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Effectiveness and cost-effectiveness of a guided and unguided internet-based Acceptance and Commitment Therapy for chronic pain: Study protocol for a three-armed randomised controlled trial.☆

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ABSTRACT

Background: Acceptance and Commitment Therapy (ACT) is an effective intervention for the treatment of chronic pain. Internet-based pain interventions might be an effective and cost-effective way to overcome treatment barriers of traditional face-to-face pain interventions such as the lack of availability and accessibility. However, little is known about the general (cost-)effectiveness of internet-based pain interventions and the specific (cost-) effectiveness of guided and unguided pain interventions. Therefore, the aim of this study is to investigate the effectiveness and cost-effectiveness of a guided and unguided ACT-based online intervention for persons with chronic pain (ACTonPain).

Methods: ACTonPain is a pragmatic three-armed randomised controlled trial comparing ACTonPain with or without therapist guidance against a waitlist control group. Both active conditions differ only with regard to guidance provided by an eCoach, who sends feedback after each module. This study aims to include 300 participants. Randomisation and allocation will be performed using permuted block randomisation with variable block sizes. The intervention contains seven ACT-based modules with interactive exercises, and audio and video clips. Furthermore, the participants have the opportunity to receive daily text messages. Online self-assessments will take place at pre- and post-treatment, as well as at 6 month follow-up. The primary outcome is pain interference. Secondary outcomes include physical and emotional functioning, pain intensity, ACT-related variables as well as health-related quality of life. Moreover, a cost-effectiveness analysis will be conducted from a societal perspective. Demographic and medical variables will be assessed on the basis of self-reports in order to detect potential moderators or mediators of the effects. The data will be analysed on an intention-to-treat basis and also using per-protocol analyses.

Discussion: This study will contribute to the evidence base of internet-based pain interventions and provide valuable information about the treatment success and cost-effectiveness regarding the intervention's level of guidance (self-help only vs. guided self-help). If ACTonPain is shown to be effective, investigations in different healthcare settings should follow, to examine possible ways of implementing ACTonPain into existing healthcare systems. The implementation of ACTonPain could help to shorten waiting times, expand access to pain treatment and, potentially, also reduce treatment costs.

☆ Trial registration: German Clinical Trial Registration (DRKS): DRKS00006183.

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1. Introduction

Chronic pain seriously affects quality of life, including physical, psychological and social functioning of the affected persons (Breivik et al., 2006; Gatchel et al., 2007). In addition, chronic pain is highly prevalent and a recent study indicated the prevalence of chronic pain in Germany to be 17% (Wolff et al., 2011); comparable to prevalence found in large scale international studies (Breivik et al., 2006; Gureje et al., 1998; IASP, 2005). Taking direct and indirect costs into account, chronic pain carries a high economic burden for societies around the world (Baumeister et al., 2012; Breivik et al., 2006; IASP, 2005; Phillips & Schopflocher, 2008; Turk, 2002).

A multidimensional and interdisciplinary treatment approach is an effective and cost-effective setting for the treatment of chronic pain (Sanders et al., 2005). Psychological interventions such as Cognitive-Behavioural Therapy (CBT) and Acceptance and Commitment Therapy (ACT) are core elements within such treatment plans (Kerns et al., 2011; Turk et al., 2011). In contrast to CBT, ACT focuses on the process and functions of emotions, thoughts or behaviour rather than on their form, frequency or appearance alone (McCracken & Vowles, 2014). According to the model of ACT, the therapeutic target is psychological flexibility, defined as "the ability to contact the present moment more fully as a conscious human being, and to change or persist in behavior when doing so serves valued ends" (Hayes et al., 2006). In order to develop psychological flexibility, the six interrelated core processes – cognitive defusion, acceptance, contact with the present moment, self-as-context, values and committed action – need to be facilitated (Hayes & Strosahl, 2004; Hayes et al., 2012; Vowles et al., 2014a). A considerable number of clinical trials highlight the potential of ACT for effectively treating chronic pain in different patient samples and clinical settings (McCracken et al., 2007; Thorsell et al., 2011; Veehof et al., 2011; Vowles et al., 2009, 2011, 2014b; Vowles & Thompson, 2011; Wetherell et al., 2011; Wicksell et al., 2009a, 2013). A meta-analysis of 22 acceptance-based interventions for chronic pain with controlled (waitlist or treatment as usual (TAU)) and non-controlled study-designs showed a small but significant effect size on pain intensity with a standardised mean difference (*SMD*) of 0.37 at post-treatment (Veehof et al., 2011). Accordingly, the effect size is comparable to those reported for CBT approaches (Eccleston et al., 2009; Hoffman et al., 2007; Morley et al., 1999), demonstrating ACT to be an alternative to CBT in the treatment of chronic pain (McCracken & Vowles, 2014; Wetherell et al., 2011).

