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## Predictors and mediators of outcome in CBT for chronic pain

### The roles of psychological flexibility and PTSD

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# Predictors and mediators of outcome in CBT for chronic pain

## The roles of psychological flexibility and PTSD

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DEPARTMENT OF PSYCHOLOGY | FACULTY OF SOCIAL SCIENCES | LUND UNIVERSITY





# Predictors and mediators of outcome in CBT for chronic pain

The roles of psychological flexibility and PTSD

Sophia Åkerblom



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DOCTORAL DISSERTATION

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To be defended at Palaestra hörsal, May 25th 2018, 10.00 am

*Faculty opponent*

Steven Linton, Örebro University

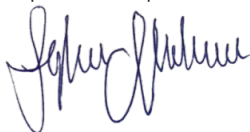
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<p><b>Abstract</b></p> <p>Chronic pain is a commonly occurring and debilitating condition, and among the costliest health problems for both the individual and society at large. Cognitive behavioral therapy (CBT) is the most widely-disseminated psychological treatment for chronic pain. Even though it is recommended and evidence-based, it yields quite modest improvements in pain-related functioning and accompanying symptoms of emotional distress. It is now generally acknowledged that further efforts are needed to improve the efficacy of CBT for chronic pain. Specifically, pain researchers have called for studies to identify mechanisms that underlie changes in treatment outcomes (mediators) and characteristics of the individual that predict improvements in these mechanisms and treatment overall (predictors and moderators).</p> <p>To address this call, the primary aim of this research program was to study whether changes in psychological flexibility mediated outcomes in a multi-disciplinary, group-based CBT program delivered at a regional specialist unit for pain rehabilitation. The secondary aim was to identify possible predictors of outcome by focusing on facets of psychological flexibility as well as the understudied influence of posttraumatic stress disorder (PTSD). This aim also included investigation of the relationships between PTSD, pain presentation, and psychological flexibility. With these two aims, we hoped to shed further light on the validity of the psychological flexibility model as an integrating, overarching model that can help define relevant treatment processes for adults presenting with chronic pain and psychiatric problems.</p> <p>Study I investigated whether pain-related acceptance, from the psychological flexibility model, and other variables posited as potential mediators in standard CBT mediated changes in pain-related outcomes measured at post-treatment and 12-month follow-up from the CBT program. The results highlighted the mediating role of pain-related acceptance across different indices of outcome.</p> <p>Study II evaluated the psychometric properties of the Swedish-language versions of the full length and shortened version of the Committed Action Questionnaire, as well as the generalizability of previous results related to committed action. The results supported the validity and reliability of the Swedish-language versions of the measure, the generalizability of earlier findings, and the relevance of committed action to health and functioning in individuals with chronic pain.</p> <p>Study III focused on the prevalence of traumatic experiences, trauma types, and PTSD in patients referred for treatment of chronic pain, and the relationship between PTSD and pain-related functioning prior to treatment. High rates of traumatic exposure and PTSD were found for chronic pain patients. The presence of PTSD in these patients was associated with worse clinical characteristics and an increased need for treatment.</p> <p>Study IV examined whether various processes from the psychological flexibility model mediated the relationship between PTSD and chronic pain. Results indicated that the relationship was mediated by pain-related acceptance, committed action, and cognitive fusion, where pain-related acceptance constituted the most influential mediator from the psychological flexibility model.</p> <p>Study V analysed whether indices of emotional distress (including PTSD) and different facets of psychological flexibility predicted pain-related outcomes at 12-month follow-up from the CBT program. Furthermore, it examined whether changes in processes from the psychological flexibility model mediated changes in pain-related outcomes. The only significant predictors of outcomes turned out to be psychological inflexibility and committed action. All available facets of psychological flexibility had mediating effects on treatment outcomes.</p> <p>Based on the results from these studies, theoretical integration within the CBT field may be facilitated by a process-focused approach including the psychological flexibility model. This model seems to be transdiagnostically and trans-situationally applicable in several ways. Its processes span problem areas with diverse backgrounds from the somatic field and chronic pain to the psychiatric field and PTSD, and appear useful not only to treatments specifically built around targeting psychological flexibility but also more broadly in CBT treatments.</p>		
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# Contents

Acknowledgements .....	7
Abstract .....	8
Summary in Swedish.....	10
List of studies .....	12
Abbreviations .....	13
Introduction .....	15
Definition, prevalence of chronic pain, and costs for society .....	15
Psychiatric comorbidity in individuals with chronic pain.....	16
Posttraumatic stress disorder and chronic pain.....	16
Treatment of chronic pain .....	17
Cognitive behavioral therapy for chronic pain .....	19
The psychological flexibility model .....	21
Predictors, moderators, and mediators of outcome in CBT for chronic pain .....	24
Predictors, moderators, and mediators related to the psychological flexibility model .....	26
General and specific aims .....	27
Methods .....	31
Designs and settings .....	31
Participants .....	31
Ethics .....	31
Inclusion and exclusion criteria.....	32
Intervention .....	32
Measures .....	33
Data analyses.....	37
Attrition analyses.....	37
Descriptive analyses .....	38
Psychometric analyses .....	38
Group differences .....	38
Indirect/mediating effects .....	39
Research studies .....	41
Study I .....	41
Study II.....	45
Study III .....	46
Study IV .....	48

Study V.....	51
Discussion.....	55
General discussion.....	55
Practice implications and further studies.....	57
Research limitations .....	60
Conclusions .....	62
References .....	63



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Lastly, I wish to thank the participants of the studies included in this dissertation.

## Abstract

Chronic pain is a commonly occurring and debilitating condition, and among the costliest health problems for both the individual and society at large. Cognitive behavioral therapy (CBT) is the most widely-disseminated psychological treatment for chronic pain. Even though it is recommended and evidence-based, it yields quite modest improvements in pain-related functioning and accompanying symptoms of emotional distress. It is now generally acknowledged that further efforts are needed to improve the efficacy of CBT for chronic pain. Specifically, pain researchers have called for studies to identify mechanisms that underlie changes in treatment outcomes (mediators) and characteristics of the individual that predict improvements in these mechanisms and treatment overall (predictors and moderators).

To address this call, the primary aim of this research program was to study whether changes in psychological flexibility mediated outcomes in a multi-disciplinary, group-based CBT program delivered at a regional specialist unit for pain rehabilitation. The secondary aim was to identify possible predictors of outcome by focusing on facets of psychological flexibility as well as the understudied influence of posttraumatic stress disorder (PTSD). This aim also included investigation of the relationships between PTSD, pain presentation, and psychological flexibility. With these two aims, we hoped to shed further light on the validity of the psychological flexibility model as an integrating, overarching model that can help define relevant treatment processes for adults presenting with chronic pain and psychiatric problems.

Study I investigated whether pain-related acceptance, from the psychological flexibility model, and other variables posited as potential mediators in standard CBT mediated changes in pain-related outcomes measured at post-treatment and 12-month follow-up from the CBT program. The results highlighted the mediating role of pain-related acceptance across different indices of outcome.

Study II evaluated the psychometric properties of the Swedish-language versions of the full length and shortened version of the Committed Action Questionnaire, as well as the generalizability of previous results related to committed action. The results supported the validity and reliability of the Swedish-language versions of the measure, the generalizability of earlier findings, and the relevance of committed action to health and functioning in individuals with chronic pain.

Study III focused on the prevalence of traumatic experiences, trauma types, and PTSD in patients referred for treatment of chronic pain, and the relationship between PTSD and pain-related functioning prior to treatment. High rates of traumatic exposure and PTSD were found for chronic pain patients. The presence

of PTSD in these patients was associated with worse clinical characteristics and an increased need for treatment.

Study IV examined whether various processes from the psychological flexibility model mediated the relationship between PTSD and chronic pain. Results indicated that the relationship was mediated by pain-related acceptance, committed action, and cognitive fusion, where pain-related acceptance constituted the most influential mediator from the psychological flexibility model.

Study V analysed whether indices of emotional distress (including PTSD) and different facets of psychological flexibility predicted pain-related outcomes at 12-month follow-up from the CBT program. Furthermore, it examined whether changes in processes from the psychological flexibility model mediated changes in pain-related outcomes. The only significant predictors of outcomes turned out to be psychological inflexibility and committed action. All available facets of psychological flexibility had mediating effects on treatment outcomes.

Based on the results from these studies, theoretical integration within the CBT field may be facilitated by a process-focused approach including the psychological flexibility model. This model seems to be transdiagnostically and trans-situationally applicable in several ways. Its processes span problem areas with diverse backgrounds from the somatic field and chronic pain to the psychiatric field and PTSD, and appear useful not only to treatments specifically built around targeting psychological flexibility but also more broadly in CBT treatments.

## Summary in Swedish

Långvarig smärta är ett vanligt förekommande och tärande tillstånd som är bland de mest kostsamma hälsoproblemen för både individen och samhället som helhet. Kognitiv beteendeterapi (KBT) är den mest spridda psykologiska behandlingen för långvarig smärta. Även om metoden är evidensbaserad och rekommenderad ger den relativt blygsamma förbättringar för smärtrelaterad funktion och medföljande emotionella symtom. Det är nu allmänt vedertaget att ytterligare ansträngningar behövs för att förbättra effektiviteten av KBT för långvarig smärta. Mer specifikt har smärtforskare förordat studier som kan identifiera mekanismer genom vilka behandlingseffekterna erhålls (mediatorer) och egenskaper hos individen som predicerar förbättringar i dessa mekanismer och behandling överlag (prediktorer och moderatorer).

Mot den bakgrunden hade detta forskningsprogram som primärt syfte att undersöka om förändringar i psykologisk flexibilitet medierade behandlingsutfallen i ett multidisciplinärt och gruppbaserat KBT-program på en regional specialistenhet för smärtrehabilitering. Det sekundära syftet var att identifiera möjliga prediktorer av behandlingsutfall genom att fokusera på olika aspekter av psykologisk flexibilitet samt det utforskade inflytandet av posttraumatiskt stressyndrom (PTSD). Detta syfte omfattade även att undersöka relationerna mellan PTSD, smärtpresentation och psykologisk flexibilitet. Med denna inriktning hoppades vi ytterligare kunna belysa den psykologiska flexibilitetsmodellens tillämplighet som en integrerande, övergripande modell som kan hjälpa till att definiera relevanta behandlingsprocesser för vuxna med långvarig smärta och psykiatriska problem.

Studie I undersökte om smärtrelaterad acceptans, från den psykologiska flexibilitetsmodellen, och andra variabler som tidigare föreslagits som mediatorer i standard-KBT medierade behandlingsutfallen vid avslut och 12-månaders uppföljning från KBT-programmet. Resultaten underströk den medierande rollen hos smärtrelaterad acceptans i förhållande till olika behandlingsutfall.

Studie II utvärderade de psykometriska egenskaperna hos de svenska översättningarna av original- och kortversionen av Committed Action Questionnaire samt generaliserbarheten av tidigare resultat kopplade till ändamålsenligt handlande. Resultaten stödde validiteten och reliabiliteten av de svenska versionerna, generaliserbarheten av tidigare resultat och relevansen av ändamålsenligt handlande i förhållande till hälsa och funktion hos personer med långvarig smärta.

Studie III fokuserade på förekomsten av traumatiska erfarenheter, traumatyper och PTSD hos patienter som hade hänvisats till behandling av långvarig smärta och på relationen mellan PTSD och smärtrelaterad funktion före behandling. Höga nivåer

av traumaexponering och PTSD påvisades för patienter med långvarig smärta. Förekomsten av PTSD hos dessa patienter förknippades med svårare kliniska karaktäristika och ökat behandlingsbehov.

Studie IV undersökte huruvida olika processer från den psykologiska flexibilitetsmodellen medierade relationen mellan PTSD och långvarig smärta. Resultaten indikerade att relationen medierades av smärtrelaterad acceptans, ändamålsenligt handlande och kognitiv fusion. Smärtrelaterad acceptans uppvisade den starkaste effekten av processerna från den psykologiska flexibilitetsmodellen.

Studie V studerade ifall emotionella svårigheter (inklusive PTSD) och olika aspekter av psykologisk flexibilitet predicerade smärtrelaterade behandlingsutfall vid 12-månaders uppföljning från KBT-programmet. Studien undersökte även om olika processer från den psykologiska flexibilitetsmodellen medierade behandlingsutfallen. De enda signifikanta prediktorerna i förhållande till behandlingsutfallen visade sig vara psykologisk inflexibilitet och ändamålsenligt handlande. Alla tillgängliga aspekter av psykologisk flexibilitet medierade behandlingsresultaten.

Utifrån resultaten i studierna verkar teoretisk integration inom KBT-fältet kunna understödjas av ett processfokuserat tillvägagångssätt som inkluderar den psykologiska flexibilitetsmodellen. Modellen förefaller ha en transdiagnostisk och transsituationell tillämplighet på flera sätt. Dess processer spänner över flera problemområden med bakgrund dels i det somatiska fältet och långvarig smärta, dels i det psykiatriska fältet och PTSD. Processerna tycks inte enbart vara användbara för behandlingar som är specifikt uppbyggda kring psykologisk flexibilitet utan även för bredare KBT-behandlingar.



## List of studies

- I. Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2015). The Mediating Role of Acceptance in Multidisciplinary Cognitive-Behavioral Therapy for Chronic Pain. *The Journal of Pain*, 16(7), 606-615.
- II. Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2016). A Validation and Generality Study of the Committed Action Questionnaire in a Swedish Sample with Chronic Pain. *International Journal of Behavioral Medicine*, 23(3), 260-270.
- III. Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2017). The Impact of PTSD on Functioning in Patients Seeking Treatment for Chronic Pain and Validation of the Posttraumatic Diagnostic Scale. *International Journal of Behavioral Medicine*, 24(2), 249-259.
- IV. Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2017). The Relationship Between Posttraumatic Stress Disorder and Chronic Pain in People Seeking Treatment for Chronic Pain: The Mediating Role of Psychological Flexibility. *Accepted for publication in Clinical Journal of Pain*.
- V. Åkerblom, S., Perrin, S., Rivano Fischer, M., & McCracken, L. M. (2018). Predictors and Mediators of Outcome in Cognitive Behavioral Therapy for Chronic Pain: The Contributions of Psychological Flexibility. *Manuscript in preparation*.

