Connolly-Gibbons et al. (2008) argue that STPP does not meet these criteria due to different STPP types studied and methodological quality of studies. Moreover, efforts to review the efficacy of STPP for depression by

means of meta-analysis (Svartberg & Stiles, 1991; Leichsenring, 2001; Churchill et al., 2001) have mainly focused on comparisons of STPP to (specific) other psychological treatments, reporting contradictory results. As these meta-analyses do not compare STPP to control conditions, it remains unclear whether STPP is an effective treatment for depression. For these reasons, STPP is currently not considered as a recommended psychotherapy in guidelines for the treatment of depression (APA, 2010; National Institute for Health and Clinical Excellence [NICE], 2009) and NICE (NICE, 2009 p. 46) calls for the comparison of the efficacy of STPP to CBT in the treatment of moderate to severe depression as one of their research recommendations to improve patient care.

SPSP is a variant in the family of STPPs, which acceptability, feasibility, and efficacy have been examined in four randomized clinical trials and a mega-analysis, which support both SPSP's relative efficacy to pharmacotherapy as a monotherapy and its incremental efficacy when combined with pharmacotherapy (de Jonghe, Kool, van Aalst, Dekker, & Peen, 2001; de Jonghe et al., 2004; Dekker et al., 2005; Dekker et al., 2008; de Maat et al., 2008). Although these studies provide initial support for SPSP in the outpatient treatment of depression, SPSP has not yet been directly compared to other forms of psychotherapy. It therefore remains unknown how SPSP compares to evidence-based psychotherapy methods.

This thesis aims to add to this issue by means of summarizing the available efficacy research with regard to STPP for depression in a meta-analysis (Chapter 4), including a number of studies regarding the efficacy of STPP for depression that were published after the meta-analyses of Leichsenring (2001) and Churchill et al. (2001) and not solely focusing on a comparison of STPP with a specific other psychotherapy method, but aiming to compare the efficacy of STPP with all other treatments as well as with control conditions. Furthermore, this thesis aims to add to this issue by means of comparing the efficacy of SPSP for moderate to severe depression with CBT in a randomized clinical trial (Chapters 6, 7, and 8).

E. It is unclear what factors moderate differential efficacy of STPP

If studies comparing different psychotherapies for depression generally fail to find significant efficacy differences in larger patient samples (e.g., Cuijpers, van Straten, Andersson, van Oppen, 2008), the question can be raised whether certain smaller subgroups of patients might benefit more from one treatment than the other and whether patient characteristics can be used to guide treatment selection. A useful distinction in this regard can be made between prognostic and prescriptive factors. Prognostic factors (or non-specific predictors of treatment outcome; Kraemer, Wilson, Fairburn, & Agras, 2002), predict outcome to a given treatment and can be used to determine which patients are more likely to respond to that given treatment relative to other patients. Van, Schoevers, and Dekker (2008), for instance, identified female gender, younger age, and duration of the depressive episode shorter than one year as prognostic factors associated with better response to psychodynamic therapy relative to patients of male gender, older age, and with longer episode duration. Although such prognostic factors can help shape expectations when starting treatment, they are of little use in deciding what treatment to select. On the other hand, prescriptive

information (or moderators; Kraemer et al., 2002) relate to different patterns of outcomes between different treatments for different types of patients and provide a basis for choosing the best treatment for a given patient.

Little is known about prescriptive factors that are associated with differential efficacy to CBT and psychodynamic therapy for depression; only three studies could be retrieved in this regard. Two studies in the same sample found that comorbid cluster-C personality disorder and treatment credibility predicted differential response within psychodynamic-interpersonal psychotherapy, but not in CBT (prognostic; Hardy et al.,1995a, b), but the investigators did not conduct the kinds of direct treatment comparisons within patient subgroups required to establish a prescriptive relationship (Driessen & Hollon, 2010). A third study found that clinically depressed family caregivers who had been caregivers for less than 44 months improved more in psychodynamic therapy than in CBT, while patients who had been caregivers longer improved more in CBT than in psychodynamic therapy (Gallagher & Steffen, 1994). Given the lack of research findings in this regard, the National Institute for Health and Clinical Excellence (NICE, 2009, p.46) called for the examination of moderators of response to CBT and psychodynamic therapy in the treatment of moderate and severe depression as a research recommendation in order to improve patient care.

The aim of this thesis is to add to this aspect of psychotherapy for depression outcome research by means of trying to identify moderators associated with differential outcomes of STPP versus other psychotherapies in a meta-analytic review (Chapter 4). Furthermore, this thesis aims to identify factors associated with differential response to CBT or SPSP within the context of a randomized clinical trial (Chapter 9). In addition, CBT moderator research is reviewed in Chapter 5.

Content of this thesis

The first half of the thesis comprises four chapters that examine different research questions with regard to the abovementioned issues A, B, D, and E by means of (systematic) reviews and meta-analyses of available outcome research. In **Chapter 2**, the possibility of a moderating relationship between pre-treatment depression severity and the outcome of psychological treatment for depression is studied in depth by means of meta-analytic techniques (Issue A). The extent of publication bias in psychological treatments for depression efficacy research is examined by means of a systematic review and meta-analysis in **Chapter 3** (Issue B). **Chapter 4** includes a meta-analytic review of the efficacy of STPP for depression and efforts to identify moderating factors of this efficacy (Issues D and E). Finally, a narrative review concerning the efficacy of CBT for depression, and moderators and mediators of CBT efficacy is reported in **Chapter 5** (Issue E).

The second half of this thesis consists of four chapters examining research questions with regard to the abovementioned issues C, D, and E in the context of a randomized clinical trial comparing the efficacy of SPSP and CBT in the outpatient treatment of depression. In **Chapter 6,** the protocol of this study is described. In **Chapter 7**, the

observer-rated and patient-rated outcomes of this study are presented employing a non-inferiority design (Issues C and D). Therapist-rated outcome measures are next reported in **Chapter 8** (Issue D). **Chapter 9** then describes efforts to identify factors associated with differential response to CBT or SPSP (Issue E).

The thesis is concluded with a general discussion of the main findings, their limitations and implications in **Chapter 10** and a summary of the content.

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