Despite the potential of various treatments for chronic pain, many affected persons remain untreated or inadequately treated (Breivik et al., 2006; Shapiro et al., 2003). Internet-based interventions might be a feasible means through which to increase uptake rates of chronic pain-specific interventions and, thus, help to improve health care for persons with chronic pain (Bender et al., 2011; Bennett & Glasgow, 2009; Eccleston, 2011; Keogh, 2013; Long & Palermo, 2009; McGeary et al., 2012; Rosser et al., 2011; Williams, 2011). To date, there is a growing evidence base for the effectiveness of internet-based CBT interventions for the treatment of chronic pain, with a considerable number of different interventions trialled (Berman et al., 2009; Eccleston et al., 2014; Keogh et al., 2010; Macea et al., 2010; Velleman et al., 2010). Two recent meta-analyses on internet-based interventions for chronic pain reported overall combined effect sizes on pain at post-treatment compared to active control, waitlist or treatment as usual of $d = .29$ (Macea et al., 2010) and $SMD = .37$ (Eccleston et al., 2014), respectively.

Despite several promising efficacy and effectiveness studies, the evidence base of internet interventions for chronic pain remains limited, with an almost exclusive focus on CBT-based pain interventions (Eccleston et al., 2014; Macea et al., 2010). To the best of our knowledge, there are only two internet intervention trials based on ACT for chronic pain, and these studies show promising effects of ACT-based interventions on pain outcomes (e.g. pain interference: $d = .33$ when compared to an online expressive writing intervention (Trompetter et al., 2014) and $d = .56$ when compared to a discussion forum for chronic pain (Buhrman et al., 2013)). Yet, none of the trials of internet interventions for chronic pain went beyond the evaluation of efficacy to focus on potential effect-modifying or mediating covariates and their cost-effectiveness (Macea et al., 2010; Rini et al., 2012). The costs of internet interventions are, once developed, substantially linked with guidance time whereby participants are provided with some form of professional support, mostly in the form of personal feedback (Ebert et al., 2014). To date, internet interventions without guidance are often found to be less effective than internet interventions including at least some guidance (Baumeister et al., 2014b; Johansson & Andersson, 2012; Richards & Richardson, 2012). One recent meta-analysis examining unguided and guided versions of an internet intervention for varying mental disorders reported an average *SMD* of 0.27 (Baumeister et al., 2014b). This finding suggests that guidance has an adherence-facilitating effect, keeping users engaged in the internet intervention (Baumeister et al., 2014b). A growing body of evidence highlights further possibilities for enhancing users' adherence to interventions, such as automated prompts, videos, audios, interactive web-design and mobile features (Ritterband et al., 2009; Wangberg et al., 2008). So far, however, little is known about the general cost-effectiveness of internet interventions and, in particular, the cost-effectiveness of guided versus unguided interventions. Based on the extant research regarding internet interventions, an unguided intervention may produce clinically significant effects at a population level (Ebert et al., 2014), due to the possible higher accessibility of unguided interventions at potentially lower costs. On the other hand, unguided interventions show higher dropout rates than their guided counterparts and thus may still be less cost-effective due to the potentially increased costs associated with dropout, such as continuous absence from work and uptake of more treatments.

1.1. Aims

To examine the effectiveness and cost-effectiveness of both guided and unguided ACT-based internet interventions, we developed both guided and unguided versions of an online interactive ACT-based intervention for chronic pain (ACTonPain). Potential effect-modifying and -mediating covariates will also be investigated in order to gain a deeper understanding of the mechanisms underlying any effects found of ACTonPain. The specific aims of the study are:

1. To examine the effectiveness of guided and unguided ACTonPain compared to a waitlist control group (WLC).
2. To examine the comparative effectiveness of guided and unguided ACTonPain.
3. To examine the cost-effectiveness of guided and unguided ACTonPain compared to WLC.
4. To examine the comparative cost-effectiveness of guided and unguided ACTonPain.
5. To investigate which factors moderate and mediate the effects of guided and unguided ACTonPain.

We hypothesise that both guided and unguided ACTonPain will be more effective and cost-effective than a waitlist control group (WLC).

2. Methods

2.1. Study design

This study is a three-armed pragmatic RCT of parallel design with guided and unguided ACTonPain intervention groups, and a WLC (see CONSORT flow diagram, Fig. 1). Participants in all intervention arms will have full access to treatment as usual, with the exception of ongoing or planned psychological pain interventions within the upcoming three months. Thus, participants can receive treatment that will be monitored in order to control for potential confounding effects. The trial will be conducted and reported in accordance with the CONSORT 2010