## Abbreviations

PTSD = Posttraumatic stress disorder

CBT = Cognitive behavioral therapy

RCT = Randomized controlled trial

BT = Behavior therapy

ACT = Acceptance and commitment therapy

CPAQ = Chronic Pain Acceptance Questionnaire

CPVI = Chronic Pain Values Inventory

CAQ = Committed Action Questionnaire

HADS = Hospital Anxiety and Depression Scale

SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey

MPI = Multidimensional Pain Inventory Version 2

NRS = Numerical Rating Scale

PDS = Posttraumatic Diagnostic Scale

PIPS = Psychological Inflexibility in Pain Scale

TSK = Tampa Scale of Kinesiophobia

MCR = Missing completely at random

MANOVA = Multivariate analysis of variance

ANOVA = Analyses of variance

CI = Confidence interval

SE = Standard error

M = Mean

SD = Standard deviation

LL = Lower limit

UL = Upper limit

DF = Degrees of freedom



# Introduction

## Definition, prevalence of chronic pain, and costs for society

Chronic pain is often defined as any pain lasting for a period of more than three months (International Association for the Study of Pain, 1986). Chronic pain of moderate to severe intensity occurs among 19% (prevalence range of 12–30%) of adults in Europe, with a prevalence of 18% in Sweden. Out of the adults suffering from chronic pain in Europe, 34% had severe pain, 46% had constant pain, 61% were less able or unable to work, 32% had lost their jobs or had changed jobs because of their pain, and 60% had visited their doctor regarding their pain two to nine times during the last six months (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). Similar to the rest of Europe, chronic pain is one of the most prevalent and costly health problems in Sweden, with the cost of chronic pain in terms of healthcare spending, lost earnings, and welfare support annually exceeding SEK 87.5 billion (SBU, 2010).

The significant cost and social burden of chronic pain in Sweden has long been recognized. Moreover, medical and non-medical treatments focused on reducing the frequency and severity of pain have proven to be largely ineffective, with an insufficient focus on interventions that help people live a more productive life despite the presence of chronic pain (Nachemson, 1994). Recognizing the scale of the problem, the Swedish government has published guidelines for the treatment of chronic pain (SBU, 2010). The government has also mandated the collection of data (including treatment outcomes) on individuals with chronic pain at all levels of the health and social welfare system, provided funding for specialist pain centres across the country as well as funding for the development and dissemination of a wide range of interventions to help identify and support individuals with chronic pain (SKL, 2015).

## Psychiatric comorbidity in individuals with chronic pain

Individuals presenting with chronic pain often suffer from a range of co-occurring psychiatric problems including depressive disorders, anxiety disorders, somatoform disorders, substance use disorders, and personality disorders (Dersh, Polatin, & Gatchel, 2002). The most commonly occurring forms of psychiatric comorbidity are disorders involving high levels of anxiety and depression (Demyttenaere et al., 2007; Gerhardt et al., 2011; Hooten, 2016; Pope, Sharma, Sharma, & Mazmanian, 2015). Prevalence estimates for depressive and anxiety disorders in pain populations range between 2-65% and 1-65% respectively (Hooten, 2016). These variations may be due to differences in assessment methods, study designs, sample sizes, pain populations, inclusion or diagnostic criteria, but also whether the focus is on symptoms or diagnoses (Andersen, Andersen, Vakkala, & Elklit, 2012; Hooten, 2016). Nevertheless, it is widely recognized that individuals with chronic pain are at a greatly increased risk of developing psychiatric problems, relative to the general population (Gerhardt et al., 2011).

### **Posttraumatic stress disorder and chronic pain**

In addition to anxiety and depressive disorders, posttraumatic stress disorder (PTSD) also appears to be common in chronic pain populations (Andersen et al., 2012). PTSD is defined by exposure to one or a number of traumatic events followed by the development of difficulties from four symptom clusters: intrusion (persistent re-experiencing of the trauma); avoidance of traumatic reminders; negative alterations in cognitions and mood; and negative alterations in arousal and reactivity (American Psychiatric Association, 2013). Recent meta-analyses report PTSD prevalence rates in chronic pain samples ranging from 1-50%, with an overall rate of 9.8% (Fishbain, Pulikal, Lewis, & Gao, 2017). This can be contrasted with the lifetime prevalence of PTSD in the general population, estimated at 6.8%, with the 12-month prevalence closer to 3.5% (Kessler, 2005; Kessler & Wang, 2008). In a recent study of adults seeking treatment from two Scandinavian pain clinics, 23% of all consecutive referrals fulfilled the DSM-IV criteria for PTSD (Andersen et al., 2012). This is consistent with rates of PTSD in adults seeking treatment for chronic pain outside of Scandinavia (Fishbain et al., 2017; Siqveland, Hussain, Lindstrøm, Ruud, & Hauff, 2017). Likewise, individuals with PTSD report high rates of chronic pain (Beckham et al., 1997; McFarlane, Atchison, Rafalowicz, & Papay, 1994; Shipherd et al., 2007). Recent meta-analyses conclude that rates of PTSD found among chronic pain samples (and vice versa) far exceed those expected by chance and that there is clear and



consistent evidence for an association between chronic pain and PTSD (Fishbain et al., 2017; Siqveland, Hussain, et al., 2017).

While there is greater recognition of the frequent comorbidity between PTSD and chronic pain, the nature of this association remains poorly understood (Jenewein, Wittmann, Moergeli, Creutzig, & Schnyder, 2009). What is known is that the presence of PTSD in chronic pain samples is associated with higher levels of physical health problems (Beckham et al., 1997); pain intensity (Geisser, Roth, Bachman, & Eckert, 1996; Jenewein et al., 2009; Phifer et al., 2011; Ruiz-Párraga & López-Martínez, 2014; Sherman, Turk, & Okifuji, 2000); pain-related disability (Morasco et al., 2013; Phifer et al., 2011; Ruiz-Párraga & López-Martínez, 2014; Sherman et al., 2000); kinesiophobia (Russek et al., 2015); emotional distress (Geisser et al., 1996; Morasco et al., 2013; Ruiz-Párraga & López-Martínez, 2014; Sherman et al., 2000); and lower levels of perceived life control (Palyo & Beck, 2005).

Overall, individuals suffering from chronic pain and comorbid anxiety, depression, and PTSD have been found to present with more severe pain and pain-related disability, have poorer prognosis and outcomes in treatment for chronic pain, and have higher healthcare costs (Linton et al., 2011; Outcalt et al., 2015; Rayner et al., 2016; Reme et al., 2012; Ruiz-Párraga & López-Martínez, 2014; Salazar et al., 2013; Trompetter, Bohlmeijer, Lamers, & Schreurs, 2016; Tunks, Crook, & Weir, 2008; Turner, Holtzman, & Mancl, 2007). It is important to recognize that PTSD is only one of several types of psychiatric disorders that are frequent among individuals with chronic pain. At the same time, there is a much longer tradition within the pain literature to investigate, conceptualize, and deal with comorbid symptoms of depression and anxiety in individuals undergoing treatment for chronic pain (Ehde, Dillworth, & Turner, 2014). In comparison PTSD is an understudied form of comorbidity in this population (Andersen, Andersen, & Andersen, 2014; Beck & Clapp, 2011). Unlike depression and anxiety, PTSD is not routinely measured in Swedish patients presenting for treatment of chronic pain, nor are PTSD measures recorded in the Swedish Quality Registry for Chronic Pain (SQRP, 2015). Thus, further studies involving measures of depression, anxiety, and particularly PTSD in chronic pain populations are warranted.

## Treatment of chronic pain

Chronic pain is a complex problem where a wide array of biological, behavioral, psychological, and social factors have been shown to be of importance to the development, maintenance, and impact of chronic pain (Gatchel & Okifuji, 2006;

McCracken & Turk, 2002; Turk, 2002). There has been more than 30 years of research on causes and maintaining factors, as well as efforts to develop treatments that reduce the severity and impact of chronic pain. Still, a significant proportion of individuals who have received various treatments for chronic pain continue to have significant pain-related disabilities, lower quality of life, and increased healthcare usage (McCracken & Turk, 2002; Turk, 2002). Indeed, meta-analytic and systematic reviews of the treatment literature find that the available evidence-based approaches, both medical and non-medical, only yield modest improvements in pain as well as in physical and emotional functioning (Hughes, Clark, Colclough, Dale, & McMillan, 2017; Turk, 2002; Turk, Wilson, & Cahana, 2011; Williams, Eccleston, & Morley, 2012).

With regard to medical treatments, systemic reviews find that pharmacological interventions, injection therapy, conservative (standard) care, surgery, and implantable devices can be of limited benefit to carefully selected patient groups and individuals. However, for the most part, these interventions have weak to modest effects on reductions in pain intensity or frequency, functional activities (including return to work), closure of disability claims, and healthcare utilization (DeBerard, Masters, Colledge, Schleusener, & Schlegel, 2001; Furlan, Sandoval, Mailis-Gagnon, & Tunks, 2006; Hornberger, Kumar, Verhulst, Clark, & Hernandez, 2008; Kroenke, Krebs, & Bair, 2009; Martin et al., 2008; McCracken & Turk, 2002; Taylor, 2006; Turk et al., 2011). In addition, medical interventions frequently involve a significantly increased risk of iatrogenic consequences and adverse events of physical, psychological, and social nature (Hornberger et al., 2008; McCracken & Turk, 2002; Taylor, 2006; Turk, 2002; Turk et al., 2011). As a result, calls have been made to de-medicalize the problems experienced by chronic pain sufferers and to redirect treatment efforts where cure is not possible to focus on self-management, functioning, quality of life, return to work, and decreasing the usage of non-beneficial health care services (McCracken & Turk, 2002; Turk, 2002; Turk et al., 2011). Treatment programs incorporating these goals are based on psychological principles, and the available evidence suggest that they outperform mixed treatment interventions provided by the primary care physician (i.e. treatment as usual) (Williams et al., 2012).

The majority of psychological treatments have drawn heavily upon principles and interventions from cognitive and behavioral therapy (CBT), originally developed for the treatment of anxiety and depression (Beck, 1964; Ellis, 1962). Other psychological treatments, such as psychodynamic, interpersonal, family, or supportive therapies are still poorly specified or inadequately examined in the pain literature (Eccleston, Morley, & Williams, 2013). The development of CBT rationales and interventions for chronic pain has, to some degree, tracked the development of CBT in a broader sense. In the 1960s and 1970s Fordyce and colleagues applied concepts from more behaviorally oriented approaches to

chronic pain (Fordyce, Fowler, & Delateur, 1968). Cognitive components were first used in treatment protocols within the chronic pain field during the 1970s (Morley & Williams, 2015). Gradually, both behavioral and cognitive methods for change were integrated into multi-component programs under the unifying label of CBT (Hayes, 2004; Morley & Williams, 2015). CBT has often been divided into separate generations (i.e., behavioral, cognitive, and contextual approaches) (Hayes, 2004; Hayes & Hofmann, 2017; Morley & Williams, 2015). On the other hand, it has been argued that interventions from all generations should be seen as a group of coherent treatment strategies (Hofmann, Sawyer, & Fang, 2010) and recent efforts have been made to bring all wings of the CBT field more closely together (Hayes & Hofmann, 2017; Hayes & Hofmann, 2018). The term CBT is used to capture the entire range of cognitive and behavioral interventions throughout the text, except where more specificity is necessary.

### **Cognitive behavioral therapy for chronic pain**

The recommended, and most commonly delivered psychological treatment for chronic pain, is multi-component CBT (Williams et al., 2012). This approach has been referred to as “traditional” CBT and it has been argued that such programs often give greater weight to cognitive concepts and didactic interventions at the expense of behavioral principles and experiential methods (Hayes, 2004). There is no single (or dominant) CBT program for chronic pain in the literature, nor any consensus regarding the number or types of interventions that should be included, the length (dose) of treatment, or delivery format (e.g., individual or group approaches) (McCracken & Morley, 2014; Morley & Williams, 2015; Turk et al., 2011).

Various assumptions underpin these CBT programs, but it is generally assumed that individuals with chronic pain have interfering emotions and beliefs about the causes of pain and how pain should be managed that help guide a range of persistent maladaptive responses. Such beliefs often revolve around the notion that their pain is misunderstood or minimized by medical professionals and loved ones. Pain sensations are also thought to signal imminent and sometimes severe physical harm (e.g., pain catastrophizing) that require the person to seek immediate medical attention and/or to discontinue any ongoing activity. The responses that gradually develop are myriad in nature, e.g., reassurance seeking from medical professionals and loved ones, opioid/substance use/abuse, restriction of physical activities, and full/partial withdrawal from social, educational, and occupational spheres of functioning (to name a few). These responses are maladaptive in the sense that they can, unintentionally: a) increase sensitivity to one’s own pain signals; b) increase the perceived severity of the pain; c) increase feelings of helplessness and isolation; d) lower mood; e) drive unnecessary healthcare usage and conflict with

healthcare professionals; and f) negatively impact the person's relationships, domestic activities, education, work, and physical health (Ehde et al., 2014; McCracken & Morley, 2014; Turk et al., 2011; Williams et al., 2012).

