Abstract

Background: Despite the demonstrated effectiveness of behavioural headache interventions, it is not yet known which intervention processes account for treatment responses. Acceptance and commitment therapy (ACT), an emerging behavioural intervention for headaches, proposes psychological flexibility (PF) processes as the mechanisms via which intervention change occurs. This is the first study examining these process of change variables on headache-related disability and quality of life (treatment outcome). Methods: Data originated from a Randomized Clinical Trial evaluating the efficacy of ACT for primary headaches. Ninety-four individuals with primary headaches (*M*=43 yrs; 84% females; *M* headache frequency/month=9.30) were randomized to either an ACT-based or a Wait-list control group (N=47 in each). Participants completed questionnaires related to their headache experiences and PF processes at pre- (T1), post-treatment (T2), and 3-month follow-up (T3). Results: Following a bootstrapped cross product of coefficients approach, results demonstrated mediating effects of headache acceptance, cognitive defusion, avoidance of headache, and mindfulness in the ACT group compared to control on parameters of headache-related disability and quality of life at post and 3-month follow-ups. Conclusions: These findings demonstrate that changes in certain PF processes lower disability and improve quality of life in headache sufferers, supporting that ACT works via its proposed mechanisms of change. Interventions for headache management may be optimized if they target increases in headache acceptance, defusion from thoughts, and mindfulness.

Mechanisms of Change in Acceptance and Commitment Therapy for Primary Headaches

Abstract

Background: Despite the demonstrated effectiveness of behavioural headache interventions, it is not yet known which intervention processes account for treatment responses. Acceptance and commitment therapy (ACT), an emerging behavioural intervention for headaches, proposes psychological flexibility (PF) processes as the mechanisms via which intervention change occurs. This is the first study examining these process of change variables on headache-related disability and quality of life (treatment outcome). Methods: Data originated from a Randomized Clinical Trial evaluating the efficacy of ACT for primary headaches. Ninety-four individuals with primary headaches (*M*=43 yrs; 84% females; *M* headache frequency/month=9.30) were randomized to either an ACT-based or a Wait-list control group (N=47 in each). Participants completed questionnaires related to their headache experiences and PF processes at pre- (T1), post-treatment (T2), and 3-month follow-up (T3). Results: Following a bootstrapped cross product of coefficients approach, results demonstrated mediating effects of headache acceptance, cognitive defusion, avoidance of headache, and mindfulness in the ACT group compared to control on parameters of headache-related disability and quality of life at post and 3-month follow-ups. Conclusions: These findings demonstrate that changes in certain PF processes lower disability and improve quality of life in headache sufferers, supporting that ACT works via its proposed mechanisms of change. Interventions for headache management may be optimized if they target increases in headache acceptance, defusion from thoughts, and mindfulness.

Keywords: Headaches; Mediation Analysis; Process of Change; Acceptance and Commitment Therapy; Intervention; Headache management; Psychological Flexibility

Introduction

Behavioral headache interventions (relaxation, biofeedback, cognitive-behavioral therapy) significantly reduce headaches burden (Penzien et al., 2015; Rains et al., 2005). They are also considered moderately effective in lowering headache severity (Day et al., 2014; Trompetter et al., 2015), showing 35-50% effectiveness (Raggi et al., 2018). What is yet unknown, is the exact change processes via which such interventions exert their effects (Penzien et al., 2015). Recent calls propose a paradigm shift in intervention science, calling for the examination of therapeutic change processes that contribute to outcomes as the key to augmenting the efficacy of psychological interventions (Gloster & Karekla, 2020; S. C. Hayes et al., 2019). Examining theorized processes that may optimize headache management can explain how and why treatment changes occur, leading to more personalized, modularized behavioral headache interventions in which key mechanisms of headache adaptation are targeted (Gilpin et al., 2019; McCracken, 2020).

Traditional Cognitive-Behavioral headache therapies (CBT) include an amalgamation of therapeutic targets, such as muscle tension reductions (Penzien et al., 2015), improving self-efficacy (Holroyd et al., 2009), decreasing catastrophizing, and cultivating positive coping skills (Penzien & Irby, 2014). These processes originate from different CBT viewpoints and are not coherent under one explicit guiding theoretical model (McCracken & Morley, 2014). As such, it is unclear which processes constitute the mechanism of change impacting treatment outcomes. Acceptance and Commitment Therapy (ACT), an emerging behavioural headache intervention (Smitherman et al., 2015), targets a narrow set of empirically driven processes which all promote Psychological Flexibility (PF) or the ability to engage with the present moment in a way that facilitates long-term valued living (Gloster & Karekla, 2020; McCracken & Morley, 2014). The PF model encompasses interrelated processes (acceptance, cognitive defusion, self-awareness, and values committed) that purport to drive changes in pain outcomes (Kemani et al., 2016; Lin et al., 2018; K. E.

Vowles et al., 2014; Wicksell, Olsson, et al., 2010). These processes expand the dominant CBT approach with practices that focus on how individuals can respond to headache with flexibility, placing the emphasis on improving daily functioning (Smitherman et al., 2015).

PF processes have previously been found to mediate treatment effects on functioning, life satisfaction, and psychological distress in chronic pain patients (Kemani et al., 2016; Lin et al., 2018; McCracken & Gutiérrez-Martínez, 2011a, 2011b; K. E. Vowles et al., 2014, 2017; Wicksell, Olsson, et al., 2010). In headache, there are cross-sectional studies indicating that higher pain acceptance and values-based actions are associated with lower depression, headache-related disability, interference, and catastrophizing (Almarzooqi et al., 2017; Chiros & O'Brien, 2011; Dindo et al., 2015; Foote et al., 2016). What is missing is the examination of PF processes, as mediators of treatment effects in headache management.

This is the first study to examine the mediating effects of the ACT PF processes for headache management. Consistent with the PF model that guide the ACT approach, we hypothesized that the PF processes will mediate the effects of ACT treatment (and not of a wait-list control) on headache-related disability and quality of life (QoL) outcomes at two-time points: post-treatment (T2) and 3-month follow-up (T3).

Method

Participants, Recruitment, and Settings

One hundred sixty-four individuals with headaches were recruited and screened via telephone through, e-mails, newsletter adverts, fliers, distributed at targeted locations (e.g., municipalities, libraries, and clinics' waiting-rooms) and private-care Neurologists, across Cyprus. For a full description of recruitment procedures please see our efficacy trial paper (Vasiliou et al., 2021). Ninety-four Greek-speaking adults (over 18 years old) met the inclusion criteria of primary headaches. Individuals were excluded if they had a condition that might preclude the accuracy of primary headache diagnosis (e.g., history of seizure, facial neuralgia or other secondary headache diagnoses), had signs of mild cognitive impairment (scored <23 on the Mini-mental Status Examination), or presented with psychiatric or other unstable conditions (psychotic or manic episode, suicide ideation or substance misuse problems). Excluded participants were referred to appropriate services. Diagnosis was established by a study Neurologist, following a neurological examination based on the International Classification of Headache Disorders-II diagnosis (Headache Classification Committee of the International Headache Society (IHS), 2013). A psychological evaluation was then conducted by doctoral level clinical psychology trainees, based on a semi-structured interview of Headache Assessment (Smitherman, 2016), to gather information about coping with headaches and rule out psychopathology.

Participants were randomly assigned to either the ACT or wait-list control (WL) groups, using a simple within-sample randomization technique (randomized in a single block to ensure group equivalency, i.e., 50% chance of allocation to either condition; (Rains & Penzien, 2005). Participants randomized in the WL group were informed that they would receive the intervention with a 4–month delay. The majority of participants in both treatment groups were women (84%), 43.90 years of age (SD=*10.35*), married (72%), with an average monthly income of 1000 euro (37%), and held a high- or vocational-school diploma (37%). Eighty-seven percent of participants received the diagnosis of migraines, 13% tension-type headache and 6.5% other primary headaches. For both groups, time since headache-suffering onset varied between 1 to 46 years (M=18.42, SD=10.81), and a mean of 9.40 headache days per month (SD=7.28; range 4 to 30 days/month). Most participants in both groups, were on prescribed medication for their headache (83.50%). Ninety-four participants provided data at T1 (47 in each group) and 61 participants provided data at T2 and T3 (31 from the ACT and 30 from the WL group). The study was approved by the Cyprus National Bioethics Committee (#EEBK/EP.2013/05), the Office of the Commissioner for Personal Data Protection (2.0.18/II) and was registered with clinical trials.gov (NCT02734992).