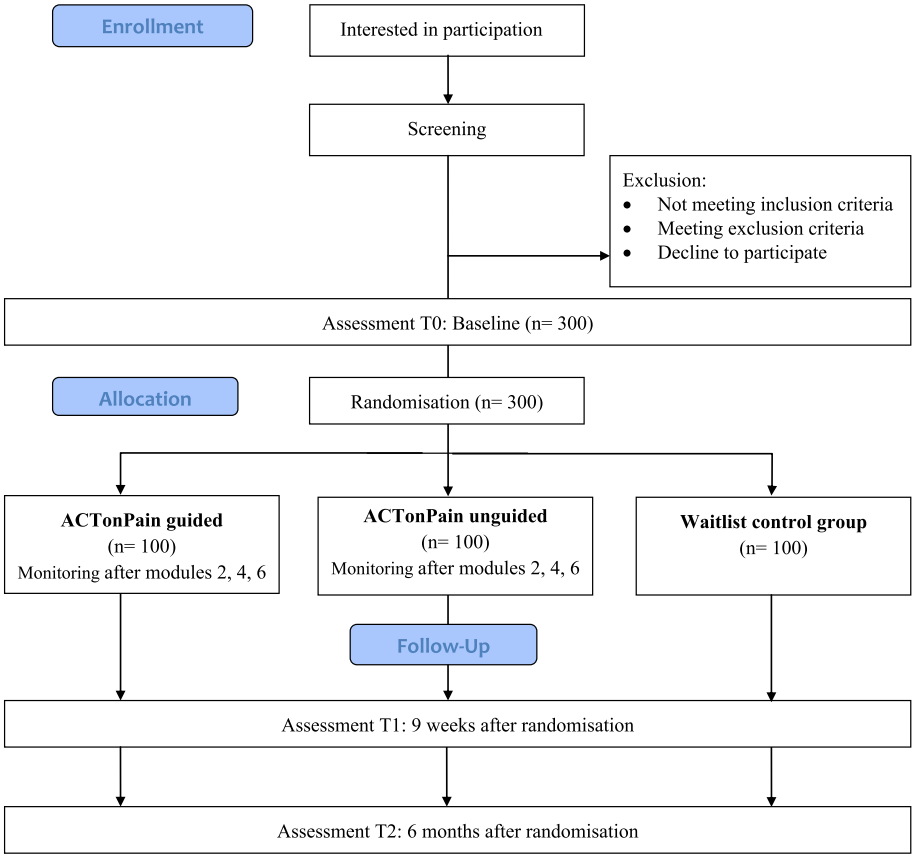

Fig. 1. Flow diagram.

Statement (Schulz et al., 2010), the CONSORT supplement for pragmatic trials (Zwarenstein et al., 2008) and the guidelines for executing and reporting internet intervention research (Proudfoot et al., 2011). Online assessments will be conducted at pre-treatment (T0) and post-treatment (nine weeks after randomisation, T1) as well as at six month follow-up (six months after randomisation, T2). Monitoring of the treatment process will take place at every second module.

All procedures are approved by the ethics committee at the Albert-Ludwigs-University of Freiburg. The trial is registered at the German Clinical Trial Register (DRKS): DRKS00006183.

2.2. Target/study population

As ACT has been shown to be effective for different samples of chronic pain patients (Vowles & Thompson, 2011), we expect ACTonPain to be suitable for the heterogeneous target population of adults with chronic pain. In order to define chronic pain, we follow the definition of the International Association of Pain (IASP), which defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey & Bogduk, 1994) and recommends six months of pain endurance as the threshold for chronic pain (Merskey & Bogduk, 1994). Inclusion criteria are 1) age ≥18 years, 2) chronic pain (duration ≥ 6 months) with 3) considerable intensity (= at least Grade II according to the Chronic Pain Grade questionnaire (CPG; Korff et al., 1992)), 4) being medically suitable for participation in an internet-based chronic pain intervention, 5) sufficient knowledge of the German language, 6) sufficient computer and internet literacy, and 7) having internet access. Exclusion criteria are 1) cancer-related pain, 2) ongoing or planned psychological pain intervention within the forthcoming three months and 3) elevated risk of suicide. Applicants for study participation with a PHQ-9 score ≥ 1 on item nine ("thoughts that you would be better off dead or of hurting yourself in some way?") will be assessed regarding their suicidal thoughts using the BDI-II suicide item (Kühner et al., 2007). In case of a score of 1 ("I have thoughts of killing myself, but I would not carry them out"), applicants will be contacted by email and asked for a non-suicidality statement. Applicants not providing the non-suicidality statement, in addition to those with a score ≥ 2 ("I would like to kill myself" or "I would kill myself if I had the chance"), will be excluded. Moreover, all applicants with an elevated risk of suicide (BDI-II Suicide Item ≥ 1) will receive an email with the urgent advice to seek help (along with relevant information on available services) from their general practitioner, the local psychiatric emergency unit or an official emergency number in case of present suicidality. This procedure will be repeated at all assessment points.

2.3. Procedure

Persons with chronic pain will be recruited through advertisements and at multidisciplinary pain clinics in Germany. Furthermore, we will request large-scale organisations for chronic pain to inform their members of the study via flyers, Facebook and on their websites. All advertisements will include a link to the open access website (https://geton-training.de), where detailed information about the study will be provided. Interested visitors may leave their email address on the website in order to receive an online information letter with detailed information regarding the study procedures. They will also be asked to provide a first and last name (which can be pseudonyms if desired) in order to receive an invitation to register with the website (on a secure web-based platform), where they can fill out the study inclusion form. Eligible participants will be asked to provide informed consent and to fill out the pre-treatment (T0) assessment. Afterwards, the participants will be randomly allocated to one of the three study conditions. After

allocation, participants will either be informed that they have been allocated to the WLC or they will receive access to ACTonPain (guided or unguided). Both interventions are provided on the same platform as the screening, online assessment and treatment process monitoring. After the follow-up (T2) assessment, the participants in the WLC will receive access to unguided ACTonPain. All data will be saved encrypted (AES 256-bit encryption).