As such, CBT programs for chronic pain deploy a range of interventions to target these emotions, pain-related beliefs, maladaptive behaviors, and to some extent the social context of the individual. Typically, CBT interventions include, but are not limited to: a) education about the nature of pain and appropriate management methods; b) efforts to foster optimism, self-efficacy, and activity through education and cognitive restructuring; c) training to use goal-setting, pacing, problem-solving, and relaxation strategies; d) behavioral activation; e) physical exercise; and f) involvement of partner/spouse or employer (where possible) in some aspect of the treatment process (Ehde et al., 2014; Turk et al., 2011). Such interventions are based upon the notion that patients benefit from having a better understanding of the links between their own pain-related beliefs, behavioral responses, mood, and overall functioning. Patients are also guided in identifying and developing more adaptive ways of thinking and behaving through a combination of didactic and experiential exercises. CBT programs for chronic pain are often delivered in group formats with multi-disciplinary inputs that provide assistance with drug (particularly opioid) dependence, as well as physical and vocational rehabilitation (Eccleston et al., 2013; Gatchel & Okifuji, 2006; Gatchel & Rollings, 2008; Turk et al., 2011).

Systematic and meta-analytic reviews have identified a large number of randomized controlled trials (RCTs) evaluating the efficacy of multi-component CBT programs (as above) for adults with chronic pain arising from a variety of conditions (but usually excluding headache and cancer-related pain) (Hoffman, Papas, Chatkoff, & Kerns, 2007; McCracken & Turk, 2002; Williams et al., 2012). The most common comparison groups in these RCTs have been no treatment or treatment as usual, the latter primarily referring to ongoing pain management by the primary care physician. In the most recent Cochrane Collaboration review, the authors identified 35 RCTs providing data on the efficacy of CBT and behavior therapy (BT) programs when compared to active treatment, treatment as usual, or no treatment control groups for adults with chronic pain (Williams et al., 2012). Treatment outcomes were indexed by pain, disability, mood, and catastrophic thinking at post-treatment and six-month follow-up.

There was no evidence for the efficacy of BT relative to treatment as usual or no treatment for any outcome, with the exception of catastrophizing at post-treatment (Williams et al., 2012). CBT fared better than BT in this meta-analysis. The comparisons to treatment as usual favored CBT with small effects on pain and disability at post-treatment but not at follow-up, small effects on mood at both time points, and moderate effects on catastrophizing at post-treatment with

insufficient data at follow-up. The effects were weaker when comparing CBT to active controls. The comparisons only yielded small effect sizes for CBT on disability and pain catastrophizing at post-treatment and disability at follow-up. The other comparisons were non-significant relative to active controls. The authors concluded that CBT has weak effects on pain itself with gains on this outcome measure disappearing at follow-up. The benefits of CBT in relation to the other outcome measures tended to fall in the small to moderate range with weaker effects or non-sustained effects at follow-up. They suggested that no additional trials of CBT are necessary, rather further efforts are needed to identify which components of the various CBT programs will work for whom and try to understand why (Williams et al., 2012).

One way to achieve this aim is to try and identify predictors, moderators, and mediators of outcome in multi-component, multi-disciplinary-delivered CBT programs for chronic pain so that they can be modified in order to improve their efficacy (Turner et al., 2007; Williams et al., 2012). As part of these efforts, and recognizing that outcomes for chronic pain may be broadly or narrowly defined, there is a need to identify processes that contribute to the persistence, severity, and interference of pain as well as the most commonly occurring forms of comorbidity in pain populations, particularly psychiatric disorders (Linton, 2013).

It is now acknowledged that chronic pain treatments need to be based more on evidence regarding the efficacy of individual treatment components for different individuals, but also on theoretically coherent models of change that can aid in the selection of such components (McCracken & Morley, 2014; Williams et al., 2012). As described above, the core assumptions of CBT programs for chronic pain include a broad remit, permitting the use of diverse interventions that may at times have seemingly contradictory aims. For example, training a person to use relaxation or visualization strategies in an attempt to reduce the intensity of their ongoing pain versus exposure exercises wherein the person engages in various activities (active and sedentary) and notices the impact of such behaviors upon their pain. Another example involves interventions where the individual is taught to identify, test, and replace negative/irrational beliefs with more helpful ones versus exercises aimed at reducing the influence of negative beliefs over ongoing behavior without altering the content of such beliefs. With such a broad remit, it is not surprising that little is known about which components of CBT are necessary or beneficial, in what combinations, and for which patients (McCracken & Morley, 2014; Williams et al., 2012).

## **The psychological flexibility model**

The psychological flexibility model can be said to be inherently integrative since it only includes six processes, all of which can be organized under one single



process termed psychological flexibility. This is defined as the ability to act effectively in accordance with one's chosen values in the presence of unpleasant thoughts, emotions, or bodily symptoms (McCracken & Morley, 2014). The six processes specified in the psychological flexibility model are: (1) *acceptance*: the ability to actively embrace unwanted private events (physical sensations, thoughts, images, and emotions); (2) *cognitive defusion*: the capacity to distance oneself from thoughts and not be ruled by the meaning and influences carried in them; (3) *contact with the present moment*: moment to moment awareness or non-judgmental contact with events as they occur; (4) *self as context*: the capacity to differentiate the processes of experiencing events, especially thoughts and feelings, from the content of these events; (5) *values*: chosen desires or qualities that can be reflected in purposive action; and (6) *committed action*: the ongoing expansion of effective behavior patterns linked to chosen values (Hayes, Luoma, Bond, Masuda, & Lillis, 2006).

Psychological flexibility is positioned as a contextual model of normal human behavior, not solely the behavior of people suffering from chronic pain or other difficulties. It is symmetrical in the sense that it attempts to explain how problems arise and may be reduced by focusing on processes of psychological flexibility and inflexibility, in other words processes promoting resilience and action versus those promoting experiential avoidance, behavioral restriction, and inactivity (McCracken & Morley, 2014). It has been argued that psychological flexibility spans a wide range of human abilities, constitutes an essential part of psychological functioning, and that psychological flexibility processes are often absent or lacking in individuals with many forms of psychopathology (Kashdan & Rottenberg, 2010; Levin et al., 2014). Psychological flexibility has even been referred to as a fundamental aspect of health, underlining the transdiagnostic applicability of the model (Kashdan & Rottenberg, 2010; Morley, Williams, & Eccleston, 2013). The model's focus on theory and data-driven change processes, targeted with a limited number of therapeutically active interventions, is consistent with recommendations for further development of psychological treatment programs for chronic pain (Williams et al., 2012).

Acceptance and commitment therapy (ACT) is a treatment primarily focusing on healthy activity and wellbeing achieved through increases in psychological flexibility (Hayes, Strosahl, & Wilson, 1999). Research based on ACT and the psychological flexibility model in relation to chronic pain has increased at a rapid pace during the last decade (McCracken & Morley, 2014). ACT is now recognized by the American Psychological Association as an empirically supported treatment with strong research support for chronic pain (Society of Clinical Psychology, 2016). A recent systematic review identified 10 RCTs of ACT for adults with chronic pain (Hann & McCracken, 2014). Comparisons across studies with non-active controls favored ACT, with small to large effect sizes on a number of

variables including physical functioning, depression, anxiety, general emotional distress, life satisfaction, and psychological flexibility. Four studies had active control groups, including more traditional CBT, applied relaxation, education, and recommended medication. One study found a large effect size for impact of disease on global functioning favoring ACT over recommended medication, whereas another study found higher satisfaction ratings for ACT as compared to more traditional CBT. There was some evidence favoring ACT over active controls when outcome was defined by changes in psychological flexibility (small to large effect sizes). Even so, the results overall found that ACT was as beneficial as (but not superior to) the active control conditions on most outcomes (Hann & McCracken, 2014).

A more recent meta-analytic review of ACT for chronic pain identified 11 RCTs (Hughes, Clark et al., 2017). The primary outcomes in the RCTs were: pain acceptance, quality of life, and functioning in the presence of pain. Secondary outcomes were: pain intensity, anxiety, depression, and psychological flexibility. Relative to no treatment or treatment as usual, ACT yielded medium to large effect sizes for measures of pain acceptance and psychological flexibility at post-treatment and follow-up. However, ACT also yielded small to moderate effect sizes for functioning and depression at post-treatment and follow-up, and for anxiety at post-treatment, relative to non-active controls. No effects were seen for quality of life and pain intensity at post-treatment. In the two RCTs involving similar active treatment control groups, comparisons favored ACT over applied relaxation showing small to large effect sizes for pain-related acceptance, functioning, and quality of life at post-treatment and follow-up, and a small effect size for depression at post-treatment. Effect sizes were generally smaller at follow-up for all comparisons. The authors noted the heterogeneity in terms of the quality of the RCTs and the need for further methodologically robust trials involving active treatment controls (Hughes et al., 2017). As with other forms of CBT, there is a need for further research identifying predictors, moderators, and mediators of outcome in ACT for chronic pain (Gilpin, Keyes, Stahl, Greig, & McCracken, 2017).

Finally, ACT and the psychological flexibility model are relatively recent additions to the CBT tradition (Hayes & Hofmann, 2017). However, as seen above, there are both points of overlap and distinction between the assumptions of the psychological flexibility model and those underpinning more traditional CBT programs applied to chronic pain. An overlapping feature is the importance of learning new or more adaptive ways of relating to one's experience of pain. A distinction emerges in relation to how this aim would be achieved through more traditional CBT interventions and how this would be achieved in treatments predicated solely upon the psychological flexibility model. Even so, it is possible that psychological flexibility can be enhanced by a variety of experiences

occurring outside of therapy or through interventions or treatments not based on the psychological flexibility model or ACT (McCracken and Morley 2014). Thus, the psychological flexibility model is a reasonable target for research that aims to identify processes that help explain why individuals do or do not respond to various CBT programs for chronic pain.

## **Predictors, moderators, and mediators of outcome in CBT for chronic pain**

Before proceeding, it is important to distinguish between mediators, predictors, and moderators of outcome (for a detailed discussion of these concepts see: Kraemer, Wilson, Fairburn, & Agras, 2002). Mediators are variables through which change takes place (MacKinnon, Fairchild, & Fritz, 2007). Knowing what processes underpin changes in pain-related disability can aid in the refinement of existing treatments and the development of new treatments for chronic pain. Predictors and moderators are characteristics of the individual (e.g., age, symptom severity, and pain beliefs) that are present prior to the start of treatment and that may influence the individual's response, regardless of whatever treatment is under study (predictor), or differentially to one treatment versus another (moderator) (Gilpin et al., 2017; Kraemer, Wilson, Fairburn, & Agras, 2002). Knowing what variables influence an individual's response to one or more treatments can aid in the process of personalizing a particular treatment to improve its efficacy or offering the individual the more suitable of the available treatments (DeRubeis et al., 2014).

As CBT has been the most researched and widely disseminated approach for chronic pain, efforts to identify predictors, moderators, and mediators of outcome have largely involved this approach. Still, relatively few studies have undertaken to measure and analyse possible mediators of outcome in multi-component CBT programs for chronic pain (Turner et al., 2007). As stated above, these programs involve a large number of components or interventions and relatedly, a wide range of possible change processes have been suggested in the literature. These include but are not limited to: coping style (Jensen, Turner, & Romano, 2001; Jensen, Turner, & Romano, 2007); self-efficacy (Turner et al., 2007); helplessness (Burns, Glenn, Bruehl, Harden, & Lofland, 2003; Burns, Johnson, Mahoney, Devine, & Pawl, 1998; Burns, Kubilus, Bruehl, Harden, & Lofland, 2003); social support from partner/family (Romano, Jensen, Turner, Good, & Hops, 2000; Romano et al., 1995); kinesiophobia (Vlaeyen & Linton, 2000; Vlaeyen, de Jong, Geilen, Heuts, & van Breukelen, 2001); and pain-related beliefs (perceived control over pain and catastrophizing) (Burns, Glenn, et al., 2003; Burns, Kubilus, et al., 2003; Jensen et al., 2001; Jensen et al., 2007; Smeets, Vlaeyen, Kester, & Knottnerus, 2006; Spinhoven et al., 2004; Turner et al., 2007). This can to some extent be

contrasted to the psychological flexibility model, where the number of processes (and interventions) is constrained.

In respect of predictors and moderators of outcomes in CBT for chronic pain, the literature is fairly sparse and the findings rather mixed (Gilpin et al., 2017). Efforts to identify demographic factors that predict outcome have been unsuccessful and there are conflicting findings when it comes to the role of pain (intensity and duration) and pain diagnosis as baseline predictors (Gilpin et al., 2017; McCracken & Turk, 2002). High levels of negative pain perceptions (McCracken & Turk, 2002); pain sites (Turner et al., 2007); non-specific physical problems (Turner et al., 2007); lower levels of pain control (McCracken & Turk, 2002); and self-efficacy (Miles et al., 2011) have been identified as predictors of poorer outcomes in BT and CBT programs for chronic pain.

Variables relating to emotional distress or functioning seem to be the most commonly studied predictors of treatment outcome in chronic pain studies. Higher levels of psychological distress (McCracken & Turk, 2002); rumination (Turner et al., 2007); stress (Turner et al., 2007); catastrophizing (Turner et al., 2007); anxiety (Trompetter et al., 2016); and depression (Miles et al., 2011; Trompetter et al., 2016) have all been found to predict worse treatment outcomes. A moderating effect of psychological well-being on better outcomes has also been shown in web-based ACT in comparison to control groups (Trompetter et al., 2016). By way of contrast, a history of depression has been identified as a moderator of improved outcomes during an online mindfulness-based intervention for chronic pain in comparison to an attention control (Davis & Zautra, 2013). Another study was unable to establish a significant association between a diagnosis of depression and outcomes in a randomized evaluation of CBT and ACT for chronic pain (Wetherell et al., 2016). Overall, a higher level of emotional distress before treatment appear to influence treatment outcomes, and then mostly in a negative way but further investigation is warranted (Miles et al., 2011; Trompetter et al., 2016; Turner et al., 2007).

