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# Acceptance for persons suffering from pain

*Evaluation of acceptance-based interventions for adults with chronic pain and children with cancer experiencing acute pain*

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**Abstract**
Thorsell Cederberg, J. 2017. Acceptance for persons suffering from pain. Evaluation of acceptance-based interventions for adults with chronic pain and children with cancer experiencing acute pain. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine* 1340. 64 pp. Uppsala: Acta Universitatis Upsaliensis. ISBN 978-91-513-0001-6.

It is increasingly clear that pain and emotions are closely interconnected. Pain does not only cause psychological distress, but psychological distress also amplifies pain through neurological mechanisms. Treatment of both chronic and acute pain would benefit from acknowledging the psychological mechanisms of pain neurophysiology. Psychological acceptance predicts increased pain tolerance and decreased pain intensity and discomfort in experimentally induced pain and improved physical and psychosocial functioning for persons with chronic pain.

The overall aim of this thesis was to evaluate acceptance-based interventions for persons suffering from pain.

In Study I the effect of a manualised ACT-based self-help intervention for adults with chronic pain was evaluated in an RCT (n=90). The results showed improvements in satisfaction with life, physical functioning and pain intensity for the ACT group. Both the ACT and the control group improved regarding depression and anxiety. In Study II the mediating effect of acceptance for treatment change was evaluated, using data from Study I (n=64). The results showed indirect effects of treatment via acceptance for physical functioning but not for satisfaction with life. In Studies III and IV, instruments to measure psychological flexibility in relation to pain were developed for children with cancer, and their parents respectively, using factor analysis. The results showed that a two-factor solution for the child scale (n=61) and a three-factor solution for the parent scale (n=243), best represented the data. In Study V, an acceptance-based intervention was preliminarily evaluated in a single-subject study (n=5) for children reporting pain during cancer treatment. The intervention consisted of an approximately 15-minute long pain exposure exercise. All participants reported reduced discomfort of pain, and three of the participants reported reduced pain intensity.

The results suggest that a manualised ACT-based self-help intervention is a valuable addition to the treatment repertoire for persons with chronic pain and that acceptance may mediate the effect of treatment on physical functioning. Furthermore, instruments to measure acceptance in the context of acute pain in children with cancer are now available, although further validation is needed. Lastly, the results indicate that an acceptance-based intervention may help children undergoing cancer treatment to cope with pain.

*Keywords:* acute pain, chronic pain, acceptance, psychological flexibility, acceptance and commitment therapy, children and adolescents, cancer

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*To Erik, Alfred and Eira*

# List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I Thorsell J, Finnes A, Dahl J, Lundgren T, Gybrant M, Gordh T, Buhrman M. (2011) A Comparative Study of 2 Manual-based Self-Help Interventions, Acceptance and Commitment Therapy and Applied Relaxation, for Persons With Chronic Pain. *Clinical Journal of Pain*, 27(8):716-723. Erratum. (2013) *Clinical Journal of Pain*, 29(5):469.

II Thorsell Cederberg J, Cernvall M, Dahl J, von Essen L, Ljungman G. (2016) Acceptance as a Mediator for Change in Acceptance and Commitment Therapy for Persons with Chronic Pain? *International Journal of Behavioral Medicine*, 23(1):21-29.

III Thorsell Cederberg J, Weineland Stranskov S, Dahl J, Ljungman G. (2017) Parents' relationship to pain during children's cancer treatment – a preliminary validation of the Pain Flexibility Scale for Parents. *Journal of Pain Research,* 10:507-514.

IV Thorsell Cederberg J, Weineland Stranskov S, Dahl J, Ljungman G. (2017) Children's and adolescents' relationship to pain during cancer treatment: a preliminary validation of the Pain Flexibility Scale for Children. *Journal of Pain Research,* 10:1171-1178.

V Thorsell Cederberg J, Dahl J, von Essen L, Ljungman G. An acceptance-based intervention for children and adolescents with cancer experiencing pain – a single subject study. *Submitted.*

# Contents

# Abbreviations

| | |
|---|---|
| AAQ-II | The acceptance and action questionnaire – 2nd version |
| ACT | Acceptance and commitment therapy |
| AFQ-Y | The avoidance and fusion questionnaire for youth |
| AR | Applied relaxation |
| BA | Behaviour analysis |
| BT | Behaviour therapy |
| CBT | Cognitive behaviour therapy |
| CI | Confidence interval |
| Df | Degrees of freedom |
| EFIC | European Pain Federation |
| FA | Functional analysis |
| FU | Follow-up |
| HADS | Hospital anxiety and depression scale |
| HMR | Hierarchical multiple regression |
| IASP | International Association for the Study of Pain |
| ICC | Intraclass correlation |
| NRS | Numerical rating scale |
| PCA | Principal component analysis |
| PCS-C | The pain catastrophizing scale for children |
| PCS-P | The pain catastrophizing scale for parents |
| PFS-C | The pain flexibility scale for children |
| PFS-P | The pain flexibility scale for parents |
| RCT | Randomized controlled trial |
| RFT | Relational frame theory |
| SD | Standard deviation |
| SE | Standard error |
| SWLS | Satisfaction with life scale |
| TAU | Treatment as usual |
| VAS | Visual analogue scale |
| WHO | World Health Organization |

# Introduction

## Pain

Pain can be described in terms of a multitude of sensory terms including temporal, spatial and thermal aspects (e.g. beating, pounding, flashing, shooting, burning, scalding), miscellaneous kinds of pressure characteristics (e.g. pricking, stabbing, cutting, pinching, cramping, tugging), brightness (e.g. tingling, stinging) and dullness (e.g. sore, heavy). Additionally, it can be described in numerous affective and evaluative terms (e.g. tiring, suffocating, intense, troublesome). Furthermore, it can be described in various other terms such as radiating, piercing, numbing, squeezing, freezing and nagging.[1] So, if all these descriptions are pain, what is pain more specifically?

According to the International Association for the Study of Pain (IASP) the definition of pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[2] It is a subjective, by definition always unpleasant, complex and multidimensional phenomenon involving biological and psychological factors.[3]

### The function of pain

Acute pain is an alarming system of the body necessary for the survival of humans and animals.[3] Acute pain has been defined as "the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus, associated with surgery, trauma or acute illness".[4] Its function is to demand attention and prioritise escape, recovery and healing. Individuals incapable of feeling pain, as in Congenital Insensitivity to Pain (CIP), are subjected to an increased risk of premature death due to unnoticed injuries and illnesses.[3] Hence, pain serves a tremendously important function.

### Classifications of pain

**Pain aetiology**

Pain is often classified according to its aetiology.[5] Nociceptive pain is the result of stimulation of nociceptors by a noxious stimulus. Neuropathic pain is caused by a dysfunction of the nervous system, peripherally or centrally.

**Type of pain**

Pain can also be classified, according to type of pain, into somatic and visceral.[5] Somatic refers to the superficial body whereas visceral refers to the internal organs.

**Duration of pain**

Finally, pain is commonly categorised according to its' duration.[6] Pain lasting up to three or four weeks is defined as acute pain, between four and 12 weeks as subacute pain and pain that persists for over three months is categorized as chronic. The distinction between acute and chronic pain is, however, not as clear cut, but should be seen as a continuum.[7] Chronic pain can simply be defined as "pain that lasts beyond the usual course of the acute disease or expected time of healing".[8]

## Pain physiology made simple

Pain starts with nerve stimulation where ascending pain impulses are sent to the brain. A descending response is then sent back from the brain to the stimulated area.[3] The nerve transmission to and from the brain can be either inhibited or facilitated. In fact, pain impulses are continuously modulated on their way through the nervous system. Acute pain can be viewed as a trigger of a cascade of processes, which induce alterations in the interactive processes of the multiple signalling pathways in the nervous system.[9,10] These processes generally wane out within a few weeks, but may, in cases of pain amplification processes, develop into chronic pain.[4] The transition from acute to chronic pain occurs gradually in discrete pathophysiological steps. Neuroplasticity, i.e. re-modelling of the neuronal structure in the brain, takes place shortly after the onset of sustained acute pain.[6] Both the duration and intensity of the pain stimulation affects peripheral and central sensitisation processes. Sensitisation refers to the facilitation of the nerve transmission of pain impulses, i.e. a pain amplification process.[3]

## Pain and the brain – the psychology of pain

Pain involves the whole biological system that is regulated by the brain. It is increasingly clear, that pain and emotions are closely interconnected - they constantly influence each other neuro-physiologically.[3] The relationship between pain and negative emotions is therefore not unidirectional, but reciprocal.[11-13] This means that pain not only causes psychological distress, but that psychological distress also amplifies the nerve transmission of pain impulses. Brain-imaging studies have shown that negative emotions, such as stress, anxiety and depressed mood, neurologically facilitate pain impulses while positive emotions, such as happiness, relaxation and love, neurologically inhibit

them.[14] How we interpret pain, what meaning we attribute to it, further affects the neurophysiology of pain.[15] If pain is perceived as a threat it is neurologically amplified.[16] Likewise, perceived uncontrollability has the same intensifying effect on the pain experience.[17] Accordingly, perception of control has an inhibitory effect on the nerve transmission of pain impulses.[18]

There is no pain centre in the brain. Instead, the brain integrates information from this complex interaction of ascending and descending signalling pathways into one output, the pain experience. The neuromatrix theory of pain acknowledges this multidimensionality of pain and suggests that pain is produced by characteristic patterns of nerve impulses called "neurosignatures" of pain.[19,20] Such patterns have been demonstrated in acute pain.[21]

In summary, pain cannot be explained or understood as merely physiological nerve stimulation, instead it is the result of the interaction of a multitude of biological and psychological processes taking place in conjunction with the nerve transmission of pain impulses. It is a whole integrated system that is highly dynamic and plastic, involving biological, cognitive, emotional, behavioural and social factors.

## Pain in children with cancer

Children with cancer suffer from multiple adverse symptoms throughout the cancer trajectory, of which pain is reported as one of the most frequent and burdensome ones.[22] Pain in children with cancer is most commonly caused by the disease itself, side effects of treatment and/or medical procedures. Pain from the disease is caused by tumour connection with bones, soft tissue, viscera or the nervous system. Pain that is caused by side effects of chemotherapy includes mucositis (painful inflammation and ulcers in the mouth and/or gastro-intestinal tract), mucosal damage, gastritis, infections and peripheral neuropathy. Pain that is caused by side effects of radiation includes myelopathy (spinal cord deficits), plexopathy (deficits in nerves, blood vessels or lymph vessels), dermatitis and burns. Painful medical procedures include surgery, lumbar punctures, bone marrow aspirations, biopsies and venepunctures. Treatment- and procedure-related pain are most common during cancer treatment.[23] Although cancer-related pain is classified as distinct from acute and chronic pain, the pain neurophysiology can be seen as communal.[4]

## The role of the parent in child coping

Having a child who is undergoing cancer treatment infers a significant amount of psychological distress for a parent.[24-26] How parents feel and behave in challenging situations affects the level of distress and coping in the children[27-32] and parental acceptance has been shown to predict lower levels of distress in the children.[33,34] The role of the parent has been stressed in interventions in paediatric cancer[35] as well as in paediatric pain.[36]

## Consequences of pain

Up to 80% of visits to physicians are accountable to pain.[6] Even short-term, pain leads to negative psychological consequences and reduced quality of life. As described, these psychological factors may amplify the pain neurophysiology and hence, increase the pain experience. Unrelieved pain may also, in the worst case scenario, lead to chronic pain.[37,38] In chronic pain, comorbidity with depression and anxiety is common,[39-41] social and professional life is negatively affected,[42,43] daily functioning impaired,[44-46] general level of activity reduced [40,47] and quality of life decreased.[48-51] According to the World Health Organization (WHO), chronic pain is one of the most underestimated challenges for the healthcare worldwide.[52] The point prevalence of chronic pain in Europe is estimated to 40-65 %.