2.4. Randomisation

Randomisation and allocation will be performed by an independent researcher not otherwise involved in the study using permuted block randomisation with variable block sizes of 6, 9 and 12 (randomly arranged) and an allocation ratio of 1:1:1. The randomisation list will be created using an automated, web-based randomisation programme (https://www.sealedenvelope.com/).

2.5. Sample size

The sample size for this study is optimised for the expected increased effectiveness of ACTonPain guided and unguided compared to WLC on the primary outcome (i.e. pain interference) at post-treatment. Furthermore, we expect the effect size for ACTonPain guided compared to WLC to be higher than for ACTonPain unguided compared to WLC (Buhrman et al., 2013; Trompetter et al., 2014). In the two internet intervention trials based on an ACT intervention for chronic pain, effect sizes of $d = .33$ (Trompetter et al., 2014) and $d = .56$ (Buhrman et al., 2013) were reported for pain interference. ACTonPain is developed with features designed to facilitate adherence and effectiveness of internet interventions (e.g. video, audio, automated prompts, text message support, and interactive web-design). Thus, we regard an average effect size of $d = 0.40$ as threshold for clinical significance for ACTonPain unguided in comparison to WLC. Accordingly, a sample size of 100 participants in each of the groups is required to detect a statistically significant difference at a power of 80% and a significance level of $p = 0.05$ (two-tailed t-test, calculated using G*Power). With regard to the comparison between unguided and guided ACTonPain, the sample size is sufficient to detect the reported average *SMD* of 0.27 (Baumeister et al., 2014b) with a power of 60% and a significance level of $p = 0.05$ (one-tailed).

2.6. Intervention development

The intervention builds on a prior ACT intervention developed by Buhrman et al. (2013) that has been shown, in a Swedish sample, to be effective for different outcomes such as pain acceptance and pain interference. We translated this intervention into German language and incorporated features to maximise the effects of ACTonPain. Consistent with the intervention by Buhrman et al. (2013), all modules consist of information, assignments, relevant metaphors and mindfulness exercises. However, contrasting the intervention by Buhrman et al. (2013) our platform – run by Minddistrict.com – provides the intervention materials as integral parts of each module, thus allowing participants to do the exercises on the spot. An integrated read-aloud function allows the participants to follow the audio-narration of each module. Furthermore, we structured the text in shorter paragraphs or tables and added illustrations, pictures and videos in order to enhance the participants' engagement, motivation and active behaviour, and to reduce study attrition. Another point of departure pertains to introducing three vignettes that are typical examples of persons with chronic pain. These vignettes are used to illustrate the information and assignments and to accompany the participants throughout the modules to enable observational learning. All changes were incorporated based on the ACT literature (Hayes & Strosahl, 2004; Strosahl et al., 2014; Wengenroth, 2012) or ACT in the treatment of chronic pain (Dahl, 2005; Vowles & Sorrell, Unpublished Therapist Guide and Patient Workbook). Considering the recommendations on adherence- and efficacy-enhancing elements of internet interventions (Andersson et al., 2009; Brouwer et al., 2011; Ritterband et al., 2009), we used a responsive web design to integrate interactive features, such as quizzes or options to read more about certain topics. Expert feedback and think-aloud interviews with three persons with chronic pain have been conducted to further improve the feasibility and acceptability of the intervention.

2.7. Intervention content

The intervention's content is structured following the procedure-recommendations by Hayes et al. (1999). The first module aims at "creative hopelessness". Participants receive information about acute and chronic pain via text and video. With the help of examples, participants identify their former strategies to manage pain in order to highlight the short- and long-term effects of these strategies. Furthermore, the concept of mindfulness is introduced and the participants schedule their strategies to manage pain as well as their mindfulness exercises for the upcoming days. A video in module two explains why acceptance can be an alternative to control and how it can be achieved. The concept of primary and secondary suffering is introduced and the participants can reflect on this concept in their everyday life. Defusion is the focus of module three. Participants learn how to take distance to negative thoughts, with a video, and formulate goals. The content of module four pertains to the self as context. In a video, participants learn about self-concept and how it can be viewed from a broader perspective. In addition, values are introduced, and these are further discussed in module five. In module six, participants work on willingness exercises in accordance with their values in life. In the last module, the participants can report their own experiences with the intervention and the goals that they set in module three. Furthermore, participants identify new goals and strategies for living a valued life in the future. For a more detailed overview of the modules and their content, see Table 1. All participants are advised to work on one module per week. Each module takes approximately 60 min to complete, depending on the time participants require for the assignment. After the first half of the module, the programme will encourage participants to take a break if needed.