Whether pre-treatment levels of PTSD influence outcomes in CBT for chronic pain remains under-investigated. A recent study on patients receiving multidisciplinary treatment for chronic pain found no significant relationship between pre-treatment levels of PTSD and pain-related outcomes (Andersen et al., 2014). Another study assessed for a history of traumatic events and current symptoms of PTSD in 63 adults undergoing treatment for chronic pain, with 32% meeting the criteria for PTSD at baseline. The authors found that baseline PTSD diagnostic status was unrelated to outcomes as indexed by a 10-point visual analogue scale for pain levels (Siqueland, Ruud, & Hauff, 2017). While interesting, the conclusions that can be drawn from this study are limited due to the small sample and the way in which pain outcomes were assessed. It is possible

that the presence of PTSD at baseline was related to the effects of treatment in terms of pain-related impairment or other important aspects of functioning. In view of the high prevalence of PTSD in chronic pain samples, further research is needed on the potential impact of PTSD on outcomes in treatment for chronic pain (Andersen et al., 2014; Beck & Clapp, 2011). Also, it is possible that identification of shared processes that influence both pain and comorbid psychiatric problems can help improve assessments and treatments (Linton, 2013).

It should be further noted that various models have been put forward to explain the relationship between PTSD and chronic pain, with many resting on the notion that common factors maintain and/or predispose a person to develop both conditions (Asmundson, Coons, Taylor, & Katz, 2002; Sharp & Harvey, 2001). Recent research has investigated some of these mechanisms, mostly using cross-sectional designs (Irwin, Konnert, Wong, & O'Neill, 2014; Morasco et al., 2013; Porter, Pope, Mayer, & Rauch, 2013; Poundja, Fikretoglu, & Brunet, 2006), which limits the inferences that can be drawn about the direction of influence. However, and of relevance to this program of research, several longitudinal studies suggest that the severity and duration of chronic pain in trauma-exposed and injured populations may be related to the development of PTSD in the immediate aftermath of the trauma. In a longitudinal study of injured accident victims, Jenewein, Wittman et al. (2009) found mutual maintenance of PTSD symptoms and pain intensity shortly after a traumatic accident, and a significant impact of PTSD symptomatology on pain intensity, but not vice versa, 6-12 months post-accident (Jenewein et al., 2009). In a longitudinal study of adults who had experienced a whiplash injury, Andersen, Karstoft et al. (2016) observed that those who had failed to recover from pain six months after the accident were more likely to suffer from PTSD symptoms. The authors also found that pain catastrophizing and fear avoidance beliefs mediated the relationship between PTSD symptoms and pain (Andersen, Karstoft, Brink, & Elklit, 2016). Still, the nature of the relationship between PTSD and chronic pain as well as the potential mediators by which they are linked remain under-investigated (Jenewein et al., 2009). Perhaps application of a more integrative psychological model to the relationship between these two conditions could facilitate clarification of key mediating variables, which could thereafter lead to improved treatments.

### **Predictors, moderators, and mediators related to the psychological flexibility model**

There is evidence of an association between facets of psychological flexibility and pain-related functioning and these processes have been shown to have mediating effects on treatment outcomes within ACT for chronic pain (Wicksell, Olsson, & Hayes, 2010; Vowles, Witkiewitz, Sowden, & Ashworth, 2014). However, pain-

related acceptance has also been associated with improved outcomes for chronic pain in more traditional CBT approaches (Baranoff, Hanrahan, Kapur, & Connor, 2013). These latter results, albeit preliminary, raise the question of whether positive outcomes in chronic pain treatments more broadly are partly mediated by changes in psychological flexibility (or processes from within the model). Most studies using processes from the psychological flexibility model have focused on changes in only one or two of the six components of the model, usually acceptance and values-based action (McCracken & Morley, 2014). Consequently, it is possible that additional processes from the model mediate outcomes in traditional CBT approaches for chronic pain. Moving beyond mediation, no studies of which we are aware, have investigated whether baseline levels of psychological flexibility predict or moderate outcomes in CBT (or ACT) for chronic pain (Gilpin et al., 2017).

It is also important to point out that processes from or similar to those from the psychological flexibility model have been linked to the severity of PTSD in studies of trauma-exposed individuals (Dick, Niles, Street, Dimartino, & Mitchell, 2014; Keith, Velezmo, & O'Brien, 2015; Miron, Sherrill, & Orcutt, 2015; Palm & Follette, 2011). Moreover, there are a limited number of studies linking pain-related acceptance to the relationship between PTSD and chronic pain (Cook et al., 2015; Ruiz-Párraga & López-Martínez, 2014, 2015). One study has incorporated the psychological flexibility model, using the processes acceptance, cognitive defusion, committed action, and values in a treatment protocol for people with chronic pain and whiplash, and found significant improvements in pain disability, functioning, and symptoms of post-traumatic stress (Wicksell, Ahlqvist, Bring, Melin, & Olsson, 2008). Such findings suggest that processes from the psychological flexibility model may influence the severity and impact of chronic pain and co-occurring psychiatric problems and may help us integrate current knowledge concerning the negative association between PTSD and chronic pain.

## General and specific aims

Chronic pain is a commonly occurring and debilitating condition, and among the costliest health problems for both the individual and society at large. Cognitive behavioral therapy (CBT) is the most widely-disseminated psychological treatment for chronic pain. Even though it is recommended and evidence-based, it yields quite modest improvements in pain-related functioning and accompanying symptoms of emotional distress, and primarily in comparison to treatment as usual or no treatment at all. It is now generally acknowledged that further efforts are needed to improve the efficacy of CBT for chronic pain. Specifically, pain researchers have called for studies to identify mechanisms that underlie changes in

treatment outcomes (mediators) and characteristics of the individual that predict improvements in these mechanisms and treatment overall (predictors and moderators).

The current studies arise from a program of research aimed at improving the efficacy of an intensive, five-week, group-based CBT program delivered to more than 200 patients per year in a specialist pain rehabilitation unit at Skåne University Hospital. This long-established program yields effect sizes for pain-related disability comparable to those found in RCTs. It is based on a broad model of CBT emphasizing the benefits of: increased awareness of the links between emotions, pain-related beliefs, behaviors, and functioning; altering maladaptive beliefs and behaviors that reduce overall functioning; and (where possible) involving partners/significant others and employers in the development of the individual's treatment plan, with the explicit aim of returning the individual to more normal levels of functioning, including returning to work.

When considering how to identify the mechanisms by which a CBT program involving such diverse interventions might work, and for whom, we also had to take the pre-existing heavy assessment burden placed upon the patients in keeping with the requirements of the Swedish Quality Registry for Pain Rehabilitation into account. The existing assessment protocol included measures of a relatively small number of putative mediators, and generally not those most frequently mentioned in the CBT literature (e.g. pain catastrophizing and coping style). Furthermore, while the assessment protocol had various measures that would allow us to examine putative predictors of outcome, including comorbid symptoms of depression and anxiety, it did not include a measure of PTSD nor was PTSD assessed via interview as part of the intake process.

Therefore, a pragmatic decision was taken to add extremely brief self-report measures of individual processes from the psychological flexibility model and a single self-report measure of PTSD to the assessment protocol. We chose measures of the six processes from the psychological flexibility model rather than a single measure of psychological flexibility, or for example, measures of pain catastrophizing and coping for two main reasons. First, for reasons given above, we believed that the psychological flexibility model was more coherent and incorporated several different change processes that, in turn, were more likely to underpin the interventions and functional goals of this CBT-based program. Second, over the medium to long term, there was an existing plan in place to slowly alter the treatment regime to include interventions from the psychological flexibility model and ACT for chronic pain.

Thus, the primary aim of this research program was to study whether changes in psychological flexibility mediated outcomes in this multi-disciplinary, group-based CBT program. The secondary aim was to identify possible predictors of

outcome by focusing on facets of psychological flexibility as well as the understudied influence of posttraumatic stress disorder (PTSD). This aim also included investigation of the relationships between PTSD, pain presentation, and psychological flexibility. With these two aims, we hoped to shed further light on the validity of the psychological flexibility model as an integrating, overarching model that can help define relevant treatment processes for adults presenting with chronic pain and psychiatric problems.

Study I investigated whether pain-related acceptance, from the psychological flexibility model, and other variables posited as potential mediators in standard CBT mediated changes in pain-related outcomes measured at post-treatment and 12-month follow-up from the CBT program. As a secondary aim the study also examined whether improvements in pain-related functioning at post-treatment and 12-month follow-up were observed and if the levels of improvements were consistent with previously published efficacy studies on CBT treatments for adults with chronic pain.

Study II evaluated the psychometric properties of the Swedish-language versions of the full length and shortened version of the Committed Action Questionnaire (CAQ), as well as the generalizability of previous results related to committed action. The study also aimed to further demonstrate the relevance of this construct to the functioning of patients with chronic pain.

Study III focused on the prevalence of traumatic experiences, trauma types, and PTSD in patients referred for treatment of chronic pain, and the relationship between PTSD and pain-related functioning prior to treatment. The study also involved an examination of the psychometric properties of a Swedish-language version of the Posttraumatic Diagnostic Scale (PDS).

Study IV was a further examination of the relationship between PTSD and chronic pain at the time of referral and prior to commencing treatment for chronic pain. In particular, the study examined whether various processes from the psychological flexibility model mediated the relationship between PTSD and chronic pain, while controlling for the effects of depression. It also included comparisons between trauma-exposed adults with and without PTSD on measures of psychological flexibility, pain severity, pain interference, and depression.

Study V examined whether indices of emotional distress (including PTSD) and different facets of psychological flexibility predicted pain-related outcomes at 12-month follow-up from the CBT program. Furthermore, it examined whether changes in processes from the psychological flexibility model mediated changes in pain-related outcomes.





# Methods

## Designs and settings

The Pain Rehabilitation Unit at Skåne University Hospital is government funded and based within the national health system, providing specialist assessments and treatment services to adults with chronic pain and related disabilities. It is the largest specialist centre for chronic pain in Region Skåne, the southernmost region of Sweden with 1.26 million inhabitants (approximately 13% of the Swedish population).

Study I and V are longitudinal treatment outcome studies assessing the group CBT program, while Study II, III, and IV are cross-sectional studies with all data collected at the time of referral.

## Participants

Participants in all five studies were consecutive referrals to the Pain Rehabilitation Unit between 2009 and 2015. The sample sizes for the studies were as follows: Study I = 409; Study II = 462; Study III = 463; Study IV = 315; and Study V = 232. Participants gave their written informed consent prior to their data being used in the studies.

## Ethics

All five studies were approved by the Regional Ethical Review Board in Lund (2013/381). This patient group is often heavily burdened by both physical and psychosocial issues. The current research project involved some minor ethical problems. A more exhaustive study of pain-related problems was carried out, but took place in conjunction with data collection already included as a clinical routine. As a consequence, the data collection could be said to involve a strain on the patient even if it did not entail any particular risks. On the other hand, this effort also resulted in the patient having more contact than usual with healthcare

staff at the clinic. Some questions of sensitive nature appeared during the data collection, possibly reminding patients of difficulties they had previously encountered and resulting in negative thoughts and feelings. In such cases, the patient or the treatment team responsible for the patient were offered the possibility to contact the research team for guidance in handling the situation. Still, focusing on their difficulties could also be healthy as this might normalize such issues and help to eventually resolve them. A document was drawn up where undesirable events connected to the research project were written down together with the actions taken in each case.

## Inclusion and exclusion criteria

Patients were assessed by a team at the unit and included in Study II if they suffered from chronic and complex non-malignant pain. To be included in Study III and IV patients also had to be assessed for or have been exposed to trauma.

Patients were included in the treatment program investigated in Study I and V if they met these criteria: 1) were between 18 and 67 years of age; 2) were able to understand Swedish; 3) had symptoms of chronic pain that interfered significantly with everyday life; 4) were fully examined medically and had received medical treatment if indicated; 5) were able to function in a group setting and take part in a five-week program, five to seven hours per day for two to four days per week; 6) were able to be an active part of the rehabilitation process and regain functioning in different areas of life; and 7) had goals that could be satisfied within the program. Patients were excluded if they met the following criteria: 1) exhibited acute or severe psychiatric disorders or symptoms; 2) were actively abusing analgesic medications (including narcotics), alcohol, or other drugs; 3) had already undergone similar treatment; 4) displayed great difficulty in terms of harbouring and handling strong emotions that could lead to emotional outbursts or self-harming behavior; 5) had health risks due to medical reasons; and 6) had social or economic difficulties or lack of social support that hindered behavior change.

## Intervention

Patients were registered in a day treatment program lasting five weeks with 18 active treatment days. The rest of the weekdays were used for home practice. After the program patients were discharged to a “homework phase” lasting for two months, where patients worked on goals in their individual rehabilitation plan. At the end of this phase, patients took part in two days of additional treatment (the

post-treatment assessment), where progress, difficulties, and future goals were in focus. Patients were then mailed questionnaires and asked to complete and return 12 months after discharge from the day treatment program (the follow-up assessment).

The treatment was a multi-disciplinary, outpatient, treatment program based on a cognitive behavioral approach, provided by three separate multi-professional teams with training in CBT and extensive knowledge of pain rehabilitation. The teams included a physician, a social worker, an occupational therapist, a physiotherapist, and a clinical psychologist. Each patient had individual appointments where an individual rehabilitation plan was formulated and then followed. The rest of the treatment was group-based and biopsychosocial in orientation, intended to help the patients develop more adaptive ways of thinking and behaving in relation to pain. Furthermore the program was designed to improve knowledge, awareness, and practical skills concerning pain and medication (physician); work-related and national insurance issues (social worker); ergonomics, time-use adaptations, problem-solving strategies, and every day occupational performance (occupational therapist); physical exercises, body awareness, and relaxation (physiotherapist); and thoughts, emotions, behaviors, communication, goal-setting methods, and behavioral activation (psychologist). To support uniformity and treatment integrity, some group sessions were co-led by the staff and team members also attended weekly team meetings. Significant others were invited to take part in education and discussions regarding pain and its consequences for a half day. The overall goals of the treatment program were: 1) to help patients improve their strategies for managing chronic pain and its consequences; 2) to improve their perceived quality of life; 3) to improve their ability to participate in everyday activities; 4) to reduce their pain experience; and 5) to increase the knowledge of significant others regarding pain and its consequences by inviting them to participate in the rehabilitation. These goals were chosen to reflect recommendations on core outcome domains in trials on patients with chronic pain (Dworkin et al., 2005; Turk et al., 2003) and to meet internationally recognized standards for medical rehabilitation (CARF, 2014).