ACT-based treatment guide

An ACT group-based treatment (see (Vasiliou et al., 2021) for more details) was developed, focusing on improving physical and psychological daily functioning and increasing QoL among individuals suffering from headaches. The intervention utilized experiential techniques, metaphors, and behavioral change practices and combined the six facets of the ACT approach along with evidence-based behavioural medicine practices, targeting common headache-related problems (e.g., sleep hygiene, how to respond to headache triggers, assertiveness training, etc.; see (Buse & Andrasik, 2009). Particularly, the intervention focused on teaching participants to flexibly respond to their headaches by: a) recognizing how avoidance of important activities increase suffering than reducing headaches; b) committing in valued areas that give meaning to ones' life while learning to engage with such activities, even in the presence of headaches (inclusion of exposure to headache); c) learning behavioral awareness skills (e.g., mindfulness) and techniques to deal with headache related thoughts (i.e., cognitive defusion, self-as-context); and d) increasing awareness of headache triggers while learning to respond in a way valued activities will not be interrupted. The intervention included nine weekly treatment sessions, lasting 1 ½ hours each. They conducted in groups of 8-10 participants and each session was led by two-co-therapists. Therapists were doctoral Clinical Psychology Trainees who received >25 hours training in the ACT approach. Treatment integrity was upheld with weekly supervision meetings with an ACT peer-reviewed trainer.

Assessment

All participants completed the same questionnaires at three different time points: pre- (T1), post-treatment (T2), and 3-month follow-up (T3). The two primary treatment outcomes, examining headache-related disability and functioning, were the dependent variables. The hypothesized mediators included the six PF processes.

Treatment Outcomes

The Henry Ford Hospital Headache Disability Inventory (b-HDI) (Jacobson et al., 1994) is a 25-item measure evaluating headache effects on daily activities in two scales: functional disability (HDI- Func; 13 items; e.g. "Because of my headaches I feel restricted in performing my routine daily activities") and emotional disability (HDI- Em; 12 items, e.g., "I am afraid to go outside when I feel that a headache is starting"). Participants' respond to one of three options, each receiving a set of points (i.e., yes=4 points, sometimes=2 points, and no=0 points). Each subscale's points are summed and higher scores indicate greater disability. b-HDI demonstrates high reliability (Cronbach's alpha = .93 for the total score, .88 for the functional and .87 for the emotional subscales) and sufficient validity with theoretically related scales.

The Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ) (Martin et al., 2000)-use permission from GlaxoSmithKline health outcome group- is a 14-item scale, assessing the impact of migraine on quality of life, over the past four weeks. It is scored on a 6-point scale (1=none of the time to 6=all of the time) and includes three dimensions: (a) Role Restrictive (MSQ-RR; 7 items)- examining the degree to which headache restricts daily activity performance, (b) Role Preventive (MSQ-RP; 4 items)- examining the number of activities interrupted by headaches, and (c) Emotional Function (MSQ-EF; 3 items)- examining the degree to which emotional reactions impact headaches. Items corresponding to each subscale are reversed and summed. Raw scores are converted into percentages for each dimension (Martin et al., 2000) and higher scores represent higher QoL. The MSQ has shown good psychometric properties across different populations (Cole et al., 2007; Rendas-Baum et al., 2013). This measure was modified in the present study, so that the word "migraine" was substituted with the word "headache" to be broadly applicable for all primary headache diagnoses. The instruments' reliability was similar to that of the original scale. Cronbach's alphas for this study were: .93 for MSQ-RR, .87 for MSQ-RP, and .83 for MSQ-EF.

Hypothesized PF Mediators

Mediators were selected based on the PF model, following recommendations from relevant scholars (Gilpin et al., 2019; Hann & McCracken, 2014), and included the following measures:

The Greek Chronic Pain Acceptance Questionnaire (G-CPAQ), Greek version: (Vasiliou et al., 2018) Original:(McCracken et al., 2004) is an 8-item scale, assessing pain acceptance or the degree to which participants engage in meaningful activities even in the presence of pain, and willingness to experience pain without trying to change, control, or struggle with it. The G-CPAQ is rated on a 7-point frequency-type scale (1=never true to 6=always true) and yields a total sum with higher scores reflecting higher pain acceptance. The G-CPAQ presents with high reliability (α=.78 in this study) and adequate construct validity with theoretically related constructs.

The Greek Psychological Inflexibility in Pain Scale (G-PIPS-II) Greek version: (Vasiliou et al., 2019), Original: (Wicksell, Lekander, et al., 2010) consists of 12 items assessing psychological inflexibility in two subscales: (a) avoidance of pain (G-PIPS-avoid; 8 items)- examining behaviors that lead to avoidance of pain and related distress; and (b) cognitive fusion (G-PIPS-fus.; 4 items)- assessing the frequency of pain-related thoughts sufferers with headache get fused with, leading to avoidance behaviors. Items are rated on a 7-point frequency-type scale (1=never true to 7=always true) and summed. Higher scores reflect higher psychological inflexibility in pain. The scale presents with good psychometric properties (Wicksell et al. 2010) and a relevant factorial structure for its Greek version (Vasiliou et al., 2019). Cronbach's alpha for this study was .90 for the total score, .90 for G-PIPS-avoid, and .68 for G-PIPS-fus subscales.

The Cognitive Affective Mindfulness Scale-Revised (CAMS-R) (Feldman et al., 2007) is a 12-item self-report questionnaire assessing mindfulness. Items are rated on a 4-point Likert scale (1=rarely to 4=almost always). Greater mindfulness qualities reflect better ability to understand what is happening inside and around the environment when individuals engage in the present moment without being judgmental. CAMS-R presents with high reliability for this study (α=.86) and adequate construct validity.

The Valuing Questionnaire (VQ), (Smout et al., 2014) is a 10-item instrument, assessing the extent to which individuals acted based on personal values during the past week. It yields two dimensions: (a) progress in identified values (VQ-Pr; 5 items, e.g., "I worked toward my goals even if I didn't feel motivated to do so") and (b) obstruction of valued living (VQ-Ob; 5 items, e.g., "When things didn't go according to plan, I gave up easily"). Items are rated on a 7-point Likert scale (0=not at all true and 6=completely true). Higher scores in VQ-Pr sub-scale represent better valued living and higher scores in VQ-Ob subscale reflect the presence of psychological barriers (e.g., disturbing thoughts, emotions, sensations) in pursuing valued living. VQ demonstrates good convergent validity and high reliability (α=.87 for VQ-Pr and .62 for VQ-Ob).

Committed Action Questionnaire (CAQ) (McCracken et al., 2015) is an 8-item scale, assessing goal-directed behaviors (McCracken, 2013). Items are rated on a frequency-type scale from 0=never true to 6=always true and summed so that higher scores reflect higher persistence in pursuing valued-driven behaviors (e.g., "I can remain committed to my goals even when there are times that I fail to reach them"). Cronbach's alpha for this study was .80.

Data Analyses Plan

Overview of Statistical Analyses

Power analysis was calculated to estimate the sample size and probability errors. Although distribution assumptions in bootstrapping cannot be achieved, we made the assumption of the sample based on the data (approximate solution) (Fritz & MacKinnon, 2007). We employed G* power analysis software (Faul et al., 2007) to calculate the joint significance test. Then we added 25% of the value to ensure some levels of security. Assuming equal size groups, for two predictors (a and b paths with no covariances) a total sample of 110 participants- 55 in each condition for $\eta_p^2 = .25$, $p < .01$ was estimated.

For all analyses, we used only the completers' data. Analyses were executed in three steps. First, we estimated bivariate Pearson correlations coefficients between primary outcomes (dependent variables) and hypothesized mediators, to explore the interrelated pattern of correlations among the examined variables and to assess multicollinearity.

Second, we ran a cross-product of the coefficient approach using a non-parametric bootstrapping approach, to identify what proposed mediators accounted for outcome changes. A non-parametric Bootstrap approach bypasses assumptions of normality, hence, is considered a statistically robust method when dealing with small samples (Preacher & Hayes, 2008). The issue of small sample size precluded us from being able to utilize a multivariate mediation model.

