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**CBT IN PRIMARY CARE - EFFECTS ON SYMPTOMS AND SICK LEAVE,
IMPLEMENTATION OF STEPPED CARE AND PREDICTORS OF OUTCOME**

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CBT IN PRIMARY CARE - EFFECTS ON SYMPTOMS AND SICK LEAVE,
IMPLEMENTATION OF STEPPED CARE AND PREDICTORS OF OUTCOME

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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*To patients, clinicians, researchers, officials and politicians,
may we unite for a fair, effective, available,
and humane care of mental health.*

ABSTRACT

Background

Common mental disorders (CMDs) cause great individual suffering and high societal costs including long-term sick leave. Cognitive behavioural therapy (CBT) can effectively treat CMDs, but access to treatment is insufficient. Moreover, sick leave is not reduced to the same extent as psychiatric symptoms after CBT. Little is known about predictors of outcome after CBT, especially concerning guided self-help.

Aims

The aim of the present thesis was to systematically review the effects and evidence of psychological treatments on sick leave and assess the effects in a meta-analysis of published treatment trials (Study I), evaluate the effect of CBT and a novel return-to-work intervention (RTW-I) on sick leave and psychiatric symptoms for patients with CMDs (Study II), test a stepped care CBT model for CMDs in primary care (Study III), and investigate predictors of outcome for guided self-help CBT (Study IV).

Methods

In Study I, a systematic review and meta-analysis (45 studies) was conducted regarding effects of psychological interventions on sick leave and symptoms. In Study II (N = 211) and III (N = 396) patients from four primary care centres in Stockholm were treated with disorder specific CBT for CMDs. In Study II, patients on sick leave were randomised to CBT, RTW-I, or a combination of the two, and were followed up one year after treatment regarding sick leave and symptoms. In Study III all patients received disorder specific guided self-help CBT for nine weeks. Non-responders were then randomised to face-to-face CBT or continued guided self-help. In Study IV predictors of outcome for guided self-help CBT in Study III were investigated.

Results

Study I showed that psychological interventions were more effective than care as usual in reducing sick leave and psychiatric symptoms but the effect sizes were small ($g = 0.15$ and 0.20 , respectively). There was no significant difference in effect between work focused interventions, problem solving therapy, CBT or collaborative care. In Study II, there was no significant difference between treatments regarding days on sick leave one year after treatment start; CBT however led to larger reduction of symptoms post-treatment than RTW-I. In Study III, 40% of patients were in remission after nine weeks of guided self-help CBT. After Step II, 39% of the non-remitted patients who had been randomised to face-to-face CBT were in remission compared to 19% of patients who received continued guided self-help ($p < 0.05$). Study IV showed that patients across all disorders benefitted from guided self-help CBT, but those with social anxiety disorder and depression reached remission to a lower extent. Higher educational level predicted remission, higher quality of life ratings predicted remission and post treatment depression ratings, and higher age at onset predicted reliable change. All investigated therapy related variables, e.g., adherence to treatment and expectancy of outcome, were positively associated to outcome.

Conclusions

Psychological interventions can reduce sick leave compared to treatment as usual, but effects are small. Adding RTW-I as investigated in the present thesis to CBT seems to have little effect on sick leave. This could be due to lack of power or that CBT also had an effect on sick

leave. Disorder specific CBT can effectively treat CMDs in primary care and using stepped care with guided self-help CBT as the initial step seem to be a resource efficient way to treat CMDs. Patients with higher education, higher ratings of quality of life and later age of onset appear to have a better outcome of guided self-help. Patients who rate treatment as credible and actively participate in therapy have a greater chance of recovering. This knowledge can be of value when making treatment recommendations.

SAMMANFATTNING

Bakgrund

Psykisk ohälsa, så som ångest, depression, stress och sömnstörningar orsakar stort individuellt lidande och genererar höga samhällskostnader främst genom sjukskrivning och ökad medicinsk vårdkonsumtion. Kognitiv beteendeterapi (KBT) kan effektivt behandla dessa tillstånd, men tillgången till behandling, särskilt i primärvården, är otillräcklig. Dessutom är effekten av psykologisk behandling på sjukskrivning oklar.

Mål

Syftet med föreliggande avhandling var att undersöka effekterna av psykologiska behandlingar på sjukskrivning (Studie I), utvärdera effekten av KBT och en intervention för arbetsåtergång på sjukskrivning och symtom (Studie II), utvärdera stegvis vård med KBT för psykisk ohälsa i primärvården (Studie III) och att undersöka prediktorer av utfall för KBT i form av guidad självhjälp (Studie IV).

Metod

I Studie I genomfördes en systematisk granskning och meta-analys (45 studier) av effekter för psykologisk behandling på sjukskrivning och symtom. I Studie II (N = 211) och III (N = 396) behandlades patienter på fyra vårdcentraler i Stockholm med diagnosspecifik KBT för psykisk ohälsa. I Studie II behandlades sjukskrivna patienter med KBT eller en intervention för arbetsåtergång (return-to-work intervention; RTW-I) och följdes upp ett år efter behandling avseende sjukskrivning och symtom. I Studie III fick alla patienter diagnosspecifik KBT som guidad självhjälp under nio veckor. De patienter som inte blivit friska randomiserades sedan till individuell KBT med veckovisa psykologträffar eller fortsatt självhjälp i steg II. I Studie IV undersöktes prediktorer av utfall för KBT som guidad självhjälp.

Resultat

Studie I visade att psykologisk behandling var effektivare än sedvanlig vård gällande minskad sjukskrivning ($g = 0.15$) och symtom ($g = 0.20$), men effekten var liten. Det var ingen signifikant skillnad i effektivitet mellan RTW-I, problemlösningsfokuserad terapi, KBT och förstärkt primärvård. I Studie II var det ingen signifikant skillnad mellan behandlingarna gällande sjukskrivning ett år efter behandlingsstart, men KBT ledde till större minskning av symtom vid behandlingsavslut än RTW-I. I Studie III var 40% av patienterna friska efter nio veckors guidad självhjälp (KBT). Efter steg II var 39% av de icke återhämtade patienterna friska efter individuell veckovis KBT jämfört med 19% av patienterna efter fortsatt självhjälp ($p < 0.05$). Denna modell av stegvis vård krävde mindre än sex behandlingssessioner per patient och resulterade i att 63% av alla patienter tillfrisknade efter behandling. Studie IV visade att patienter med ångest, depression, stress och sömnstörningar alla förbättrades av behandlingen, men patienter med socialt ångestsyndrom och depression nådde remission i lägre utsträckning. Högre utbildningsnivå predicerade tillfrisknande, högre självskattad livskvalitet predicerade förbättring och minskad nedstämdhet och högre debutålder predicerade förbättring. Alla terapiorelaterade variabler, t ex följsamhet till behandling och förväntat utfall, var positivt förknippade med behandlingsresultatet.

Slutsatser

KBT är en effektiv behandling av psykisk ohälsa i primärvården. Stegvis vård med guidad självhjälp som inledande insats tycks vara ett resurseffektivt sätt att behandla psykisk ohälsa samtidigt som behandlingseffekten bibehålls. Psykologiska behandlingar kan minska sjukfrånvaro jämfört med sedvanlig behandling, men effekterna är små. RTW-I utvecklad för Studie II var inte mer effektiv än KBT när det gällde minskad sjukfrånvaro. Detta kan bero på bristande power eller att även KBT haft en effekt på sjukskrivning. Patienter med högre utbildning, högre skattad livskvalitet och som insjuknat senare i livet tycks få bättre behandlingseffekt av guidad självhjälp. Patienter som skattar behandlingen som trovärdig och deltar aktivt i terapin har större chans att tillfriskna.

LIST OF SCIENTIFIC PAPERS

- I. Salomonsson, S., Hedman-Lagerlöf, E., & Öst, L-G. (In press). Sickness absence: A Systematic Review and Meta-Analysis of Psychological Treatments for Individuals on Sick leave due to Common Mental Disorders. *Psychological Medicine*.
- II. Salomonsson, S., Santoft, F., Lindsäter, E., Ejeby, K., Ljótsson, B., Öst, L-G., Ingvar, M., Lekander, M., Hedman-Lagerlöf, E. (2017). Cognitive-behavioural therapy and return-to-work intervention for patients on sick leave due to common mental disorders: a randomised controlled trial. *Occupational and Environmental Medicine*, 74(12), 905-912. doi: 10.1136/oemed-2017-104342
- III. Salomonsson, S., Santoft, F., Lindsäter, E., Ejeby, K., Ljótsson, B., Öst, L-G., Ingvar, M., Lekander, M., Hedman-Lagerlöf, E. (2017). Stepped care in primary care - guided self-help and face-to-face cognitive behavioural therapy for common mental disorders: a randomised controlled trial. *Psychological Medicine*, 1-11. doi: 10.1017/s0033291717003129
- IV. Salomonsson, S., Santoft, F., Lindsäter, E., Ejeby, K., Öst, L-G., Lekander, M., Ljótsson, B., & Hedman-Lagerlöf, E. (Manuscript). Predictors of outcome in Guided self-help Cognitive Behavioural Therapy for Common Mental Disorders in Primary Care.

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LIST OF ABBREVIATIONS

AD	Adjustment disorder
CBT	Cognitive behavioural therapy
CMDs	Common mental disorders
CSR	Clinician Severity Rating
DSM	Diagnostic and Statistical Manual of Mental Disorders
ED	Exhaustion disorder
GAD	Generalized anxiety disorder
ICD	International Statistical Classification of Diseases and Related Health Problems
IAPT	Improving Access to Psychological Treatments
MDD	Major depressive disorder
NICE	National Institute for Health and Clinical Excellence
OCD	Obsessive compulsive disorder
OECD	Organisation for Economic Co-operation and Development
PD	Panic disorder
PST	Problem solving therapy
PTSD	Post-traumatic stress disorder
QOLI	Quality Of Life Inventory
RTW-I	Return-to-work Intervention
SAD	Social anxiety disorder

1 INTRODUCTION

When I first started working as a clinical psychologist 12 years ago, at a child and adolescent outpatient clinic, I was confused and upset. The gap between the treatment methods and structure I had just learnt at the University and the methods used in practice was striking. Being novice, I found it hard to balance learning from experienced clinicians and integrating scientific methods from my training. Changing structures met hard resistance.

After less than two years I was recruited by a friend to primary care, and the setting and challenges turned out to be quite different. At the primary care centre, where I now have worked for 10 years, there was a great demand for psychological treatments in general and CBT in particular. There were no old bad habits to fight, instead there was a total lack of routines and experience regarding psychological treatments. The needs from patients with mental disorders were vast. Initially, we were three novice psychologists and one counsellor working with all patients of all ages, all types of problems, serving a primary care clinic of 30, 000 inhabitants and a specialist assignment to work with patients from the entire Stockholm County with stress-related disorders and sick leave. The workload was massive but it was energising to work with a manager with interest in treatment of mental disorders and great power of initiative. I was also very grateful to work with primary care patients, so many seemed to benefit from psychological treatments, and with general practitioners, I find them to be effective, competent and happy to cooperate.

Initially, we did not have the resources to work in a systematic evidence-based manner. But step-by-step, with conviction, in collaboration with a growing body of skilled psychologists, expert supervision, and means for research and care improvement, we managed to develop an evidence-based structure. I consider our work to be pioneering, and I am very proud to be part of it. My intentions are to bring evidence-based treatments to patients, and bring real clinical challenges to research. In my opinion, the work we have done, integrating psychologists in primary care, in close collaboration with general practitioners, implementing structured assessments, systematic evaluation and stepped care CBT, has shown to be effective, resource efficient, feasible and a much appreciated model that could successfully be disseminated if supported with the right investments and intentions.

Many challenges remain, for example in the areas of stress-related disorders, sick leave, predictors and moderators of change, and treatments for patients who do not respond to CBT. Our work may constitute a building brick in a greater attempt to deliver good treatments to people who suffer from mental disorders. Fortunately, digitalisation will transform the format and new knowledge will constantly improve treatments and reach new populations.