## Measures

Data were collected from self-report measures from the Swedish Quality Registry for Pain Rehabilitation and from other measures not currently available in this database assessing processes from the psychological flexibility model and PTSD (SQRP, 2015). Outcome measures in the studies were selected to cover the overall goals in the treatment program and to reflect identified core domains in chronic

pain: pain, physical functioning or pain-related functioning, and emotional functioning (Dworkin et al., 2005; Turk et al., 2003).

### **Chronic Pain Acceptance Questionnaire (CPAQ)**

Pain-related acceptance was measured with the full length version of the CPAQ (McCracken, Vowles, & Eccleston, 2004) and the eight-item short form version (CPAQ-8) (Fish, McGuire, Hogan, Stewart, & Morrison, 2010). These measures assess acceptance for people with chronic pain using two subscales: activity engagement and pain willingness. All items are rated on a seven-point scale (0 = never true; 6 = always true). The total scores were used, with higher scores representing greater acceptance of pain. The English original versions of the CPAQ as well as the Swedish versions used have satisfactory psychometric properties (Fish et al., 2010; McCracken et al., 2004; Rovner, Arestedt, Gerdle, Börsbo, & McCracken, 2014; Wicksell, Olsson, & Melin, 2009; Vowles, McCracken, McLeod, & Eccleston, 2008).

### **Chronic Pain Values Inventory (CPVI)**

Values-based action was assessed with the CPVI, which is a 12-item measure of engagement in valued activities for chronic pain patients (McCracken & Yang, 2006). The importance of activities in six different domains (family, intimate/close interpersonal relations, friends, work, health, and personal growth/learning) is rated by respondents on a six-point scale (0 = not at all important; 5 = extremely important). Thereafter the degree of success in behaving according to their values in these domains is rated on a six-point scale (0 = not at all successful; 5 = extremely successful). A mean success rating and a mean discrepancy rating can be computed. The mean success rating was used to measure values-based action (Åkerblom, Perrin, Rivano Fischer, & McCracken, 2017), where higher scores represent greater success. Consistent with the English original, the Swedish version has demonstrated satisfactory validity and reliability (McCracken & Yang, 2006; Åkerblom et al., 2017).

### **Committed Action Questionnaire (CAQ)**

Committed action was assessed using the full length version of the CAQ (McCracken, 2013) and the eight-item short version (McCracken, Chilcot, & Norton, 2014), each item being rated on a seven-point scale (0 = never true, 6 = always true). Factor analysis has indicated two subscales in both versions with positively and negatively phrased items respectively. Higher scores represent greater levels of committed action or goal-directed, flexible persistence. Both the

original English version of the CAQ-18 and the CAQ-8 exhibit acceptable internal consistency and validity (McCracken, 2013; McCracken et al., 2014). The psychometric properties of the Swedish versions were reported in Study II.

### **Hospital Anxiety and Depression Scale (HADS)**

Anxiety and depression were assessed with the 14-item HADS which was developed to measure the frequency of anxiety and depression symptoms during the past week in medical settings (Zigmond & Snaith, 1983). Each item is scored on a four-point frequency/severity scale and each subscale has seven items with scores ranging from 0–21. Higher scores indicate greater anxiety/depression. In line with the English original, the Swedish version used has been shown to exhibit satisfactory validity and internal consistency with regard to the total, anxiety, and depression scales (Lisspers, Nygren, & Soderman, 1997; Zigmond & Snaith, 1983).

### **Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)**

Physical functioning, vitality, mental health, social functioning, and general health were assessed with these specific subscales in the SF-36, which is a commonly used self-report measure of non-disease-specific health and functioning. It consists of 36 items belonging to eight different subscales, where scores on each subscale are transformed to a 0-100 scale. Higher scores represent a better health state. In accordance with the English original (Ware & Sherbourne, 1992), the Swedish version used in this context has satisfactory validity and internal reliability with regard to the subscales (Sullivan, Karlsson, & Ware, 1995).

### **Multidimensional Pain Inventory Version 2 (MPI)**

Life control, affective distress, social support, pain interference, and pain severity were assessed using the respectively named subscales from Part 1 of the MPI (Version 2), which focuses on the perception of pain and pain-related consequences (Rudy, Turk, Zaki, & Curtin, 1989). The life control subscale assesses the perceived ability to solve problems and feelings of personal mastery and competence. The affective distress subscale assesses low mood, irritability, and tension. The social support subscale measures appraisal of support received from spouse, family, and significant others. The pain interference subscale measures pain-related life interference in different areas of functioning, such as family and marital functioning, work and work-related activities, and social and recreational activities. The pain severity subscale measures severity of pain and related suffering. Each item is rated on a seven-point scale (0 = never; 6 = very

often) and the mean score can be calculated for each scale. The MPI possesses satisfactory internal consistency and validity (Kerns, Rudy, & Turk, 1985) and a Swedish version was used in this context (Nyberg, Novo, & Sjolund, 2011).

### **Numerical Rating Scale (NRS)**

Pain intensity was measured using the NRS, which is a widely-used measure of pain in both research and clinical settings. It consists of a single item wherein the patient rates the intensity of their pain over the past week on an 11-point scale (0 = no pain; 10 = worst possible pain) and it constitutes a valid and sensitive measure (Ferreira-Valente, Pais-Ribeiro, & Jensen, 2011; Jensen & Karoly, 1992).

### **Posttraumatic Diagnostic Scale (PDS)**

PTSD symptoms and PTSD diagnostic status were measured with the PDS (Foa, Cashman, Jaycox, & Perry, 1997). The PDS is a self-report measure consisting of 49 items separated into four parts, where Part 1 is a trauma checklist; Part 2 asks respondents to describe their most upsetting traumatic event (when it happened, if anyone was injured, perceived life threat, and whether the event resulted in feelings of helplessness or terror); Part 3 measures the severity of the 17 symptoms included in the DSM-IV for PTSD; and Part 4 measures interference in social, occupational, or other important areas of functioning. It is possible to calculate a total severity score, with scores ranging from 0–51 (1–10 = mild; 11–20 = moderate; 21–35 = moderate to severe; >36 = severe). In order to enable an assessment of diagnostic status, participants who reported a trauma, the required number and type of symptoms, and distress or impairment in line with the DSM-IV PTSD criteria were categorized as having a current diagnosis of PTSD. The following criteria had to be met: (A) having experienced, witnessed, or been confronted with an event that involved actual or threatened death, serious injury, or threat to the physical integrity of oneself or others and responded with intense fear, helplessness, or horror; (B) one or more symptoms of re-experiencing; (C) three or more symptoms of avoidance and numbing; (D) two or more symptoms of hyperarousal; (E) symptom duration of more than a month; (F) clinically significant distress or impairment in two or more areas of functioning. In order to be categorized as not having PTSD participants reported a trauma but either too few symptoms or insufficient distress or impairment. The original scale has acceptable internal consistency and validity (Foa et al., 1997) and the psychometric properties of a Swedish version were investigated in Study III.

## **Psychological Inflexibility in Pain Scale (PIPS)**

Cognitive fusion and psychological inflexibility were assessed using the PIPS. The PIPS is a 12-item measure assessing psychological *inflexibility* through two subscales: avoidance of pain and fusion with pain thoughts (Wicksell, Lekander, Sorjonen, & Olsson, 2010). Each item is rated on a seven-point scale (1 = never true; 7 = always true), with higher scores representing greater levels of cognitive fusion and psychological inflexibility. The original Swedish version possesses acceptable reliability and validity (Wicksell, Lekander, et al., 2010).

## **Tampa Scale of Kinesiophobia (TSK)**

Kinesiophobia was measured with the 17-item TSK (Vlaeyen, Kole-Snijders, Boeren, & Van Eek, 1995). Items are rated on a four-point scale (1 = strongly disagree; 4 = strongly agree) with scores ranging from 17–68. Higher scores represent greater fear of movement and (re)injury. The English original and the Swedish version of the TSK, have been shown to have acceptable validity and reliability (Roelofs et al., 2007; Swinkels-Meewisse et al., 2003; Vlaeyen et al., 1995).

## **Data analyses**

### **Attrition analyses**

In order to investigate the potential influence of missing data in Study I a series of t-tests were performed. Patients with missing data were compared to those without missing data and no differences were found in relation to any of the studied variables. Hence, data appeared to be missing completely at random. Furthermore, treatment outcomes when only using cases with complete data did not differ from outcomes when using cases with (partial) missing data. Lastly, sensitivity analyses identified four different missing data patterns in the dataset which were shown to be unrelated to treatment outcome. As a result, all available data were used and cases were excluded analysis by analysis if they had missing values on the time variable, the covariates, or if they had missing values on all variables except the time variable and the covariates.

In Studies II-V, Little's missing completely at random (MCAR) test was performed to ascertain that all data were missing completely at random. Thereafter, missing values were imputed using the Expectation-Maximization method (Schafer & Graham, 2002) in the cross-sectional studies with very low



levels of missing data. Study V had a longitudinal design with higher levels of missing data at the variable level at post-assessment and at follow-up. In this study missing data were imputed on the item level, while all available data were used when data were missing on the variable level. Generally, outliers were identified and the affected values were winsorized and included in all subsequent analyses.

## **Descriptive analyses**

In Study III, the prevalence of traumatic exposure and PTSD were investigated in a sample of patients seeking treatment for chronic pain. Different trauma types were also studied and patients were asked to identify their primary traumatic (or most upsetting) event.

## **Psychometric analyses**

The internal consistency and reliability of the CAQ (CAQ-18 and CAQ-8) and the PDS were examined in Study II and III via inter-item correlations, item-total correlations, and Cronbach's alpha. Validity was assessed via pairwise Pearson correlations between the investigated measures and measures assessing convergent constructs. Confirmatory factor analyses were undertaken using maximum likelihood estimation procedures to assess the structural validity of the measures. Several studies have investigated the factor structure of the PDS and concluded that the observed factors do not reliably correspond to the three symptom clusters described in DSM-IV (Griesel, Wessa, & Flor, 2006; Hearn, Ceschi, Brillon, Fürst, & Van der Linden, 2012; Powell & Rosner, 2005). Consequently, we analysed whether a better fit to the data could be obtained by using the four-factor Emotion Numbing model (King, Leskin, King, & Weathers, 1998), similar to the updated DSM-5 symptom clusters (Charak et al., 2014; Forbes et al., 2011), as compared to the three-factor solution corresponding to the DSM-IV PTSD criteria. The incremental validity of the CAQ was also investigated using a series of hierarchical regression analyses. More specifically, it was investigated whether the CAQ (CAQ-18 and CAQ-8) was able to account for variance in patient functioning over and above the effect of measures of pain-related acceptance and kinesiophobia.

## **Group differences**

To evaluate differences within and between groups, different parametric analyses were used. In Study I and V, descriptive statistics were produced to present demographic and clinical characteristics within the treatment group at pre-treatment and outcome at post-treatment and 12-month follow-up. Effect sizes

were calculated for each outcome measure over the observed time intervals (pre to post-treatment and pre-treatment to follow-up). In order to correct for correlated data, within-subjects effect sizes (Cohen's *d*) were calculated (Dunlap, Cortina, Vaslow, & Burke, 1996).

In Study III, differences in clinical characteristics between three groups of patients with chronic pain were explored at the time of referral for assessment; those fulfilling criteria for PTSD, those exposed to trauma not fulfilling criteria for PTSD, and those not exposed to trauma. A multivariate analysis of variance (MANOVA) was conducted to test whether a linear combination of clinical characteristics differed between these three subgroups. Subsequently, a series of univariate analyses of variance (ANOVAs) were conducted as follow-up tests to the MANOVA. Post hoc analyses were performed to examine mean differences across the three groups in relation to all clinical characteristics.

As a part of Study IV, participants with and without PTSD were compared on demographic variables, pain interference, pain severity, and the potential mediators (pain-related acceptance, committed action, values-based action, cognitive fusion, and depression) at the time of referral for assessment of chronic pain using independent sample t-tests. Effect sizes (Cohen's *d*) were calculated with adjustments made for differing sample sizes.

A range of pre-treatment variables, including PTSD, depression, anxiety, and psychological inflexibility, were explored as possible predictors of treatment outcome one year following treatment using separate linear regression models in Study V.

## **Indirect/mediating effects**

Mediation analyses were conducted to examine the effect of a mediating variable (M) on the relationship between an independent (X) and a dependent (Y) variable. The indirect or mediating effect refers to processes through which changes occur (MacKinnon et al., 2007). In Study I and V, longitudinal models were used to assess the indirect effects of the proposed mediators. More specifically, we explored whether changes in the outcome measures over time were mediated by changes in the proposed mediators over time. The term mediation is commonly used in between-group designs. However, in these studies, time was used as a proxy for treatment and the term mediator was specifically applied to the observed within group effect over time in a single treatment cohort. The understanding of mediation processes can be enhanced by using single treatment conditions. However, such designs yield weaker evidence than studies using a control group and random assignment (Maric, Wiers, & Prins, 2012).