In summary, pain reduces the quality of life for the patient, both short- and long-term, and imposes high expenses on healthcare systems.[52] Given the complexity of pain neurophysiology, treatment of pain, both chronic and acute, requires a multimodal approach acknowledging the multidimensionality of pain[6,53-55] including its psychological mechanisms.

# Acceptance of pain

Psychological interventions incorporating mindfulness and acceptance have been shown to predict increased pain tolerance, decreased pain intensity and decreased discomfort of pain in experimentally induced pain.[56-63] Psychological acceptance has also been shown to be helpful for persons suffering from chronic pain.[64-66] Mindfulness and acceptance entails a focused, attentive, non-reactive stance towards unpleasant stimuli with the aim to simply observe ongoing internal experiences without further mental evaluation,[67,68] as opposed to getting absorbed or occupied analysing or trying to control or avoid them. Acceptance in this way enables the possibility to simply notice internal events, such as reactions and impulses, and then *choose* one's actions, rather than rigidly reacting to these internal events. At the same time this position seems to attenuate the pain experience. Mindfulness as a mechanism of change has been shown to have a mechanistically distinct pain-relief function compared to placebo and sham-mindfulness.[69] The definition of psychological acceptance of chronic pain is "living with pain without reacting to, judging or attempting to reduce or avoid it".[70] It entails an active willingness to engage in meaningful activities in the presence of pain, in the service of living a vital life. It does not mean resigning to or ignoring pain, but rather flexibly relating to pain as part of one's experience while at the same time continuing to *live*, guided by what is important in life, and in that particular situation. Acceptance-based treatment, Acceptance and Commitment Therapy (ACT), has been shown to improve physical as well as psychosocial functioning for both adults and children

with chronic pain[71] and is considered to have strong research support for chronic pain.[72] ACT is not only a set of psychological interventional techniques, but a whole philosophical and theoretical framework.[73]

## A contextual behavioural perspective

Mindfulness and acceptance has historically been practiced in eastern Buddhist traditions for thousands of years.[74,75] Modern mindfulness and acceptance has naturally developed from these traditions. Modern mindfulness and acceptance has however, as operationalised in ACT, progressed within the realm of a contextual behavioural scientific framework.[76] Contextual behavioural science is founded upon distinct philosophical and theoretical paradigms.[73]

### Functional contextualism

The philosophical foundation of contextual behavioural science is *functional contextualism.*[73] Like any philosophy of science it infers certain assumptions about the world, conditions under which the system is based. The functional part of the term refers to the fact that all behaviour has a function, i.e. serves a purpose. Put another way, all behaviour takes place because it is reinforced in one way or another. The contextual part of the term refers to the fact that everything happens in a context and should be analysed in light of that context. A behavioural chain can and may be divided into smaller analytical parts if it is helpful to do so but these smaller parts are generally not considered relevant without the context in which they appear. Behaviour and context are seen as intertwined and can generally not be analysed meaningfully as separated from each other. Behaviour and context is seen as a "whole" in that sense. In functional contextualism the truth criterion is viewed differently than in some other philosophies of science, such as in realism, where truth is absolute and something to merely uncover. In functional contextualism, there is no "truth" in an ontological sense. What is "true" is what works. Functional contextualism is pragmatic in that way. What works is further dependent on what is trying to be achieved and under which circumstances. This pragmatic stance extends to all knowledge, which further infers that knowledge is not, in an epistemological sense, "true" either, rather it is assessed based on if it is useful or not. Whether knowledge is useful or not is, again, assessed according to what is trying to be achieved and under what circumstances. The pragmatic stance of functional contextualism opens up to the ongoing contingencies in any given moment and context. Opening up to the ongoing contingencies creates a foundation for flexibility, a possibility to relate to these contingencies in a flexible pragmatic way to serve the purpose for one's action at that given moment.

In short, functional contextualism is guided by the workability of a behaviour in a given context, in relation to a certain purpose.

## Relational Frame Theory (RFT)

The theoretical foundation of contextual behavioural science is Relational Frame Theory (RFT), which is an empirically grounded theory of human language.[73] RFT elaborates upon how humans verbally relate to the world within and around us and demonstrates the interconnection between language and thinking and how thinking is, in fact, verbal behaviour. Like any behaviour, it is learned and governed by behavioural principles.

RFT is based upon three principal features of human verbal behaviour; 1) mutual entailment, 2) combinatorial entailment and 3) transformation of stimulus functions. Mutual entailment refers to the process of deriving a bidirectional relation between stimulus events based on a unidirectional relation. If A is related to B, then we derive that B is related to A. Combinatorial entailment refers to the process of deriving relations between stimulus events based on their relation to other related stimulus events. If A is related to B and B is related to C, then we derive that C is also related to A. Transformation of stimulus functions is the process where the function, i.e. meaning, of a certain stimulus event transforms to other related stimulus events. Note that the relations derived may be completely arbitrary. The term relational frame refers to a specific pattern of contextually controlled and arbitrarily applicable relational responding involving these three principal features of verbal behaviour. Humans have the ability to derive stimulus functions to infinity. Once stimulus relations are derived they are part of the relational network and seem impossible to delete, even with contradictory information or training. What we can do is to add other stimulus relations to increase flexibility to our relational responding.

Furthermore, RFT demonstrates the difference between rule-governed and contingency-governed behaviour. Rules tend to have a narrowing effect on our awareness of the ongoing contingencies in the world within and around us. This narrowing of our awareness hence restricts our ability to relate to these contingencies and in that way restricts our behavioural repertoire. In that mode we are not as apt to respond flexibly but rather rigidly to the ongoing contingencies within and/or around us. A restricted rigid behavioural repertoire inhibits our ability to actually do what works and, hence, to achieve our goals and purposes. Contingency-governed behaviour, on the other hand, is sensitive to the ongoing contingencies within and around us which lets us respond more flexibly. A flexible pragmatic behavioural repertoire tends to be more useful for us in achieving our goals and purposes in life.

If there is a neural network of integrated processes constituting pain as in the neuromatrix of pain theory, there is also a network, or “neuromatrix”, of

experiences and relations, created by an interplay of genetic factors and learning. One could say that we also have "neurosignatures" of relational framing, or verbal behavioural responding.

## Learning theory

Learning theory is developed within the behaviour therapy (BT) tradition.[77] BT is called the first wave of Cognitive Behaviour Therapy (CBT). After BT came cognitive therapy, which was incorporated into BT, and is called the second wave of CBT. ACT and other therapies incorporating mindfulness and acceptance strategies are called the third wave of CBT.[76,78] Although philosophically and theoretically distinct from traditional CBT, this incorporation into CBT is based on the shared foundation upon learning theory and behaviour principles.

### Classical and operant conditioning

Classical and operant conditioning are central to learning theory.[79] Classical conditioning is about stimulus-controlled responses. It is the process where an association between a naturally existing stimulus and a previously neutral stimulus is created, resulting in a conditioned response. Pavlov's Dogs is a classic example of classical conditioning, where the dogs started to salivate (a conditioned response) on the sound of a bell (conditioned stimulus) by repeated pairing of the bell with the food (unconditioned stimulus). In short, classical conditioning is about how we can associate practically everything to anything by learning. Operant conditioning is about consequence-controlled responses. It is the process in which behaviours are governed by their consequences. Behaviours can be strengthened, which increases their likelihood, or punished, which reduces their likelihood. Technically, reinforcement and punishment can be both positive and negative. In short, operant conditioning is about how behaviours are shaped and maintained by their consequences.

#### *Behaviour analysis*

Based on behaviour principles, behaviour analysis is the foundation for any therapeutic intervention within the CBT framework, including ACT. The behaviour analysis is a systematic mapping of a person's goals and behavioural repertoire in relation to those goals. It includes step-by-step analyses of a behaviour in a particular context, including how an antecedent triggers a response followed by a set of consequences, and how these consequences relate to short and long-term goals. This step-by-step analysis is called functional analysis (FA), which focuses on the functions of behaviours rather than their topography.[80,81]

## Psychological flexibility

So, if a flexible behavioural repertoire is more useful to meet the challenges of life and to achieve our purposes, then how do we help people to apply that? In ACT, this is promoted by fostering *psychological flexibility* around impairing life experiences, such as pain.[73] By responding psychologically flexibly to those impairing life experiences we can find ways to move forward and engage in a vital valued life in the presence of difficulties in life. Contact with the present moment, as fostered in mindfulness, and acceptance, are two important processes of psychological flexibility. Theoretically it further consists of the processes; *defusion*, i.e. de-literalisation of language by altering its function (as opposed to its form), *self-as-context*, i.e. detachment from restricting self-conceptualisations and promotion of a broader perspective of the self, *values clarity*, i.e. clarification of values and undermining of values-inconsistent verbal and overt behaviour, and *commitment*, i.e. engagement in values-consistent activities. These latter processes may not be as obvious as mindfulness and acceptance for pain interventions, particularly in a single interventional exercise as compared to in a whole ACT-treatment programme, but they are important aspects of psychological flexibility and indeed applicable on a moment-to-moment basis as well.

# Concluding remarks – a contextual behavioural perspective on pain

Pain is a dynamic, plastic and complex system of an integration between biological and psychological processes.[3] This complexity and multidimensionality needs to be acknowledged and assessed in the treatment of pain.[6,53-55] In the chronic pain area, multimodal treatments in general and psychological treatments in particular, have been used for decades and been shown to be effective.[82] Still, the mechanisms of change need to be further investigated in order to optimise psychological treatments for chronic pain.

Although interventions addressing psychological aspects of the pain experience are commonly used in the acute pain area as well, psychological interventions are generally not part of the standard care. When applied, they have traditionally been used to address the negative psychological consequences of pain in sustained acute pain. Given the reciprocity of pain physiology and psychological processes, psychological interventions are most likely to also have an effect on the pain per se. Furthermore, the need to improve acute pain management in order to prevent the pain from becoming chronic has been emphasised.[7,53,83]

From a contextual behavioural perspective a reduction in pain intensity is of less relevance than the pain in relation to values-consistent engagement. This means that what is important is whether the pain interferes with daily

living or not, i.e. if one can continue to engage in meaningful life activities in the presence of pain or if pain constitutes an obstacle for that. Nevertheless, if our interventions have a decreasing effect on the pain intensity for persons suffering from pain, we should of course take advantage of this beneficial effect. Caution must however be observed so that the intervention is not used as an avoidant coping strategy, which may contradict the intent of the intervention if it were undermining psychological flexibility. Although avoidant coping strategies may be effective short-term, avoidance and context insensitivity have been proposed as mediators for emotional dysfunction and pain problems long-term.[84] However, no single coping strategy would be considered problematic if applied flexibly. Again, it is not the topography but the function of a behaviour that is important.