Gustavsberg, December 2017

2 BACKGROUND

2.1 COMMON MENTAL DISORDERS

2.1.1 Definition

Common mental disorders (CMDs) refer to the most prevalent mental disorders, often defined as depression and anxiety disorders (National Institute for Health and Clinical Excellence [NICE], 2011). In primary care, insomnia (Ohayon, 2002) and stress-related disorders such as adjustment disorders (Casey, 2014), are also found to be highly prevalent. In the present thesis, CMDs refer to anxiety disorders, depression, insomnia and adjustment disorders as defined according to Diagnostic and Statistical Manual of Mental Disorders (DSM) IV (American Psychiatric Association [APA], 1994) and ICD-10 (World Health Organization, 1993).

2.1.2 Prevalence and consequences

CMDs represent one of the largest burdens of disease in western countries with a point prevalence of 20% (Kessler et al., 2005; Fernandez et al., 2012; Ohayon, 2002). Women are 40-60% more likely than men to develop these disorders (Kessler, Berglund, et al., 2005; Zhang & Wing, 2006). CMDs lead to a substantial reduction of functioning (Wells et al., 1989), quality of life (Comer et al., 2011), and lead to most long-term sick leave of all medical conditions (Henderson et al., 2011). Moreover, the medical costs in primary care for patients with depression and anxiety are estimated to be doubled compared to other patient groups (Simon, Ormel, VonKorff, & Barlow, 1995). In total, the cost of mental disorders are comparable to those of physical disorders, and the bulk of costs are work related (Smit et al., 2006).

2.1.3 Anxiety disorders

2.1.3.1 Definition

Fear is a normal part of life, motivating humans to fight or flight upon presenting threats (Barlow, 2002). Anxiety refers to exaggerated reactions to a threat, or to anticipated threats that are not actually present (Barlow, 2002). For some people, symptoms of anxiety and avoidance of anxiety provoking situations become a hindrance to everyday life. Several disorders share these common factors but vary regarding what types of situations are perceived as threatening. In DSM-IV, anxiety disorders include generalised anxiety disorder (GAD), social anxiety disorder (SAD), panic disorder (PD), obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and simple phobias (Brown, Di Nardo, Lehman, & Campbell, 2001).

2.1.3.2 Prevalence, prognosis and consequences of anxiety disorders

Lifetime prevalence of anxiety disorders has been estimated to 29% (Kessler, Berglund, et al., 2005), twelve-month prevalence estimate to 18%, and median age of onset for anxiety disorders to 11 years (Kessler, Chiu, Demler, & Walters, 2005). Anxiety disorders tend to become chronic and have a low degree of spontaneous recovery (Penninx et al., 2011; Yonkers, Bruce, Dyck, & Keller, 2003).

Quality of life is strongly affected for patients with anxiety disorders. A meta-analysis including 23 studies of patients with anxiety disorders (N = 2892) compared their ratings of quality of life with the ratings of non-clinical samples. Results showed a large effect size indicating poorer quality of life for patients with anxiety disorders (Olatunji, Cisler, & Tolin, 2007). This was true for patients with all types of anxiety disorders, but analysis of specific domains showed that patients with PTSD may be particularly impaired by their disorder (Olatunji et al., 2007).

Several studies point out the high direct and indirect costs of anxiety disorders (Greenberg et al., 1999; Simon et al., 1995). Patients with anxiety disorders, seem to have especially increased costs of non-psychiatric medical treatments (Lepine, 2002). In 2006, the estimated annual cost of each anxiety disorder was €3,600. Being most prevalent among mental disorders, this makes anxiety disorders most cost some among psychiatric conditions (Smit et al., 2006).

2.1.4 Depression

2.1.4.1 Definition

Depression is a common but serious disorder with depressed mood and loss of interest, for at least two weeks, as core criteria (APA, 2013). Depression causes severe symptoms that affect how one feels, thinks, and handles daily activities, such as sleeping, eating, or working (APA, 2013). The depressed mood is often associated with a lack of activity, initiative, pleasurable activities and problem solving (e.g., Ramnerö, Folke, & Kanter, 2015). The essential composition of depression is hard to define, and the disorder should perhaps not be seen as a distinct syndrome but rather be understood as a term that helps summarize a set of phenomena (e.g., Ramnerö et al., 2015; Stringaris, 2017).

2.1.4.2 Prevalence, prognosis and consequences of depression

The life time prevalence of depression has been estimated to 21% (Kessler, Berglund, et al., 2005), twelve-month prevalence to 10% and median age of onset for depression is estimated to be 30 years (Kessler, Chiu, et al., 2005). Depression is less chronic than anxiety disorders (Penninx et al., 2011), and often has a spontaneous recovery, but about 50% of patients seem to have recurrent episodes (Eaton et al., 2008).

Even though depression is slightly less prevalent and less chronic than anxiety disorders, the consequences of depression are serious. Depression was the fourth leading cause of disease burden in 2000 (Üstün, Ayuso-Mateos, Chatterji, Mathers, & Murray, 2004). Several studies have confirmed that depression and depressive symptoms have a great impact on a person's wellbeing and function (e.g. Berlim & Fleck, 2007; Wells et al., 1989). Patients with depression have reductions in their functioning (Wells et al., 1989) and quality of life, comparable to patients with chronic medical conditions such as hypertension, rheumatoid arthritis and diabetes (Berlim & Fleck, 2007). Depression is estimated to be more cost some per case than anxiety disorders, with an estimated annual cost of €5,000 per affected individual (Smit et al., 2006).

2.1.5 Insomnia

2.1.5.1 Definition

Definitions of insomnia usually include the following aspects: (1) a difficulty of falling asleep, staying asleep or obtaining restorative sleep; (2) this difficulty is present despite adequate opportunity and circumstance to sleep; (3) this impairment in sleep is associated with daytime impairment or distress; and (4) this sleep difficulty occurs at least 3 times per week and has been a problem for at least 1 month (Roth, 2007).

2.1.5.2 Prevalence, prognosis and consequences of insomnia

Insomnia has an estimated point prevalence of 6% but as many as 30% in the population suffer from symptoms of insomnia (Ohayon, 2002). Insomnia can be a situational, recurrent, or persistent problem with an onset often associated with life events or sleep schedule changes (Morin & Benca, 2012). The prevalence of insomnia seem to be quite stable from 15 to 45 years, but symptoms seem to be more prevalent among elderly, starting from the age of 45 (Ohayon, 2002). Among elderly it's been found that 50% of patients with insomnia still fulfil diagnostic criteria three years later (Foley, Monjan, Simonsick, Wallace, & Blazer, 1999).

Insomnia has been coupled to several negative consequences. Patients with insomnia show reduced work productivity and absenteeism, and are three times more likely than controls to have an accident (Roth, 2007). Further, insomnia has a stronger association with psychiatric disorders, especially depression, than any other medical illness (Morin & Benca, 2012; Roth, 2007).

2.1.6 Stress-related disorders

2.1.6.1 Definition

Adjustment disorder (AD) is a condition strongly tied to acute and chronic stress. AD is defined as the experience of an identifiable psychosocial stressor (not of catastrophic type) and the onset of clinically significant emotional or behavioural symptoms within three months of the event. AD can be defined as chronic if the stressor remains, but symptoms should not persist after the removal of the stressor (Carta, Balestrieri, Murru, & Hardoy, 2009; World Health Organization, 1993).

In Sweden, exhaustion disorder (ED), registered as a reaction to severe stress, has been added to the ICD-10 (Swedish National Board of Health and Welfare, 2003). ED resembles AD, but in ED, the stressor must have been present for at least six months. Mental and physical exhaustion are core diagnostic criteria. Further, patients often need of prolonged recovery in response to psychological stress and display daily difficulties regarding sleep, concentration, memory, ability to manage duties or to do things under pressure, emotional lability and irritability, and substantial bodily weakness. Symptoms must be present daily for at least two weeks and cause significant suffering or impaired functioning (Swedish National Board of Health and Welfare, 2003).

2.1.6.2 Prevalence and consequences of stress-related disorders

Adjustment disorder have been criticized for its vague criteria and lack of valid diagnostic instruments (Patra & Sarkar, 2013) and as a consequence, AD has not been included in most major epidemiological studies of psychiatric disorders (Casey, 2014). When AD has been included, the diagnostic process has been conducted in two steps, where AD has been considered a secondary disorder after the exclusion of anxiety and depressive disorders. This has resulted in prevalence estimations of <1% (Gradus, 2017), but many studies maintain that the disorder is highly prevalent and typically seen in primary care settings. Estimations of prevalence vary greatly between 1 and 18%. (Carta et al., 2009).

Exhaustion disorder has even more unclear prevalence rates, however, some survey studies have been conducted. In one study of patients in primary care, 30% reported symptoms that indicate ED (Wiegner, Hange, Björkelund, & Ahlborg, 2015), in another study, 9% of primary care patients fulfilled diagnostic criteria (Glise, Wiegner, Ahlborg, & Jonsdottir, Manuscript.), and in a German study of exhaustion symptoms in the general population, 6% showed exhaustion symptoms with serious mental impairments (Stobel-Richter, Daig, Brahler, & Zenger, 2013). In a study of human service workers, 16% indicated clinical levels of exhaustion (Glise, Hadzibajramovic, Jonsdottir, & Ahlborg, 2010), and in another study of a working sample, 8-14% reported clinical levels of exhaustion (Persson, Österberg, Viborg, Jonsson, & Tenenbaum, 2016).

Five-year follow-ups show that about 20% of patients with AD develop another psychiatric disorder, most commonly depressive disorder or alcoholism (Carta et al., 2009). There is little research regarding ED, but in a study of 232 patients treated with multi modal treatment, one third still fulfilled criteria 18 months after treatment start, suggesting lingering symptoms among many of these patients (Glise, Ahlborg, & Jonsdottir, 2012).

Stress-related disorders and work stress have shown to increase the risk of anxiety, depression (Kalia, 2002; Melchior et al., 2007), and insomnia (Jansson & Linton, 2006). These patients also show impaired physical and mental functioning, more work days lost, increased impairment at work, and a high use of health care services (Kalia, 2002). Adjustment disorders are the most prevalent psychiatric condition leading to sick leave in many western countries (Koopmans et al., 2011; Swedish Social Insurance Agency, 2014b), and AD has repeatedly been shown to increase the risk of suicide attempts (Casey, Jabbar, O'Leary, & Doherty, 2015; Gradus et al., 2010).

AD is considered a mild mental disorder, less severe and disabling than other psychiatric disorders considering chronicity and hospitalisation (Looney & Gunderson, 1978). ED on the other hand, is considered to be a severe reaction to stress, often with long lasting symptoms and reduced function (Swedish National Board of Health and Welfare, 2003). The Swedish National Board for Health and Welfare, publish recommendations regarding sick leave for different disorders, and recommendations regarding exhaustion disorder are the most prolonged of all CMDs with 6-12 months' sick leave.

2.1.7 Aetiology and CMDs from a learning theory perspective

There is high comorbidity between all CMDs (Kessler, Berglund, et al., 2005) which may be accounted for by similarities in their aetiology. Anxiety and depression are considered emotional disorders and patients usually show increased emotional reactivity. For example,

instead of adaptive strategies to deal with stressful emotions patients engage in behaviours to alter, avoid, or control emotional responding (Farchione et al., 2012).

The aetiology of CMDs remain largely unknown and the risk of developing a CMD is affected by both hereditary and environmental factors in heterogeneous and complex processes where biological and environmental factors interact (e.g., Barlow, 2002; Ramnerö et al., 2015; Stringaris, 2017). Anxiety and depression share many common factors, hypothesised to play a significant part in the development of these disorders. These factors include a tendency for neuroticism (Brown, 2007), early negative life experiences (Chorpita & Barlow, 1998), and dysfunctional emotion regulation (Braunstein, Gross, & Ochsner, 2017; De Castella, Platow, Tamir, & Gross, 2017). Some patterns are more specific for different disorders and these are summarised below.

Patients with pathological anxiety show excessive attention to threat stimuli, perceive ambiguous or nonthreatening situations and symptoms as overly dangerous (Barlow, Allen, & Choate, 2016), and react with indiscriminate conditioned fear to threats and safe situations (Waters & Craske, 2016). This can lead to maladaptive strategies, mainly threat monitoring and threat avoidance, resulting in cognitive distress (worry and rumination) and high behavioural avoidance (Waters & Craske, 2016).