In Study IV, mediation analyses were performed to assess the effect of psychological flexibility and depression on the relationship between PTSD and chronic pain, as measured by pain severity and interference, at the time of referral for assessment of chronic pain. Mediation models should be chosen on the basis of assumptions that are either invoked based on theory or fulfilled by design features (Thoemmes, 2015). In line with these recommendations, the models in this study were based on earlier longitudinal research having emphasized the long-term influence of PTSD symptoms on pain intensity (Jenewein et al., 2009) and having identified mediators of the relationship between PTSD symptoms and pain intensity (Andersen et al., 2016). The models were also based on cross-sectional research aimed at identifying mediators of the relationship between PTSD and chronic pain (Irwin et al., 2014; Morasco et al., 2013; Porter et al., 2013; Poundja et al., 2006). Furthermore, they were strengthened by the current data, where the trauma producing the PTSD symptoms was shown to precede the administration of the pain measures and the psychological flexibility measures by an average of three to five years.

Regardless, the criterion of temporality, where a change in the mediator comes before a change in the dependent variable, was not met in the current studies and as a result no firm conclusions about the direction of causation could be made. On the other hand, the studies followed several recommendations for mediation analysis by utilizing adequate sample sizes, using measures with sound psychometric properties, and examining multiple mediators simultaneously (Kazdin, 2007; Maric et al., 2012).

In all studies the significance of the indirect effect was estimated using the product of coefficients, which directly assesses the significance of the indirect or mediating effect (MacKinnon et al., 2007). Individual mediation effects were first established by examining all mediators separately. Subsequently, all significant individual mediators were examined together in a model of parallel mediation to analyse the relative importance of each mediator in relation to the outcomes.

# Research studies

## Study I

### Introduction

The primary aim of this study was to investigate whether pain-related acceptance, from the psychological flexibility model, mediated changes in outcome over time in a CBT treatment program for chronic pain. This included comparing how pain-related acceptance performed in relation to three other variables posited as potential mediators in standard CBT: life control, affective distress, and social support. In addition, we analysed whether improvements on measures of pain interference, pain intensity, and depression at post-treatment and 12-month follow-up were observed and if the levels of improvement were consistent with previously published efficacy studies of CBT treatments on adults with chronic pain.

### Methods

Participants (N=409) took part in a five-week outpatient multidisciplinary program with self-report data collected at assessment, post-treatment, and at 12-month follow-up. For each outcome measure effect sizes over the observed time intervals were calculated. In order to examine whether changes in pain interference, pain intensity, and depression (outcome measures) over time were mediated by changes in pain-related acceptance, life control, affective distress, and social support (mediators) multilevel models were used. The effect of time on the mediator was represented by the *a*-path and the effect of the mediator on the outcome controlling for time was represented by the *b*-path. The total effect of time on outcome was represented by the *c*-path and the direct effect of time on outcome when controlling for the mediator was represented by the *c'*-path (Table 1 and 2).

**Table 1 Results of univariate mediator analyses**

Outcome	N	Mediator	Indirect Effects		Results for Indirect Effects <i>a*b</i>		
			Path	Point-estimate (SE)	Point-estimate (SE)	95% CI	
						Lower	Upper
Pain interference							
	233	Pain acceptance	a	.331* (.030)	-.153* (.024)	-.214	-.114
			b	-.462* (.050)			
	235	Life control	a	.372* (.039)	-.095* (.017)	-.139	-.068
			b	-.256* (.034)			
	235	Affective distress	a	-1.381* (.211)	-.079* (.016)	-.120	-.053
			b	.057* (.006)			
235	Social support	a	-.744* (.167)	-.019* (.008)	-.039	-.007	
		b	.026* (.008)				
Pain intensity							
	237	Pain acceptance	a	.337* (.031)	-.167*(.040)	-.270	-.101
			b	-.495* (.112)			
	238	Life control	a	.374* (.038)	-.239* (.037)	-.334	-.178
			b	-.638* (.070)			
	238	Affective distress	a	-.279* (.042)	-.143* (.029)	-.217	-.095
			b	.511* (.065)			
238	Social support	a	-.150* (.033)	-.014 (.012)	-.043	.005	
		b	.091 (.072)				
Depression							
	235	Pain acceptance	a	.326* (.031)	-.556* (.080)	-.761	-.425
			b	-1.704* (.193)			
	236	Life control	a	.371* (.038)	-.537* (.072)	-.722	-.418
			b	-1.447* (.126)			
	236	Affective distress	a	-.272* (.042)	-.097* (.017)	-.140	-.069
			b	.355* (.028)			
236	Social support	a	-.148* (.033)	.018 (.024)	-.044	.058	
		b	-.124 (.167)				

Notes: The indirect effect is statistically significant if the confidence interval does not include zero. A 95 % confidence interval (CI) is equivalent to a value of  $p < .05$ . Asterisks (\*) indicate a statistically significant effect. Information in this table has been updated since publication, see <http://dx.doi.org/10.1016/j.jpain.2016.08.004>.

## Results

Results indicated that effect sizes for the investigated treatment were within the ranges reported in the literature on CBT for chronic pain. The univariate multilevel analyses for the mediating effects on each outcome variable can be seen in Table 1. Changes in pain interference during treatment were mediated individually by changes in each of the proposed mediators, whereas changes in pain intensity and depression were only mediated by changes in pain-related acceptance, life control, and affective distress. The multivariate multilevel analyses for the mediating effects including all significant mediators from the previous analyses have been tabulated in Table 2. Only changes in life control and affective distress were simultaneous and significant mediators for outcome as indexed by pain intensity. Changes in pain-related acceptance, life control, affective distress, and social support all mediated change in pain interference during treatment, while changes in pain-related acceptance, life control, and affective distress all significantly and simultaneously mediated change in depression. Pain-related acceptance was the strongest mediator for both pain interference and depression.

## Discussion

In accordance with past empirical evidence and the treatment objectives in ACT, pain-related acceptance was of little importance to pain intensity. In relation to the other outcomes, pain-related acceptance was the strongest mediator. Accumulating results like these highlight pain-related acceptance as a potential key mechanism by which CBT treatments achieve improvements across different outcomes. Possibly, increased effectiveness in such treatments can be reached through more focused targeting of pain-related acceptance.

**Table 2 Results of multivariate mediator analyses**

		Total, Direct, and Indirect effects		Results for Indirect Effects $a*b$			
Outcome	Mediator	Path	Point-estimate (SE)	Point-estimate (SE)	95% CI		Proportion of effect mediated ( $a*b$ )/c
Pain interference							
N=228		Total c	-.156* (.031)				
		Direct c´	.040 (.036)				
	Pain acceptance	a	.322* (.029)	-.113* (.019)	-.163	-.081	.72
		b	-.352* (.044)				
	Life control	a	.368* (.038)	-.024* (.012)	-.054	-.005	.15
		b	-.066* (.031)				
	Affective distress	a	-.286* (.041)	-.020* (.007)	-.038	-.009	.13
		b	.168* (.032)				
Social support	a	-.153* (.034)	-.048* (.012)	-.079	-.029	.31	
	b	.132* (.034)					
Pain intensity							
N=231		Total c	-.453* (.059)				
		Direct c´	-.117 (.082)				
	Pain acceptance	a	.324* (.030)	-.057 (.036)	-.150	.003	na
		b	-.174 (.112)				
	Life control	a	.372* (.037)	-.168* (.038)	-.266	-.105	.37
		b	-.452* (.090)				
	Affective distress	a	-.290* (.041)	-.064* (.025)	-.128	-.023	.14
		b	.222* (.078)				
Depression							
N=229		Total c	-.804* (.115)				
		Direct c´	-.036 (.129)				
	Pain acceptance	a	.322* (.030)	-.296* (.070)	-.476	-.181	.37
		b	-.918* (.194)				
	Life control	a	.368* (.037)	-.261* (.055)	-.403	-.171	.32
		b	-.709* (.135)				
	Affective distress	a	-.286* (.041)	-.240* (.048)	-.364	-.160	.30
		b	.839* (.122)				

Notes: The indirect effect is statistically significant if the confidence interval does not include zero. A 95 % confidence interval (CI) is equivalent to a value of  $p \leq .05$ . Asterisks (\*) indicate a statistically significant effect. Information in this table has been updated since publication, see <http://dx.doi.org/10.1016/j.jpain.2016.08.004>

# Study II

## Introduction

The aims of this study were to analyse the psychometric properties of the Swedish-language versions of the full length CAQ (CAQ-18) and the shortened CAQ (CAQ-8), the generalizability of previous results related to committed action, and the importance of this construct to the functioning of patients with chronic pain.

## Methods

Participants were 462 consecutive referrals to the Pain Rehabilitation Unit at Skåne University Hospital. Inter-item correlations, item-total correlations, and Cronbach's alpha were used to estimate reliability. To examine whether the factor structures in the current sample matched the two-factor models found in the original validation studies, confirmatory factor analyses were used. Correlation analyses of the CAQ-18 and CAQ-8 were conducted with theoretically related concepts and indices of pain-related functioning. To test the incremental validity of the measure a series of hierarchical regression analyses were undertaken.

## Results

High levels of internal consistency and acceptable relationships with theoretically related concepts and several indices of patient functioning were shown in these Swedish-language versions of the CAQ (CAQ-18 and CAQ-8). Furthermore, the CAQ demonstrated satisfactory structural validity and incremental validity.

## Discussion

The development, translation, and further validation of the CAQ and other measures from the psychological flexibility model are essential elements when it comes to evaluating the utility of this model to the treatment of chronic pain. The results from this study supported the validity and reliability of the Swedish-language versions of the CAQ, the generalizability of earlier findings, and the relevance of committed action to health and functioning in individuals with chronic pain. Going forward this measure can facilitate research on processes of change within the psychological flexibility model.



# Study III

## Introduction

The aims of this study were threefold. The first aim was to assess the psychometric properties of a Swedish version of the Posttraumatic Diagnostic Scale (PDS). The second aim was to study the prevalence of traumatic experiences, trauma types, and posttraumatic stress disorder (PTSD) in a sample of patients seeking treatment for chronic pain. The third aim was to examine how indices of pain-related functioning varied with a history of traumatic exposure and PTSD diagnostic status, as assessed by the PDS.

## Methods

Participants were 463 consecutive patients with chronic pain referred for assessment at the Pain Rehabilitation Unit at Skåne University Hospital. Inter-item correlations, item-total correlations, and Cronbach's alpha were used to examine the internal consistency and reliability of the PDS. Pearson correlations with convergent constructs were conducted and confirmatory factor analyses were undertaken using maximum likelihood estimation procedures to examine the structural validity of the PDS. The prevalence of trauma, trauma types, and PTSD were also examined in this patient group. Differences in clinical characteristics between three groups of patients with chronic pain were explored; those fulfilling criteria for PTSD, those exposed to trauma not fulfilling criteria for PTSD, and those not exposed to trauma.

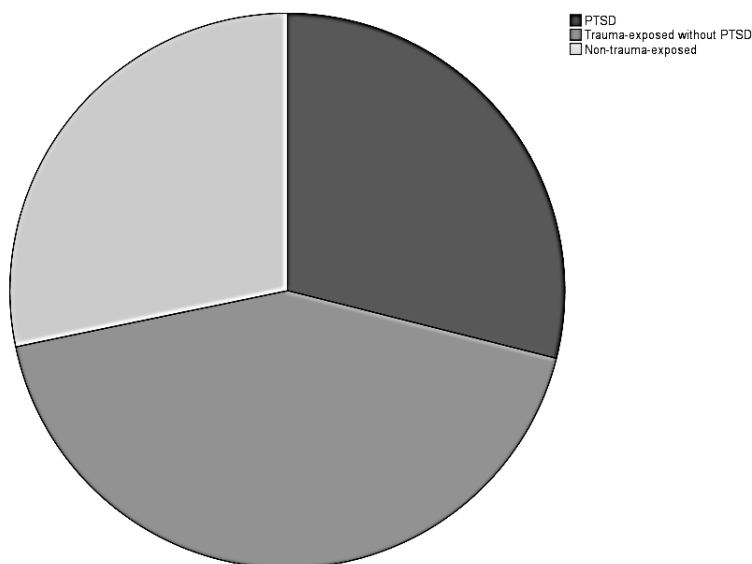


Figure 1 Percentage of three subgroups of chronic pain patients; those fulfilling criteria for PTSD; those exposed to trauma not fulfilling PTSD criteria; and those not exposed to trauma.

## Results

High levels of internal consistency and a factor structure in accordance with those reported in previous validation studies using trauma samples were seen for this translated version of the PDS. A majority (71.8%) reported one or more traumatic events, with almost one-third (28.9%) of the patients fulfilling criteria for a current PTSD diagnosis based on their responses from the PDS (Figure 1). Significant differences were observed between the analysed groups. The post hoc comparisons showed that the patients fulfilling criteria for PTSD reported significantly higher levels of pain interference, kinesiophobia, anxiety, and depression as well as significantly lower levels of life control, compared to trauma-exposed patients not fulfilling criteria for PTSD as well as non-trauma-exposed patients (Table 3). No differences were observed between the trauma-exposed group not fulfilling criteria for PTSD and the non-exposed group.

**Table 3 Differences in clinical characteristics between patients fulfilling criteria for PTSD (Group 1), trauma-exposed patients not fulfilling criteria for PTSD (Group 2) and non-trauma exposed patients (Group 3)**

Variable	F	M (sd)			Mean differences		
		Group 1 (n=127)	Group 2 (n=188)	Group 3 (n=124)	1 vs 2	1 vs 3	2 vs 3
Pain duration	.22	7.24 (7.32)	7.74 (7.32)	7.78 (7.50)	-.50	-.54	-.04
Number of pain sites	3.61*	15.93 (9.14)	15.24 (9.02)	13.08 (8.28)	.68	2.85*	2.16
Pain intensity	3.59*	7.67 (1.56)	7.24 (1.54)	7.56 (1.39)	.43*	.11	-.33
Pain interference	9.19**	5.00 (.88)	4.59 (.91)	4.59 (.94)	.41**	.41**	-.00
Life control	12.61**	1.89 (1.05)	2.47 (1.14)	2.47 (1.05)	-.58**	-.57**	.01
Physical functioning	4.73**	42.53 (24.03)	50.20 (21.25)	48.71 (21.88)	-7.67**	-6.17	1.50
General health	3.82*	32.62 (17.18)	37.60 (18.95)	38.42 (18.92)	-4.99	-5.80*	-.82
Anxiety	33.49**	13.46 (4.38)	9.66 (4.52)	9.40 (4.71)	3.80**	4.06**	.26
Depression	17.75**	11.81 (4.40)	9.14 (4.43)	8.92 (4.40)	2.67**	2.89**	.22
Kinesiophobia	13.32**	46.16 (9.21)	41.08 (9.02)	41.55 (8.92)	5.08**	4.61**	-.47

Notes: All alpha levels were adjusted using the Bonferroni correction. Degrees of freedom were: df1 = 2, df2 = 436. Pain duration was measured in years. Pain intensity was assessed with the Numerical Rating Scale, pain interference and life control with the Multidimensional Pain Inventory, physical functioning and general health with the Medical Outcomes Study 36-Item Short-Form Health Survey, anxiety and depression with the Hospital Anxiety and Depression Scale, and kinesiophobia with the Tampa Scale of Kinesiophobia.\*P < .05; \*\*P < .01.