Pain is initially a physical sensation followed by a reaction comprised of thoughts, emotions and physical tension, which in turn triggers more pain. Pain will quickly be conditioned as aversive. The behavioural response is typically avoidant behaviour, seeking to alleviate the aversive stimulus. This response will be reinforced and maintained as it alleviates the pain short-term. This whole behavioural chain will now be experienced as pain, which is far more than the original physical sensation. A behavioural repertoire based on an avoidant response pattern manifests pain as aversive and sensitises the system to pain. Furthermore, it is rigid and inflexible. The purpose of the interventions in this thesis is to promote psychological flexibility of pain and in that way expand the behavioural repertoire for persons suffering from pain. Given the foundation upon which ACT rests, this is done by cultivating a non-reactive stance towards pain stimuli, adding and transforming the stimulus functions of pain, changing perspective and the context in which pain appears[85] and promoting a contingency-governed and values-consistent behavioural repertoire, through experiential interventions. A flexible behavioural repertoire would help persons suffering from pain to meet the challenge of experiencing pain and enabling engagement in life at the same time, moment by moment.

# Aims

## Overall aim

The overall aim of this dissertation project was to evaluate acceptance-based interventions for persons suffering from pain, in the service of helping these persons to cope with the pain and find a way to continue to live their lives in the presence of pain.

## Specific aims

**Study I**

The aim of Study I was to evaluate a manualised ACT-based self-help intervention for adults with chronic pain.

**Study II**

The aim of Study II was to evaluate acceptance as a mediating variable for treatment change in an ACT intervention for adults with chronic pain, using the data from Study I.

**Study III**

The aim of Study III was to develop and preliminarily evaluate an instrument to measure level of acceptance in parents of children undergoing cancer treatment experiencing pain.

**Study IV**

The aim of Study IV was to develop and preliminarily evaluate an instrument to measure level of acceptance in children with cancer experiencing pain.

**Study V**

The aim of Study V was to preliminarily evaluate an acceptance-based intervention for children experiencing pain during cancer treatment.

# Hypotheses

## Study I

The hypothesis in Study I was that a manualised ACT-based self-help intervention would be equally, or more, effective than a treatment as usual, AR, in self-help format for persons with chronic pain, with regards to satisfaction with life, physical functioning, depression and anxiety. Furthermore, participants in the ACT group were hypothesised to report increased acceptance in comparison to the AR group.

## Study II

The hypothesis in Study II was that acceptance would mediate the effect of treatment on satisfaction with life and physical functioning, in Study I.

## Study III and IV

The hypotheses underlying the aims of Study III and IV were that acceptance-based interventions can help both children with cancer experiencing pain and their parents to cope better and that acceptance would mediate this effect. Instruments to measure acceptance in children experiencing pain during cancer treatment, and their parents, were therefore developed and evaluated in Study III and IV.

## Study V

The hypothesis in Study V was that an acceptance-based intervention would have an effect on discomfort of pain for children experiencing pain during cancer treatment.

# Methods

## Design

An overview of the characteristics of the studies is presented in Table 1.

Study I is a randomised controlled trial (RCT) with follow-up (FU) assessments at six and 12 months post intervention. Study II is a mediation study using data from Study I. Studies III and IV are psychometric studies with a cross-sectional design. Study V is a pilot-study to a planned RCT evaluating an acceptance-based intervention for children with cancer experiencing pain, adopting a single-subject AB design with a non-concurrent multiple baseline.

Table 1. *Overview of Studies I-V.*

| Study | Design | Participants | Data collection |
|---|---|---|---|
| I | RCT | 90 adults with chronic pain who started treatment in Study I | Self-report via internet |
| II | Mediation study | 64 adults with chronic pain who completed treatment in Study I | Self-report via internet |
| III | Psychometric, cross-sectional | 243 parents of children undergoing cancer treatment, experiencing pain | Self-report via pen and paper |
| IV | Psychometric, cross-sectional | 61 children undergoing cancer treatment, experiencing pain | Self-report via pen and paper |
| V | Single-subject | Five children reporting pain during cancer treatment | Oral self-report |

## Procedure and participants

An overview of participant characteristics is presented in Table 2.

Table 2. *Overview of participant characteristics in Studies I-V.*

| Characteristic | Study I and II* | Study III | Study IV | Study V |
|---|---|---|---|---|
| Sample | Chronic pain | Parents of children with cancer | Children with cancer | Children with cancer |
| Mean age (SD) | 46.0 (12.3) | Children: 7.58 (5.12) | 12.7 (3.4) | 12.8 (4.0) |

| | | | | |
|---|---|---|---|---|
| | | Children: | | |
| Age range (yrs) | 18-73 | 0-18 | 7-18 | 7-18 |
| | ♂ 36 % | ♂ 40 % | ♂ 54 % | 3 ♂ |
| Gender | ♀ 64 % | ♀ 60 % | ♀ 46 % | 2 ♀ |
| | | Children: | | |
| Mean pain (SD) | 8.1 (1.7) | 1.3 (1.9) | 1.1 (1.3) | 5.9 (2.4) |
| Type of pain | All types of chronic pain excluding malignancies | Children: Cancer-, treatment-, procedure-related | Cancer-, treatment-, procedure-related | Inflammatory, post-operative, neuropathic |
| Duration of pain | 96 % >1 year | Acute | Acute | Acute |

In Studies I-IV pain was assessed using the Numerical Rating Scale (NRS), in Study V using the Faces Pain Scale-Revised (FPS-R) and the Visual Analogue Scale (VAS). *The numbers differ slightly between the studies, due to different N's.

## Studies I and II

Participants in Study I were recruited from the Pain Clinic at Uppsala University Hospital. Eligibility included a chronic pain diagnosis, accessibility for treatment during seven weeks and sufficient literacy skills in Swedish. Other planned psychological treatment during the study period was an exclusion criterion. Participants were identified, contacted via telephone and informed about the study by a psychologist at the clinic. Information about the study was also sent out via mail along with a consent form. Persons who agreed to participate were randomised into an intervention or a control group. Ninety participants started treatment and were included in the statistical analyses in Study I. Since data from Study I was used in Study II, the recruitment procedure was the same across the two studies. However, the statistical analyses of Study II included only participants who had completed treatment in Study I (n=64).

## Studies III and IV

Studies III and IV are twin studies and the procedure adopted for the two studies was identical. Patients were identified by the Swedish Childhood Cancer Registry. In Study III, parents of all children, 0-18 years of age (n=483), undergoing cancer treatment in Sweden at the time of study were invited to participate. In Study IV, all children aged 7-18 years, were invited to participate in the study (n=231). Potential participants were contacted via mail. The study material included information about the study, background questions, the test version of the scale, evaluation questions and measures for validation. Consent was given through participation in the study. Additionally, in Study IV, written parental consent was required for participants under 15 years of age.

A reminder was sent out two weeks after the invitation. For test-retest-analysis, the measures were sent out again one month after the collection of the first measurement. All study material was coded.

### Study V

Participants in Study V were recruited from the paediatric haematology and oncology ward and outpatient clinic at the Children's University Hospital in Uppsala. Children from four to 18 years of age reporting pain were eligible. Insufficient knowledge of Swedish was an exclusion criterion. Potential participants were identified by nurses and/or doctors on the ward or in the clinic and informed about the study by a research nurse, who also collected written consent for participation. Ten children were invited to participate, one of whom declined and nine accepted. Two small children who had accepted to participate changed their minds and were excluded. For two adolescents the measurements and intervention were not possible to carry out during their pain episodes due to other appointments, and they were consequently excluded. Five participants were included in the study. Participant A was a seven-year-old boy, diagnosed with osteosarcoma, with inflammatory nociceptive pain due to mucositis, a condition of painful inflammation and ulcers in the mouth and/or gastro-intestinal tract caused by the cancer treatment. Participant B was a 12-year-old-boy, diagnosed with osteosarcoma, with post-operative nociceptive pain due to surgery and neuropathic pain due to post-operative complications. Participant C was a 13-year-old girl, diagnosed with neurofibromatosis and a peripheral malignant nerve sheath tumour in the thorax, with post-operative nociceptive pain due to a gastrostomy. Participant D was a 14-year-old girl, diagnosed with thrombocytopenia and a pain condition of unclear aetiology. Her pain had worsened over the last year and further intensified during the week before the study. Participation in the study was occasioned by inflammatory post-operative pain with possible neuropathic components. Participant E was an 18-year-old boy, diagnosed with osteosarcoma, with post-operative nociceptive pain due to surgery. Written informed consent for publication of case details was collected.

## Measures

### Studies I and II

Self-report assessments were carried out at pre, post and six and 12-month FU including measures of satisfaction with life, physical functioning, depression and anxiety, pain intensity and acceptance.

**Satisfaction with life**

Satisfaction with life was measured by the Satisfaction with Life Scale (SWLS)[86] which measures a general level of satisfaction. It consists of five statements, such as "If I could live my life over, I would change almost nothing", by which the respondents rate their agreement on a scale from 1 = "Strongly disagree" to 7 = "Strongly agree". A higher total score indicates a higher level of satisfaction. The SWLS correlates with other measures of subjective well-being and Cronbach's alpha has been shown to be $\alpha$=0.88.[87-89]

**Physical functioning**

Physical functioning was measured by five items from the Örebro Musculoskeletal Pain Questionnaire (ÖMPQ)[90,91] targeting the respondents' ability to carry out light work, walk for an hour, take care of household chores, shop for groceries and sleep. The items are rated on a scale from 0 = "Cannot do that at all due to pain" to 10 = "Can do that without pain problems" and a higher score indicates a higher level of functioning.

**Depression and anxiety**

Depression and anxiety were measured by the Hospital Anxiety and Depression Scale (HADS)[92] consisting of two subscales with seven items each. The depression subscale consists of statements such as "I can laugh and see the funny side of things" and "I feel as if I am slowed down". The anxiety subscale consists of statements such as "I feel tense or 'wound up'" and "I can sit at ease and feel relaxed". The HADS correlates with other measures of depression and anxiety, its factor structure has been supported and Cronbach's alpha has been shown to be $\alpha$=0.82 for the depression scale, $\alpha$=0.84 for the anxiety scale and $\alpha$=0.90 for the total scale.[93] Higher scores indicate higher levels of depression and anxiety.

**Pain intensity**

Pain intensity was measured by one item, "How much pain have you experienced in the last week?", from the ÖMPQ on a Numerical Rating Scale (NRS). The NRS is a numbered pain scale from 0 = "No pain at all" on the left side to 10 = "Unbearably lot of pain" on the right. Respondents rate their pain by choosing a score corresponding to their level of pain intensity. The NRS correlates with other pain measures and has been shown to be sensitive to change.[94,95] A higher score indicates a higher level of pain.

**Acceptance**

Acceptance was measured by the Chronic Pain Acceptance Questionnaire (CPAQ)[96] consisting of the subscales Activity Engagement (11 items) and Pain Willingness (nine items). The Activity Engagement subscale measures engagement in meaningful life activities in the presence of pain and includes

statements such as “When my pain increases, I can still take care of my responsibilities” and “It’s a relief to realize that I don’t have to change my pain to get on with my life”. The Pain Willingness subscale measures whether the respondent is willing to experience pain and to what extent he/she tries to avoid or control pain. It includes statements such as “I need to concentrate on getting rid of my pain” and “Keeping my pain level under control takes first priority whenever I’m doing something”. Respondents rate their agreement with the statements on a scale from 0 = “Never true” to 6 = “Always true”. Some items are reversed and a higher score indicates a higher level of acceptance. The CPAQ correlates negatively with measures of physical disability and psychological ill health and Cronbach’s alpha has been shown to be $\alpha$=0.78-0.82.[97]

## Studies III and IV

In Studies III and IV new scales for measuring acceptance in children with cancer experiencing pain, and their parents, were developed. Two measures for validation were used in each study.