Stress is a risk factor for depression, and is hypothesised to trigger depressive behaviours and states by decreasing rewards and positive reinforcement and presenting uncontrollable aversive events (e.g., Dimidjian, Barrera, Martell, Munoz, & Lewinsohn, 2011; Ramnerö et al., 2015). This can cause passive coping strategies such as rumination, which in turn lead to more depressed mood and less healthy, positive behaviours (Schmaling, Dimidjian, Katon, & Sullivan, 2002). Behaviours that would typically produce positive consequences are instead followed by aversive consequences, such as guilt or anxiety (Ferster, 1973). Another important aspect is that depressed patients typically show excessively negative beliefs about themselves, the world, and the future, which may lead to misinterpretation of experiences and thus confirm negative biases (Beck, Rush, Shaw, & Emery, 1979).

Patients with adjustment disorder or exhaustion disorder often show a similar tendency as patients with depression and anxiety, of emotional reactivity and aversive consequences to behaviours that usually are perceived as positive, but these disorders also specifically seem to be maintained by a deficit of recuperation (Geurts & Sonnentag, 2006). This is similar to insomnia which can be described as a disorder of hyper arousal, experienced throughout the entire day (Morin & Benca, 2012). For both insomnia and adjustment disorders, cognitive factors such as worry and rumination, seem to play an important role to initiate and maintain the disorders (Eisma et al., 2015; Morin & Benca, 2012; Servant, Pelissolo, Chancharme, Le Guern, & Boulenger, 2013). For example, patients with adjustment disorders or insomnia may get hyper aroused as a consequence of thinking about stressful events and problems and therefore not manage to relax. Indeed, reducing anxious arousal has been shown to lead to decreased insomnia (McGowan, Espejo, Balliett, & Werdowatz, 2016). Similar to depression, behaviours that would typically produce positive consequences are instead followed by aversive consequences (Ferster, 1973). For example, patients may engage in activities such as working hard or trying to solve a problem and avoid more relaxing activities and thoughts due to aversive consequences, e.g., a person may feel shame or guilt if taking a rest instead of working or helping friends or family. Thus, instead of fulfilling their own needs and

balancing effort and relaxation, patients' strategies could include increased effort and focus on satisfying the needs of others.

2.2 COGNITIVE BEHAVIOURAL THERAPY (CBT)

CBT is based on a number of main principles. They include the idea that psychological problems are based, in part, on learned patterns of unhelpful behaviour and ways of thinking (American Psychological Association, 2017). Underlying theories of CBT are learning theory (e.g., Mineka & Zinbarg, 2006) and cognitive theory (e.g., Beck, 1993). CBT techniques are designed to alter and change behaviours and thoughts that maintain patients' symptoms and prevent them from living their lives according to their goals (American Psychological Association, 2017).

2.2.1 Core interventions

CBT usually includes psychoeducation about a person's symptoms, cognitive interventions to recognise unhelpful thinking and evaluate them in light of reality, and behavioural techniques to change behaviours that maintain the problems (American Psychological Association, 2017). Several disorder-specific CBT protocols have been developed that explicitly address maintenance factors for various disorders. These disorder-specific treatments display substantial variation in techniques, but all share the same core model and approach to treatment. (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012).

CBT for anxiety disorders includes several components. A main intervention is exposure to feared stimuli, in order to become more discriminate of different stimuli and learn more adaptive strategies than avoidance (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). CBT can also target patterns of excessive attention to threat stimuli by, for example, practicing to shift focus of attention (Mörtberg, Hoffart, Boecking, & Clark, 2015). Patients' tendency to perceive situations as overly dangerous can be challenged in behavioural experiments where patients engage in a feared situation and thoroughly record if their feared catastrophic outcome occurs (Clark et al., 1994).

Based on the assumption that depression is maintained by dysfunctional negative beliefs and maladaptive passive coping strategies as a response to stressful events and emotions, CBT for depression focus on behavioural activation to reconnect to activities that can be naturally reinforcing (Lejuez, Hopko, Acierno, Daughters, & Pagoto, 2011), and challenging of depressed thoughts (Beck et al., 1979). Behavioural activation is a core intervention in CBT for depression whereas cognitive restructuring is an essential part of cognitive therapy but not included in the behavioural approaches (Dimidjian et al., 2011).

CBT for adjustment disorders often include behavioural activation, exposure, cognitive restructuring, as described above, but also puts an emphasis on relaxation strategies and problem solving (van der Klink, Blonk, Schene, & van Dijk) since these aspects are hypothesized to maintain symptoms of stress and exhaustion.

CBT for insomnia, in addition to the above, have specific strategies concerning stimulus control and sleep restriction (Morin et al., 2006). Stimulus control is a behavioural treatment for insomnia designed to help patients establish a reliable sleep-wake rhythm, reinforce the bed and bedroom as cues for sleep, and weaken their association to activities that may hinder sleep (Sharma & Andrade, 2012). Sleep restriction is also a behavioural technique based on the principle that the longer you stay awake, the less likely you are to

remain awake, and the more likely you are to feel sleepy (Sharma & Andrade, 2012). A goal with the intervention is to increase sleep efficiency, i.e., the proportion of time spent in bed actually sleeping. When sleep efficiency is improved the scheduled time for sleep is gradually increased back to a normal pattern (Sharma & Andrade, 2012).

2.2.2 Effectiveness of CBT

The effectiveness of CBT in clinical settings has been widely studied. Based on the body of research, CBT is first hand choice for the treatment of anxiety disorders (NICE, 2011; Swedish National Board of Health and Welfare, 2010) and primary insomnia (Swedish agency for health technology assessment and assessment of social services [SBU], 2010). Regarding depression, CBT is first hand choice together with other specific short term psychotherapies and in some cases medication (NICE, 2011; SBU, 2004; Swedish National Board of Health and Welfare, 2010). For AD and ED, there is insufficient research but some support for CBT (Hofmann et al., 2012; van der Klink & van Dijk, 2003), physical exercise and problem solving therapy (Arends et al., 2012).

Regarding anxiety disorders, CBT is a reliable first hand choice. Meta-analyses of CBT for anxiety disorders have reported effect sizes (d) between 0.87 and 1.31 when comparing CBT to waitlist. For GAD the estimated effect size is $d = 0.87$ (Cuijpers et al., 2014), for SAD $d = 0.93$ (Mayo-Wilson et al., 2014), for PD $d = 1.02$ (Sanchez-Meca et al., 2010), for PTSD $d = 1.22$ (Cusack et al., 2016) and for OCD $d = 1.31$ (Öst et al., 2015).

For depression, the estimated effect size compared to waitlist is $d = 0.71$ (Cuijpers et al., 2013). CBT for depression seems to yield similar effects as pharmacological treatments and treatments of interpersonal therapy and in some cases short term psychodynamic therapy (Cuijpers et al., 2013; Hofmann et al., 2012).

CBT for insomnia (CBT-I) has been shown to be more effective than control treatments with effect sizes on subjective and objective sleep measures varying from small to large (Morin et al., 2006; Trauer, Qian, Doyle, Rajaratnam, & Cunnington, 2015).

Two meta-analyses with approximately 3000 participants each, found a significant, medium to large effect size for CBT on work related stress (Richardson & Rothstein, 2008; van der Klink, Blonk, Schene, & van Dijk, 2001). Studies on the effectiveness of interventions for AD and ED are scarce. A few studies with different psychotherapeutic approaches have shown promising results in the treatment of AD, and it is generally agreed that psychotherapeutic treatments are preferable (Casey, 2014; Maercker & Bachem, 2015), though it has been found that many patients (37%) with AD are in fact treated with medication in primary care (Fernandez et al., 2012). Three meta-analyses that evaluated the effect of interventions (mainly CBT) for AD (Arends et al., 2012), stress-related disorders including ED (Perski, Grossi, Perski, & Niemi, 2017), and alleviated burnout symptoms (Ahola, Toppinen-Tanner, & Seppänen, 2017) found no significant effect on symptoms compared to control groups. All of these meta-analyses report limitations regarding methodological quality and heterogeneity of included studies and a small number of studies eligible for inclusion.

There are several reviews and meta-analyses that have evaluated the effect of CBT on anxiety and depression in primary care, and they all find treatment to be effective both compared to waitlist and primary care treatment-as-usual (Khoury & Ammar, 2014; Seekles et al., 2013;

Twomey, O'Reilly, & Byrne, 2015). For insomnia, studies have shown positive outcome when applied in primary care settings, but I have found no meta-analysis on the subject (Bothelius, Kyhle, Espie, & Broman, 2013; Davidson, Dawson, & Krsmanovic, 2017)

2.2.3 Guided self-help CBT

Guided self-help refers to treatment delivered via, for example, a book or the internet through which the patient learns about the disorder and how to apply treatment techniques to their own problems while receiving limited support by a clinician. CBT delivered as guided self-help has been shown to have positive effects on symptoms in the treatment of anxiety (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014), depression (Cuijpers, Donker, van Straten, Li, & Andersson, 2010; Karyotaki et al., 2017) and insomnia (Ho et al., 2015), with effect sizes comparable to traditional face-to-face CBT, though the effects in regular clinical settings have not been fully tested.

Interventions for stress-related disorders have not been adequately tested regarding face-to-face treatments and naturally it is the same case regarding self-help interventions (Maercker & Bachem, 2015). However, considering the characteristics of AD as a minor mental disorder, it may very well be suitable with guided self-help treatments, and has been tested as such in a few studies with encouraging results (Bachem & Maercker, 2016; Persson Asplund et al., 2017).

2.2.4 Stepped care

The use of guided self-help within a stepped care model has been suggested as a viable solution to improve accessibility to evidence-based psychological treatments of mental disorders (Andrews, 2006; National Collaborating Centre for Mental Health, 2009). Stepped care including guided self-help has also been implemented in the English initiative Improving Access to Psychological Treatments (IAPT; Clark, 2011). The core idea of a stepped care model is that patients should be treated at the lowest appropriate service level and stepped up to more advanced care only when clinically indicated. Some recent studies have tested stepped care models for anxiety and depression with mixed results (Seekles et al., 2011; Tolin et al., 2011; Nordgreen et al., 2016; van Straten et al., 2015). A small study of patients with obsessive-compulsive disorder (OCD) showed comparable and good results of stepped care CBT compared to face-to-face CBT (Tolin et al., 2011) as did a study of patients with social anxiety disorder and panic disorder (Nordgreen et al., 2016). In another study, 120 patients with anxiety or depression received stepped care with watchful waiting, guided self-help, problem solving therapy and medication. This stepped care showed no difference from care as usual (Seekles et al., 2011). A meta-analysis of stepped care for depression analysed 10 studies with 4580 patients. The interventions varied in content, number of steps and length of treatment and had an overall small effect (Cohens' $d = 0.34$) compared to care as usual (van Straten et al., 2015). In sum, results have been mixed, possibly related to methodological problems, at least for depression (van Straten et al., 2015). To the best of my knowledge, there has been no previous study of stepped care CBT that has included the whole range of patients with anxiety, depression, insomnia, adjustment disorder and exhaustion disorder. This is important since this is what constitutes the broad range of CMDs in primary care. Moreover, to our knowledge, there is no previous study evaluating whether non-responders to guided self-help CBT benefit from being stepped up to face-to-face CBT.

2.3 PREDICTORS OF OUTCOME

Even though CBT is an effective treatment of CMDs, response rates vary between 50% for depression and GAD and 70-80% for more specific anxiety disorders such as panic disorder and social anxiety disorder (Hofmann et al., 2012). Analysing predictors of treatment outcome is important in order to learn more about what treatment works for whom (Kraemer, Wilson, Fairburn, & Agras, 2002). Empirical data on predictors can be used to make more informed recommendations, for example, for whom to recommend guided self-help and for whom to recommend traditional face-to-face CBT.

A predictor is a baseline variable that affects treatment outcome (Kraemer et al., 2002). Predictors of outcome for CBT can be classified into three general categories: patient demographics, e.g., gender and age, clinical characteristics, e.g., symptom levels, and therapy process variables, e.g. expectancy of treatment (Hedman, Lindefors, et al., 2013). Predictors of treatment outcome have been of increasing interest the last decades (Brandenburg, 2017). However, small study samples and differences between studies regarding treatments, patients and outcome have made it difficult to determine distinct predictors and more research is needed (Brandenburg, 2017; Eskildsen, Hougaard, & Rosenberg, 2010).

Regarding demographic predictors, most studies on CBT for anxiety disorders have not found significant predictors (Brandenburg, 2017; Eskildsen et al., 2010), whereas for depression, being married has repeatedly shown to have a positive effect on treatment outcome (Hamilton & Dobson, 2002).