2.8. SMS coach

ACTonPain provides participants with optional supportive text messages. The messages are automatically sent and are designed to support the participants' efforts to integrate the techniques that they have learned during the programme into everyday life. The contents of the messages include a) reminders to complete the mindfulness exercises and weekly assignments, b) repetition of the modules' content, and c) motivation enhancement. Participants can choose between an intensive (two SMSs a day) and a light (one SMS every second day) version. Such SMS prompts have been shown to be very beneficial in internet interventions (Brouwer et al., 2011; Childs et al., 2011; Fry & Neff, 2009; Heber et al., 2013; Nobis et al., 2013; Ritterband et al., 2009; Webb et al., 2010).

2.9. Administrative and technical support

In order for the study and the intervention to be carried out, participants in both ACTonPain groups will receive administrative and technical support in the use of the intervention (e.g. forgot the password, cannot play videos or audios). The administrative support includes answering questions via mail regarding participation in the study and reminding the participants to complete the informed consent or assessments. Given the likelihood of dropout from the post-treatment and follow-up assessments, especially in the unguided ACTonPain group, participants will be contacted by phone after having first received two letters reminding them to complete the assessments.

Table 1
Overview of the intervention's content.
Modified from Buhrman et al. (2013).

Module	Information	Audio files	Assignments
1	Information about the programme and acute and chronic pain (video) and its life consequences. Introduction to mindfulness.	• Mindfulness 1: Awareness of breathing • Metaphor (creative hopelessness): "The man in the hole"	Practice and register mindfulness. Participants are asked to write down everything they have done to reduce/manage their pain and record their behaviours and sensations during increased pain situations (functional analysis) for a week.
2	Information about control and acceptance (video). Introduction to primary and secondary suffering, short- and long-term consequences.	• Mindfulness 2: Body scan • Metaphors (control and acceptance): "The shark trap" and "The radio"	To practice and register mindfulness. To register primary and secondary pain (to distinguish physiological and psychological consequences of pain) for a week. An acceptance record is introduced.
3	Information about thoughts and emotions (video) and goal setting.	• Mindfulness 3: Sitting meditation • Metaphor (defusion): "The bus"	To practice and register mindfulness. Different defusion exercises. To formulate goals.
4	Information about self as context (video). To live a good life despite pain.	• Mindfulness 4: Sitting meditation • Observing thoughts metaphor (distinction between self and psychological content): "The chess board" exercises "self as context".	To practice and register mindfulness. Values assessment. Self as context exercises.
5	Information about values (video) and committed action.	• Mindfulness 5: Sitting meditation-observing feelings • Metaphors (values): "The farewell party"	To practice and register mindfulness. Values compass.
6	Information about willingness, committed action (video) and living according to ones values.	• Mindfulness 6: Mindfulness in daily life. • Metaphor (committed action): "My party"	To practice and register mindfulness. Different willingness exercises.
7	Summary of the programme and information about maintenance.	• Mindfulness 7: mindfulness in daily life • Metaphor (values) "The skier"	Maintenance plan. Evaluation of goals.

2.10. Guidance

Guidance is provided in the guided version of ACTonPain by trained eCoaches (psychologists) throughout the programme. The eCoaches will be trained and supervised weekly by a clinical psychologist (HB). A small picture of the eCoach is provided, making it clear to participants who is responsible for their support. The main task of the eCoaches is to provide feedback by regarding the completed modules in order to increase participants' motivation and adherence (Andersson et al., 2009; Brouwer et al., 2011; Mohr et al., 2011; Paxling et al., 2013; Ritterband

Table 2
Key variables and measurements.

Variables	Measurement	Screening	T0	Monitoring[1]	T1	T2
Inclusion and exclusion criteria						
Chronic pain	SR	X				
Chronic pain stage	CPG	X				
Ongoing or planned psychological pain intervention within the forthcoming three months	SR	X				
Medically suitable	SR	X				
Cancer related pain	SR	X				
Suicidality	PHQ-9 and BDI-II suicide item	X	X		X	X
Further inclusion criteria (≥18 years of age, sufficient knowledge of the German language, sufficient computer and internet literacy as well as internet access)	SR	X				
Primary outcome						
Pain interference	Interference Scale of MPI		X		X	X
Secondary outcomes						
Physical functioning	BPI		X		X	X
Emotional functioning	PHQ-9 & GAD-7		X		X	X
Pain intensity	NRS		X		X	X
Participants' rating of overall improvement	PGIC				X	X
Health related quality of life	EQ-5D, AQoL 8D & SF-12		X		X	X
ACT-related variables						
Chronic pain acceptance	CPAQ		X	X	X	X
Psychological flexibility	FAH-II		X	X	X	X
Intervention costs	TiC-P		X		X	X
Covariates						
Demographic variables (sex, age, education, social support)	SR	X				
Prior pain treatment, pain type, duration, course and chronicity	SR	X				
Comorbidities	SR	X				
Participants' evaluation of the intervention[1]						
Participant adherence	Attrition rate				X	X
Participant satisfaction	CSQ-8				X	X