To evaluate the mean value for the a*b product (and the obtained score distribution) across the conditions (ACT vs. WL), we ran analyses based on 5000 bootstrap resampling. Mediation (indirect effect) occurs if the strength of the relation between the predictor and outcomes is reduced (i.e., non-significant) when a mediator is added (A. F. Hayes & Preacher, 2014). The a*b product calculates corrections for bias with a point to estimate the indirect effects and provides the CIs of these effects (Bootstrap distribution is adjusted for bias and skewness when CIs equate p<.05; (Preacher & Hayes, 2008). If lower and upper bounds of CIs do not include zero, then indirect effects are significant at the level values as indicated in the analyses at BCa 95% or BCa 90% CI. The normal theory (Sobel) test was also examined (z scores), but the interpretation of indirect effects was based on CIs not including the zero value, rather than the formal tests of significance (Shrout & Bolger, 2002).

Selection of Mediators

The hypothesized mediators (change scores) were selected based on an a-priory decision of relevance to the underlying theoretical rationale (specificity criterion) (Kraemer et al., 2002). Both outcomes and mediators consisted of pre- to post-treatment (T1-T2) and pre to 3 months follow-up (T1-T3) change scores. Completers' only data was used to assess whether the change scores in the mediators drive changes in targeted headache related outcomes. We expected that the proposed mediators (ACT processes) should account for the specified headache-related treatment outcomes.

Specificity and timeline are the two main criteria when assessing mediating effects in treatment outcomes (A. F. Hayes & Preacher, 2014). Given the observed significant changes on both process and outcome variables at post assessment, we run further analyses of mediation to also address the timeline criterion. In a series of post-hoc analyses, we tested all the mediators with and without change scores (controlling for the treatment outcomes T1 scores). Table 1 presents all variables examined at each time point in the tested mediation models. Analyses were performed with SPSS version 22, utilizing the macros for bootstrapping procedures (see (A. F. Hayes & Preacher, 2014). On the supplementary table S1, we present a series of *t*-tests for independent samples with Bonferroni corrections, to show the comparability of the two groups on primary outcomes $p<.008$ (.05 divided by the six variables; 3 for each treatment outcome variable) and mediators $p<.006$ (.05 divided by the 7 ACT process variables); both change scores. To allow examination of findings with a critical interpretation, standardized estimates, their corresponding SE, and the exact *p* values are reported on the supplementary Tables S2, S3, and S4.

Results

Preliminary and Descriptive Characteristics

Visual inspection of histograms, skewness, kurtosis, stem-and-leaf, and normality plots showed that scores on all measures followed a normal distribution. Multivariate normality was also met. Further, visual inspection of missing data (10.52% at post-intervention) and Little's MCAR test (x^2=55.802, *df*=5, Sig=.63) showed no systematic pattern of missing data. Attrition rates were found to be similar to other behavioral headache trials, including 17.08% at T1, 24% at T2, and 35% at T3. Missing per item rates was negligible, ranging from 0-2.92% with only MSQ-RR at T1 reaching 6.33% items missing.

Pearson's Coefficient Correlation Analyses

Tables 2 and 3 present the results of the correlation analyses, assessing the overall relationships between the treatment outcomes and the hypothesized mediators at T1-T2 and T1-T3 (all change scores). Overall, correlations were in the expected directions and multicollinearity was not an issue.

Test of Indirect (mediation) effects

Figure 1 about here

As Figure 1 shows, mediation analyses were run in relation to the two outcome variables: headache-related disability (HDI) and QoL (MSQ). BCa 95% CI are used to present the findings from the mediation analyses. Table 4 presents the mediation effects on the two outcomes (BCa 95% CI) in a form of a matrix (grid). Supplementary Tables S2 & S3 present the exact values of the mediations, including normal theory (parametric) findings.

Mediators of change on Headache-related Disability (HDI)

Change scores between pre and post of headache acceptance and avoidance of headache mediated the effects of treatment on general headache-related disability, functional, and emotional disability sub-scales (HDI- Func & HDI-Em; see Table S2). There were no mediating effects for fusion with headache related thoughts, values progress and obstruction, mindfulness, and committed action.

Acceptance and cognitive fusion change scores from pre to follow-up, showed maintenance of mediating effects on the general headache related disability and in its two sub-scales (HDI-Func. and HDI-Em.; See Table S3). Avoidance of headache change scores (T1-T3) mediated the effects of treatment on both general and emotional headache-related disability (see Table S3). Also, committed action, values progress, and mindfulness change scores (T1-T3) mediated the effects of treatment on functional related disability (HDI- Func; See Table S3). There were no other mediating effects at T1-T3 for any of the other ACT processes.

Mediators of change on Headache-Specific QoL (MSQ)

At T1-T2, headache acceptance and mindfulness change scores exerted mediating effects on the role-restrictive dimension of the QoL scale (MSQ-RR; see Table S4). No other mediating effects were found for any of the other proposed mediators for any of the other dimensions of QoL.

At T1-T3 (see Table S5), only change scores in headache acceptance mediated the effects of treatment on the role restrictive dimension of the QoL scale (RR-MSQ). No other mediating effects were observed.

Additional Post Hoc Analyses

To increase confidence in our findings that our hypothesized mediators (change scores) accounted for the treatment outcomes (changes occurred due to the mediating effects of ACT processes during the intervention phase), we performed a series of post hoc analyses to examine if the mediators at post-treatment (not change scores) predict changes on the two outcome variables at two times (T2 & T3), while controlling for the pre-treatment scores (T1). These analyses tested if the level the proposed process variables at post have a functional importance for changes in the treatment outcomes.

Effects of mediators Headache-related Disability (HDI) controlling for pre-treatment changes

At T2, headache acceptance, avoidance of headache, fusion with headache -related thoughts, committed action, and values obstruction, all mediated the effects of treatment on the three headache-related disability sub-scales when controlling for their pre-treatment (T1) scores (BCa 95% CI). Values progress was additionally found to mediate the effects of treatment on general headache-related disability.

At T3, headache acceptance, avoidance of headache, and committed action mediated the effects of treatment on headache-related disability sub-scales, when controlling for their pre-treatment (T1) scores (BCa 95% CI). Further, fusion with headache -related thoughts mediated the effects of treatment on emotional headache-related disability (HDI-Em.; BCa 95% CI).

Effects of mediators Headache-specific QoL (MSQ) controlling for pre-treatment changes

At T2, headache acceptance, avoidance of headache, and committed action mediated the effects of treatment on the three-headache specific QoL dimensions when controlling for their pre-treatment (T1) scores (BCa 95% CI).

At T3, headache acceptance, avoidance of headache, fusion with headache related thoughts, and committed action mediated the effects of treatment in the role preventive dimension of the QoL scale only (MSQ-RP; BCa 95% CI). Additionally, avoidance of headache, committed action, and values obstruction mediated the effects of treatment on the role emotional dimension of the QoL scale (MSQ-EM; BCa 95% CI).

Discussion

Examination of proposed therapeutic mechanisms of change as mediators of treatment effects in headache management presents with a solid first step in the identification of common and unique processes that may inform how behavioral headache therapies can improve upon their effectiveness (Nicholson et al., 2005). This study explored the effects of PF processes as mediators of treatment change in ACT compared to control for headache management. In our previous RCT (Vasiliou et al., 2021) significant improvements on several functional treatment outcomes were found for ACT compared to WL control, demonstrating the effectiveness of this intervention approach. Extending these findings, the present study is the first in the relevant behavioral headache literature to examine whether ACTs' theoretically hypothesized PF processes mediate the effects of treatment on headache-related outcomes of disability and QoL parameters. Findings corroborated with cross-sectional studies, showing the potential central role of PF processes in headache and its contribution to patients' functioning (Almarzooqi et al., 2017; Chiros & O'Brien, 2011; Foote et al., 2016). In line with the ACT theoretical model, improvements in headache acceptance and decreases in avoidance of headache mediated headache-related disability (total, functional, and emotional) both at post-treatment and 3-months follow-up. Also, at 3-months follow-up an increase in cognitive defusion mediated all aspects of headache-related disability, whereas increases in mindfulness mediated functional headache-related disability. Similarly, headache acceptance and mindfulness were the PF processes found to mediate role restrictive QoL parameter outcomes at post-treatment with only headache acceptance being a significant mediator at the 3-months follow-up.