### Background questions

Background questions in Studies III and IV included age, gender, diagnosis, possible date of end of treatment, current level of pain and discomfort, highest, lowest and average level of pain during the past week, average level of discomfort of pain during the past week and type of pain. Pain and discomfort was rated on an NRS scale, from 0 = “No pain/discomfort at all” to 10 = “Unbearably lot of pain/discomfort”.[95] Additionally, in Study III, information about the relationship with the child was also requested.

### Development of the Pain Flexibility Scale, for Children (PFS-C), and for Parents (PFS-P)

Three psychologists familiar with the concept of acceptance, both theoretically and clinically, were involved in the development of the PFS-C and the PFS-P. Firstly, a sketch of possible dimensions of acceptance was formed. Secondly, transferable items from the CPAQ[96] were re-formulated to correspond to the context of pain in children with cancer. Thirdly, new items were created in line with the sketch of dimensions. In Study IV the language was particularly adjusted to suit children. Fourthly, pre-tests were carried out. For the child scale no adjustments were called upon but for the parent scale some adjustments were made according to feedback from the pre-tests. The final test versions included 38 items for the child scale and 37 items for the parent scale.

**Measures used for validation**

In Study III, the Pain Catastrophizing Scale for Parents (PCS-P) and the Acceptance and Action Questionnaire (AAQ-II) were used as validation measures. In Study IV, the Pain Catastrophizing Scale for Children (PCS-C) and the Avoidance and Fusion Questionnaire for Youth (AFQ-Y) were used.

*The Pain Catastrophizing Scale for Parents (PCS-P)*

The PCS-P measures parents' catastrophizing thoughts about their children's pain.[98,99] It consists of 13 statements, such as "When my child has pain, I feel I can't stand it anymore" and "When my child has pain, I keep thinking about how badly I want the pain to stop", by which parents rate their agreement on a scale from 0 = "Not at all" to 4 = "Extremely much". A higher score indicates a higher level of catastrophizing thoughts. It correlates with measures of parental distress and child functioning and disability and Cronbach's alpha has been shown to be $\alpha$=0.93.

*The Acceptance and Action Questionnaire (AAQ-II)*

The AAQ-II measures level of experiential avoidance in general.[100,101] The short version of six items was used.[102] Respondents rate their agreement with statements such as "I'm afraid of my feelings" and "I worry about not being able to control my worries and feelings" on a scale from 0 = "Never true" to 6 = "Always true". Higher scores indicate higher levels of experiential avoidance. The AAQ-II correlates with other measures of mental health and Cronbach's alpha has been shown to be $\alpha$=0.78-0.88.

*The Pain Catastrophizing Scale for Children (PCS-C)*

The PCS-C measures catastrophizing thoughts in children with pain.[98,103] It consists of 13 items, such as "I become afraid that the pain will get worse" and "I keep thinking about how much it hurts", by which the children rate their agreement on a scale from 0 = "Not at all" to 4 = "All the time". Higher scores indicate higher levels of catastrophizing. The PCS-C correlates with measures of depressed mood and trait anxiety in children and Cronbach's alpha has been shown to be $\alpha$=0.87.

*The Avoidance and Fusion Questionnaire for Youth (AFQ-Y)*

The AFQ-Y measures general level of psychological inflexibility in youths,[104,105] where psychological inflexibility is conceptualised by experiential avoidance and fusion, i.e. the tendency to take thoughts literally. Respondents rate their agreement with eight statements, such as "My thoughts and feelings mess up my life" and "I am afraid of my feelings", on a scale from 0 = "Not at all true" to 4 = "Very true". The AFQ-Y correlates with anxiety, physical symptoms, problem behaviour and general quality of life. Cronbach's alpha has been shown to be $\alpha$=0.83.

## Study V

In Study V, assessments included five baseline measurements and one post measurement. Pain intensity and discomfort of pain were assessed. The Faces Pain Scale-Revised (FPS-R) and the Visual Analogue Scale (VAS) were used to assess both outcome variables. Feasibility was assessed with regards to treatment acceptability and implementation.[106] Treatment acceptability was assessed by calculating the proportion of children accepting to participate in the intervention and the children's reports of their experience of and intention to use the intervention in the future. Implementation was assessed by calculating the degree to which the children could complete the intervention. Additionally, prior to onset of the intervention, the children were asked about what they normally do to cope with pain.

**The Faces Pain Scale-Revised (FPS-R)**

The FPS-R is developed to measure pain in children.[107,108] The scale consists of six faces representing different levels of pain intensity, from "No pain" on the left hand side of the scale, to "Very much pain" on the right. The children are asked to rate which facial expression that corresponds to their level of pain. The FPS-R is recommended from four years of age.[109] It correlates with other pain measures[108] and inter-rater agreement between children's and nurses' ratings is high.[110]

**The Visual Analogue Scale (VAS)**

The VAS is a pain scale consisting of a 100 mm long horizontal line with the endpoints "No pain" on the left hand side and "Worst imaginable pain" on the right.[111] Respondents rate their level of pain intensity by making a mark on the line. The mark corresponds to a score, from 0 to 10, shown on the reverse side of the scale. The VAS is recommended from eight years of age.[109] It correlates with other pain measures and has been shown to be sensitive to change.[94]

# Interventions

## Studies I and II

Two interventions were delivered in Study I, Acceptance and Commitment Therapy (ACT) and Applied relaxation (AR), of which AR had formerly been evaluated for chronic pain[112,113] and served as an active treatment control intervention. The interventions were manual-based self-help treatments with an initial and a concluding 90-minute face-to-face session and weekly therapist support via telephone. The participants worked with assigned chapters of the treatment manual for seven weeks with scheduled weekly 30-minute telephone sessions. A detailed description of the content of each chapter of the

treatment manuals is provided in Table 1 in Paper I.[114] The participants also had the opportunity to e-mail their therapist as required throughout the treatment.

**The ACT intervention**

The initial face-to-face session of the ACT intervention included the mapping of the participant's pain strategies, identification of his/her values in life, a review of the impact of the different pain strategies on short- and long-term goals, a discussion about to what extent the participant was living in accordance with his/her values and finally, the introduction of the treatment manual *Living beyond your pain*.[115] During the self-help phase the participants worked through the treatment manual. The chapters covered perspective-taking on own thoughts and self-conceptions, mindfulness and acceptance strategies, identification of obstacles to living in accordance with one's values and the creation of a plan for committed action. During the telephone sessions, the topic of the previous week was discussed. The concluding face-to-face session of the treatment consisted of a discussion about the participant's values in life, the obstacles to living in accordance with these values and the action plan for engaging in meaningful life activities.

**The AR intervention**

The initial face-to-face session of the AR intervention included the mapping of challenging pain situations, a discussion about AR as both a coping and a preventive strategy, a practical introduction in the form of an exercise and the introduction of the treatment manual, a self-help version of the original AR manual.[116] During the self-help phase the participants worked through the treatment manual, which gradually increased in level of difficulty. The chapters covered differentiation between tension and relaxation, cue-controlled, i.e. self-instructed, relaxation, application of relaxation in different situations, fast relaxation and application of relaxation to everyday life activities (including difficult situations). The telephone sessions were focused on a discussion about how to practically apply the week's exercises. The concluding face-to-face session of the treatment consisted of a discussion about how to continue to practice and maintain the acquired skills and the creation of a maintenance programme.

## Study V

The intervention delivered in Study V was an approximately 15-minute long pain exposure exercise. The aim of the exercise was to teach the children to practice a non-reactive perspective on painful stimuli in order to cultivate psychological flexibility of pain. Firstly, the exercise consisted of instructions to practice attentive focus on the breathing, bodily sensations, thoughts and feelings. Secondly, the instructions included noticing the painful stimuli while

simultaneously maintaining an attentive focus on the breathing and on the painful stimuli themselves. Thirdly, a non-reactive perspective on pain was further cultivated by instructions to zoom in on the pain area, noticing the physical sensations of the pain stimuli, again while simultaneously maintaining an attentive focus.

## Data analyses

In Studies I-IV, the statistical analyses were carried out using SPSS,[117] from version 17.0 in Study I to version 24.0 in Study IV.

### Study I

Descriptive statistics were used to provide an overview of variable means. Preliminary analyses including *t*-tests and $\chi^2$-tests were performed to investigate differences between groups at pre-treatment. The Mixed Model Repeated Measures (MMRM) was used to evaluate the effect of the interventions.[118] An intent-to-treat (ITT) sample was used in the analysis including all participants who had started treatment. In MMRM, all data from all participants is calculated including the "missingness" of missing data.[119] A more detailed description of the MMRM analysis used in Study I can be found under "Statistical Methods" in Paper I.[114] Post hoc tests were performed to investigate the specific effects from the MMRM. Effect sizes were interpreted according to the guidelines by Cohen[120] where an effect size of $d = 0.2 – 0.49$ is considered a small effect, 0.5 – 0.79 a medium effect and ≥0.8 a large effect. The level of significance was set at standard, $p<.05$.

### Study II

Descriptive statistics were used to provide an overview of means and change scores and to explore correlations between variables. A bootstrapped cross product of coefficients approach was used to investigate the indirect effect of the intervention via acceptance on satisfaction with life and physical functioning.[121] A description of the cross product coefficients approach for investigating indirect effects and bootstrapping is provided under "Tests of indirect effects" in Paper II.[66] The analyses were performed with 10 000 samples, no imputation and bias-corrected confidence intervals (CIs) of 95 and 90%. Indirect effects with CIs not including "0" at CI=95 were interpreted conventionally as statistically significant and at CI=90 as a trend. Intervention was analysed as the independent variable with two levels: ACT and AR. Post-intervention assessment scores on acceptance, depression and anxiety were analysed as mediating variables. The latter two were included to assess the specificity of acceptance as a mediator. Change scores on satisfaction with life

and physical functioning were analysed as outcome variables. Two change scores were calculated: from pre-assessment to follow-up at six and 12 months. Indirect effects are reported as unstandardised units. Supplementary analyses were performed in two steps. Firstly, the indirect effect analyses were performed again including potential covariates. This is a way to investigate the indirect effect of treatment via the mediator on change in the outcome variables while at the same time controlling for other variables. Change in pain intensity from pre- to post-assessment and post-assessment scores in the outcome variable were used as covariates. Only changes in physical functioning were included as outcomes in the supplementary analyses given that no indirect effect of treatment was found for satisfaction with life. Secondly, Hierarchical Multiple Regression (HMR) analyses were carried out to investigate the specific effects of the two treatments and to provide information about the unique contribution of the predictor variables of the analyses.[122]

## Studies III and IV

In Studies III and IV, initial analyses of the test scales were performed. Internal consistency was calculated to assess the suitability to conduct factor analyses of the scales. Frequency distributions were examined to screen for invariability in responses to the separate items and the total scales. Inter-item and item-total correlations were inspected to identify items that did not correlate sufficiently with the others or the total scale. In Study III, ICC was calculated to assess dependence in data between pairs (i.e. parents of the same child).[123] A one-way random model was used assessing the single measures value.[124] An ICC of <0.40 indicates poor inter-rater agreement, 0.40 – 0.59 fair, 0.60 – 0.74 good and ≥0.75 excellent.[125] Preliminary factor analyses were carried out and eigenvalues, the scree plots and pattern matrices were evaluated to select the number of factors for final analyses. In addition to these parameters, in Study III, parallel analysis was performed using the Monte Carlo PCA program. Factor analyses were carried out using Principal Component Analysis (PCA).[122] Internal consistency was calculated for the total scales and the subscales. In Study III, test-retest reliability was calculated using Pearson for the total scale and Spearman's rho for the subscales. Convergent validity was assessed by correlations with other measures using Spearman's rho. In Study IV, test-retest reliability was calculated using ICC.[126] A two-way random effects model with absolute agreement was used assessing the single measures value.[127] Correlations with other measures to assess convergent validity was calculated using Pearson. Correlation coefficients were interpreted in accordance with the guidelines by Cohen[120], where $r = 0.10 – 0.29$ is considered a small, 0.30 – 0.49 a medium, and 0.5 – 1 a large correlation.[120]

## Study V

The primary analysis in Study V was visual inspection of the data. In addition, the two-standard-deviation-band (2-SD-band) method was used which shows the interval of plus/minus two standard deviations (SDs) from the mean of the baseline measurements.[128]

# Results

## Studies I and II

Mean scores from the four assessments on outcome measures in Studies I and II are presented in Table 3.