1: ACTonPain groups only; ACTonPain: Acceptance and Commitment Therapy based online intervention for chronic pain; AQoL = Assessment of Quality of Life; BDI-II = Beck Depression Inventory II; BPI = Brief Pain Inventory; CPAQ = Chronic Pain Acceptance Questionnaire; CPG = Chronic Pain Grade; CSQ-8 = Client Satisfaction Questionnaire; FAH-II = Fragebogen zu Akzeptanz und Handeln II, German version of the Acceptance and Action Questionnaire – II; GAD-7 = Generalised Anxiety Disorder Screener; IG = intervention group; MPI = Multidimensional Pain Inventory; NRS = Numerical Rating Scale; PGIC = Patient Global Impression of Change scale; PHQ-9 = Patient Health Questionnaire-9; SF-12 = Short Form 12-item survey; SR = self-report assessment; PSEQ = Pain Self-Efficacy Questionnaire; TiC-P = Trimbos/iMTA questionnaire for costs associated with psychiatric illness.

et al., 2009; Webb et al., 2010). The eCoaches send weekly standardised feedback that is specific to the participants' assignments via email within two work days of module completion. Feedback includes: positive reinforcement that integrates the assignments of the participants, and encouraging the participant to continue working with the programme. The eCoaches will spend approximately 2 h in total per participant. Furthermore, participants and eCoaches can contact each other any time. The eCoaches will be supervised by experienced clinical psychologists (HB, ML). If a participant does not complete a module within one week, the eCoach will send a reminder email to complete the module within the next two days. After this deadline, the participant's access to the intervention will be deactivated, however, access can be reactivated again upon request.

2.11. Outcome measures

For the selection of the primary and secondary outcomes, we considered the recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT; Dworkin et al., 2005; Dworkin et al., 2008). In addition, we will assess ACT-related variables, health-related quality of life, intervention costs as well as the participants' satisfaction with the intervention as secondary outcomes. Demographic and medical variables will be examined as potential moderating or mediating variables. For an overview of all variables and measurements, see Table 2. All assessments will be conducted via online self-report; with online administration of assessments likely to yield equivalent psychometrics as their paper-and-pencil counterparts (Buchanan, 2003).

2.11.1. Primary outcome

2.11.1.1. Pain interference. The Interference Scale of the Multidimensional Pain Inventory (MPI; Flor et al., 1990; Kerns et al., 1985) measures the degree of pain interference with regard to all-day activities (Kerns et al., 1985). The Interference Scale of the German version of the MPI consists of 10 questions. The participants will have to respond on a 7-point scale ranging from 0 = "no interference/change" to 6 = "extreme interference/change". The internal consistency is $\alpha = 0.94$ with a test–retest coefficient of $r = 0.78$.

2.11.2. Secondary outcomes

2.11.2.1. Physical functioning. Following the IMMPACT recommendations (Dworkin et al., 2005, 2008), the interference items of the Brief Pain Inventory (BPI; Radbruch et al., 1999) will be used to assess physical functioning in addition to the MPI Interference Scale. In contrast to the MPI-D, the 7 BPI interference items assess pain interference in relation to sleep, mood, social relations, and enjoyment of life (Keller et al., 2004). On an 11-point scale (0 = "does not interfere", 10 = "completely interferes"), participants will indicate how much pain has interfered "in the past 24 h" with different functional aspects (Keller et al., 2004). Both questionnaires (BPI and MPI Interference Scale) are reliable ($\alpha = 0.88$) and valid measures of the interference of pain with physical functioning (Flor et al., 1990; Keller et al., 2004).

2.11.2.2. Emotional functioning. According to the IMMPACT recommendations, depression and anxiety belong to the most important dimensions of emotional functioning in participants with chronic pain (Dworkin et al., 2005). Thus, we will assess emotional functioning with the Patient Health Questionnaire (PHQ-9; Kroenke & Spitzer, 2002) and the Generalised Anxiety Disorder Screener (GAD-7; Löwe et al., 2008). Although the PHQ-9 is shorter than most other measures for the assessment of depressive symptoms (e.g. the Beck Depression Inventory with 21 items (Beck et al., 1961)), it shows comparable sensitivity and specificity to many other depression inventories (Kroenke, Spitzer & Williams, 2001) and excellent internal consistency ($\alpha = 0.89$) (Kroenke et al., 2001). In the PHQ-9, each of the 9 DSM-V criteria can be scored from 0 = "not at all" to 3 = "nearly every day". The sum-score ranges from 0 to 27 and the cut-off points of 5, 10, 15, and 20 represent the thresholds for mild, moderate, moderately severe, and severe depression, respectively (Kroenke & Spitzer, 2002; Kroenke et al., 2001). The 7-item Generalised Anxiety Disorder Screener (GAD-7) describes the most prominent diagnostic features of the DSM-V diagnostic criteria A, B, and C for generalised anxiety disorder with a high internal consistency ($\alpha = 0.89$) (Löwe et al., 2008). The 7 core symptoms of GAD can be scored from 0 = "not at all" to 3 = "more than half the days" during the last 2 weeks. Therefore, GAD-7 scores range from 0 to 21 and the cut-off points of 5, 10 and 15 represent the thresholds for mild, moderate and severe anxiety symptom levels, respectively (Löwe et al., 2008).