## Discussion

High rates of traumatic exposure and PTSD were found among chronic pain patients. The presence of PTSD in these patients was associated with worse clinical characteristics and an increased need for treatment. Self-report measures, such as the PDS, seem valid for screening purposes in this population and can be implemented with low costs.

## Study IV

### Introduction

The aim of the study was to examine the relationship between PTSD and chronic pain and in particular whether various indices of psychological flexibility mediated the relationship between these two conditions. First, we compared trauma-exposed adults with and without PTSD on measures of psychological flexibility, pain severity, pain interference, and depression in a sample seeking treatment for chronic pain. Second, we examined whether psychological flexibility mediated the relationship between PTSD and pain severity/interference at the time of referral for assessment of chronic pain, controlling for depression.

## Methods

Participants were 315 people seeking treatment for chronic pain reporting at least one traumatic experience. Differences between participants with and without PTSD on pain interference, pain severity, and the potential mediators (psychological flexibility and depression) were explored through independent sample t-tests. The effects of psychological flexibility and depression on the relationship between PTSD and pain severity/interference were assessed using mediation analyses (Figure 2). Psychological flexibility was indexed by pain-related acceptance, committed action, values-based action, and cognitive fusion.

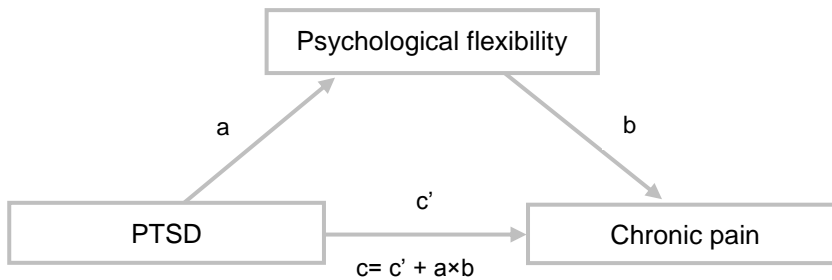


Figure 2 The effect of PTSD (yes/no) on the mediator was represented by the *a*-path and the effect of the mediator on chronic pain controlling for PTSD was represented by the *b*-path. The total effect of PTSD on chronic pain was represented by the *c*-path and the direct effect of PTSD on chronic pain, when controlling for the mediator, was represented by the *c'*-path. The mediating or indirect effect was the effect of the mediator on the relationship between PTSD and chronic pain and the cross-product  $a \times b$  directly assessed the significance of this effect.

## Results

Significantly higher levels of pain severity, pain interference, depression, and cognitive fusion and lower levels of pain-related acceptance and committed action were seen in participants reporting symptoms consistent with a diagnosis of PTSD as compared to those reporting symptoms below the diagnostic threshold for PTSD. Pain-related acceptance, committed action, cognitive fusion, and depression were identified as individual mediators of the relationship between PTSD (diagnostic status) and chronic pain as indexed by both pain severity and interference. When significant mediators on the univariate level were examined in a multivariate fashion, pain-related acceptance, cognitive fusion, and depression were identified as mediators of the relationship between PTSD and pain severity/interference (Table 4). Taken together, the most influential mediator from the psychological flexibility model was pain-related acceptance. Comparable levels of explained variance and consistent result patterns were found using PTSD symptom severity and the PTSD symptom clusters as independent variables in corresponding mediation analyses.

**Table 4 Results of the multivariate mediator analyses between PTSD diagnostic status and pain severity and pain interference**

Dependent Variable	Mediator	Total Direct & Indirect Effects		Results for Indirect Effects <i>a*b</i>		
		Path	Effects	Point-estimate (SE)	95% CI LL, UL	<i>P<sub>M</sub></i> <u>ab</u> c
Pain severity						
		Total c	.27* (.10)			
		Direct c´	.03 (.09)			
	Pain acceptance	a	-7.81* (1.96)	.09* (.04)	.03, .18	.33
		b	-.01* (.00)			
	Committed action	a	-9.52* (1.81)	-.03 (.03)	-.10, .02	ns
		b	.00 (.00)			
	Cognitive fusion	a	1.16* (.47)	.05* (.03)	.01, .12	.19
		b	.05* (.01)			
	Depression	a	2.67* (.51)	.12* (.04)	.06, .21	.44
		b	.05* (.01)			
Pain interference						
		Total c	.41* (.10)			
		Direct c´	.06 (.08)			
	Pain acceptance	a	-7.81* (1.96)	.15* (.05)	.07, .25	.37
		b	-.02* (.00)			
	Committed action	a	-9.52* (1.81)	-.03 (.02)	-.09, .01	ns
		b	.00 (.00)			
	Cognitive fusion	a	1.16* (.47)	.03* (.02)	.00, .09	.07
		b	.03* (.01)			
	Depression	a	2.67* (.51)	.20* (.05)	.12, .30	.49
		b	.07* (.01)			

Notes: LL = lower limit; UL = upper limit. Unstandardized coefficients are reported and the indirect effect is statistically significant if the confidence interval (CI) does not include zero. Asterisks (\*) indicate a statistically significant effect.

## Discussion

The relationship between PTSD and chronic pain was mediated by processes from the psychological flexibility model in people seeking treatment for chronic pain. Possibly, the psychological flexibility model can be useful as an overarching model for understanding the relationship between PTSD and chronic pain. Targeting of pain-related acceptance, committed action, and cognitive fusion

(among other processes) during treatment may be of value for people exhibiting these combined problems.

## Study V

### Introduction

The first aim of this study was to investigate whether a range of pre-treatment variables, including PTSD, depression, anxiety, and different facets of psychological flexibility predicted outcome in a CBT program for chronic pain one year following treatment. The second aim was to examine the mediating effects of processes from the psychological flexibility model on treatment outcome.

### Methods

Participants were 232 patients taking part in a multidisciplinary program with assessment at pre-treatment, post-treatment and at 12-month follow-up. First, we analysed whether baseline values for depression, anxiety, PTSD, and different facets of psychological flexibility individually predicted treatment outcome at 12-month follow-up, as indexed by pain intensity, pain interference, and depression. Second, we explored whether changes in different facets of psychological flexibility (acceptance, committed action, cognitive fusion, and values-based action) over time (pre-treatment to follow-up) mediated changes in pain intensity, pain interference, and depression over time (pre-treatment to follow-up), controlling for the CBT-compatible-processes of kinesiophobia and life control.

### Results

The only significant predictors of outcome one year following treatment turned out to be psychological inflexibility for pain interference and depression, and committed action for depression. Participants who at baseline reported higher levels of pain inflexibility had significantly worse pain interference and depression, while individuals who reported lower levels of committed action had significantly worse depression. Psychological inflexibility, pain-related acceptance, committed action, cognitive fusion, and values-based action all had significant, separate mediating effects on outcomes at a univariate level, with the strongest effects being seen for psychological inflexibility. On a multivariate level, the most influential mediators of the sub-processes from the psychological

flexibility model were pain-related acceptance, committed action, and values-based action (Table 5).

**Table 5 Multivariate mediation analyses including the sub-processes from the psychological flexibility model**

Dependent Variable	N	Mediator	Results for Indirect Effects	
			<i>a*b</i>	
			Point-Estimate (SE)	95% CI LL, UL
Pain intensity	133	Acceptance	-.121 (.150)	-.413, .176
		Committed action	-.016 (.040)	-.119, .048
		Cognitive fusion	-.017 (.113)	-.248, .193
		Values-based action	.221 (.098)	.061, .441
		Life control	.268 (.102)	.100, .504
		Kinesiophobia	.222 (.102)	.035, .438
Pain interference	135	Acceptance	.189 (.077)	.055, .365
		Committed action	.036 (.022)	.006, .099
		Cognitive fusion	.026 (.074)	-.125, .163
		Values-based action	.067 (.042)	-.004, .161
		Life control	.104 (.044)	.031, .211
		Kinesiophobia	.082 (.051)	-.012, .191
Depression	133	Acceptance	.322 (.280)	-.169, .958
		Committed action	.295 (.132)	.087, .613
		Cognitive fusion	-.369 (.282)	-1.003, .105
		Values-based action	.280 (.192)	-.060, .690
		Life control	.828 (.231)	.453, 1.368
		Kinesiophobia	.196 (.210)	-.216, .617

Notes: LL = lower limit; UL = upper limit. The indirect effect is statistically significant if the confidence interval (CI) does not include zero.

## Discussion

The view that the processes from the psychological flexibility model are transdiagnostic and trans-situational is supported by the results in this study, as they seem to underlie improvement in a more CBT-oriented treatment approach and for a population with diverse problems cutting across diagnostic categories, including both somatic and psychiatric complaints. More exact targeting of the

processes from the psychological flexibility model may improve outcomes in chronic pain treatments. An increased focus on this model may also speed up integration within the field of CBT in general, but further studies using controlled longitudinal designs are needed.





# Discussion

## General discussion

Given the costs of chronic pain for both the individual and society, a primary aim must be the development and dissemination of more effective interventions for individuals suffering from these conditions. To achieve this aim, increased efforts are needed to identify the treatment processes that help people live more productive and rewarding lives despite the presence of chronic pain. Information about therapeutically active treatment processes can assist in the development of treatment programs that better target such processes and thus lead to improved outcomes.

The primary aim of this research program was to increase our understanding of how changes in psychological flexibility during a multicomponent, multidisciplinary CBT program for chronic pain were related to outcome. Current psychological treatments for chronic pain only produce small to medium effect sizes. More and more studies are trying to identify which treatment components work for which type of patient and try to understand why (Turner et al., 2007; Williams et al., 2012). The results from Study I and V highlight the importance of processes from the psychological flexibility model as mediators of outcomes in CBT for chronic pain, and support the trans-situational properties of these processes, as they seem to operate within a CBT treatment based on a traditional model. Possibly, a processes-focused approach informed by the psychological flexibility model can be useful for theoretical integration within the field of CBT and can help speed up development within CBT treatments for chronic pain.

The secondary aim of the research program was to identify predictors of treatment outcome, which might inform future efforts to modify or supplement treatment programs for chronic pain in order to improve outcomes. There is a small but growing body of literature attempting to identify predictors (Gilpin et al., 2017; McCracken & Turk, 2002), with at times conflicting results. As part of Study V, and to add to the literature, we investigated a range of pre-treatment variables as possible predictors of outcome, particularly focusing on PTSD and other indicators of emotional distress as well as processes from the psychological flexibility model. Overall, the results suggested that pre-treatment characteristics such as patient demographics, pain duration, and emotional distress as indexed by anxiety,

depression, and PTSD did not predict outcomes. These findings differ from previous studies where higher levels of anxiety and depression have been found to predict worse treatment outcomes (Linton et al., 2011; Miles et al., 2011; Trompetter et al., 2016; Turner et al., 2007). In contrast, psychological inflexibility and lower levels of committed action predicted poorer outcomes, suggesting that patients with these characteristics may benefit from more intensive targeting of these processes during treatment.

Regarding emotion-related predictors, a sub-aim of this research program was to examine how one particular and understudied form of psychiatric comorbidity – PTSD – related to pain presentation, psychological flexibility, and treatment outcome. Study III aimed to expand the knowledge base on the prevalence of PTSD in adults seeking treatment for chronic pain, finding similarly high levels as in previous studies (Andersen et al., 2012; Fishbain et al., 2017). The findings from Study III also lend some support to the view that there is a negative interaction between the symptoms of PTSD and chronic pain, as the patients with comorbid PTSD were shown to have much poorer pain presentations at pre-treatment than those without PTSD, and regardless of traumatic exposure.

The influence of PTSD on outcomes in treatment for chronic pain is an understudied area. We have only identified two previous studies that have investigated this possibility (Andersen et al., 2014; Siqveland, Ruud, et al., 2017). Similar to those results, the findings from Study V suggested that pre-treatment levels of PTSD were unrelated to outcomes as indexed by pain intensity, pain interference, and depression. Still, no studies that we are aware of have studied whether empirically supported treatments for chronic pain also have beneficial effects for PTSD symptoms (Andersen et al., 2014; Beck & Clapp, 2011; Siqveland, Ruud, et al., 2017).

Taken together, clarification of components in psychological treatments that underlie these conditions and can be used to target both the adverse impact of PTSD and improve pain-related functioning are needed. One clear contribution of the psychological flexibility model is that it places less emphasis on disorder-specific treatment protocols and instead focus on a more limited range of therapeutically-active interventions that aim to reduce experiential avoidance and increase psychological flexibility, i.e. processes that work across different diagnostic boundaries (Hayes & Hofmann, 2017; McCracken & Morley, 2014). In Study IV, processes from the psychological flexibility model were found to mediate the relationship between PTSD and pain severity/interference in adults seeking treatment for chronic pain. Hence, processes from the psychological flexibility model appear to contribute to the interaction between PTSD and chronic pain. These results strengthen the transdiagnostic applicability of the model, since

it seems able to link specific somatic and psychiatric problems together through its processes.