Table 3. *Mean scores (SD) on the outcome measures at the different assessments.*

| | M (SD) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Pre* (n=90)** | | **Post (n=56)** | | **6-month FU (n=53)** | | **12-month FU (n=32)** | | **Scale range** |
| | **ACT** | **AR** | **ACT** | **AR** | **ACT** | **AR** | **ACT** | **AR** | |
| Satisfaction with life | 17.0 (6.5) | 16.9 (6.8) | 21.5 (7.1) | 18.0 (7.1) | 18.9 (6.4) | 16.6 (7.2) | 21.1 (6.1) | 16.5 (8.4) | 0-35 |
| Physical function-ing | 5.3 (2.2) | 4.6 (2.2) | 6.2 (2.3) | 4.8 (2.5) | 6.3 (2.2) | 4.9 (2.7) | 6.3 (2.4) | 5.1 (3.3) | 0-10 |
| Acceptance of pain | 47.5 (16.9) | 47.0 (14.7) | 62.5 (18.7) | 51.8 (19.0) | 57.9 (19.6) | 53.4 (18.9) | 60.8 (15.2) | 50.5 (23.3) | 0-120 |
| Depression | 8.7 (4.5) | 9.0 (4.3) | 6.6 (4.6) | 7.3 (4.8) | 7.0 (4.8) | 8.0 (5.4) | 7.2 (5.3) | 7.5 (4.7) | 0-21 |
| Anxiety | 9.2 (4.6) | 8.1 (4.9) | 7.6 (4.6) | 7.4 (5.3) | 8.5 (4.6) | 7.2 (4.9) | 6.4 (3.4) | 7.5 (4.2) | 0-21 |
| Pain intensity | 7.9 (1.6) | 8.3 (1.7) | 7.2 (2.0) | 7.9 (2.1) | 7.6 (1.9) | 7.8 (2.0) | 7.0 (2.3) | 8.4 (2.2) | 0-10 |

*The numbers differ slightly between the studies, due to different N's.

### Study I

The results from the MMRM in Study I are presented in Table 4.

Table 4. *Results from the MMRM (n=90).*

| | **Treatment** | | | **Time** | | | **Treatment x Time** | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ***Df*** | ***F*** | ***p*** | ***Df*** | ***F*** | ***p*** | ***Df*** | ***F*** | ***p*** | ***d*** |
| Satisfaction with life | 1, 94 | 2.75 | 0.101 | 3, 145 | 4.19 | *0.007* | 3, 145 | 2.14 | 0.098 | 0.31 |
| Physical functioning | 1, 78 | 5.55 | *0.021* | 3, 44 | 0.99 | 0.407 | 3, 44 | 1.62 | 0.198 | 0.39 |
| Acceptance of pain | 1, 97 | 4.20 | *0.043* | 3, 95 | 9.85 | *0.001* | 3, 95 | 3.96 | *0.010* | 0.42 |
| Depression | 1, 95 | 0.63 | 0.428 | 3, 125 | 4.82 | *0.003* | 3, 125 | 1.11 | 0.347 | 0.22 |
| Anxiety | 1, 94 | 0.46 | 0.501 | 3, 101 | 8.00 | *0.001* | 3, 101 | 0.92 | 0.433 | 0.20 |
| Pain intensity | 1, 74 | 4.01 | *0.049* | 3, 45 | 2.00 | 0.127 | 3, 45 | 1.37 | 0.264 | 0.35 |

*P*-values in italics= statistically significant.

**Satisfaction with life**

The MMRM showed a significant effect of time and a trend towards an interaction effect between treatment condition and time on satisfaction with life. For the ACT group, there were significant improvements from pre-treatment to post-treatment [estimate=4.29, standard error (SE)=1.03, *t* (150.0)=4.17, *p*<0.005, 95% CI=2.25, 6.32, effect size=0.75, a medium effect], to 6-month FU [estimate=2.15, SE=1.03, *t* (149.95)=2.09, *p*=0.038, 95% CI=0.12, 4.18, effect size=0.38, a small effect], and to 12-month FU [estimate=3.10, SE=1.24, *t* (150.72)=2.51, *p*=0.013, 95% CI=0.66, 5.54, effect size=0.54, a medium effect]. There were no significant changes for the AR group.

**Physical functioning**

There was a significant effect of treatment condition on physical functioning. For the ACT group, there were significant improvements from pre-treatment to post-treatment [estimate=0.83, SE=0.32, *t* (60.41)=2.58, *p*=0.012, 95% CI=0.19, 1.47, effect size=0.46, a small effect] and to 6-month FU [estimate=0.67, SE=0.29, *t* (64.14)=2.27, *p*=0.026, 95% CI=0.08, 1.26, effect size=0.47, a small effect]. There were no significant changes for the AR group.

**Acceptance of pain**

There were significant effects of treatment condition, time and treatment by time on acceptance of pain. For the ACT group, there were significant improvements from pre-treatment to post-treatment [estimate=14.76, SE=2.44, *t* (121.50)=6.05, *p*<0.005, 95% CI=9.93, 19.59, effect size=1.10, a large effect], to 6-month FU [estimate=10.54, SE=2.83, *t* (102.56)=3.72, *p*<0.005, 95% CI=4.92, 16.16, effect size=0.65, a medium effect], and to 12-month FU [estimate=12.96, SE=3.61, *t* (50.05)=3.59, *p*=0.001, 95% CI=5.72, 20.20, effect size=0.74, a medium effect]. There were no significant changes for the AR group.

**Depression and anxiety**

There was a significant effect of time on depression. For the ACT group there were significant improvements from pre-treatment to post-treatment [estimate=-2.14, SE=0.61, *t* (104.37)=-3.52, *p*=0.001, 95% CI=-3.34, -0.93, effect size=-0.63, a medium effect], to 6-month FU [estimate=-1.39, SE=0.63, *t* (100.90)=-2.20, *p* =0.030, 95% CI=-2.65, -0.14, effect size=-0.40, a small effect], and to 12-month FU [estimate=-1.75, SE=0.83, *t* (80.17)=-2.11, *p*=0.038, 95% CI=-3.40, -0.95, effect size=-0.44, a small effect]. For the AR group, there was a significant improvement from pre-treatment to 12-month FU [estimate=-1.87, SE=0.89, *t* (77.62)=-2.11, *p*=0.038, 95% CI=-3.63, -0.10, effect size=-0.47, a small effect].

There was a significant effect of time on anxiety. For the ACT group, there were significant improvements from pre-treatment to post-treatment [estimate=-1.77, SE=0.52, *t* (110.75)=-3.43, *p* =0.001, 95% CI=-2.79, -0.74, effect size=-0.62, a medium effect] and to 12-month FU [estimate=-2.65, SE=0.75, *t* (54.94)=-3.56, *p*=0.001, 95% CI=-4.14, -1.16, effect size=-0.75, a medium effect]. For the AR group, there was a significant improvement from pre-treatment to 12-month FU [estimate=-1.99, SE=0.79, *t* (53.80)=-2.51, *p*=0.015, 95% CI=-3.58, -0.40, effect size=-0.56, a medium effect].

**Pain intensity**

There was a significant effect of treatment condition on pain intensity. For the ACT group, there were significant improvements from pre-treatment to post-treatment [estimate=-0.78, SE=0.38, *t* (61.11)=-2.05, *p*=0.045, 95% CI=-1.54, -0.02, effect size= -0.37, a small effect] and to 12-month FU [estimate=-1.09, SE=0.46, *t* (43.84)=-2.36, *p*=0.023, 95% CI=-2.03, -0.16, effect size=-0.47, a small effect]. There were no significant changes for the AR group.

## Study II

The results from the mediation analysis are presented in Table 5. No indirect effect of treatment via any of the mediators was found on satisfaction with life. For physical functioning, a statistically significant indirect effect of treatment via acceptance was found at the 6-month FU. A marginally significant indirect effect of treatment via acceptance was found at the 12-month FU. No indirect effects of treatment via anxiety or depression were found.

Table 5. *Results from the mediation analysis.*

| Outcome | Mediator | Indirect effect | Bootstrap results for indirect effects | |
|---|---|---|---|---|
| | | | 95% CI | 90% CI |
| **Satisfaction with life** | | | | |
| Pre to 6-month FU (n=43) | Acceptance | 0.33 | −0.582, 2.609 | −0.378, 2.175 |
| | Depression | 0.09 | −0.601, 0.512 | −0.409, 0.367 |
| | Anxiety | -0.00 | −0.601, 0.512 | −0.409, 0.367 |
| Pre to 12-month FU (n=27) | Acceptance | 0.89 | −1.421, 6.260 | −1.036, 5.228 |
| | Depression | 0.18 | −1.153, 3.644 | −0.859, 2.869 |
| | Anxiety | 0.05 | −1.327, 1.628 | −1.009, 1.229 |
| **Physical functioning** | | | | |
| Pre to 6-month FU (n=43) | Acceptance | 0.33 | *0.005, 1.021* | - |
| | Depression | 0.11 | −0.119, 0.519 | −0.068, 0.452 |
| | Anxiety | -0.03 | −0.376, 0.129 | −0.287, 0.085 |
| Pre to 12-month FU (n=27) | Acceptance | 0.68 | −0.005, 2.122 | *0.089, 1.827* |
| | Depression | 0.20 | −0.249, 1.704 | −0.142, 1.322 |
| | Anxiety | 0.18 | −0.199, 1.079 | −0.145, 0.888 |

The indirect effect is statistically significant at CI=95% and marginally significant at CI=90%, when the CI does not include 0.

**Supplementary analyses**

The results from the covariate mediation analysis are presented in Table 6. When controlling for pain intensity there was a marginally significant indirect effect of treatment via acceptance on physical functioning at the 6-month FU. The HMR analysis showed that acceptance explained an additional 17% of the variance in change at the 6-month FU for the ACT group ($\Delta F=4.21$, $p=0.05$). The indirect effect of treatment via acceptance on change at the 12-month FU was statistically significant, where the HMR analysis showed that acceptance explained an additional 26% of the variance for the ACT group ($\Delta F=3.58$, $p=0.09$).

When controlling for earlier change in physical functioning, there were marginally significant indirect effects of treatment via acceptance on change to both FUs. The HMR analysis showed that acceptance explained an additional 35% of the variance in change at the 12-month FU ($\Delta F=5.43$, $p=0.04$).