Beyond presenting which PF processes mediate outcomes, these findings propose which processes should constitute personalized, modularized therapeutic targets if the aim is to decrease disability because of headaches. Increasing headache acceptance and mindful awareness emerged as the processes that impact headache disability. In patients who exhibit restrictions with daily functioning performance (e.g., in leisure activities, professional tasks, daily errands) and increased emotional burden due to headaches (e.g., frustration and distress) interventions should, based on this study's findings, employ processes that target reducing avoidance in headache. Differences in the mediation pathways at post versus 3-month follow-up, propose that certain processes (e.g., values-based activities) lose their functional importance as time-since-treatment passes and thus may need to be boosted over time.

With respect to our exploration of the predictive ability of the ACT processes on outcomes when controlling for earlier effects (pre-treatment levels of mediators), these data further support that the PF mediating effects occurred primarily due to the effects of treatment. This finding provides tentative support the temporal criterion of mediation. Nevertheless, an intense temporal assessment of the processes of change across sessions as the treatment upfolds, can shed more light on the key functional pathways that can define which processes change and at which time within the course of the treatment. Such granular understanding of the PF processes for headache management can have clinical implications, suggesting personalized, modularized components that can further augment treatment effects.

Yet, not all proposed processes of change emerged as significant mediators. Values-based progress and obstructions, along with committed action did not mediate the effects of ACT on headache disability and QoL. Two potential explanations for this may relate to the specific sample recruited for this trial and the emphasis and timing of these processes during treatment. In terms of the sample, we recruited a rather heterogenous sample of community dwellers suffering from headache who appear to be higher functioning than individuals who tend to typically seek clinical services (Ziegler & Paolo, 1995). This probably resulted in a ceiling effect in these process variables, since participants were already committed and active. Indeed, a recent trial examining ACT for high-frequency migraine demonstrated improvements and greater effects on valued living in patients with more disability compared to community controls (Grazzi et al., 2019). Regarding emphasis and timing during treatment, valued living and committed action components were introduced towards the end of the intervention and as such, may have received less emphasis, compared to acceptance of headache that was introduced earlier and fortified throughout. In terms of time, it may be that the 3-month range is too short a period for information consolidation to occur especially for processes requiring individuals to take effective actions, guided and motivated by values, even in the presence of aversive experiences, such as headaches. This may be particularly relevant in individuals who suffer from headaches who appear with low headache self-awareness and motivation and as such may need more practice for consolidation to occur (Lipton, Stewart & Liberman, 2002). New findings from a recently conducted RCT provides more evidence for the belated effects of some ACT processes in headache sufferers (Grazzi et al., 2021). Notably, in this study mediating effects of mindfulness emerged at post-treatment in the role restrictive parameter of QoL, followed by increases in functioning at 3-month follow-up. This supports that for some PF processes to mediate treatment effects (i.e., mindfulness), some time to consolidate the skill, is needed. This is consistent with findings from the pain literature, showing belated improvements (e.g., of 6 months) in some PF processes (McCracken & Gutiérrez-Martínez, 2011a; K. Vowles et al., 2010; K. E. Vowles et al., 2011; K. E. Vowles & McCracken, 2008).

It should be noted, that based on the PF theoretical model, all processes are interconnected and behavioral changes can occur as a result of changes in other processes (Day et al., 2014; Karademas et al., 2017; Trompetter et al., 2015). Based on the PF model, altering the function of headache-related thoughts by changing individuals’ relationship to their thoughts (rather than changing the content of thoughts) can result in shifting attention from the content of the headache-related thoughts to engaging in committed value-based activities (e.g., "even if I have a headache, I will go out with my friends") (Garland et al., 2015; Hayes-Skelton et al., 2015; McCracken et al., 2014; Vasiliou et al., 2019; K. E. Vowles et al., 2009). It may be the case that changes in avoidance of headache facilitate changes in committed action (found to not be a significant mediator in this study), and committed action may not work as a primary mediator but be driven by other key mediating effects (Almarzooqi et al., 2017). To investigate this hypothesis however, full examination of temporality is required.

Findings should be interpreted in light of some limitations. First, the sample size was relatively small not allowing for multivariate mediation analyses. Second, given the community-based and relatively highly active sample of this study, the generalizability to severe headache populations with comorbidities or other medical complexities should be considered with caution. Third, the use of retrospective self-reports and the shared content in some measure items (e.g., G-CPAQ, G-PIPS-II, HDI) may have inflated errors in the relations among the variables. Finally, causality cannot be implied and mediation models may falsely assume that therapeutic change is a linear and unidirectional process when in reality it is multidimensional, complex, and differs across individuals (Hofmann, Curtiss & Hayes, 2020). Methods of direction dependence are needed (i.e., latent growth curve modelling; (Wiedermann & von Eye, 2015) to identify whether changes in putative mediators temporarily precede changes in targeted functional outcomes. Also, idiographic dynamic network approaches have recently been proposed (Hofmann, Curtiss & Hayes, 2020) and need to be developed and investigated in future studies.

These limitations notwithstanding, present findings provide significant theoretical and clinical implications. Theoretically, findings lend further support for the PF processes as plausible mechanisms of change in a previously treatment improvements, observed in a 9-weekly ACT group-based intervention (Vasiliou et al., 2021). Yet, findings raised questions for future investigations in regard to the interconnectedness among the processes and how these may impact functionality and QoL. Clinically, these findings provide initial foci for therapeutic targets. Maximizing acceptance and minimizing headache avoidance and values obstructions emerged as key processes to augment patients' daily functioning and QoL. Provided that numerous individuals who suffer with headaches, may never succeed in becoming permanently headache -free, our findings propose therapeutic processes which can diminish the extensive burden for those who suffer from headaches.

Future studies should replicate and extend these findings. It is important to examine mediators at multiple time points during (i.e., session by session changes) and longitudinally after treatment (e.g., at 6 or 12-months follow-up), to further clarify temporal relationships and whether mediators change prior to changes in the outcome. In addition to mediators, it is important to examine moderators that co-occur with headaches (e.g., psychiatric comorbidity, high body mass index; (Bond et al., 2018) or moderators that are related to treatment (e.g., treatment expectations, therapists' competence, treatment delivery methods; (Rief & Anna Glombiewski, 2017). Knowledge of these moderators in combination with mediators of processes of intervention change along with utilization of new methodologies (e.g., Ecological Momentary Assessments) can leverage personalization and individualization of treatments with the potential to further improve their effectiveness and efficiency (Gloster et al., 2020; S. C. Hayes et al., 2019; McCracken, 2020; Nicholson et al., 2005; Villatte et al., 2016).

In conclusion, findings demonstrate that ACT intervention improvements in disability, functioning, and QoL for those suffering from primary headaches, occurred via changes in headache acceptance, defusion from headache related thoughts, and mindfulness. Focusing on optimizing headache adjustment via flexible responses to it not driven by attempts to prevent or control headache, provides a novel approach in headache management.

As accumulating evidence shows, this approach can help sufferers re-establish optimal daily functioning even when headache is present and doing so becomes an important step to reducing disability and increasing QoL.

References

Almarzooqi, S., Chilcot, J., & McCracken, L. M. (2017). The role of psychological flexibility in migraine headache impact and depression. *Journal of Contextual Behavioral Science*, *6*(2), 239–243. https://doi.org/10.1016/j.jcbs.2017.04.004

Bond, D. S., Thomas, J. G., Lipton, R. B., Roth, J., Pavlovic, J. M., Rathier, L., O’Leary, K. C., Evans, E. W., & Wing, R. R. (2018). Behavioral Weight Loss Intervention for Migraine: A Randomized Controlled Trial: Weight Loss and Migraine. *Obesity*, *26*(1), 81–87. https://doi.org/10.1002/oby.22069

Buse, D. C., & Andrasik, F. (2009). Behavioral Medicine for Migraine. *Neurologic Clinics*, *27*(2), 445–465. https://doi.org/10.1016/j.ncl.2009.01.003

Chiros, C., & O’Brien, W. H. (2011). Acceptance, appraisals, and coping in relation to migraine headache: An evaluation of interrelationships using daily diary methods. *Journal of Behavioral Medicine*, *34*(4), 307–320. https://doi.org/10.1007/s10865-011-9313-0