Concerning clinical predictors, comorbidity has been shown to predict worse outcome CBT for insomnia (van de Laar, Pevernagie, van Mierlo, & Overeem, 2015). For patients with anxiety disorders, having a comorbid mood disorder may predict worse outcome, while comorbid anxiety does not seem to influence treatment effect (Brandenburg, 2017; Eskildsen et al., 2010). For patients with depression, comorbid anxiety does not seem to clearly affect outcome (Hamilton & Dobson, 2002). Higher baseline symptom scores may predict higher end score but not necessarily affect the change score regarding CBT for anxiety, depression and insomnia (Brandenburg, 2017; Eskildsen et al., 2010; Hamilton & Dobson, 2002; Van Houdenhove, Buyse, Gabriels, & Van den Bergh, 2011).

Increasing emphasis has been put on the impact of treatment related variables on outcome (Brandenburg, 2017; Hedman et al., 2012; Meyer et al., 2002; Simon & Perlis, 2010). Some studies have shown that patients are more likely to benefit from treatment if they believe in the treatment, (Chambless et al., 2017; Chambless, Tran, & Glass, 1997; Hamilton & Dobson, 2002; Hedman et al., 2012; Wampold, 2015) or find the treatment logical (Carter et al., 2011). Research has also shown that adhering to treatment (Hedman et al., 2012) and conducting homework assignments (Mausbach, Moore, Roesch, Cardenas, & Patterson, 2010) are associated with better treatment outcome for both anxiety, depression (Cowan et al., 2008) and insomnia (Harvey, Inglis, & Espie, 2002). There is limited research on predictors of guided self-help CBT and results are inconclusive (Haug, Nordgreen, Öst, & Havik, 2012; Hedman et al., 2012; Hoifodt & Mittner, 2015).

Thus, there are few predictors that have repeatedly been shown to impact outcome and findings are seldom consistent over studies. There is therefore a need for predictor analyses in large scale studies in clinical settings, especially regarding guided self-help.

2.4 TREATING CMDs IN PRIMARY CARE

2.4.1 Organisation and mission

Primary care in Sweden, as in most developed countries, constitutes a foundation for the health care system by providing first line of care. In Sweden, there are more than 1100 public and private primary care units. Primary care services with four to six GPs, and other personnel (often nurses, physiotherapists, occupational therapists, psychologists, and social welfare counsellors), is the most common form of primary care practice in Sweden. (Anell, Glenngård, & Merkur, 2012)

The mission of primary care in Stockholm County is defined by the assignment to family doctors, which controls the caregiver's responsibilities, target group, competence of personnel and remuneration. It states that the caregiver should respond to the needs of medical treatment for both physical and mental disorders that do not require the resources of specialist care. It also states that psychological treatments should be aimed primarily at problems such as anxiety, depression, stress, addiction or psychosocial crisis (Stockholm County Council, 2016).

2.4.2 CMDs in primary care

Both worldwide and in Sweden, the vast majority of patients with CMDs are treated in primary care (Henderson, Glozier, & Holland, 2005; Wicks, Kosidou, & Dalman, 2017). Studies suggest that in one year 10-15% of the population will consult a primary care clinician for a mental health problem (deGruy, 1996). Among patients in primary care, 20-25% have been shown have a diagnosable mental disorder, with mood, anxiety, substance abuse, and somatoform disorders being most common. The comorbidity between these disorders is high, around 30-50% (Ormel et al., 1994; Spitzer et al., 1994). Several studies show that there are many patients in primary care with sub-threshold mental disorders, who show high impairment, are at risk of developing CMDs (Cuijpers & Smit, 2004), respond to psychological treatments and therefore also are important and meaningful to detect and offer treatment (Buntrock et al., 2016; Cuijpers & Smit, 2008; deGruy, 1996).

Worldwide, treatment of mental disorders is highly underdeveloped (Layard, 2014). A minority seeks and receive treatment and of those who do receive treatment, few obtain evidence-based interventions (Wolitzky-Taylor et al. 2015). Patients with CMDs are often treated with psychotropic medication, even though psychological treatments are recommended by treatment guidelines and preferred by most patients (Fernandez et al., 2012; van Schaik et al., 2004). Lack of resources and lack of qualified therapists have been pointed out as important explanations for this situation (Shafran et al. 2009; Layard & Clark, 2014).

In Sweden, the situation is similar. The National Board of Health and Welfare stated in their report (2007) that there is a lack of psychologists and counsellors in primary care and that there is a great need for professionals trained in CBT, in order to offer patients in primary care evidence-based treatments. The Swedish Centre for Epidemiological Studies (Stockholm County) confirms this picture. In their analysis of care for mental health in primary care, they report that 2% of male patients in primary care see a psychologist or counsellor and 5% of female patients (Wicks et al., 2017). Among patients that do see a psychologist or counsellor, there is no report on what kind of treatment patients receive nor the outcome of the treatment.

2.5 SICK LEAVE

2.5.1 Definitions

Sick leave refers to compensated work days lost due to illness (Organisation for Economic Co-operation and Development [OECD], 2010). The costs for sickness benefits due to CMDs have increased substantially in developed countries during the last decades (Henderson, Harvey, Overland, Mykletun, & Hotopf, 2011). As a consequence, research on treatments of CMDs has put more emphasis on its effects on sick leave (Nigatu et al., 2016). There has been a great variety in outcome measures, but most commonly outcome has been defined as participants' total days on sick leave or days until full or partial return to work (RTW; Arends et al., 2012).

2.5.2 Amplitude and consequences

Costs for CMDs are substantial and mainly affect the work sector (OECD, 2012). A conservative estimate of the costs of poor mental health are 3-4% of the gross domestic product in the European Union (OECD, 2012). In OECD countries 6% of the working-age population rely on disability benefits on average, and up to, 10-12% in some of the northern and eastern countries (OECD, 2010). Sweden had the highest rates of sickness disability of all OECD countries in 2002; the rates have decreased but are still among the highest in developed countries (OECD, 2009). High rates of long-term sickness absence, and many young people with mental disorders are specific characteristics behind high rates of sickness disability in Sweden.

CMDs cause most long-term sick leave of all medical conditions (Henderson et al., 2011). Depression and anxiety are the most prevalent mental disorders (Kessler et al., 2005), but in addition work stress (OECD, 2012), adjustment disorders (Koopmans et al., 2011) and exhaustion disorders (The Swedish Social Insurance Agency, 2014b) are important causes of sick leave.

Depression and low self-rated health are risk factors for longer sick leave periods (Nielsen et al., 2012) and only 20% of people who have been on sick leave for at least six months will return to work in the following five years. Further, long periods of sick leave may itself affect a person's health, wellbeing and access to the labour market negatively (Rahman, Alexanderson, Jokinen, & Mittendorfer-Rutz, 2016; Vingard, Alexanderson, & Norlund, 2004).

2.5.2.1 Rules and regulations

Policies for benefits and rehabilitation seem to greatly impact sickness disability rates (OECD, 2012). The Netherlands is a country that had similar high rates as Sweden but have worked strategically and managed to decrease sickness absence (Koning & Lindeboom, 2015). Increased economic responsibility for employers in preventing long-term sickness absence, with a strong emphasis on early interventions is suggested as an important factor behind this change. Evidence-based guidelines regarding treatment and sick leave for occupational services and primary care are also suggested to have played an important role (Hulshof, 2015).

2.5.2.2 Risk factors

There are several risk factors for sick leave due to CMDs. Women have a higher risk of sick leave compared to men (SBU, 2003). Having the main responsibility for home and family also increases the risk of sick leave (Clays, Kittel, Godin, Bacquer, & Backer, 2009). In Sweden, this risk is the highest two years after the birth of a second child, when both parents usually go back to work (Swedish Social Insurance Agency, 2014a). Moreover, aspects of work seem to affect the risk of sick leave. Not having the opportunity to influence your work situation increases the risk of sick leave (SBU, 2003), as do having lower educational level and lower salary (Swedish Social Insurance Agency, 2014a). Occupations in human services such as the areas of education, health care and social services have an increased risk of sick leave (Swedish Social Insurance Agency, 2014a). All of these factors are important to bear in mind even though the work in this thesis focuses on psychological interventions aimed at the individual to reduce sick leave.

2.5.3 Return-to-work interventions

Research on interventions to facilitate patients' return to work (RTW-I) is at an early stage and little is known about effective interventions to prevent sick leave or facilitate return to work after sick leave. Psychological treatments can reduce symptoms, but it is less clear if they affect sick leave. In some studies psychological treatments have reduced (van der Klink, Blonk, Schene, & van Dijk, 2003) or prevented (Hägglund, Johansson, & Laun, 2014) sick leave, but in other studies they have not (Ejeby et al., 2014).

Interventions to prevent or reduce sick leave differ between published studies. In some studies the psychological treatment itself is proposed to enhance the patients' health and as a consequence work functioning, and therefore prevent or reduce sick leave. In other studies a specific intervention is added to the psychological treatment to address work related issues and facilitate RTW. And in yet other studies RTW-I is the focus of treatment arguing that if problems at work are addressed and RTW occurs, this will also reduce the patient's symptoms.

Interventions in previous research have been based on different approaches. Some studies have shown that a combination of CBT techniques and work focus can be effective to enhance RTW (Lagerveld, Brenninkmeijer, Blonk, Twisk, & Schaufeli, 2016). Graded exposure to the workplace (van der Klink et al., 2003), and early contact with the workplace (Hoefsmit, Houkes, & Nijhuis, 2012) have also indicated to facilitate RTW. Other studies have had a positive effect on RTW using problem solving therapy (PST; Arends et al., 2012).

The topic has been investigated in a recent meta-analysis (Nigatu et al., 2016) where RTW after clinical or work-focused interventions was evaluated for patients with CMDs. The meta-analysis included 16 trials with 3345 subjects. The authors found that the interventions shortened the time until full RTW by 13 days, but found no support for an effect on the proportion of patients on sick leave. Doki and colleagues (2015), conducted a similar meta-analysis with 1554 workers with mental problems, evaluating the effect on sick leave for interventions by occupational health services on workers with or without sick leave. They found an overall decrease by 6.6 sick days when including workers both with and without prior sick leave, but no effect when analysing the subgroups separately. In another meta-analysis the effects on RTW after treatment for depression were studied (Nieuwenhuijsen et al., 2014). In this meta-analysis 23 studies were included, with 5996 participants, and results

showed that adding a work-directed intervention to a psychological or pharmacological intervention reduced the number of days on sick leave compared to no work-directed intervention (Nieuwenhuijsen et al., 2014). They also found that enhancing primary or occupational care with CBT reduced sick leave compared to usual care. A fourth meta-analysis investigated the effect on sick leave after psychological treatments of adjustment disorder (Arends et al., 2012). In this analysis 10 studies with 1546 participants were included. This study found that CBT did not significantly reduce days on sick leave compared to no treatment. They found that problem solving therapy (PST) significantly enhanced partial work resumption at one-year follow-up compared to non-guideline based care. Yet another meta-analysis focused on workplace interventions to prevent work disability in workers on sick leave, including different type of disabilities (van Vilsteren et al., 2015). In this review only five studies concerned mental disorders, interventions were aimed at the workplace, and not symptom reduction. The authors found no effect on sick leave for the interventions and found the evidence to be of low quality. The results in these meta-analyses are thus somewhat inconsistent, but as additional studies are published in a rapid pace further systematic reviews and meta-analyses are warranted to investigate the effect of psychological treatments on sick leave. In addition, two of the prior meta-analytic studies were restricted to depression (Nieuwenhuijsen et al., 2014) and adjustment disorder (Arends et al., 2012) respectively, and not the whole spectrum of CMDs, which could have reduced statistical power. One of the published meta-analysis restricted outcomes to proportion of employees who returned to work after the intervention and time until full RTW (Nigatu et al., 2016), which might exclude studies with other relevant measures of sick leave and absenteeism. Further, this latter meta-analysis did not include psychiatric symptoms as an outcome. Doki et al. (2015) restricted the analysis to occupational health services, not including important studies from health care services, nor including effects on symptoms, and van Vilsteren et al. (2015) focused on work interventions and only included five studies on mental disorders.