Table 6. *Results from the covariate mediation analysis.*

| Covariate | Outcome: Physical functioning | Indirect effect via acceptance | Bootstrap results for indirect effects controlling for covariates | |
|---|---|---|---|---|
| | | | 95% CI | 90% CI |
| Pain intensity | Pre to 6-month FU | 0.242 | −0.016, 0.959 | *0.008, 0.824* |
| | Pre to 12-month FU | 0.946 | *0.116, 2.579* | - |
| Physical functioning at post assessment | Pre to 6-month FU | 0.199 | −0.020, 0.773 | *0.003, 0.680* |
| | Pre to 12-month FU | 0.836 | −0.036, 2.771 | *0.091, 2.346* |

The indirect effect is statistically significant at CI=95% and marginally significant at CI=90%, when the CI does not include 0.

# Study III

The parents' reports of the children's level of pain and discomfort are shown in Table 7.

Table 7. *Parents' reports of the children's level of pain and discomfort.*

| | Measurement 1 (n=243) | | Measurement 2 (n=117) | |
|---|---|---|---|---|
| | M (SD) | Min-max | M (SD) | Min-max |
| Current pain | 1.30 (1.93) | 0-10 | 1.22 (1.78) | 0-10 |
| Current discomfort | 1.25 (1.85) | 0-9 | 1.26 (1.87) | 0-10 |
| Most pain last week | 2.29 (2.60) | 0-10 | 2.09 (2.59) | 0-10 |
| Least pain last week | 0.80 (1.55) | 0-10 | 0.68 (1.22) | 0-6 |
| Average pain last week | 1.43 (1.80) | 0-8 | 1.28 (1.64) | 0-7 |
| Average discomfort last week | 1.58 (2.05) | 0-10 | 1.50 (1.99) | 0-10 |

## Factor analysis

Frequency distributions showed limited variability for four items, which was, however, considered acceptable. Internal consistency of the test scale was good (α=0.87). Twelve items had corrected item-total correlations below 0.3 and were eliminated from further analysis. A presentation of these items is provided under "Factor analysis" in Paper III. The ICC was 0.195 indicating no dependence in data between pairs. Bartlett's test of sphericity was significant, the Kaiser-Meyer-Olkin (KMO) index was 0.91 and preliminary factor analyses showed no items consistently loading independently. PCA was performed on the remaining 25 items. Oblique rotation was used given indications of interdependence between factors. The preliminary factor analyses yielded four factors with eigenvalues above 1. The scree plot showed an ambiguous result, indicating one or three factors to retain. Parallel analysis indicated three factors and the component matrices two. Based on this information along with evaluation of the pattern matrices and the theoretical coherence between items a three-factor solution was chosen, with Promax rotation. Variance explained by this solution was 56%; 39% by the first, 10% by the second and 7% by the third factor. Two items, #5 and #25, had factors loading below 0.4. Item 5 also had low communality and was eliminated. Twenty-four items were included in the final solution. The theoretical analysis of the factors yielded the factor labels: 1) *Pain resistance*, 2) *Valued action* and 3) *Pain fusion*. The first factor, *Pain resistance*, is characterised by attempts to resist, avoid or control the feelings that having a child in pain infers and by a kind of reactivity to the child's pain in which the pain is experienced as a threat and something unbearable. The second factor, *Valued action*, is characterised by continuing to engage in daily life in the presence of pain and worry. The third factor, *Pain fusion*, is characterised by rule-governed verbal behaviour about pain, i.e. judgements and rules about pain itself and how it affects oneself and the child, and a literalisation (i.e. *fusion*) of this evaluative verbal behaviour. The scale was named the *Pain Flexibility Scale for Parents (PFS-P)*. The final factor solution is presented in Table 8. Scale range is 0-144 for the total scale; 0-54 for the *Pain resistance* subscale, 0–54 for the *Valued action* subscale and 0–36 for the *Pain fusion* subscale.

Table 8. *Factors, factor labels, items, factor loadings and communalities for the final factor solution (n=243).*

| Factor | Factor label | Item | | Factor loading | Communality |
|---|---|---|---|---|---|
| 1 | Pain resistance | 35 | I do things to flee from my worry over my child's pain. | 0.955 | 0.507 |
| | | 10 | I need to control my worry over my child's pain. | 0.671 | 0.605 |
| | | 7 | I need to focus on getting rid of the worry over my child's pain. | 0.634 | 0.532 |
| | | 17 | I have to struggle to do things when my child is in pain. | 0.623 | 0.533 |
| | | 15 | I am afraid of my child's pain. | 0.587 | 0.638 |
| | | 21 | My child's pain always feels like a threat to me. | 0.542 | 0.543 |
| | | 34 | If I try to feel what I really actually feel, it is more difficult. | 0.530 | 0.308 |
| | | 24 | Seeing my child in pain is too difficult for me. | 0.491 | 0.361 |
| | | 30 | I can't think about anything else when my child is in pain. | 0.387 | 0.592 |
| 2 | Valued action | 27 | I continue doing things even when I am worried about my child being in pain. | 0.829 | 0.668 |
| | | 14 | Even though it is difficult to see my child in pain I have learned that I can actually handle it. | 0.816 | 0.569 |
| | | 8 | There are many things I can do simultaneously while worrying over my child being in pain. | 0.804 | 0.601 |
| | | 29 | I feel that I can cope with my worry. | 0.755 | 0.721 |
| | | 2 | Even if it is difficult for me to see my child in pain I know that I can handle it. | 0.751 | 0.510 |
| | | 18 | I can focus on other things even while I am worried about my child being in pain. | 0.640 | 0.620 |
| | | 28 | When my child is experiencing pain, I can do nothing else. | 0.548 | 0.618 |
| | | 31 | I continue to do things that are important to me even while I am worried about my child being in pain. | 0.536 | 0.601 |
| | | 25 | My child's pain needs to pass before I can focus on anything else. | 0.373 | 0.643 |
| 3 | Pain fusion | 4 | Sometimes it feels ok for me when my child is in pain. | 0.740 | 0.464 |
| | | 3 | I refuse to allow my child to be in pain. | 0.716 | 0.450 |
| | | 13 | I am very affected by my child being in pain. | 0.688 | 0.650 |
| | | 6 | My child should never have to experience pain. | 0.644 | 0.466 |
| | | 9 | My child being in pain makes me worried. | 0.580 | 0.606 |
| | | 11 | Worrying over my child's pain is always difficult for me. | 0.454 | 0.535 |

## Reliability and validity

Means, standard deviations, score ranges, internal consistencies, test-retest correlations and coefficients for the correlations with the validation measures for the total scale and the subscales are presented in Table 9. All correlations were significant ($p$<0.01) and all correlation coefficients were large, except the correlation between the pain fusion subscale and the AAQ-II, which was medium. Controlling for change in level of pain did not affect the correlations.

Table 9. *Mean (SD), score range, internal consistency and correlation coefficients for the total scale and the subscales.*

| | M (SD) | Min-max | Cronbach's α | Correlations | | |
|---|---|---|---|---|---|---|
| | | | | Test-retest (*r/π*) | PCS-P (*π*) | AAQ-II (*π*) |
| PFS-P | 69.7 (24.8) | 10-122 | 0.93 | 0.87 | -0.84 | -0.63 |
| Pain resistance | 25.6 (11.0) | 0-54 | 0.86 | 0.82 | −0.78 | -0.64 |
| Valued action | 33.5 (10.3) | 1-54 | 0.89 | 0.80 | −0.65 | -0.56 |
| Pain fusion | 10.6 (7.2) | 0-29 | 0.81 | 0.76 | −0.69 | -0.40 |

PFS-P= the Pain Flexibility Scale for Parents, PCS-P= the Pain Catastrophizing Scale for Parents, AAQ-II= the Acceptance and Action Questionnaire – 2nd version.

# Study IV

The children's reports of level of pain and discomfort are shown in Table 10.

Table 10. *The children's reports of level of pain and discomfort.*

| | Measurement 1 (n=59) | | Measurement 2 (n=40) | |
|---|---|---|---|---|
| | M (SD) | Min-max | M (SD) | Min-max |
| Current pain | 1.1 (1.6) | 0-8 | 0.8 (1.1) | 0-5 |
| Current discomfort | 1.0 (1.7) | 0-7 | 0.6 (0.9) | 0-3 |
| Most pain last week | 2.5 (2.5) | 0-9 | 2.1 (2.4) | 0-10 |
| Least pain last week | 0.5 (1.3) | 0-7 | 0.3 (0.7) | 0-3 |
| Average pain last week | 1.4 (1.5) | 0-6 | 1.1 (1.5) | 0-7 |
| Average discomfort last week | 1.5 (2.0) | 0-8 | 1.2 (1.6) | 0-7 |

## Factor analysis

Frequency distributions showed that data on some items were skewed, which was, however, considered acceptable. Internal consistency of the test scale was acceptable (α=0.78). Initially, eleven items had corrected item-total correlations below 0 and were eliminated from further analysis. After the elimination of these eleven items, five items had corrected item-total correlations below 0.3 and were eliminated. After the elimination of these five items, the corrected item-total correlation for another item was reduced to below 0.3;

consequently this item was also eliminated. This further reduced the corrected item-total correlation for another item, which was also eliminated. Information regarding these deleted items is provided under "Factor analysis" in Paper IV. PCA was performed on the remaining 20 items. Bartlett's test of sphericity was significant, the Kaiser-Meyer-Olkin (KMO) index was 0.76 and preliminary factor analyses showed no items consistently loading independently. Interdependence between factors was indicated and oblique rotation was used. The preliminary factor analyses extracted six factors with eigenvalues above 1. The scree plot indicated two factors to retain. The component and the pattern matrices supported a two-factor solution, which was chosen. All items had factor loadings above 0.4, and communalities above 0.3, and were therefore kept. Hence, 20 items were included in the final solution. Promax rotation was used. Variance explained by the solution was 54%; 37% by the first and 17% by the second. The theoretical analysis of the factors generated the following factor labels: 1) *Valued action* and 2) *Pain resistance.* The first factor, *Valued action*, is characterised by continuing to engage in daily life in the presence of pain, and also by a non-evaluative perspective of pain in relation to one's ability to cope with it. The second factor, *Pain resistance*, is characterised by attempts to resist, avoid or control pain and the feelings that being in pain infers. It is also characterized by a kind of reactivity to pain where the pain is experienced as threatening and unbearable. The scale was named the *Pain Flexibility Scale for Children (PFS-C)*. The final factor solution is presented in Table 11. Scale range is 0-120 for the total scale; 0–54 for the *Valued action* subscale and 0–66 for the *Pain resistance* subscale.