Cole, J. C., Lin, P., & Rupnow, M. F. T. (2007). Validation of the Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v. 2.1) for patients undergoing prophylactic migraine treatment. *Quality of Life Research*, *16*(7), 1231–1237. https://doi.org/10.1007/s11136-007-9217-1

Day, M. A., Thorn, B. E., & Rubin, N. J. (2014). Mindfulness-based cognitive therapy for the treatment of headache pain: A mixed-methods analysis comparing treatment responders and treatment non-responders. *Complementary Therapies in Medicine*, *22*(2), 278–285. https://doi.org/10.1016/j.ctim.2013.12.018

Dindo, L., Recober, A., Marchman, J., O’Hara, M., & Turvey, C. (2015). Depression and Disability in Migraine: The Role of Pain Acceptance and Values-Based Action. *International Journal of Behavioral Medicine*, *22*(1), 109–117. https://doi.org/10.1007/s12529-014-9390-x

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*(2), 175–191. https://doi.org/10.3758/BF03193146

Feldman, G., Hayes, A., Kumar, S., Greeson, J., & Laurenceau, J.-P. (2007). Mindfulness and Emotion Regulation: The Development and Initial Validation of the Cognitive and Affective Mindfulness Scale-Revised (CAMS-R). *Journal of Psychopathology and Behavioral Assessment*, *29*(3), 177–190. https://doi.org/10.1007/s10862-006-9035-8

Foote, H. W., Hamer, J. D., Roland, M. M., Landy, S. R., & Smitherman, T. A. (2016). Psychological flexibility in migraine: A study of pain acceptance and values-based action. *Cephalalgia*, *36*(4), 317–324. https://doi.org/10.1177/0333102415590238

Fritz, M. S., & MacKinnon, D. P. (2007). Required Sample Size to Detect the Mediated Effect. *Psychological Science*, *18*(3), 233–239. https://doi.org/10.1111/j.1467-9280.2007.01882.x

Garland, E. L., Farb, N. A., R. Goldin, P., & Fredrickson, B. L. (2015). Mindfulness Broadens Awareness and Builds Eudaimonic Meaning: A Process Model of Mindful Positive Emotion Regulation. *Psychological Inquiry*, *26*(4), 293–314. https://doi.org/10.1080/1047840X.2015.1064294

Gilpin, H. R., Stahl, D. R., & McCracken, L. M. (2019). A theoretically guided approach to identifying predictors of treatment outcome in Contextual Cognitive Behavioural Therapy for chronic pain. *European Journal of Pain*, *23*(2), 354–366. https://doi.org/10.1002/ejp.1310

Gloster, A. T., & Karekla, M. (2020). Gloster, A.T. & Karekla, M. (2020). A multi-level, multi-method approach to testing and refining intervention targets. In S.G. Hoffman & S. Hayes (Eds.), Beyond the DSM. Oakland, CA: Context Press/New Harbinger Publications. In *Beyond the DSM* (p. 304). Oakland, CA: Context Press/New Harbinger Publications. https://www.newharbinger.com/beyond-dsm

Gloster, A. T., Rinner, M. T. B., Ioannou, M., Villanueva, J., Block, V. J., Ferrari, G., Benoy, C., Bader, K., & Karekla, M. (2020). Treating treatment non-responders: A meta-analysis of randomized controlled psychotherapy trials. *Clinical Psychology Review*, *75*, 101810. https://doi.org/10.1016/j.cpr.2019.101810

Grazzi, L., Andrasik, F., Rizzoli, P., Bernstein, C., Sansone, E., & Raggi, A. (2021). Acceptance and commitment therapy for high frequency episodic migraine without aura: Findings from a randomized pilot investigation. *Headache: The Journal of Head and Face Pain*, head.14139. https://doi.org/10.1111/head.14139

Grazzi, L., Bernstein, C., Raggi, A., Sansone, E., Grignani, E., Searl, M., & Rizzoli, P. (2019). ACT for migraine: Effect of acceptance and commitment therapy (ACT) for high-frequency episodic migraine without aura: preliminary data of a phase-II, multicentric, randomized, open-label study. *Neurological Sciences*, *40*(S1), 191–192. https://doi.org/10.1007/s10072-019-03802-w

Hann, K. E. J., & McCracken, L. M. (2014). A systematic review of randomized controlled trials of Acceptance and Commitment Therapy for adults with chronic pain: Outcome domains, design quality, and efficacy. *Journal of Contextual Behavioral Science*, *3*(4), 217–227. https://doi.org/10.1016/j.jcbs.2014.10.001

Hayes, A. F., & Preacher, K. J. (2014). Statistical mediation analysis with a multicategorical independent variable. *British Journal of Mathematical and Statistical Psychology*, *67*(3), 451–470. https://doi.org/10.1111/bmsp.12028

Hayes, S. C., Hofmann, S. G., Stanton, C. E., Carpenter, J. K., Sanford, B. T., Curtiss, J. E., & Ciarrochi, J. (2019). The role of the individual in the coming era of process-based therapy. *Behaviour Research and Therapy*, *117*, 40–53. https://doi.org/10.1016/j.brat.2018.10.005

Hayes-Skelton, S. A., Calloway, A., Roemer, L., & Orsillo, S. M. (2015). Decentering as a potential common mechanism across two therapies for generalized anxiety disorder.

Journal of Consulting and Clinical Psychology, *83*(2), 395–404. https://doi.org/10.1037/a0038305

Headache Classification Committee of the International Headache Society (IHS). (2013). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia: An International Journal of Headache*, *33*(9), 629–808. https://doi.org/10.1177/0333102413485658

Holroyd, K. A., Labus, J. S., & Carlson, B. (2009). Moderation and mediation in the psychological and drug treatment of chronic tension-type headache: The role of disorder severity and psychiatric comorbidity. *PAIN®*, *143*(3), 213–222. https://doi.org/10.1016/j.pain.2009.02.019

Jacobson, G. P., Ramadan, N. M., Aggarwal, S. K., & Newman, C. W. (1994). The Henry Ford hospital headache disability inventory (HDI). *Neurology*, *44*(5), 837–837.

Karademas, E. C., Karekla, M., Flouri, M., Vasiliou, V. S., Kasinopoulos, O., & Papacostas, S. S. (2017). The impact of experiential avoidance on the relations between illness representations, pain catastrophising and pain interference in chronic pain. *Psychology & Health*, *32*(12), 1–16. https://doi.org/10.1080/08870446.2017.1346193

Kemani, M. K., Hesser, H., Olsson, G. L., Lekander, M., & Wicksell, R. K. (2016). Processes of change in Acceptance and Commitment Therapy and Applied Relaxation for long-standing pain. *European Journal of Pain*, *20*(4), 521–531. https://doi.org/10.1002/ejp.754

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and Moderators of Treatment Effects in Randomized Clinical Trials. *Archives of General Psychiatry*, *59*(10), 877. https://doi.org/10.1001/archpsyc.59.10.877

Lin, J., Klatt, L.-I., McCracken, L. M., & Baumeister, H. (2018). Psychological flexibility mediates the effect of an online-based acceptance and commitment therapy for chronic pain: An investigation of change processes. *PAIN*, *159*(4), 663–672. https://doi.org/10.1097/j.pain.0000000000001134

Martin, B. C., Pathak, D. S., Sharfman, M. I., Adelman, J. U., Taylor, F., Kwong, W. J., & Jhingran, P. (2000). Validity and Reliability of the Migraine-Specific Quality of Life Questionnaire (MSQ Version 2.1). *Headache: The Journal of Head and Face Pain*, *40*(3), 204–216. https://doi.org/10.1046/j.1526-4610.2000.00030.x

McCracken, L. M. (2013). Committed Action: An Application of the Psychological Flexibility Model to Activity Patterns in Chronic Pain. *The Journal of Pain*, *14*(8), 828–835. https://doi.org/10.1016/j.jpain.2013.02.009

McCracken, L. M. (2020). Necessary components of psychological treatment for chronic pain: More packages for groups or process- based therapy for individuals? *European Journal of Pain*, *24*(6), 1001–1002. https://doi.org/10.1002/ejp.1568

McCracken, L. M., Barker, E., & Chilcot, J. (2014). Decentering, rumination, cognitive defusion, and psychological flexibility in people with chronic pain. *Journal of Behavioral Medicine*, *37*(6), 1215–1225. https://doi.org/10.1007/s10865-014-9570-9