2.6 SUMMARY REGARDING GAPS OF KNOWLEDGE

Research and guidelines stress the high prevalence of CMDs (Kessler, Berglund, et al., 2005), their great cost for the individual (Üstün et al., 2004) and society (Henderson et al., 2005), the existence of effective psychological treatments (NICE, 2011; Hofmann et al., 2012) and the lack of treatment accessibility (Wolitzky-Taylor, Zimmermann, Arch, De Guzman, & Lagomasino, 2015), especially in primary care (NICE, 2011; Swedish National Board of Health and Welfare, 2007).

Against this backdrop, there are important gaps of knowledge that this thesis aims to investigate:

1. Are psychological treatments effective also to reduce sick leave?
2. Can a specific intervention to aid return to work be added to CBT to reduce sick leave among sick-listed primary care patients with CMDs?
3. Is stepped care CBT, with guided self-help and face-to-face treatment, a resource efficient way to treat patients with CMDs in primary care?
4. What factors predict positive outcome in guided self-help CBT?

3 AIM OF THE THESIS

3.1 STUDY I

The aim of Study I, a systematic review and meta-analysis, was to meta-analytically investigate the effect of psychological treatments on reducing sick leave among individuals with symptoms of depression, anxiety, stress or insomnia.

3.2 STUDY II

The aim of Study II was to evaluate CBT, RTW-I and a combination of the two (COMBO) in a clinically representative sample of primary care patients on sick leave due to CMDs. We hypothesised that RTW-I, with or without CBT, would lead to reduced sick leave compared to CBT alone. We also expected that CBT, with or without RTW-I, would lead to superior reduction of psychiatric symptoms compared to RTW-I alone.

3.3 STUDY III

The aim of Study III was to evaluate a stepped care model with guided self-help CBT and face-to-face CBT, in a clinically representative sample of patients in primary care with symptoms of CMDs. In Step I the aim was to estimate pre- to post-treatment symptom changes after guided self-help for CMDs. We expected that approximately 50% of the patients would be in remission after Step I. In Step II the aim was to evaluate the additive effect of face-to-face CBT versus continued guided self-help CBT for patients who were not in remission after Step I. We hypothesised that face-to-face treatment would yield a significant additive effect compared to continued guided self-help.

3.4 STUDY IV

The aim of Study IV was to investigate the predictive value of clinical and demographic pre-treatment characteristics on the outcome of guided self-help CBT for CMDs investigated in Study III. A secondary aim was to study the relationship between therapy-related variables, (e.g., adherence and treatment expectancy), and treatment outcome. We also explored potential differences in treatment effects between the specific psychiatric disorders that are classified as CMDs.

4 THE EMPIRICAL STUDIES

4.1 STUDY I: SICKNESS ABSENCE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF PSYCHOLOGICAL TREATMENTS FOR INDIVIDUALS ON SICK LEAVE DUE TO COMMON MENTAL DISORDERS

4.1.1 Methods

This was a systematic review and meta-analysis of original studies investigating the effect of psychological treatments on sick leave for patients with CMDs or non-patients with symptoms of CMDs and at risk for sick leave.

In order for a study to be included in this meta-analysis the following criteria had to be fulfilled: (1) the *population* consisted of adult individuals fulfilling diagnostic criteria for, or having symptoms of depression, anxiety, stress or insomnia, (2) the subjects were randomly allocated to conditions in the trial and received a psychological *intervention*, (3) there could be any kind of *comparison* condition, (4) the *outcomes* were measures of sick leave or absenteeism from work, and (5) the study was published in an English language journal.

Measures of sick leave at follow-up, continuous or categorical data, were the primary outcomes. Secondary outcomes were ratings of psychiatric symptoms, continuous or dichotomous, at post and follow-up.

The main analysis was between-group effects with follow-up data on measures of sick leave in the intervention group compared to the control condition(s). Assessment of heterogeneity was calculated using I^2 , and publication bias was assessed using Egger's (1997) regression intercept and Duval & Tweedie's (2000) trim-and-fill-method. The included studies were assessed for risk of bias using the Cochrane collaboration risk-of-bias criteria (Higgins et al., 2011). Psychotherapy Outcome Study Methodology Rating Form (Öst, 2016) was used to assess methodological quality.

4.1.2 Results

Of 2240 screened studies, 45 met all review criteria and were included in the study. The total number of participants was 10708. The studies were carried out in The Netherlands (21), the Nordic countries (Denmark, Finland, Norway, Sweden; 10), The United States (7), Great Britain (3), Germany (3) and India (1). The average score on the scale of methodological quality (total score range 0-44) was 16.0 (SD = 3.8), ranging from 4-23. The item yielding the lowest scores was; "Control of concomitant treatments".

The overall Hedges' g was small (0.15) but significantly different from zero (95% CI: 0.09-0.21). Overall, 52% of the patients were considered responders concerning sick leave at follow-up. There was no significant indication of publication bias using Egger's regression intercept (0.70, $t = 1.30$, $p = 0.20$). Duval and Tweedie's trim-and-fill method did not suggest any study to be trimmed. Since heterogeneity was significant, moderator analysis in the form of meta-regression was conducted on continuous variables and subgroup analysis on dichotomous data. None of the analyses yielded significant effects. The meta-analytic results regarding effects on psychological symptoms at post-treatment was small (Hedges' $g = 0.21$; CI = 0.13-0.29) but significantly different from zero. Indices of heterogeneity were not significant. At follow-up, 56% of participants were considered responders.

4.1.3 Discussion

The findings showed a small but significant effect on both sick leave and psychiatric symptoms for all interventions compared to care as usual. At follow-up, a majority of the participants were considered responders concerning sick leave (52%) and symptoms (56%).

Earlier meta-analyses on the subject have yielded various results, possibly due to a low number of included studies and lack of power. The effects on sick leave in the present meta-analysis is comparable to the meta-analysis of Nigatu (2016) on workers with CMDs. There were no significant differences in effects between different types of interventions, nor was there a difference between patients on sick leave and those at risk for sick leave. Few studies on psychotherapy include measures of sick leave. The included studies, thus, represent a small proportion of all psychological interventions for patients with CMDs. This makes it difficult to generalise the results to all psychological interventions. Altogether, even though the effect on sick leave was small, it may very well be of high societal relevance considering the high costs of sick leave due to CMDs (OECD, 2012).

Effect sizes on psychological symptoms were small (Hedges' $g = 0.21$) when pooling all treatments. In meta-analyses of CBT for anxiety and depression effect sizes varies between 0.71-1.31 when comparing CBT to waitlist and moderate to large effect sizes when comparing to care as usual or control conditions (Cuijpers et al., 2013; Hofmann et al., 2012). There are several possible explanations for the small effects on symptoms for the included interventions in this study. It could be that patients in the present meta-analysis had less severe symptoms than most studies on psychotherapy for anxiety and depression. There may have been a floor effect with less room for improvement when symptoms were mild at pre-treatment. Another possible explanation is the variation of symptoms and disorders. Many of the studies included patients with elevated levels of stress, anxiety, depression or pain. It could be that this reflects a population with less distinct symptoms for which traditional CBT has not been developed or evaluated. Yet another possible explanation is that many of the studies do not have the same methodological quality of the psychological treatment as gold standard treatments for anxiety and depression. Many of the studies were conducted in a work setting and the expertise may be better regarding occupational aspects than psychiatric symptoms. None of the studies describe interventions to be disorder specific, gold standard CBT with a clear description of the therapists' adherence and competence as is customary in high-quality psychotherapy studies.

The small effects, the lack of difference in effect between interventions, the variation in measures, and the variation and low ratings of methodological quality, imply that there is room for improvements. Studies on psychotherapy should add measures of sick leave to evaluate the effect of treatments on RTW. Studies aimed at RTW should investigate high quality psychotherapy with training and measurement of therapists' competence and compliance. Further, it is of utmost importance to establish common measures of sick leave and RTW to be able to better compare effects from different studies. Days on sick leave one year after randomisation, and days until full and partial RTW are today the most common measures of sick leave. Since benefits and regulations vary between countries and seem to greatly affect sick leave (OECD, 2012), it is also important to study the impact of these systems.

4.2 STUDY II: COGNITIVE BEHAVIOURAL THERAPY AND RETURN-TO-WORK INTERVENTION FOR PATIENTS ON SICK LEAVE DUE TO COMMON MENTAL DISORDERS – A RANDOMISED CONTROLLED TRIAL

4.2.1 Methods

4.2.1.1 Context and setting

Study II was conducted at four primary care clinics in Stockholm, three public and one private, situated in different areas and serving 10 000 to 35 000 inhabitants each. The clinics are situated in areas with different socioeconomic status. Fourteen psychologists, with 1-8 years of experience of working with CBT, worked at these clinics the two years these studies were running. Before the studies, all psychologists received 2-3 days training in each protocol followed by supervision every other week by supervisors specialized in the protocols used in the studies. Manuals and session checklists were used to aid the adherence to the protocols.

4.2.1.2 Inclusion and procedure

The study was a parallel randomised controlled superiority trial where 211 patients on sick leave due to CMDs were randomised to CBT, RTW-I or COMBO. Patients were recruited consecutively from routine primary care and treated at these clinics from September 1, 2012, until October 31, 2014. There were no self-referrals or media advertisements. Potential patients underwent a structured psychiatric assessment conducted by licensed psychologists using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) with additional criteria for exhaustion disorder.

Inclusion criteria were: (a) current sick leave since at least one month and maximum six months (50-100% of full time) due to a mental disorder of major depression, social anxiety disorder (SAD), generalised anxiety disorder (GAD), panic disorder (PD) with or without agoraphobia), obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), specific phobia, insomnia, adjustment disorder or exhaustion disorder, (b) a score of 4-6 on the 0-8 Clinician Severity Rating (CSR; Di Nardo, Moras, Barlow, Rapee, & Brown, 1993), (c) age of 18 to 65 years, (d) if on medication for a CMD, the dosage had to be stable since at least 12 weeks and kept constant throughout the treatment period, (e) low risk of suicide, (f) no current psychosis, bipolar disorder, dementia, self-harm or eating disorder, (g) no current substance abuse and (h) ability to read Swedish.

4.2.1.3 Primary outcomes

Primary outcomes were days on sick leave and proportion of patients on sick leave. Data were collected from the registry of The Swedish Social Insurance Agency, 12 months after treatment start and included all sick leave periods exceeding 14 days that had been approved by The Swedish Social Insurance Agency. The primary outcome measure of psychiatric symptoms was CSR (Brown et al., 2001), a clinician-administered measure where the severity of the psychiatric disorder is rated according to a 0-8 severity scale.

4.2.1.4 Treatments

4.2.1.4.1 CBT

Treatments were based on available evidence-based CBT protocols for each specific disorder. Depending on psychiatric disorder, the length of CBT varied between 8 and 14 weekly sessions. Table 1 presents the treatment protocols used in the trials.

Table 1.
Treatment protocols used in study

Disorder	CBT manual	No of sessions	Reference
Depression	Brief behavioural activation	10	(Lejuez et al., 2011)
GAD	Applied relaxation	8	(Öst, 1987)
SAD	Cognitive Therapy	14	(Clark et al., 2003)
OCD	Exposure with response prevention*	20	(Foa et al., 2005)
PD	Cognitive Therapy	10	(Clark et al., 1994)
PTSD	Cognitive Therapy	16	(Ehlers et al., 2005)
Insomnia	CBT	6	(Morin, 1993)
Adjustment and Exhaustion disorder	CBT	10	Unpublished manual, see Methods

Note. GAD, Generalised anxiety disorder; SAD, Social anxiety disorder; OCD, Obsessive compulsive disorder; PD, Panic disorder; PTSD, Post-traumatic stress disorder; CBT, Cognitive behavioural therapy.

*A slightly modified manual was used that also entailed a meta-cognitive component.

As no evidence-based treatments exist for adjustment and exhaustion disorder, these disorders were treated with a CBT protocol that has been developed by our research group and tested in clinical practice since 2007. The main components, behavioural activation, exposure, practicing and planning for recuperation, and problem-solving, are the same that have been used in the few existing previous studies of CBT for stress that also have shown effect (van der Klink et al., 2001).

4.2.1.4.2 RTW-I

RTW-I was an intervention with the specific aim of aiding a person on sick leave due to CMDs back to a sustainable and healthy work situation. Because no previously tested RTW-I is an established evidence-based treatment and because there was no available treatment manual in Swedish, we designed an RTW-I based on the previous literature and our clinical experience of working with sick-listed patients with CMDs. The intervention was based on basic CBT principles such as psychoeducation, exposure, behavioural activation and problem solving techniques (e.g., Farchione et al., 2012; Ferster, 1973; Lewinsohn & Clarke, 1999), graded exposure to the workplace (van der Klink et al., 2003), and early contact with the workplace (Hoefsmit et al., 2012). The treatment consisted of four central modules: (1) conceptualisation, (2) psychoeducation, (3) planning, and (4) monitoring and included one or two meetings with the patient's general practitioner, employer and administrator at the insurance agency. These modules were worked through in 10 sessions over a period of 20 weeks, initially weekly then more sparsely.