2.11.2.3. Pain intensity. Pain intensity will be assessed on an 11-point Numerical Rating Scale (NRS). The participants will evaluate their worst, least and average pain during the last week from 0 to 10, with 0 = "no pain" and 10 = "pain as bad as you can imagine". The mean of the three scales will be calculated. On average, a reduction of approximately two points, or a reduction of approximately 30%, in the NRS represents a clinically important difference.

2.11.2.4. Persons' rating of overall improvement. Following the IMMPACT recommendations, the Patient Global Impression of Change scale (PGIC; Guy, 1976) will be used to measure the participants' global improvement with treatment. On a 7-point scale that ranges from "very much improved" to "very much worse", with "no change" as the mid-point, participants rate their improvement with treatment during a clinical trial (Richardson et al., 2012). Furthermore, participants will be asked via open ended questions about potential negative effects as an aspect that has been less focused in previous studies of internet interventions (Rozental et al., 2014).

2.11.2.5. Health related quality of life. To assess health-related quality of life, we will use the Short Form 12 (SF-12; Luo et al., 2003), the EuroQol (EQ-5D; Rabin & Charro, 2001) and the Assessment of Quality of Life (AQoL; Hawthorne et al., 1999). The SF-12 is divided into physical and mental health and covers eight health domains: physical functioning, role limitations, pain, general health perception, vitality, mental health, emotional role and social functioning (Luo et al., 2003). In addition, we will use the EQ-5D as a widely applied, valid and reliable measure of quality of life, with five items related to mobility, self-care, common activities, pain/discomfort, and anxiety/depression, as well as a visual analogue scale concerning health state (Rabin & Charro, 2001). For sensitivity analyses, we will use the AQoL-8D, an instrument that is sensitive to health states, especially in regard to the following psychosocial dimensions (Hawthorne et al., 1999): Independent Living, Happiness, Mental Health, Coping, Relationships, Self-Worth, Pain, Senses.

2.11.2.6. ACT-related variables. To assess psychological flexibility as the core target of ACT, the Acceptance and Action Questionnaire — II (AAQ-II; Bond et al., 2011), German version: Fragebogen zu Akzeptanz und Handeln II (FAH-II; Hoyer & Gloster, 2013) will be used. This questionnaire consists of 7 items and shows good to excellent psychometric properties in a German sample (Hoyer & Gloster, 2013). On a 7-point scale that ranges from 0 = "never true" to "always true", participants rate processes of experiential avoidance and psychological inflexibility.

Moreover, we will use the Chronic Pain Acceptance Questionnaire (German version: CPAQ-D; Nilges et al., 2008). On a 7-point scale that ranges from 0 = "never true" to "always true", participants rate their activity engagement and pain willingness on 20 items. This is a well validated measure (Wicksell et al., 2009b).

2.11.2.7. Treatment process. In order to investigate treatment processes that are postulated in ACT-theory that contribute to the treatment outcomes, we will use the FAH-II and the CPAQ-D.

2.11.2.8. Cost measures. The economic evaluation, from a societal perspective, will consider all direct and indirect costs and will be assessed with the Trimbos/iMTA questionnaire for costs associated with psychiatric illness (TiC-P; Hakkaart-van et al., 2002), adapted to the context of costs associated with chronic pain. The TiC-P is an internationally established instrument for the assessment of mental health related direct and indirect costs. With this questionnaire, participants register direct costs (e.g. health service uptake or medication). Indirect costs, such as the number of 'work loss' days (absenteeism from work) or the number of 'work cut-back' days (reduced productivity at work) can be recorded.

2.11.2.9. Covariates. As potential moderating or mediating variables, demographic variables (sex, age, education and social support), prior pain treatments, pain characteristic (type, duration, course or cause, based on the German Pain Questionnaire; Deutscher Schmerz-Fragebogen, AG der Deutschen Gesellschaft zum Studium des Schmerzes) and comorbidities will be assessed by participants' self-report.

2.11.2.10. Participants' evaluation of the intervention (active groups only). The participants' intervention adherence will be estimated based on the attrition rate (i.e. percentage of participants who no longer log into the intervention). The participants' satisfaction with the internet-based intervention will be measured with the Client Satisfaction Questionnaire (CSQ-8; Attkisson & Zwick, 1982) in German (Fragebogen zur Patientenzufriedenheit; ZUF-8; Schmidt et al., 1989, adapted to the online intervention context).

2.12. Statistical analyses

In all analyses, missing data will be imputed using multiple imputations. All data will be analysed on an intention-to-treat basis. Additionally, per-protocol analyses for participants who have completed at least five of the seven modules and all assessments will be carried out in order to estimate the impact of intervention adherence on study results. In the analyses, we will not adjust for multiple testing.

2.12.1. Clinical analysis

We will perform a repeated measures MANCOVA to compare the three groups with time as the repeated dimension, and the primary and secondary outcome measures as dependent variables. In this model, control variables will be the pre-test scores of the dependent variables, and treatment condition, age and sex will be included as fixed effects. Treatment process variables will be analysed in a repeated-measures MANCOVA by controlling for the pre-test scores and will be explored using multilevel modelling procedures. Cohen's *d* and a 95% confidence interval will be calculated to measure the between-group effect size at post-treatment and follow-up. Additionally, clinical significance analyses, such as number needed to treat (NNT) will be conducted.