McCracken, L. M., Chilcot, J., & Norton, S. H. (2015). Further development in the assessment of psychological flexibility: A shortened Committed Action Questionnaire (CAQ-8). *European Journal of Pain*, *19*(5), 677–685. https://doi.org/10.1002/ejp.589

McCracken, L. M., & Gutiérrez-Martínez, O. (2011a). Processes of change in psychological flexibility in an interdisciplinary group-based treatment for chronic pain based on Acceptance and Commitment Therapy. *Behaviour Research and Therapy*, *49*(4), 267–274. https://doi.org/10.1016/j.brat.2011.02.004

McCracken, L. M., & Gutiérrez-Martínez, O. (2011b). Processes of change in psychological flexibility in an interdisciplinary group-based treatment for chronic pain based on Acceptance and Commitment Therapy. *Behaviour Research and Therapy*, *49*(4), 267–274. https://doi.org/10.1016/j.brat.2011.02.004

McCracken, L. M., & Morley, S. (2014). The Psychological Flexibility Model: A Basis for Integration and Progress in Psychological Approaches to Chronic Pain Management. *The Journal of Pain*, *15*(3), 221–234. https://doi.org/10.1016/j.jpain.2013.10.014

McCracken, L. M., Vowles, K. E., & Eccleston, C. (2004). Acceptance of chronic pain: Component analysis and a revised assessment method. *Pain*, *107*(1), 159–166. https://doi.org/10.1016/j.pain.2003.10.012

Nicholson, R. A., Hursey, K. G., & Nash, J. M. (2005). Moderators and Mediators of Behavioral Treatment for Headache. *Headache: The Journal of Head and Face Pain*, *45*(5), 513–519. https://doi.org/10.1111/j.1526-4610.2005.05103.x

Penzien, D. B., & Irby, M. B. (2014). Insights on Treatment Mechanisms of Cognitive-Behavioral Migraine Therapy. *Headache: The Journal of Head and Face Pain*, *54*(9), 1439–1440. https://doi.org/10.1111/head.12433

Penzien, D. B., Irby, M. B., Smitherman, T. A., Rains, J. C., & Houle, T. T. (2015). Well-Established and Empirically Supported Behavioral Treatments for Migraine. *Current Pain and Headache Reports*, *19*(7), 34. https://doi.org/10.1007/s11916-015-0500-5

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, *40*(3), 879–891. https://doi.org/10.3758/BRM.40.3.879

Raggi, A., Grignani, E., Leonardi, M., Andrasik, F., Sansone, E., Grazzi, L., & D’Amico, D. (2018). Behavioral Approaches for Primary Headaches: Recent Advances. *Headache: The Journal of Head and Face Pain*, *58*(6), 913–925. https://doi.org/10.1111/head.13337

Rains, J. C., & Penzien, D. B. (2005). Behavioral Research and the Double-Blind Placebo-Controlled Methodology: Challenges in Applying the Biomedical Standard to Behavioral Headache Research. *Headache: The Journal of Head and Face Pain*, *45*(5), 479–486. https://doi.org/10.1111/j.1526-4610.2005.05099.x

Rains, J. C., Penzien, D. B., McCrory, D. C., & Gray, R. N. (2005). Behavioral Headache Treatment: History, Review of the Empirical Literature, and Methodological Critique. *Headache: The Journal of Head and Face Pain*, *45*(s2), S92–S109. https://doi.org/10.1111/j.1526-4610.2005.4502003.x

Rendas-Baum, R., Bloudek, L. M., Maglinte, G. A., & Varon, S. F. (2013). The psychometric properties of the Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ) in chronic migraine patients. *Quality of Life Research*, *22*(5), 1123–1133. https://doi.org/10.1007/s11136-012-0230-7

Rief, W., & Anna Glombiewski, J. (2017). The role of expectations in mental disorders and their treatment. *World Psychiatry*, *16*(2), 210–211. https://doi.org/10.1002/wps.20427

Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: New procedures and recommendations. *Psychological Methods*, *7*(4), 422–445. https://doi.org/10.1037/1082-989X.7.4.422

Smitherman, T. A. (2016). *Clinician's Manual on Migraine*. ADIS. https://www.springer.com/la/book/9783319027760

Smitherman, T. A., Wells, R. E., & Ford, S. G. (2015). Emerging Behavioral Treatments for Migraine. *Current Pain and Headache Reports*, *19*(4), 13–18. https://doi.org/10.1007/s11916-015-0486-z

Smout, M., Davies, M., Burns, N., & Christie, A. (2014). Development of the Valuing Questionnaire (VQ). *Journal of Contextual Behavioral Science*, *3*(3), 164–172. https://doi.org/10.1016/j.jcbs.2014.06.001

Trompetter, H. R., Bohlmeijer, E. T., Fox, J.-P., & Schreurs, K. M. G. (2015). Psychological flexibility and catastrophizing as associated change mechanisms during online Acceptance & Commitment Therapy for chronic pain. *Behaviour Research and Therapy*, *74*, 50–59. https://doi.org/10.1016/j.brat.2015.09.001

Vasiliou, V. S., Karademas, E. C., Christou, Y., Papacostas, S., & Karekla, M. (2021). Acceptance and Commitment Therapy for Primary Headache Sufferers: A Randomized Controlled Trial of Efficacy. *The Journal of Pain*, *22*(2), 143–160. https://doi.org/10.1016/j.jpain.2020.06.006

Vasiliou, V. S., Karekla, M., Michaelides, M. P., & Kasinopoulos, O. (2018). Construct validity of the G-CPAQ and its mediating role in pain interference and adjustment. *Psychological Assessment*, *30*(2), 220–230. https://doi.org/10.1037/pas0000467

Vasiliou, V. S., Michaelides, M. P., Kasinopoulos, O., & Karekla, M. (2019). Psychological Inflexibility in Pain Scale: Greek adaptation, psychometric properties, and invariance testing across three pain samples. *Psychological Assessment*, *31*(7), 895–904. https://doi.org/10.1037/pas0000705

Villatte, J. L., Vilardaga, R., Villatte, M., Plumb Vilardaga, J. C., Atkins, D. C., & Hayes, S. C. (2016). Acceptance and Commitment Therapy modules: Differential impact on treatment processes and outcomes. *Behaviour Research and Therapy*, *77*, 52–61. https://doi.org/10.1016/j.brat.2015.12.001

Vowles, K. E., & McCracken, L. M. (2008). Acceptance and values-based action in chronic pain: A study of treatment effectiveness and process. *Journal of Consulting and Clinical Psychology*, *76*(3), 397–407. https://doi.org/10.1037/0022-006X.76.3.397

Vowles, K. E., McCracken, L. M., & O'Brien, J. Z. (2011). Acceptance and values-based action in chronic pain: A three-year follow-up analysis of treatment effectiveness and process. *Behaviour Research and Therapy*, *49*(11), 748–755. https://doi.org/10.1016/j.brat.2011.08.002

Vowles, K. E., Wetherell, J. L., & Sorrell, J. T. (2009). Targeting acceptance, mindfulness, and values-based action in chronic pain: Findings of two preliminary trials of an outpatient group-based intervention. *Cognitive and Behavioral Practice*, *16*(1), 49–58. https://doi.org/10.1016/j.cbpra.2008.08.001

Vowles, K. E., Witkiewitz, K., Levell, J., Sowden, G., & Ashworth, J. (2017). Are reductions in pain intensity and pain-related distress necessary? An analysis of within-treatment change trajectories in relation to improved functioning following interdisciplinary acceptance and commitment therapy for adults with chronic pain. *Journal of Consulting and Clinical Psychology*, *85*(2), 87–98. https://doi.org/10.1037/ccp0000159

Vowles, K. E., Witkiewitz, K., Sowden, G., & Ashworth, J. (2014). Acceptance and Commitment Therapy for Chronic Pain: Evidence of Mediation and Clinically Significant Change Following an Abbreviated Interdisciplinary Program of Rehabilitation. *The Journal of Pain*, *15*(1), 101–113. https://doi.org/10.1016/j.jpain.2013.10.002

Vowles, K., McCracken, L., & Zhao-O'Brien, J. (2010). Acceptance and values-based action in chronic pain: An analysis of treatment outcomes and processes three years after treatment completion. *The Journal of Pain*, *11*(4), 748–755. https://doi.org/10.1016/j.jpain.2010.01.228

Wicksell, R. K., Lekander, M., Sorjonen, K., & Olsson, G. L. (2010). The Psychological Inflexibility in Pain Scale (PIPS) – Statistical properties and model fit of an instrument to assess change processes in pain related disability. *European Journal of Pain*, *14*(7), 771.e1-771.e14. https://doi.org/10.1016/j.ejpain.2009.11.015

Wicksell, R. K., Olsson, G. L., & Hayes, S. C. (2010). Psychological flexibility as a mediator of improvement in Acceptance and Commitment Therapy for patients with chronic pain following whiplash. *European Journal of Pain*, *14*(10), 1059.e1-1059.e11. https://doi.org/10.1016/j.ejpain.2010.05.001

Wiedermann, W., & von Eye, A. (2015). Direction of effects in mediation analysis. *Psychological Methods*, *20*(2), 221–244. https://doi.org/10.1037/met0000027

Ziegler, D. K., & Paolo, A. M. (1995). Headache symptoms and psychological profile of headache-prone individuals: a comparison of clinic patients and controls. *Archives of neurology*, *52*(6), 602-606.