4.2.1.4.3 COMBO

In COMBO the treatments were combined, starting with three RTW-I sessions (the first three modules), followed by CBT for the specific disorder where a brief evaluation on the RTW-progress was added at the end of each session. RTW-I sessions were then scheduled flexibly according to the needs of the individual patient. Depending on the specific disorder and CBT protocol, the COMBO treatment thus varied between 10 and 25 sessions during a period of maximum 25 weeks.

4.2.1.5 Statistical analysis

Continuous data were analysed using mixed effects models or *t*-tests, dichotomous data using χ^2 tests. In analysis of between-group differences using mixed models the interaction effect of group and time was the central estimate of treatment effect. Analyses of sick leave were adjusted for sick leave days one year before randomisation. We also calculated effect sizes (ES) using Cohen's *d*. Data were analysed using intention to treat, i.e., all patients who were randomised into the trial were included irrespective of whether they completed the treatment or not.

4.2.2 Results

There was no data loss concerning sick leave. On average, patients completed 93 % of the sessions in all conditions. Days on sick leave and sick leave status are presented in Table 2. One year after treatment start there was no significant difference between treatments regarding days on sick leave.

Table 2.
Days on sick leave and sick leave status

		CBT (n = 64)	RTW-I (n =67)	COMBO (n = 80)
Days on sick leave	Mean (SD)	146.5 (124.3)	123.5 (104.5)	133.0 (109.2)
0-12 months after randomisation	Median (IQR)	135.3 (216.6)	102.0 (88.3)	96.8 (162.3)
Sick leave status	No sick leave n (%)	33 (52)	36 (54)	42 (53)
6 months after randomisation	Part-time sick leave n (%)	15 (23)	22 (33)	23 (29)
	Full-time sick leave n (%)	16 (25)	9 (13)	15 (19)
12 months after randomisation	No sick leave n (%)	49 (77)	53 (79)	64 (80)
	Part-time sick leave n (%)	7 (11)	5 (7)	9 (11)
	Full-time sick leave n (%)	8 (13)	9 (13)	7 (9)

Note. CBT, Cognitive behavioural therapy; RTW-I, Return-to-work-intervention; COMBO, Combined treatment.

There were no differences in proportion of patients on full-time sick leave, part-time sick leave or without sick leave at follow-ups six months after randomisation ($p = .499$) or one year after randomisation ($p = .831$). The mixed model analysis showed a significant difference (pre to post) on the primary outcome CSR ($p = .034$) indicating superior reduction of psychiatric symptoms after CBT compared to RTW-I. Improvements were sustained at 1YFU and patients in all conditions had reached similar symptom levels. In

total, 140 patients (67% of the total sample, counting non-data providers as still fulfilling diagnostic criteria) did not fulfil criteria for their principal disorder at post-treatment.

4.2.2.1 Additional data

As the CBT intervention for AD and ED has not been previously tested and because this was by far the largest subgroup of disorders ($n = 152$), we conducted a post-hoc subgroup analysis, not yet published. Patients diagnosed with AD or ED were combined into Subgroup 1 and patients diagnosed with depression, any of the anxiety disorders or insomnia ($n = 59$) were combined into Subgroup 2.

4.2.2.1.1 Subgroup analysis of sick leave

In Subgroup 1, patients with AD or ED, there was no difference in days on sick leave between treatments the year after randomisation ($p = .260-.586$). As shown in Table 3, differences in observed number of sick days were small.

In Subgroup 2, patients with primary depression, anxiety, or insomnia, there were large differences between treatments regarding days on sick leave one year after randomisation. Estimated data showed that patients had 92.0 (CI: 24.4-159.6; $p = .010$) days less on sick leave after RTW-I compared to CBT and 75.8 (CI: 13.5-138.1; $p = .021$) days less of sick leave after COMBO compared to CBT. The difference of 14.9 (CI: -74.3-44.4) days less on sick leave after RTW-I compared to COMBO was not significant ($p = .624$).

Table 3.

Mean days on sick leave (observed data) one year after treatment start

	CBT		RTW-I		COMBO	
	M	SD	M	SD	M	SD
Subgroup 1 $n = 152$	136.5	119.5	147.8	115.7	132.1	105.4
Subgroup 2 $n = 59$	189.5	140.9	107.1	93.0	100.2	101.1

Note. CBT, Cognitive behavioural therapy; RTW-I, Return-to-work-intervention; COMBO, Combined treatment; M, mean days on sick leave; SD, standard deviation. Subgroup 1 = Patients with adjustment or exhaustion disorder; Subgroup 2 = Patients with depression, anxiety, or insomnia.

4.2.2.1.2 Subgroup analysis: CSR

In Subgroup 1 there was a significant interaction effect of time and group (pre to post) on the CSR ($p = .016$) indicating superior reduction of stress-related symptoms after CBT compared to RTW-I. There was no significant difference between COMBO and RTW-I or CBT pre to post. From post to 1YFU there was no difference between treatments. In Subgroup 2 there was no significant difference between treatments regarding CSR (pre to post or post to 1YFU).

4.2.3 Discussion

There were no differences in reduced sick leave between treatment conditions. CBT led to superior reduction of psychiatric symptoms post-treatment compared to RTW-I on the primary outcome CSR. However, at 1YFU there were no longer a difference between

treatments. Overall, within-group effect sizes (d) from pre- to post-treatment were large in all treatment groups on all measures of psychiatric symptoms and the effects were maintained at 1YFU.

In the subgroup analysis, patients with depression, anxiety, or insomnia who received RTW-I or COMBO had 76 to 92 days less on sick leave compared to patients who received CBT the year after treatment start, indicating a large, significant effect for these patients. In contrast, there was no difference in sick leave between treatments for patients with AD or ED. Interestingly, CBT led to large improvements for patients with AD or ED regarding psychiatric symptoms and the difference between CBT and RTW-I was larger for these disorders. As the subgroup analysis were conducted post-hoc and Subgroup 2 consisted of only 59 patients, conclusions should be drawn with caution.

There are several possible explanations for the lack of effects on sick leave. Patients were treated in primary care by psychologists primarily experienced in CBT for CMDs. In many previous studies, treatments have been carried out by occupational therapists, occupational physicians or labour experts (e.g., Arends et al., 2012; Nigatu et al., 2016). It is possible that the setting and the therapists had too little connection to or expertise regarding the actual workplace to affect sick leave.

Another possible explanation is the comparison with gold-standard CBT. Even though disorder-specific CBT is the recommended treatment for CMDs, it is rare that patients receive these treatments. Care as usual, often limited to a few sessions with a physician, is by far the most common comparison of previous RTW-I studies (Nigatu et al., 2016). Thus, the CBT arm was a more intensive and extensive control condition than in previous RTW-I studies and therefore a tougher comparison. At 1YFU roughly 80% of patients in all conditions had resumed full RTW, 10% worked part-time and 10% were on full-time sick leave, leaving somewhat limited room for improvement. Meta-analyses of psychological interventions for individuals with CMDs on sick leave have found effects ranging from 0-17 days of reduced days on sick leave or days until RTW for psychological interventions compared to care as usual (Arends et al., 2012; Doki et al., 2015; Nieuwenhuijsen et al., 2014; Nigatu et al., 2016). The difference in days on sick leave between CBT and RTW-I in the present study was a non-significant difference of 20 days. Possibly the study was underpowered to detect such a difference. The lack of data on sick leave periods shorter than 14 days could also have reduced differences and power.

The largest group in our sample was patients with exhaustion disorder. As previously mentioned, the guidelines of the Swedish National Board of Health and Welfare recommend sick leave 6–12 months for ED. This differs markedly from the recommendations for depression, anxiety and insomnia where sick leave should either be avoided or restricted to 2 to 6 weeks, preferably part time (Swedish National Board of Health and Welfare, 2016). Benefits and regulations strongly affect sick leave and the lack of difference between treatments regarding sick leave in the current study could reflect that guidelines regarding sick leave for ED is a stronger predictor of sick leave than the contents of the treatments used.

4.3 STUDY III: STEPPED CARE IN PRIMARY CARE – GUIDED SELF-HELP AND FACE-TO-FACE COGNITIVE BEHAVIOURAL THERAPY FOR COMMON MENTAL DISORDERS: A RANDOMISED CONTROLLED TRIAL

4.3.1 Methods

4.3.1.1 Setting, inclusion and procedure

Study III was conducted parallel to Study II, i.e., patients were recruited and treated at four primary care clinics in Stockholm County 2012-2014. This multi-site-study tested a stepped care model in the treatment of consecutively referred primary care patients with symptoms of CMDs. In Step I, all patients (N = 396) received guided self-help CBT in a pretest-posttest effectiveness trial. In Step II, patients with remaining clinically relevant psychiatric symptoms, including both patients not in remission and patients with missing data (N = 214), were offered to participate in a randomised controlled trial (RCT). Of these, 161 (75%) accepted and were randomised to face-to-face CBT (n = 80) or continued guided self-help CBT (n = 81).

Inclusion criteria were, (a) mild to moderate symptoms of depression, SAD, GAD, PD (with or without agoraphobia), OCD, insomnia, AD or ED, (b) a score of 2-6 on CSR (Di Nardo et al., 1993), (c) age of 18–65 years, (d) if on medication for a CMD, the dosage had to be stable since at least 12 weeks and kept constant throughout the treatment period, (e) low risk of suicide, (f) no current psychosis, bipolar disorder, dementia, self-harm or eating disorder, (g) no current substance abuse and (h) ability to read Swedish. Patients with PTSD or specific phobia were not included since we had no guided self-help treatments for these disorders. The sample (N = 396) consisted of 286 women (72%) and 110 men (28%). The mean age was 37.2 years (SD = 11.4). In this sample, 206 patients (52%) had at least one comorbid disorder.

4.3.1.2 Primary outcomes

The primary outcome was remission, defined as the patient rated below a pre-established cutoff on a disorder-specific scale measuring symptoms of the patient's principal disorder. The disorder-specific scales were Montgomery Åsberg Depression Rating Scale-Self Rated (MADRS-S; Svanborg & Åsberg, 1994), The Penn State Worry Questionnaire (Meyer, Miller, Metzger, & Borkovec, 1990), Liebowitz Social Anxiety Scale-Self report (Fresco et al., 2001), Obsessive–Compulsive Inventory-Revised (Foa et al., 2002), The Panic Disorder Severity Scale-Self-rated (Houck, Spiegel, Shear, & Rucci, 2002), Insomnia Severity Index (Bastien, Vallieres, & Morin, 2001), Perceived Stress Scale (Cohen S, 1988), and Shirom-Melamed Burnout Questionnaire (Melamed, Kushnir, & Shirom, 1992). Patient ratings were obtained pre-treatment, weekly during treatment, post-Step I, post-Step II and at follow-up six months (6MFU) and one year (1YFU) after post-Step II. Pre-treatment, 333 patients (84%) rated over the clinical cutoff on their principal disorder scale.

4.3.1.3 Treatments

Table 4 presents the treatment protocols used in the trial.

4.3.1.3.1 Guided self-help CBT

Guided self-help in Study III was delivered via disorder-specific self-help books and face-to-face guidance sessions with a therapist. The books contained week-by-week programs with psychoeducation, illustration of the maintenance of symptoms and weekly exercises to record thoughts, feelings, and changing behaviours assumed to maintain the disorder. Treatments lasted nine weeks and therapists saw patients for two sessions, 30-45 minutes each. There was no other support online or via telephone. In the first session, patients received the disorder-specific self-help book and received instructions on how to work with the program. Therapists encouraged patients to schedule their therapy at home with weekly sessions of reading and planning, as well as daily recordings and experiments. After four weeks patients came back for a second guidance session. The guided self-help books used in this trial to treat depression, insomnia, PD, and SAD were based on internet programs of guided self-help CBT that have been tested with large effects in several RCTs and in routine practice with more than 1500 patients (Hedman et al., 2011; Hedman et al., 2014; Hedman, Ljotsson, et al., 2013; Kaldo et al., 2015). The guided self-help treatments for OCD and GAD were also based on evidence-based treatments, i.e., exposure with response prevention (Foa et al., 2005) and applied relaxation (Öst & Breitholtz, 2000), respectively, but the self-help books had not previously been tested. For AD and ED, a manual developed by the research group was used in a self-help format as described in Study II.