## Practice implications and further studies

The data collected from these studies were meant to add to the scientific knowledge base and to help develop more effective treatments for individuals with chronic pain. The results from Study I and V showed that acceptance, committed action, and values-based action as well as cognitive fusion and psychological inflexibility partly underpinned the gains made in a multicomponent, multidisciplinary CBT program for chronic pain. They further suggested that more precise monitoring and targeting of these processes within current CBT approaches should be investigated as one way to improve outcomes for adults seeking treatment for chronic pain.

Results from Study V showed that baseline scores on the overarching measure of psychological inflexibility (PIPS) predicted several indicators of worse outcome, while the measure of committed action (CAQ) predicted only one indicator of worse outcome. Thus, administration of a single self-report measure of psychological inflexibility during the assessment phase might be sufficient to identify patients who might benefit from additional interventions targeting all aspects of psychological flexibility. As part of any effort to individualize treatment based on pre-treatment levels of psychological flexibility, further efforts will be needed to identify which indices of flexibility are most relevant as predictors. Onward, it might be possible to identify patients who score in the lower percentiles on one or more of the measures of psychological flexibility, and to supplement their standard group treatment with one-to-one or small-group interventions aiming to increase their levels of psychological flexibility. These supplemental interventions during the day treatment program could be further supplemented by the patient's use at home (nights and weekends) of an internet-based program that targets psychological flexibility.

The results of Study V highlighted the need for further reflection upon the value of assessment of different psychiatric disorders in relation to the treatment of individuals with chronic pain. Pre-treatment levels of PTSD were unrelated to pain outcomes. In other words, patients with PTSD benefitted from treatment despite this aspect of comorbidity. Administering self-report measures of PTSD are not costly but it does add to the measurement burden experienced by the patients. At present, it does not appear as if the benefits of screening for PTSD at baseline and then monitoring this condition during treatment *clearly* outweigh the additional burden this assessment places on patients, if clinical utility of such screening is

only defined as reductions in pain-related disability during treatment. However, it is important to again note that no studies that we are aware of have investigated the effect of pain treatment on PTSD symptomatology, even though this is of clinical and theoretical interest (Andersen et al., 2014; Beck & Clapp, 2011; Siqveland, Ruud, et al., 2017). We aim to present such data in an upcoming study and hope these results can provide some guidance on the necessity of PTSD-screening prior to pain treatment. Also, there is a substantial evidence base indicating that the presence of untreated PTSD places the individual at greatly increased risk of a range of negative (mental) health related outcomes (Beckham et al., 1997; Geisser et al., 1996; Morasco et al., 2013; Ruiz-Párraga & López-Martínez, 2014; Sherman et al., 2000). Thus, screening might be more useful for clinics focusing on assessment rather than treatment.

It also remains possible that modifying chronic pain treatments to further increase changes in psychological flexibility can have additional benefits for patients with comorbid PTSD. The results of Study IV suggested that such an outcome is plausible. Previous research has also highlighted the relationship between psychological inflexibility and having comorbid disorders in comparison to only having one diagnosis, indicating the relevance of this process to individuals with multi-problem clinical presentations, who are more difficult to treat and have worse levels of functioning (Levin et al., 2014). In addition, delivery of a relatively brief, evidence-based treatment for PTSD might improve outcomes for both PTSD and chronic pain. In fact, such an investigation using a single-case design is currently underway where we give a sample of four patients with PTSD individual prolonged exposure therapy as a supplement before their pain treatment. Their outcomes in this PTSD-focused treatment are examined, as well as how changes in PTSD are related to their outcomes in the pain treatment. This is then compared to a cohort of chronic pain patients with comorbid PTSD who receive no individual treatment before their pain treatment.

Still, it is important to acknowledge the possibility that a separate targeted treatment for comorbid PTSD in patients with chronic pain before or after receiving intensive treatment for pain will have no or very modest effects on their pain outcomes, and that this approach is simply not cost effective. Disorder specific approaches to assessment and treatment have dominated the way in which mental problems have been conceptualized, researched, and treated for many years (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015). The idea that psychiatric disorders are best described using dimensional continua rather than categorical entities has been put forward and research and clinical evidence have shown that a categorical diagnostic schema does not fully reflect the realms of clinical concerns in many patients (Clarke & Kuhl, 2014). In relatively recent times, there has been an increased interest in transdiagnostic processes and treatment interventions that go beyond diagnostic boundaries (Craske, 2012).

These approaches are thought to facilitate treatment implementation and to enhance outcomes for the full range of disorders or problem areas in a given patient (Craske, 2012). Transdiagnostic processes and interventions might be particularly important within the field of chronic pain since pain adjustment incorporates a wide range of social, psychological, and biological factors, often described by a biopsychosocial model (McCracken & Morley, 2014), and the results from these studies lend some support to such a notion.

The transdiagnostic approach focuses on identification and targeting of shared, key temperamental, psychological, cognitive, emotional, interpersonal, and behavioral mechanisms underlying a wide range of diagnostic presentations (Harvey, Watkins, Mansell, & Shafran, 2004). At present there are two transdiagnostic approaches, where the first mainly builds on generic restructuring of CBT interventions to focus on disorders within a diagnostic cluster (e.g., anxiety disorders or eating disorders). The second cuts across all diagnostic categories, is comprised of acceptance-based interventions, and includes the psychological flexibility model (Craske, 2012). The psychological flexibility model is built around a dimensional conceptualization of pathology and health. Using this standpoint, psychological (in)flexibility is argued to influence all aspects of human behavior and functioning and to exist along a continuum from healthy to more impaired, where variations are more linked to level of inflexibility rather than qualitative, categorical differences between people with and without diagnoses (Hayes, Vilatte, Levin, & Hildebrandt, 2011). Thus, the psychological flexibility model may offer a solid theoretical and practical framework for developing and implementing transdiagnostic approaches.

In spite of an overarching aim of truly transdiagnostic treatments, research on the relationship between psychological flexibility and specific disorders can still deepen our knowledge regarding how treatments based on psychological flexibility are most effectively applied to an individual with, for example, recurring intrusive recollections of a traumatic event and persistent pain, particularly when these two phenomena are not linked to the same traumatic event. Diagnostic labels can act as helpful heuristics in the sense that they can narrow the scope of investigation to experiences that have problematic meanings for the individual, and then derive interventions that can target shared underlying mechanisms for the "symptoms" from the broader psychological flexibility model (Levin et al., 2014). Also, the form of problematic behaviors varies across individuals, even if they often can be conceptualized as having shared psychological functions (Hayes et al., 1996). Hence, to get improved treatment effects for the full range of problems for an individual, interventions in group settings may need to incorporate the dominating problem areas and triggers related to other symptoms besides pain. This is not routinely done in a pain setting, but could be incorporated using a psychological flexibility approach. Up until now,

investigations of the relationship between psychological flexibility and specific disorders have primarily focused on a more narrow range of problem areas, such as anxiety disorders (Levin et al., 2014; Venta, Sharp, & Hart, 2012), rather than the equally frequently comorbid phenomena of psychiatric and somatic complaints. Also, to a large extent the transdiagnostic literature has not investigated psychological flexibility in relation to comorbidity (Levin et al., 2014), nor the relationship between pain and emotion (Linton, 2013). Consequently, there is scope for investigating psychiatric comorbidities such as depressive disorders, anxiety disorders, and PTSD together with psychological flexibility and chronic pain, especially in lack of a fully working dimensional diagnostic approach (Clarke & Kuhl, 2014).

Six domains have been suggested as core outcome domains for chronic pain trials: pain, physical functioning, emotional functioning, participant ratings of global improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition (e.g. adherence to the treatment regimen and reasons for premature withdrawal from the trial). Numerous outcome measures related to the recommended core domains have appeared in the research literature (Turk et al., 2003). Of course, there is a need to look at broader domains of functioning and there are many supplemental outcome domains that have not been researched to the same extent, such as health care utilization, work ability, return to work, and medication use. Further studies are needed to develop, validate, and analyse measures of these aspects of functioning, but also to find out how to optimize results in these domains. It is still uncertain whether processes from the psychological flexibility model are related to such outcomes.

## Research limitations

There are certain statistical and design limitations that need to be considered in the current studies. The studies were conducted as a part of a real-world setting in a tertiary specialist unit for chronic pain. Hence, the studies included heterogenic samples with significant comorbidities, large sample sizes, and limited exclusion criteria, all of which contribute to the validity of the studies and heighten the translatability of the results to clinical practice and populations with complex clinical pictures that are frequently excluded from RCTs. On the other hand, the generalizability of the findings can be limited due to the relatively high levels of women and participants having studied at university level in the analysed samples. These real-world studies also had some drawbacks including threats to validity as the treatment outcome studies lacked randomisation and control groups. It is also difficult to separate the effects of treatment from a number of confounding variables. Variables that might have affected the results include maturation, other

significant events occurring between the beginning of treatment and the 12-month follow up, the chosen statistical methods and measures, attrition, and the diverse practice setting, where treatment was delivered by different multidisciplinary teams with varying levels of education and experience. There were missing data in all studies, but overall the missingness was shown to be completely random (Little, 1988).

Mediation studies can be viewed as falling on a continuum or ladder of evidence with the strongest evidence being found in studies with random assignment and control groups. However, studies at all levels can inform us about mediation processes (Maric et al., 2012). The current mediation studies can be said to fall in the lower end of this continuum, since Study I and V involved a single treatment condition using a longitudinal design and Study IV was based on cross-sectional data. The criterion of temporality, where change in the mediator precedes change in the dependent variable, was not met since the process variables were either measured cross-sectionally or at the same time intervals as the outcome measures. As a consequence, strong conclusions regarding the direction of causation among the variables cannot be made. The identified relationships provide a basis for additional work investigating mediators using controlled, randomized longitudinal designs.

All measures were based on self-reports and no semi-structured clinical interviews were conducted. In other words, participants had not been clinically diagnosed with depression, anxiety, or PTSD. Furthermore, the PTSD diagnostic status was based on the DSM-IV criteria since the Posttraumatic Diagnostic Scale for DSM-5 had not yet been developed at the beginning of data collection. Information can be lost by mainly investigating PTSD diagnostic status as compared to overall symptom severity, since participants who were exposed to trauma but did not self-report symptoms in accordance with a diagnosis could still have debilitating symptoms. Despite the mild symptoms reported in this group, and in the absence of structured diagnostic interviews, it is impossible to say with certainty that everyone from the group did not meet diagnostic criteria at the time.

Finally, since the studied CBT treatment was built around multiple components and delivered by multidisciplinary teams, it is difficult to pinpoint which interventions that have the strongest impact on the identified mediators. However, these studies were not intended to clarify the impact of individual components on processes from the psychological flexibility model. If improved outcomes are to be achieved in multidisciplinary, multi-component CBT programs, further studies are needed to identify specific components that are “active” in relation to facets of psychological flexibility, other relevant mediators, and outcome.



## Conclusions

CBT is the most-widely used and recommended psychological treatment for chronic pain, but it only yields modest improvements in pain-related functioning and related symptoms. The results from these studies suggest that more precise assessment and targeting of facets from the psychological flexibility model may improve outcomes of chronic pain treatments based within the CBT field.

Up until now CBT treatments for chronic pain have taken a broad focus on processes for change and included diverse methods and types of interventions often with multidisciplinary inputs. A large number of potential change processes have been investigated in chronic pain trials, without revealing which processes are most important in relation to treatment outcomes (Turner et al., 2007; Williams et al., 2012; Vowles, Wetherell, & Sorrell, 2009). This search for new and more influential variables seems to create expansion of the field rather than simplification or integration (McCracken & Morley, 2014). As mentioned above, CBT rationales and interventions have sometimes been divided into three separate waves or generations (Hayes, 2004; Hayes & Hofmann, 2017). However, there have always been overlaps between the different waves such as shared techniques and strategies, particularly when focusing on behavioral interventions. In accordance with this, interventions from all generations can be viewed as one set of coherent treatment strategies (Hofmann et al., 2010). Recent efforts have been made to move beyond division and bring all wings of CBT and evidence-based therapy more generally together by using a process-based approach (Hayes & Hofmann, 2018). Based on the results from these studies, theoretical integration within the field of CBT may be facilitated by such a process-focused approach including the psychological flexibility model. This model seems to be transdiagnostically and trans-situationally applicable in several ways. Its processes span problem areas with diverse backgrounds from the somatic field and chronic pain to the psychiatric field and PTSD, and appear useful not only to treatments specifically built around targeting psychological flexibility but also more broadly in CBT treatments.

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## Predictors and mediators of outcome in CBT for chronic pain

Chronic pain is a commonly occurring and debilitating condition, and among the costliest health problems for both the individual and society at large. Cognitive behavioral therapy (CBT) is the most widely-disseminated psychological treatment for chronic pain. Even though it is recommended and evidence-based, it yields quite modest improvements in pain-related functioning and accompanying symptoms of emotional distress. It is now generally acknowledged that further efforts are needed to improve the efficacy of CBT for chronic pain. Specifically, pain researchers have called for studies to identify mechanisms that underlie changes in treatment outcomes (mediators) and characteristics of the individual that predict improvements in these mechanisms and treatment overall (predictors and moderators).

To address this call, the primary aim of this research program was to study whether changes in psychological flexibility mediated outcomes in a multi-disciplinary, group-based CBT program delivered at a regional specialist unit for pain rehabilitation. The secondary aim was to identify possible predictors of outcome by focusing on facets of psychological flexibility as well as the understudied influence of posttraumatic stress disorder (PTSD). This aim also included investigation of the relationships between PTSD, pain presentation, and psychological flexibility. With these two aims, we hoped to shed further light on the validity of the psychological flexibility model as an integrating, overarching model that can help define relevant treatment processes for adults presenting with chronic pain and psychiatric problems.