Table 1:
Overview of Mediators and Outcome Variables Examined

Variables	Time score	
Mediators		
Pain Acceptance (G-CPAQ**)** Pain Fusion (G-PIPS-fus**)** Pain avoidance (G-PIPS-avoid) Committed Actions (CAQ**)** Value Progress (VQ-Ob**)** Value Obstructions (VQ-Pr**)** Mindfulness (CAMS-R**)**	T1-T2 change scores	T1-T3 change scores
Outcomes (Dependent variables)		
General Disability (HDI**)** Functional Disability (HDI-Func) Emotional Disability (HDI-Em.) Role Restrictive (MSQ-RR) Role Preventive (MSQ-RP) Role Emotional (MSQ-EF)	T1-T2 change scores	T1-T3 change scores

Note 1: The independent variable in all mediation models tested was the treatment condition (the conditions (ACT=0 vs. WL=1) which were coded following Hayes et al., 2014 indicator coding approach. Given the small number of participants per group, multiple simple mediation analyses were run per mediator. To reduce statistical errors resulting from running multiple simple mediation analyses, a stricter 95%, instead of 90%, BCa CI was set. 95% was therefore used to interpret the mediation effects.
Note 2: Analyses were examined in two ways: (a) in terms of the effects of treatment on outcomes' (HDI and MSQ) pre to post change scores (T1-T2) through all the possible mediators, and (b) in terms of the effects of treatment on outcomes pre to 3-month follow-up change scores (T1-T3) through the same possible mediators (see Figure 1).
Note 3: G-CPAQ= The Greek Chronic Pain Acceptance Questionnaire; G-PIPS-II =The Greek Psychological Inflexibility in Pain Scale; CAQ =Committed Action Questionnaire; VQ= The Valuing Questionnaire; CAMS-R=The Cognitive Affective Mindfulness Scale-Revised**;** HDI=The Henry Ford Hospital Headache Disability Inventory; MSQ=The Migraine-Specific Quality of Life Questionnaire.

Table 2:

Descriptive Statistics and Correlations between change scores from treatment outcomes with change scores from mediators both from T1 to T2.

	Variables	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
1	HDI-T													
2	HDI-Func.	.92**												
3	HDI-EM	.93**	.73**											
4	MSQ-RR	-.40**	-.44**	-.32**										
5	MSQ-RP	-.34**	-.35**	-.31**	.82**									
6	MSQ-EM	-.47**	-.38**	-.49**	.63**	.57**								
7	G-CPAQ	-.38**	-.41**	-.30*	.44**	.34**	.29*							
8	G-PIPS-Fus.	.33**	.28*	.31*	-.10	-.09	-.21	-.33**						
9	G-PIPS-av.	.32**	.31**	.30*	-.20	.44	-.20	-.47**	.54**					
10	CAQ	-.03	.04	-.08	.07	-.24	.14	-.09	-.15	-.18				
11	VQ-Pr.	.-.15	-.12	-.16	.12	.08	.07	.02	-.02	-.13	.31			
12	VQ-Ob.	.18	.21	.15	.30	-.20	-.03	-.03	.03	.20	-.34**	-.31**		
13	CAMS-R	-.09	-.08	-.06	.05	.07	-.19	-.08	.09	-.14	.19	.43**	-.28*	
	M	10.71	5.86	6.34	-13.15	2.90	-8.88	-2.53	2.53	4.16	-1.36	-.40	1.25	-1.28
	SD	20.02	9.10	11.01	19.44	21.79	23.02	5.52	4.35	9.24	6.29	5.48	6.50	4.25

Notes: T1-T2=Pre and Post change scores; HDI-T=Headache Disability Inventory- Total; HDI-Func.=Headache Disability Inventory- Functional; HDI-EM=Headache Disability Inventory- Emotional; MSQ-RR=Migraine-specific Quality of Life-Role Restrictive; MSQ-RP=Migraine-specific Quality of Life-Role Preventive; MSQ-EM=Migraine-specific Quality of Life- Emotional Role; G-CPAQ=Greek Chronic Pain Acceptance Questionnaire; G-PIPS-av.=Greek Psychological Inflexibility in Pain Scale- avoidance; G-PIPS-fus.=Greek Psychological Inflexibility in Pain Scale-Fusion; CAQ=Committed Action Questionnaire; VQ-Pr.=Values Questionnaire Progress; VQ-Ob.=Values Questionnaire Obstruction; CAMS-R=Cognitive and Affective Mindfulness Scale-Revised; Mean, SD= Standard Deviation, ***p < .000, ** p < .01, * p < .05.

Table 3:

Descriptive Statistics and Correlations between change scores from treatment outcomes with change scores from mediators both from T1 to T3.

	Variables	1	2	3	4	5	6	7	8	9	10	11	12	13
1	HDI-T													
2	HDI-Func.	.93**												
3	HDI-EM	.94**	.75**											
4	MSQ-RR	-.58**	-.62**	-.48**										
5	MSQ-RP	-.65**	-.62**	-.59**	.73**									
6	MSQ-EM	-.50**	-.46**	-.48**	.61**	.67**								
7	G-CPAQ	-.48**	-.46**	-.43**	.32*	.29*	.39**							
8	G-PIPS-av.	.43**	.38**	.43**	-.22	-.21	-.36**	-.68**						
9	G-PIPS-Fus.	50**	.42**	.50**	-.19	-.20	-.28*	-.53**	.51**					
10	CAQ	-.08	-.09	-.06	.25	.05	.11	.05	-.18	-.12				
11	VQ-Pr.	-.05	-.04	-.04	.13	.07	-.14	-.19	.17	.01	.23			
12	VQ-Ob.	.35**	.42**	.23	-.34**	-.35**	-.06	-.19	.10	.01	-.37**	-.31*		
13	CAMS-R	-.34**	-.32*	-.32**	.31*	.21	.02	.16	-.31*	-.23	.32**	.54**	-.37**	
	M	10.71	13.68	5.87	7.29	6.34	6.39	-3.29	2.98	5.01	-1.17	-1.10	.09	-.81
	SD	20.02	18.63	9.99	9.54	11.01	10.38	6.78	5.24	8.08	4.35	5.25	5.90	3.51