Table 11. *Factors, factor labels items, factor loadings and communalities for the final solution (n=61).*

| Factor | Factor label | Item | | Factor loading | Communality |
|---|---|---|---|---|---|
| 1 | Valued action | 18 | I can focus on other things even while I am in pain. | 0.892 | 0.746 |
| | | 27 | I continue doing things even when I am in pain. | 0.871 | .758 |
| | | 31 | I continue to do things that are important to me even while I am in pain. | 0.843 | 0.674 |
| | | 28 | When I am in pain, I can do nothing else. | 0.806 | 0.703 |
| | | 8 | There are many things I can do simultaneously while being in pain. | 0.805 | 0.605 |
| | | 29 | I feel that I can cope with the pain. | 0.791 | 0.610 |
| | | 25 | The pain needs to pass before I can focus on anything else. | 0.674 | 0.696 |
| | | 38 | Being in pain is too difficult for me. | 0.471 | 0.397 |
| | | 30 | I can't think about anything else when I am in pain. | 0.455 | 0.508 |

| | | | | | |
|---|---|---|---|---|---|
| 2 | Pain resistance | 10 | I need to control my worry over the pain. | 0.759 | 0.526 |
| | | 9 | Being in pain makes me worried. | 0.731 | 0.496 |
| | | 7 | I need to focus on getting rid of the pain. | 0.722 | 0.483 |
| | | 16 | I avoid movements or situations that might increase the pain. | 0.677 | 0.455 |
| | | 13 | Being in pain affects me very much. | 0.656 | 0.635 |
| | | 21 | The pain always feels like a threat to me. | 0.649 | 0.460 |
| | | 15 | I am afraid of pain. | 0.647 | 0.478 |
| | | 11 | The pain is always scary. | 0.601 | 0.351 |
| | | 6 | Pain is always bad. | 0.587 | 0.389 |
| | | 5 | It's impossible to do anything when I am in pain. | 0.559 | 0.334 |
| | | 17 | I have to struggle to do things when I am in pain. | 0.443 | 0.408 |

## Reliability and validity

Means, standard deviations, score ranges, internal consistencies, test-retest correlations and coefficients for the correlations with the validation measures for the total scale and the subscales are presented in Table 12. The test-retest correlations showed good agreement for the total scale and fair agreement for the subscales. Controlling for change in level of pain had negligible effect on these correlations. The correlations with the PCS-C were large for the total scale and the Valued action subscale and medium for the Pain resistance subscale. Controlling for change in level of pain had no effect on the correlations with the total scale and the Valued action scale but a small effect for the Pain resistance subscale, for which the correlation changed from $r$=0.43 to $r$=0.41. The correlations with the AFQ-Y were medium for the total scale and the Pain resistance subscale and small for the Valued action subscale. Controlling for level of pain had no effect on the correlation with the Valued action subscale but a small effect for the total scale, which changed from $r$=-0.36 to $r$=-0.33, and the Pain resistance subscale, which changed from $r$=-0.32 to $r$=-0.28. Hence, for the Pain resistance subscale controlling for level of pain changed the correlation from medium to small. Regarding all other effects of change in level of pain, these did not change the interpretation of the strength of the correlation. All correlations were significant ($p$<.05).

Table 12. *Mean (SD), score range, internal consistency and correlation coefficients for the total scale and the subscales.*

| | M (SD) | Min-max | Cronbach's α | Correlations | | |
|---|---|---|---|---|---|---|
| | | | | Test-retest ($ICC_{2,1}$) | PCS-C *(r)* | AFQ-Y *(r)* |
| PFS-C | 66.4 (21.8) | 15-116 | 0.91 | 0.61 | -0.65 | -0.36 |
| Valued action | 33.4 (12.2) | 0-54 | 0.91 | 0.56 | -0.68 | -0.27 |
| Pain resistance | 32.8 (13.2) | 8-65 | 0.87 | 0.56 | -0.43 | -0.32 |

PFS-C= the Pain Flexibility Scale for Children, PCS-C= the Pain Catastrophizing Scale for Children, AFQ-Y= the Avoidance and Fusion Questionnaire for Youth.

# Study V

Pain intensity and discomfort ratings are presented for each participant, in Figures 1-5. The 2-SD interval is shown in each graph. The baselines varied from 25 minutes to 5 hours and 10 minutes.

## Participant A

For Participant A there was no variation in the data across baseline measurements and the standard deviation was therefore "0". Baseline measurements were taken at; 53, 35, 23, 10 and 0 minutes prior to intervention.

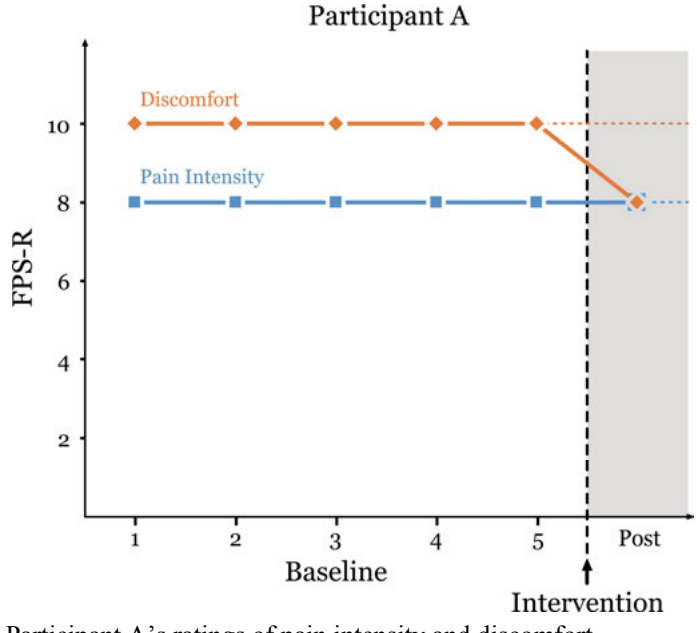


*Figure 1.* Participant A's ratings of pain intensity and discomfort.

## Participant B

For Participant B, baseline measurements were taken at; 25, 20, 15, 5 and 0 minutes prior to intervention.

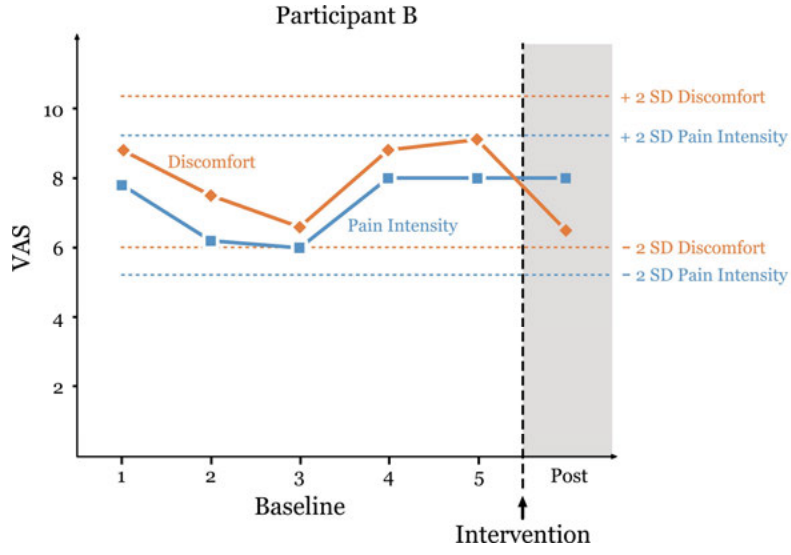


*Figure 2.* Participant B's ratings of pain intensity and discomfort.

## Participant C

For Participant C, baseline measurements were taken at; 50, 35, 20, 5 and 0 minutes prior to intervention.

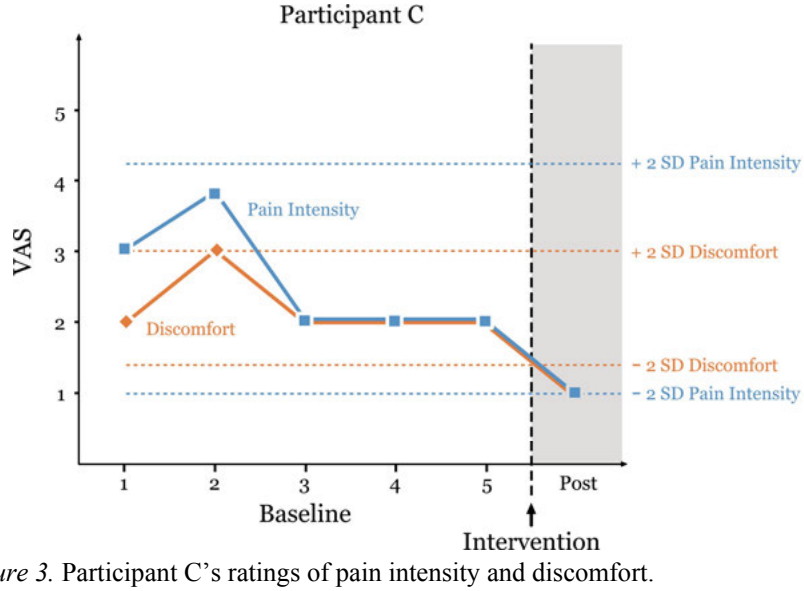


*Figure 3.* Participant C's ratings of pain intensity and discomfort.

## Participant D

For Participant D, baseline measurements were taken at; 25, 15, 10, 5 and 0 minutes prior to intervention.

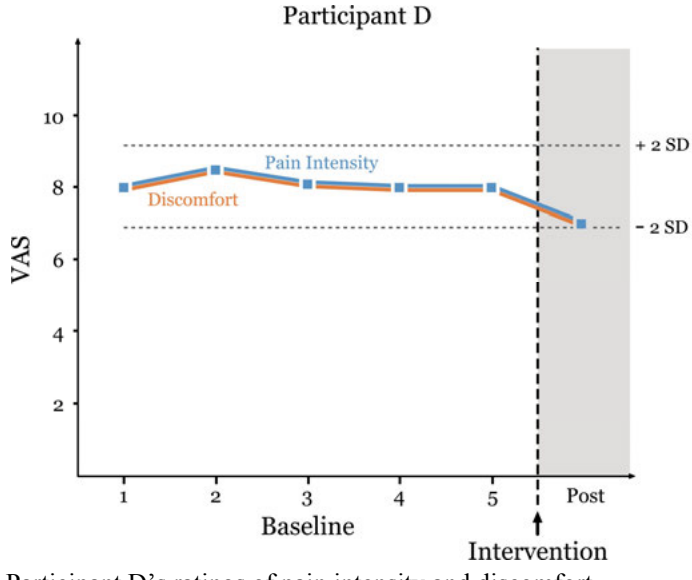


*Figure 4.* Participant D's ratings of pain intensity and discomfort.

## Participant E

For Participant E, baseline measurements were taken at; 5 hours 10 minutes, 2 hours 20 minutes, 1 hour 20 minutes, 5 minutes and 0 minutes prior to intervention. Shortly after the end of the intervention, Participant E coughed and vomited. Due to his very recent lung surgery this caused a quick recurrence of pain. He then expressed a wish to carry out the exercise once more. Due to these circumstances the design was expanded to ABAB with a non-concurrent baseline for Participant E. Post 3 was taken 5 minutes after Post 2.

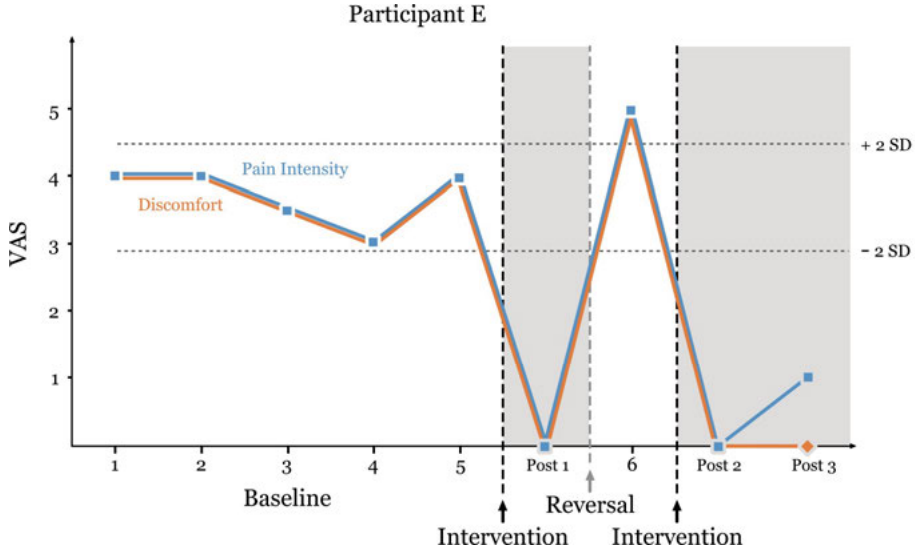


*Figure 5.* Participant E's ratings of pain intensity and discomfort.