4.3.1.3.2 Face-to-face CBT

Treatments were based on available evidence-based CBT protocols for each specific disorder as described in Study II. The standard lengths of protocols were 10 weekly sessions, with exception for insomnia with five sessions and social anxiety disorder with 14 recommended sessions. In this individualized treatment, therapist and patient summarised lessons learned during guided self-help and then the treatment continued according to the patient's needs.

Table 4.

Treatment protocols used in study

Disorder	Face-to-face	Guided self-help
Depression	Brief behavioural activation (Lejuez et al., 2011)	CBT (Andersson, 2007)
GAD	Applied relaxation (Öst, 1987, 2006)	Applied relaxation (Öst, 1987, 2006)
SAD	Cognitive Therapy (Clark et al., 2003)	CBT (Furmark, 2013)
PD	Cognitive Therapy (Clark et al., 1994)	CBT (Carlbring, 2011)
OCD	Exposure with response prevention (Foa et al., 2005)	Exposure with response prevention (Asplund, 2012)
Insomnia	CBT (Morin, 1993)	CBT (Jernelöv, 2008)
AD and ED	CBT (Unpublished manual, see Methods)	CBT (Unpublished manual, see Methods)

Note. GAD, Generalised anxiety disorder; SAD, Social anxiety disorder; PD, Panic disorder; OCD, Obsessive compulsive disorder; AD, Adjustment disorder; ED, Exhaustion disorder; CBT, Cognitive behavioural therapy

4.3.2 Results

Figure 1 shows participant flow, number of patients in remission at each step, and attrition throughout the trial. On average, patients in Step I completed 1.9 (SD = 0.4) of the planned two guided self-help sessions. In Step II, patients in face-to-face CBT completed on average 6.2 sessions (SD = 2.9) which corresponds to 76% of the planned treatment

sessions. For the full stepped care model, this means that if all patients that did not respond to guided self-help were stepped up to face-to-face treatment, an average of 5.7 sessions per patient would be required.

After nine weeks of guided self-help CBT, 134 patients (40%) of the 333 patients that rated over cutoff pre-Step I, rated under cutoff for clinical symptoms and were considered in remission. Face-to-face treatment was significantly more effective than continued guided self-help in Step II. At 6MFU and 1YFU, the observed rates of patients in remission, were higher in the face-to-face group compared to guided self-help, but differences no longer reached statistical significance.

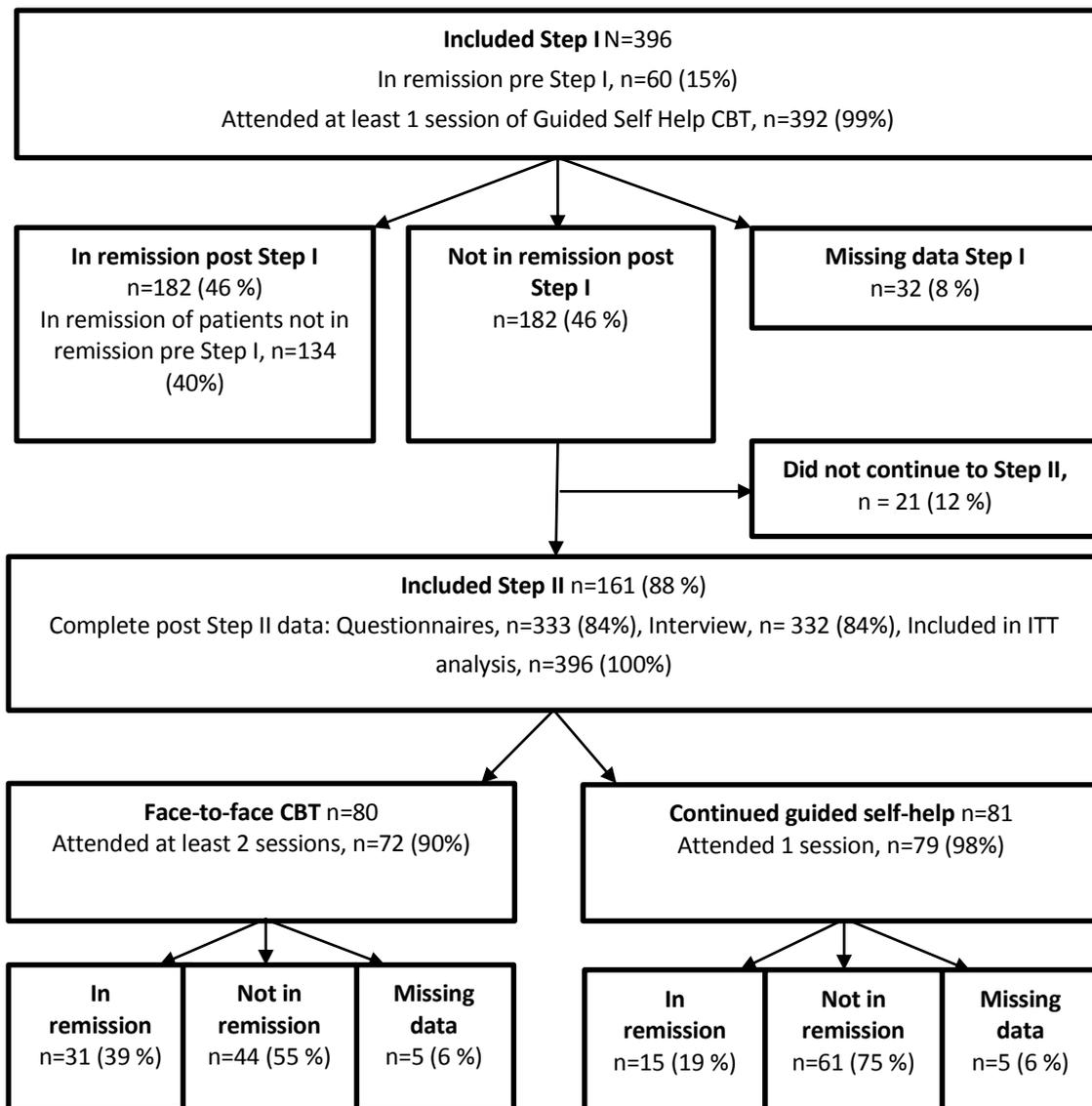


Figure 1. Participant flow, number of patients in remission at each step, and attrition throughout the trial.

CBT, Cognitive Behavioural Therapy; Step I, an open trial with nine weeks of guided self-help CBT; Step II, a randomised controlled trial with guided self-help CBT or Face to face CBT.

4.3.3 Discussion

This is to my knowledge the first study to employ a rigorous method to investigate the additional effect of face-to-face CBT after guided self-help CBT. The results showed a substantial decrease of symptoms after guided self-help for CMD and an additional effect of face-to-face treatment compared to guided self-help for non-responders. After the initial step with nine weeks of guided self-help, 40% of patients with pre-treatment ratings at clinical levels, were in remission. In the face-to-face group, 39% achieved remission compared to 19% in the continued guided self-help group, a statistically significant difference. This indicates that stepping up patients to face-to-face CBT is of additional clinical value for those who do not respond to guided self-help CBT.

In total, 63% would be in remission after treatment with this stepped care model. Because a large proportion of patients would remit after Step I, and not need face-to-face treatment, the average number of sessions required for each patient to achieve this remission rate would be 5.7. In other words, using this stepped-care model would lead to remission for nearly two thirds of the patients, and this would be achieved with approximately 50% of the therapist resources required in conventional face-to-face CBT. These results are well in line with previous evaluations of stepped care for CMDs (e.g., Gyani, Shafran, Layard, & Clark, 2013; Nordgreen et al., 2016). Given the lack of trained therapists, especially in primary care, this stepped care model presents an appealing alternative to provide more patients with evidence-based care.

Strengths of the present study were the large, consecutively included primary care sample comprising all of the highly prevalent CMDs, the use of reliable and valid instruments, relatively low data attrition, 1YFU after treatment, and the randomised controlled design in Step II. Limitations were that the treatment in Step I was not compared with a control group, that not all non-remitted patients after Step I continued to Step II, and that adherence to protocols and competence of therapists were not measured.

4.4 STUDY IV: PREDICTORS OF OUTCOME IN GUIDED SELF-HELP COGNITIVE BEHAVIOURAL THERAPY FOR COMMON MENTAL DISORDERS IN PRIMARY CARE

4.4.1 Methods

This was a study with a repeated measurement design investigating the predictive value of clinical and demographic pre-treatment characteristics on the outcome of guided self-help CBT for CMDs. A secondary aim was to study the relationship between therapy-related variables, such as adherence and treatment expectancy, and treatment outcome. We also explored potential differences in treatment effects between the specific psychiatric disorders that are classified as CMDs. The study included patients (N = 396) who received guided self-help in a pretest-posttest effectiveness trial conducted in a primary care setting (Study III, Step I).

Demographic data were collected during the initial assessment. The following demographic characteristics were investigated as potential predictors: age, presence of major life stressor, being unemployed or on sick leave, educational level, heredity for mental disorders, marital status, and having children or not.

The investigated potential clinical predictors were pre-treatment symptom severity of the principal disorder, comorbid major depression, comorbid anxiety disorder (any type), age at onset of principal disorder, pre-treatment scores on HADS anxiety scale (Zigmond & Snaith, 1983), MADRS-S (Svanborg & Asberg, 1994), and Quality of Life Inventory (QOLI; Frisch, 1992).

To explore the impact on outcome of participants' view of treatment credibility and expectancy, the Credibility Scale (C-scale) was used (Borkovec & Nau, 1972). Assessor estimation of positive outcome was conducted by the psychologist at pre-treatment with a one item question "To which extent do you believe that the patient will improve from the treatment" rated on a Likert scale (range 0-10). After treatment, therapists rated patient's adherence to treatment according to three alternatives; completed according to plan, partially completed, dropped out. Additionally, the number of missed sessions were recorded.

Differences in outcome for the respective disorders were analysed using χ^2 -tests. Logistic regression using remission and reliable change as dependent variables was performed to identify significant single predictors and secondly, a multiple regression model was conducted. Linear regression analyses with post-treatment depression ratings (MADRS-S), were conducted to identify significant predictors and subsequently a multiple regression model was applied. Therapy-related variables were analysed separately.

4.4.2 Results

The overall remission rate was 40% and 49% of the participants reached reliable change after the nine weeks of guided self-help CBT. Analyses of differences between disorders in outcome were significant both regarding remission rates ($p < .001$) and reliable change ($p = .012$). Among patients with MDD and SAD about 25% reached remission. This was a significantly lower remission rate compared to patients with GAD (48%) and AD (59% [$p < .001-.012$]). On the other hand, patients with GAD reached reliable change to a lower extent (30%) than patients with AD (55%), MDD (53%) and SAD (53% [$p < .002-.008$]).

In the final multiple regression model, pre-treatment ratings of quality of life ($p = .043$) and educational level remained significant ($p = .003$). Only 22% of patients who had a pre-treatment QOLI score below 0 reached remission, whereas 51% of patients with a QOLI score ≥ 0 were in remission post-treatment. Concerning educational level, every increased level of education improved the chance of reaching remission. For patients with nine years of compulsory school, the chance of reaching remission after treatment was 20%, for patients with 2-3 years of secondary school the remission rate after treatment was 32%, and patients who had studied at college or university, had a 47% chance of reaching remission after treatment. Age at onset was the only significant predictor of reliable change ($p = .044$), i.e., older age at onset was associated with higher chance of reliable change. Higher pre-treatment ratings of quality of life predicted lower depressive symptom ratings post-treatment ($p = .012$).

All treatment related variables, i.e., higher treatment credibility, psychologists' rating of higher probability of positive treatment outcome, patients missing fewer sessions and therapists' rating higher patient adherence to treatment, increased the chance of remission and reliable change ($p = .012 - .0001$). Regarding post-treatment depression ratings, all treatment related variables, except missed sessions, were strongly associated to a positive outcome ($p = .012 - .0001$).