2.12.2. Moderator and mediator analyses

Moderator and mediator analyses will be conducted including potential moderators and mediators as interactions with treatment condition and as independent variables in the main effect analyses. Potential moderators and mediators include the abovementioned covariates and will be analysed in explorative analyses.

2.12.3. Economic analyses

The intervention's cost-effectiveness will be assessed from a societal perspective and will include direct and indirect costs and outcomes. The incremental cost-effectiveness ratio (ICER) for the comparators 1) ACTonPain guided vs. WLC, 2) ACTonPain unguided vs. WLC and 3) ACTonPain guided vs. ACTonPain unguided will be estimated based on the pre-post, as well as the pre-follow-up, differences in costs and effects of the condition. A cost-effectiveness acceptability curve will also be calculated. To estimate the cost-utility of the intervention, quality adjusted life years (QALYs) will be calculated. Furthermore, we will use bootstrapping to quantify the uncertainty around the ICER that will be shown on the cost-effectiveness plane and as a cost-effectiveness acceptability curve.

3. Discussion

In this study protocol, we describe the study design of a randomised controlled trial that evaluates the effectiveness and cost-effectiveness of ACTonPain, an internet-based Acceptance and Commitment Therapy for chronic pain. We expect that persons with chronic pain will benefit at a clinically significant level from ACTonPain guided and unguided when compared to a waitlist control group. From an economic viewpoint, investigating the relationship between treatment (cost-)effectiveness and the intervention's level of guidance (self-help only vs. guided self-help) is an important research question. Furthermore, we will examine factors that moderate and mediate the effects of ACTonPain in order to improve our understanding of what makes an ACT-based internet intervention for persons with chronic pain effective.

This trial has some limitations. First, the external validity of our study may be limited, given that previous studies indicate that participants in internet trials tend to be better educated and thus not representative of the general population (but see (Titov et al., 2010)). In a recent investigation, we identified low levels of acceptance of internet interventions as a potential barrier to uptake in the population of patients with chronic pain (Baumeister et al., 2014c). In accordance with this finding, we will use different ways of advertising and channels of information to increase favourable attitudes and uptake rates regarding our intervention (Andersson & Titov, 2014; Baumeister et al., 2014a, 2014c; Ritterband et al., 2009). Further studies should focus on the effectiveness and reach of internet-based interventions for patients with chronic pain in different routine healthcare settings. Second, we decided not to base our secondary comparison of the two versions of ACTonPain on an a-priori power calculation, in favour of the feasibility of recruitment. However, this comparison will still be better powered than most previous studies (Baumeister et al., 2014b), providing important information on the differential effects of unguided and guided interventions. Third, focusing on specific conditions and recruiting well-diagnosed persons are important for an internet intervention to be effective (Andersson et al., 2009; Andersson & Titov, 2014). In this trial, however, we will not conduct intensive diagnostic procedures such as interviews and medical examinations in order to differentiate between specific pain syndromes. While in-depth diagnosis is a preferable but costly measure for all clinical trials, chronic pain is seen as a disease of its own right (IASP, 2005) that can be validly assessed by self-reports and targeted despite the individual syndromes of each person.

There are also several strengths of this study: The content of this intervention was further developed on the basis of an already existing intervention for chronic pain in Sweden that showed to be effective in terms of pain acceptance and pain impairment (Buhrman et al., 2013). The combination of the internet and ACT can provide an affordable and effective solution for the abovementioned health care problems regarding the high prevalence of chronic pain; a disease that has high treatment costs and a low number of treatment sites. Moreover, this intervention offers advantages over traditional face-to-face therapy for both clients and health care professionals (Macea et al., 2010). Another strength of the study is the evaluation of the cost-effectiveness of ACTonPain guided and unguided in addition to the evaluation of the effectiveness of both ACTonPain versions. Although the cost-effectiveness of internet interventions in comparison to face-to-face therapy is often highlighted in many publications, the specific potential of guided and unguided internet interventions remains uncertain (Macea et al., 2010). With the analyses of treatment processes, we will also be able to investigate the features and specific processes of the treatment and

this will give us a deeper understanding of how certain ACT-specific processes contribute to the intervention's outcomes.

4. Conclusions

We present the design of our study aimed at improving interference from chronic pain. If this first stand-alone structured psychological treatment proves to be effective, it can be part of the routine care of patients with chronic pain. Should the intervention ultimately be shown to be successful, it can be further investigated and implemented, with minimal adaptation costs, into different healthcare settings as a stand-alone treatment or as part of a stepped treatment programme (Korff & Moore, 2001; Williams, 2011).

Competing interests

None.

Authors' contributions

JL and HB initiated this study. All authors contributed to the design of this study and developed the intervention content and the assessment. JL is responsible for recruitment. JL wrote the draft of the manuscript. ML provided expertise on chronic pain and psychological pain interventions. All authors contributed to the further writing of the manuscript and approved the final version of the manuscript.

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