# Discussion

## Main findings

The results show that the hypotheses of the studies were mainly supported.

As hypothesised in Study I, the ACT intervention was equally as effective as the AR intervention with regards to depression and anxiety. Regarding satisfaction with life there was a marginally significant interaction effect between time and treatment condition and regarding physical functioning there was an effect of treatment condition. The post hoc analyses showed that these effects were explained by improvements for the ACT group, which hence, shows that ACT was more effective than AR on these outcomes. Acceptance has been found to correlate with satisfaction with life and physical functioning[129-131] and the ACT group reported a higher level of acceptance, both with regards to activity engagement and pain willingness, at post and FU assessments. As hypothesised in Study II, acceptance was found to mediate the effect of treatment on physical functioning. However, no indirect effect of treatment was found for satisfaction with life. With regards to pain, the ACT group reported decreased pain intensity at post and 12-month FU. Pain reduction is not in focus in ACT, but has previously been reported following an ACT intervention.[132-134] Taken together, the results are theoretically consistent and in line with previous research, except for the lack of indirect effect of treatment via acceptance on satisfaction with life.

The main results of Studies III and IV were the factor solutions for the Pain Flexibility Scale for Children and for Parents respectively. A three-factor solution represented the data best for the parent scale, whereas a two-factor solution was found to best represent the data for the child scale. The term "psychological flexibility" was chosen, as the composition of the scales is more theoretically consistent with that concept as opposed to only "acceptance". Given the psychometric nature of these studies, the underlying hypotheses must be tested in other studies.

As hypothesised in Study V, the results indicate that an acceptance-based intervention for children experiencing pain during cancer treatment reduces discomfort of pain. Level of pain intensity was reduced for three of the five participants. Again, the main focus of an ACT intervention is not on pain reduction, although this has been reported in previous studies targeting chronic pain[132-134] and experimentally induced acute pain where increased pain tolerance was shown following acceptance and mindfulness tasks.[63] Furthermore,

the results show that an experiential pain exposure exercise was implementable for and found acceptable by the children/adolescents in the study.

For a more detailed discussion of the results of the studies, see each respective paper.

## Methodological considerations

The studies of this thesis used different designs and analytical methods, which can be seen as a strength in so much as it, by using different methods, broadens the knowledge base of acceptance for persons suffering from pain. The methodological considerations of the separate studies are discussed below.

### Studies I and II

Study I is an RCT and Study II a mediation study using data from Study I. Randomisation strengthens the external validity, i.e. the extent to which the results can be generalised to the population. Using control groups strengthens the internal validity, i.e. the probability that effects in outcomes are in fact due to the intervention and not to confounding factors. The aim of Study I is, however, somewhat problematic given that it is, in fact, two-folded. In the case of evaluating ACT for chronic pain, randomised controlled trials using treatment as usual as a control condition is optimal. In the case of evaluating a self-help format it could be argued that a comparison with a face-to-face format would have been preferable. Furthermore regarding the design of the studies, measurements were taken at pre and post intervention and at six and 12 months FU. With regards to Study II, this is a significant limitation. Continuous assessments throughout the treatment would have been preferable in order to assess the process of change in the variables, and in that way, to more thoroughly investigate the indirect effects of the treatments.

The sample of Study I represents persons with chronic pain who started treatment. Two hundred and two potential patients were offered participation, 87 of whom declined. It is hard to know whether these persons differed in any meaningful way from the persons who accepted to participate. Of the 115 participants who accepted, more participants allocated to AR dropped out after receiving information on treatment allocation. The two groups did not, however, differ on any of the demographic or outcome variables at pre-treatment assessment. Regarding power, the sample size was satisfactory at the start of Study I. Given the attrition, the power was decreased, which constitutes a significant problem in both Studies I and II. The attrition also limits the generalisability of the results of Study I. Given the fact that bibliotherapy is associated with high attrition rates[135] this should have been taken into consideration and compensated for by including more participants from the beginning. In mediation studies, the indirect effects of treatments are investigated and the results

should apply to persons who have undergone the specific treatment. It could be argued that the attrition, therefore, does not affect the generalisability of the findings in Study II.

Another important methodological consideration in Studies I and II is the issue of experimenter bias. This concerns the fact that the experimenter, in this case the therapists, subconsciously behaves differently towards participants of the intervention and the control group, which may affect the results of the study.[136] This would be of great concern for the internal validity of a study. The same therapists carried out the intervention for both the ACT and the TA group. The use of a double-blind procedure was not plausible. However, the fact that the therapists were trained in both ACT and TA, that TA was an evaluated treatment and shown to be effective for the population, hence increasing its credibility in the eyes of the therapists, that the intervention was primarily manualised and that the assessments were carried out via an online self-report survey system all contribute to reducing the risk of this threat.

## Studies III and IV

Studies III and IV are psychometric studies with a cross-sectional design. All children undergoing cancer treatment in Sweden at the time of study, and their parents, were offered participation. The study information specified that the studies were intended for children experiencing pain during cancer treatment, and their parents respectively. In that respect, it was hence, a prerequisite that the children who had not experienced any pain during their cancer trajectory, and their parents respectively, would not participate. The background questions did not, however, include information about whether the participant, or their child respectively, had experienced any pain during cancer treatment. This is a considerable limitation inferring the risk that children who had not experienced any pain, and their parents respectively, participated in the study. One's relationship to pain is indeed affected by the presence or absence of pain. Therefore, the inclusion of non-pain-responders would affect the generalisability of the results. The risk of including non-pain-responders is, however, considered small given the specification in the study information, the high prevalence of pain in the paediatric cancer population and the fact that the comments provided by the respondents revealed that the children had, in fact, experienced pain. Furthermore regarding the sample, it is, again, difficult to know whether the persons who accepted to participate differed from the ones who did not respond or declined, in any other meaningful way. With regards to age, the span in Study IV ranged from seven to 18 years, and younger children participated to the same extent as adolescents. With regards to the size of the samples, this was well above the required number of participants for Study III, but small for Study IV, particularly given the statistical method use, i.e. factor analysis. Further validation of test scales is always important. For the PFS-C it is, due to the small sample size of Study IV, essential.

### Study V

Study V had a single-subject AB design with a non-concurrent baseline. An ABAB design was not considered adequate since a reversal effect was considered improbable. Another way to improve internal validity is by using a multiple baseline. If effects are seen regardless of length of baseline, causality is strengthened.

Regarding measurements, several data points in the B-phase may be preferable since more data points give more reliable data. Given the nature of the intervention this was not applicable in the study. Furthermore, a C-phase with several assessments would have provided information about the process post intervention. Given the numerous medical and miscellaneous appointments that the children have daily, and the many confounding factors that these imply, this was not implemented due to practical difficulty and uncertainty about what information this data would yield.

The main analytical approach was visual inspection of the data, which traditionally has been the main analysis in single-subject research.[128] A more statistical approach was also applied, the 2-SD-band method. This method was not ideal considering its assumption of normal distribution in the baseline phase and the presumption of several data points in the B-phase. It was still considered that the method contributed to the interpretation of the data since it provides an indication of the likely data interval, had the intervention not been introduced. Other statistical methods for single-subject research are available today, such as the percentage of non-overlapping data (PND) method[137] and the non-overlap of all pairs (NAP) method[138], but they were not implementable due to too few data points post intervention.

Both boys and girls, and children from the age of seven to 18 years, participated. Furthermore, the participants reported both nociceptive and neuropathic pain. These circumstances would potentially strengthen the generalisability of the results. However, given the design of the study the results cannot be seen as generalisable but should be seen as tentative and warranting further investigation.

## Ethical considerations

All studies of this thesis have been approved by the Regional Ethical Review Board in Uppsala, Sweden [Dnr 2008/001; 2014/375; 2012/126].

Written informed consent was obtained in Studies I and II, by a parent for children under the age of 15 in Study IV, and in Study V. Consent was implied by participation in Study III and for adolescents from 15 years of age in Study IV.

The use of control groups occasions some ethical consideration. It may be considered unethical to withhold a treatment that may be beneficial from a

group of participants.[139] Wait list or active treatment-controls and informed consent are ways to solve this dilemma.[140]

The procedure of Studies III and IV also deserves some attention regarding ethics. Taking into consideration the presumably stressful situation that these children and their families go through, it may seem unethical to ask for their attention and time, given that there were no benefits from participation for them. The purpose of the study, to develop an instrument to measure acceptance in the context of acute pain in children with cancer, and in that way enabling the evaluation, and eventually the development, of interventions that may help the children, and their parents, to cope during these difficult circumstances, was considered to compensate for this inconvenience. As a symbolical compensation, and token of gratitude, the participants were included in a lottery of ten movie tickets per study.

# Conclusions and implications

Study I found support for the effectiveness of a manualised ACT-based self-help intervention with therapist support for persons with chronic pain. Since the study was published, ACT has gained strong research support for chronic pain.[72] Manualised self-help interventions add flexibility to the treatment repertoires for different populations and increase the availability of treatments. As such, the ACT intervention of Study I is an important addition. In order to evaluate the specific effect of a manualised self-help intervention it should, however, be evaluated in comparison to a face-to-face format.

Study II found support for acceptance as a mediator of ACT-treatment for change in physical functioning. This is an important addition to the knowledge base of acceptance of pain. Increasing knowledge of mediators and moderators of treatments for chronic pain enables development towards optimisation of treatments for this group. No indirect effect of treatment via acceptance was found for satisfaction with life. This is not in line with previous research, and is interpreted to be on account of too low power in the study. Acceptance is, as mentioned, one aspect of psychological flexibility. Other aspects deserve attention as well. For instance, self-as-context (or perspective-taking of the self), has recently been shown to improve functioning for persons with chronic pain.[85] Further investigation of the different aspects of psychological flexibility is warranted.

On the basis of Studies III and IV, psychometrically sound scales for measuring acceptance in children experiencing pain during cancer treatment, and their parents, are now available. This enables the evaluation of acceptance as a mechanism of change in the context of acute pain in children with cancer. This will hopefully contribute to the development of acceptance-based inter-

ventions, and optimisation of treatment for children and adolescents with cancer who experience pain. Further validation of the scales is important, and for the child scale, essential.

Study V found preliminary support for the feasibility of an acceptance-based intervention for children and adolescents experiencing acute pain during cancer treatment. Furthermore, pain intensity was reduced for three of the participants while discomfort of pain was reduced for all of the five participants. The results are highly tentative given the design (and number of participants) of the study. Yet, the results warrant further evaluation of acceptance-based interventions that have the potential of helping children with cancer experiencing pain and their parents to cope better during the challenges of cancer treatment.

## Future perspectives

Acceptance-based treatments have the potential of helping persons suffering from pain to cope. Investigating mediators of treatments provide a step forward in the efforts towards the optimisation of treatments for persons in pain. We need to continue with this work. Apart from investigating mediating effects of different mechanisms in our treatments we also need to explore and investigate moderators of treatments. This work is underway, and needs to proceed. There is, furthermore, endless knowledge about how our brains work that is yet to be unfolded. Increasing knowledge about the neurology of pain will help us to move forward towards finding better ways to help persons in pain.

We all need to join forces in this work.

# Acknowledgements

Research is indeed a challenging endeavour in many ways. But with the right people around you it can also be quite inspiring. When completing this thesis I have been supported by many people. Those I would like to thank in particular are:

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