4.4.3 Discussion

Higher ratings of quality of life predicted greater chance of remission and lower end state of depressive symptoms. Older age at onset was associated with greater chance of reliable change and higher education level was positively associated with remission. All therapy-related variables, i.e., higher treatment credibility, assessor estimating higher probability of positive outcome, fewer missed sessions and therapists' assessing good patient adherence to treatment, were strongly associated with increased chance of remission, reliable change and lower end state rating of depressive symptoms.

Overall, guided self-help CBT was an effective treatment. The effect sizes for the individual disorders ($d = 0.63-1.58$) were in the range of previous studies of guided self-help CBT (Andersson, Carlbring, Ljótsson, & Hedman, 2013; Hirai & Clum, 2006). Patients with depression and SAD had a lower chance of reaching remission than patients with GAD and AD. However, patients with GAD reached reliable change to a lower degree than patients with AD, depression and SAD. AD is considered to be a milder form of mental disorder than anxiety disorders and depression (Carta et al., 2009; Casey, 2014), and, thus, it is reasonable that these patients improve to a greater extent.

Clinicians' pre-treatment estimation of outcome strongly predicted outcome, so considering clinicians' assessment can be important when deciding if a patient should be treated with guided self-help or face-to-face therapy. Our results also show that the clinician could be helped by assessing how credible the patient views the treatment before making a treatment recommendation. Emphasising and following patients' adherence to treatment appear to increase treatment outcome. The data from this study indicate that the clinician should think twice before recommending guided self-help CBT for a given patient with a low educational level, who has had the disorder since early in life, has a low quality of life, and perceives the treatment as non-credible. The treatment plan may benefit from an extended discussion with the patient regarding treatment preferences, and if treatment with guided self-help CBT is still commenced, treatment progress and adherence should preferably be

followed closely. A risk of engaging in treatments that have no effect is that patients may not be motivated to engage in subsequent treatments that may have a greater chance of being successful. Gold standard, face-to-face CBT or pharmacotherapy could be considered as first hand treatment for these patients. However, since there are no established predictors of outcome for face-to-face CBT or SSRIs either, one cannot conclude that these treatments would be more effective. Rather, the presence of these negative predictors call for a more extensive discussion with the patient regarding treatment alternatives and preferences, and a more thorough monitoring on treatment progress.

More large-scale moderator studies on guided self-help CBT in clinical settings would strengthen the knowledge regarding what treatment works for whom. More studies on differences in outcome between different disorders would be helpful to guide treatment recommendations and organisation of care. The present study replicates findings that few demographic variables, except educational level, predict outcome and maybe future research should focus on clinical and treatment related variables to increase the knowledge of factors that can improve chances of successful treatment outcome.

5 GENERAL DISCUSSION

The overall aim of this thesis was to implement and evaluate evidence-based CBT, to evaluate CBT for adjustment and exhaustion disorders, and to evaluate an intervention to reduce sick leave (RTW-I) among patients with CMDs in primary care. Specifically, I and my colleagues wanted to evaluate the effects on reduced symptoms and sick leave, effectiveness of stepped care CBT and predictors of outcome for guided self-help CBT.

5.1 EFFECTIVENESS OF PSYCHOLOGICAL TREATMENTS ON SICK LEAVE

Study I showed that psychological interventions had a significant but small effect in reducing sick leave compared to treatment as usual. There were no differences between the different types of interventions. Even though the effect was small, this could be of importance considering the high costs for sick leave (OECD, 2010).

Study II showed no significant difference in sick leave between RTW-I and CBT. There are several possible explanations. Considering the small effect on sick leave in Study I and previous meta-analyses (Nigatu et al., 2016), Study II could be underpowered to detect potential differences. Patients all received active treatments and there was no untreated control group or care as usual. It could be that all patients in fact reduced sick leave more than patients in general receiving care as usual. Another possible explanation is that RTW-I was suboptimal to reduce sick leave. Early interventions and contact with employer have been pointed out as key factors for RTW. In Study II patients were on sick leave for 1-6 months when included and perhaps interventions should rather be introduced at the very beginning of a sick leave spell. In RTW-I, patients, physicians, employers and officials from the insurance agency were all involved. However, this constitutes quite a large group with a possibility of confusion of responsibility. In The Netherlands, where sick leave has been reduced in general, key changes have been regulations (Hulshof, 2015), evidence-based guidelines for treatment and sick leave concerning AD in occupational and primary care (van der Klink & van Dijk, 2003), and increased responsibility for employers in preventing sick leave (Koning & Lindeboom, 2015). These may be crucial aspects to prevent sick leave also in Sweden. The subgroup analysis in Study II revealed differences between different disorders. RTW-I yielded no additional effect on sick leave for patients with AD or ED, whereas for patients with anxiety disorders, depression or insomnia, RTW-I had a large effect on reduced sick leave. Future studies need to replicate these findings in studies with sufficient power and explore if there are specific characteristics among patients with AD and ED that hinder RTW.

5.2 EFFECTIVENESS OF PSYCHOLOGICAL TREATMENTS ON PSYCHIATRIC SYMPTOMS

CBT is an effective treatment of CMDs in primary care (Study II and III) with effect sizes and remission rates comparable to prior literature of face-to face CBT (Hofmann et al., 2012) and guided self-help CBT (Cuijpers et al., 2010). It is notable that the effects were as strong for patients with adjustment and exhaustion disorders (Study II, III and IV), where previous research is limited (Carta et al., 2009). Effects were maintained at follow-ups after 6 and 12 months (Study II and III), but interestingly patients who received the RTW-I and continued guided self-help had by then also improved to almost the same symptom levels as those who received face-to-face CBT.

5.2.1 Stepped care

The stepped care model (Study III) yielded an overall remission rate of 63%, well in line with previous studies of face-to-face CBT (Hofmann et al., 2012) and stepped care models (Gyani et al., 2013; Nordgreen et al., 2016; Seekles, van Straten, Beekman, van Marwijk, & Cuijpers, 2011). The results were obtained using less than six sessions, a reduction of approximately 50% compared to evidence-based face-to-face CBT (Layard, Clark, Knapp, & Mayraz, 2007).

5.2.2 Predictors of outcome in guided self-help CBT

Overall, guided self-help CBT was a useful treatment. The effect sizes for the individual disorders ($d = 0.63-1.58$) were in the range of previous studies of guided self-help CBT (Andersson, Carlbring, Ljótsson, & Hedman, 2013; Hirai & Clum, 2006). Patients with depression and social anxiety disorder had a lower chance of reaching remission but our results suggest that these patients still make substantial improvements.

Significant predictors for positive outcome after guided self-help CBT were higher quality of life ratings, higher educational level, older age at onset, patients rating higher treatment credibility and clinicians rating higher probability of positive treatment response. These factors could be further investigated in research and considered by therapists when planning for guided self-help CBT. Attending sessions and working actively with treatment assignments improved the likelihood of positive treatment outcome and should be emphasised.

5.3 CLINICAL IMPLICATIONS

Patients in primary care with anxiety, depression, insomnia, adjustment or exhaustion disorders can be effectively treated with stepped care CBT. Many patients will benefit from guided self-help CBT but stepping up non-remitters to face-to-face treatment will increase remission rates with 50%. Treatments can be delivered at primary care centres of different sizes, in different socioeconomic areas providing that the therapist have proper training in the treatment methods.

Patients with lower education, younger age at onset, lower ratings of quality of life and where both patient and clinician doubt the efficacy of guided self-help, have a reduced chance of reaching remission after guided self-help CBT. These patients should be closely monitored and treatment plans should emphasise patients' preferences.

Regarding sick leave, evidence-based treatments seem to prevent and reduce sick leave to some extent compared to treatment as usual. Hopefully research will find interventions and methods to further improve this outcome.

5.3.1 Barriers to implementation

To spread this model of evidence-based care, efforts are needed. Research strongly support that investments in psychological treatments will pay back double in terms of reduced medical costs (Chiles, Lambert, & Hatch, 1999), increased tax revenues and reduced benefit usage (Layard et al., 2007). Considering that mental disorders are estimated to be just as prevalent, impairing and costly as physical disorders, it seems reasonable, cost-effective and fair to make investments in effective mental health care accordingly. Implementation will be

possible with investments in therapists in primary care and specific training for these therapists to follow evidence-based treatments. Other necessary investments are continuous monitoring of outcome and delivery of treatments. These are the same core factors that have been successfully implemented in the English initiative Improving Access to Psychological Treatments (Clark et al., 2017; Gyani et al., 2013). Currently, access to therapists and evidence-based treatments is very low. Initiatives to train clinicians in primary care and supply an evidence-based structure with stepped care treatments and monitoring of outcome, are strongly indicated to increase quality and effectiveness of treatments given in primary care and to reduce societal costs. However, without further investments, access to treatment will still be unacceptably low. Expanding accessibility of internet treatments with therapist support will most certainly be part of the solution to reach remote areas in Sweden where access to therapists are scarce. National initiatives to provide these structures, competence and platforms could enable quality work for therapists working alone in primary care settings around the country.

5.4 FUTURE DIRECTIONS

There are many important research questions for future investigations. The research on assessment and treatment of adjustment- and exhaustion disorders have only just begun. Considering their high impact on sick leave, it is of high priority to develop effective treatments and sound diagnostic instruments for these disorders. Sick leave remains a challenge for Sweden and many developed countries. Implementing evidence-based psychological treatments will probably reduce sick leave to a small, but clinically relevant extent. Future interventions to increase job satisfaction and prevent sick leave are important. Closer cooperation with the workplace and changes of rules regarding sick leave regulations have the potential to greater impact these factors.

Implementation of evidence-based, stepped care psychological treatments is an urgent task. The current knowledge is sufficient for implementation, but future research can improve treatments with further knowledge regarding predictors of outcomes and expanding treatments to patients with other languages and cultures, and other disorders such as somatoform disorders.

5.5 LIMITATIONS

In Study I, it was a limitation that the search was restricted to the PubMed data base and that only one researcher performed the search in the database. The inclusion of a wide range of symptoms and interventions may also make the results difficult to interpret. In the clinical trials, Study II and III, treatments were conducted by well-trained psychologists under supervision, but it was a limitation that adherence to treatment and competence in treatment delivery were not assessed. Increased power to detect differences would probably have strengthened Study II. In Study II it also would have been interesting with an untreated or care as usual control group in order to compare effects on sick leave to other studies and primary care in general. However, in terms of evaluating the specific effect of RTW-I, it was a strength with CBT and Combo as well-defined control groups, representing evidence-based, recommended treatments. A fourth treatment condition would also further diminish power to detect differences. An important limitation in Study III and IV was the lack of control group in the first step of guided self-help and a lack of power to fully examine disorder specific differences.

5.6 ETHICAL CONSIDERATIONS

All clinical studies (II and III) were approved by the Regional Ethics Committee in Stockholm. CBT is first hand choice treatment for the conditions of patients included in this project. In primary care in Stockholm today a minority of the patients receive the recommended treatments. This project has enabled 540 patients to receive CBT; evidence-based face-to face therapy, guided self-help, CBT with an additional component to increase return to work, or experimental CBT for stress-related disorders. Sixty-seven patients have received the experimental return-to-work intervention with minimal CBT components. This group did not receive the treatment in accordance with national guidelines and this is a notable ethical consideration. Our hope was that this group would still benefit from basic CBT-psychoeducation, that the help to reduce sick leave would enhance health and that the study would contribute to important knowledge regarding how to best treat patients with common mental disorders and how to best support their return to work. Results showed that patients who received RTW-I reduced their symptoms substantially and at follow-up after one year their symptom-level was as low as that of patients who had received CBT. Participants shared information that could be considered as private such as sick leave status and psychiatric symptoms. This information was be handled confidentially and according to clinical routine practice and health care legislation. All participants provided written informed consent and were informed that participation in the study was voluntary, and that refraining from participation or dropout would not affect their care at the clinic in any way, in line with the Declaration of Helsinki Ethical Principles.

6 CONCLUSIONS

Common mental disorders; anxiety, depression, insomnia, adjustment and exhaustion disorders are highly prevalent in primary care and cause reduced quality of life and impaired functioning often with sick leave as a result. CMDs can effectively be treated with stepped care CBT. Guided self-help CBT is effective as a first step, but stepping up patients to face-to-face treatments when needed will increase remission rates substantially. Sick leave is reduced to a small extent by psychological treatments compared to treatment as usual but there is a need for more effective treatments to improve this outcome.

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