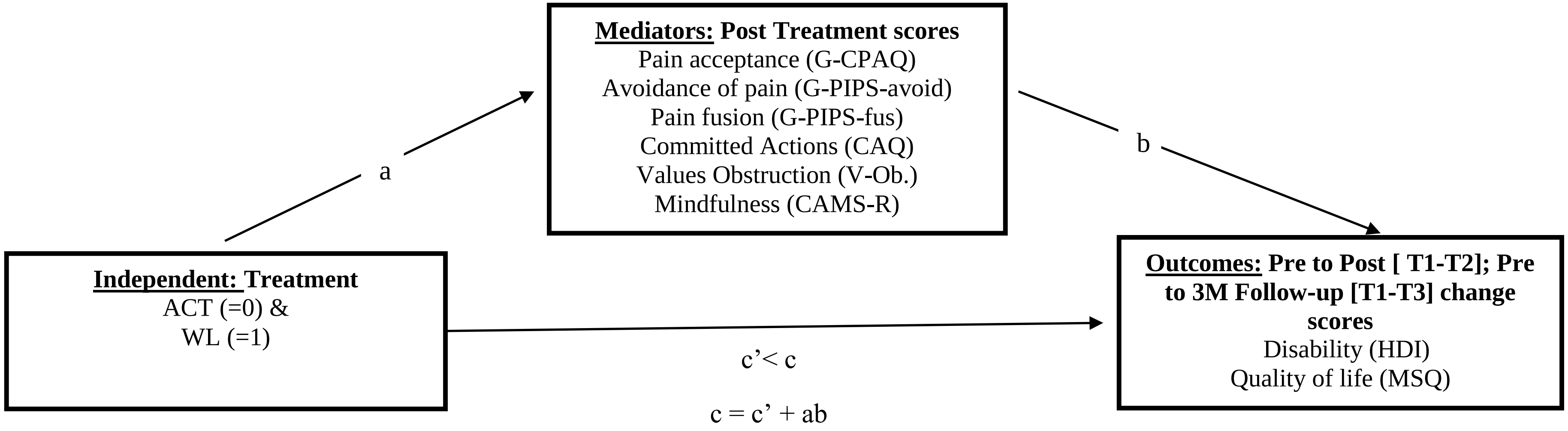
Notes: T1-32=Pre and 3M-FUP change scores; M=HDI-T=Headache Disability Inventory- Total; HDI-Func.=Headache Disability Inventory- Functional; HDI-EM=Headache Disability Inventory- Emotional; MSQ-RR=Migraine-specific Quality of Life-Role Restrictive; MSQ-RP=Migraine-specific Quality of Life-Role Preventive; MSQ-EM=Migraine-specific Quality of Life- Emotional Role; G-CPAQ=Greek Chronic Pain Acceptance Questionnaire; G-PIPS-av.=Greek Psychological Inflexibility in Pain Scale- avoidance; G-PIPS-fus.=Greek Psychological Inflexibility in Pain Scale-Fusion; CAQ=Committed Action Questionnaire; VQ-Pr.=Values Questionnaire Progress; VQ-Ob.=Values Questionnaire Obstruction; CAMS-R=Cognitive and Affective Mindfulness Scale-Revised; Mean, SD= standard Deviation, ***$p < .000$, ** $p < .01$, * $p < .05$.

Table 4:
Results from Mediation Analyses with Disability and its Subscales as Outcome Variables

		Headache-related Disability (HDI)			**Headache specific quality of life scale (MSQ)**		
Time point	Process variables (Mediators)	HDI- Total	HDI- Functional	HDI- Emotional	MSQ-RR	MSQ-RP	MSQ-EM
T1-T2	Acceptance (G-CPAQ)						
	Avoidance of pain (G-PIPS-avoid.)						
	Fusion with pain-related thoughts (G-PIPS-Fus.)						
	Committed Actions (CAQ)						
	Values progress (VQ-Pro.)						
	Values obstruction (VQ-Ob.)						
	Mindfulness (CAMS-R)						
T1-T3	Acceptance (G-CPAQ)						
	Avoidance of pain (G-PIPS-avoid.)						
	Fusion with pain-related thoughts (G-PIPS-Fus.)						
	Committed Actions (CAQ)						
	Values progress (VQ-Pro.)						
	Values obstruction (VQ-Ob.)						
	Mindfulness (CAMS-R)						

Note 1:T1=pre-treatment; T2= Post-treatment; T3= 3-Months follow-up; G-CPAQ= The Greek Chronic Pain Acceptance Questionnaire; G-PIPS-II =The Greek Psychological Inflexibility in Pain Scale; CAQ =Committed Action Questionnaire; VQ= The Valuing Questionnaire; CAMS-R=The Cognitive Affective Mindfulness Scale-Revised**.** HDI=The Henry Ford Hospital Headache Disability Inventory; MSQ=The Migraine-Specific Quality of Life Questionnaire.
Note 2: Black colored boxes represent mediation effects of the ACT treatment on outcomes at BCa 95% CI (See supplementary table S2 for bootstrap results for indirect effects: bias corrected & accelerated confidence internals. White boxes= no mediation effect.

Figure 1: *Schematic Representation of the Hypothesized Mediation model (Mediators Entered One at a Time).*



Notes: c= total effect (X→Y); c'= direct effect; c'+ab= indirect effect; Mediation (indirect effect; c'+ab) occurs if the strength of the relation between the predictor and outcomes (this is the c path; total) is reduced when a mediator is added. In this case, when the total (c) and indirect effects (c'+ab) are not significant (Hayes, 2013), a mediation exists. The independent variable was coded following Hayes et al., 2014 indicator coding approach.

Supplementary Table S1: Between Group Comparisons for the Outcomes (Dependent variables) and Mediators at T1-T2 and T1-T3 Change Scores

	Group	M (*SD*)	t	*p*-value	Effect sizes (*d*)[1]
Outcome Variables (change scores)					
HDI: T1-T2	ACT	16.67 (*19.89*)	2.40	.001	.55
	WL	5.90 (*19.02*)			
HDI: T1-T3	ACT	20.06 (*19.69*)	2.85	.006	.72
	WL	7.29 (*15.28*)			
HDI-Func: T1-T2	ACT	9.35 (*9.34*)	2.86	.005	.66
	WL	3.05 (*9.72*)			
HDI-Func: T1-T3	ACT	10.97 (*9.12*)	3.27	.002	.83
	WL	3.61 (*8.60*)			
HDI-Em: T1-T2	ACT	8.53 (*11.42*)	1.57	.120	.36
	WL	4.57 (*10.46*)			
HDI-Em: T1-T3	ACT	9.10 (*11.66*)	2.11	.039	.54
	WL	3.68 (*8.26*)			
MSQ-RR: T1-T2	ACT	-16.72 (*20.80*)	-1.45	.152	.33
	WL	-10.27 (*18.02*)			
MSQ-RR: T1-T3	ACT	-20.37 (*19.78*)	-2.75	.008	.70
	WL	-8.29 (*14.33*)			
MSQ-RP: T1-T2	ACT	-.33 (*22.71*)	-.1.16	.246	.27
	WL	5.53 (20.92)			
MSQ-RP: T1-T3	ACT	-15.81 (20.58)	-2.34	.022	.60
	WL	-3.39 (*21.11*)			
MSQ-EF: T1-T2	ACT	-11.57 (*24.08*)	-.917	.362	.21
	WL	-6.67 (*22.16*)			
MSQ-EF: T1-T3	ACT	-.14.62 (*21.60*)	-1.40	.168	.35
	WL	-4.52 (*34.01*)			
Mediators (change scores)					
Pain Acceptance (G-CPAQ) T1-T2	ACT	-4.14 (5.*18*)	-2.45	.01	.58
	WL	-1.02 (5.*46*)			
Pain Acceptance (G-CPAQ) T1-T3	ACT	-5.49 (*5.09*)	5.09	.01	.72

	WL	-.86 (*7.64*)			
Pain Fusion (G-PIPS-fus.) T1-T2	ACT	3.76 (4.*62*)	2.39	.02	.57
	WL	1.34 (3.*76*)			
Pain Fusion (G-PIPS-fus.) T1-T3	ACT	4.74 (5.17)	2.91	.01	.77
	WL	.96 (4.63)			
Avoidance of Pain (G-PIPS-avoid) T1-T2	ACT	7.30 (*7.55*)	2.41	.02	.65
	WL	2.24 (*7.97*)			
Avoidance of Pain (G-PIPS-avoid) T1-T3	ACT	6.79 (7.77)	2.37	.02	.58
	WL	1.62 (9.93)			
Committed Actions (CAQ) T1-T2	ACT	-1.73 (5.*79*)	-.48	.63	.11
	WL	-1.00 (6.80)			
Committed Actions (CAQ) T1-T3	ACT	-1.83 (4.10)	-1.25	.21	.33
	WL	-.41 (4.59)			
Values Progress (VQ-Pr.) T1-T2	ACT	-79 (*4.34*)	-.58	.56	.14
	WL	-.03 (*6.44*)			
Values Progress (VQ-Pr.) T1-T3	ACT	-1.10 (4.22)	.01	.99	.01
	WL	-1.11 (6.27)			
Values Obstructions (VQ-Ob) T1-T2	ACT	3.00 (*6.77*)	2.24	.02	.54
	WL	-.39 (5.*87*)			
Values Obstructions (VQ-Ob) T1-T3	ACT	2.25 (6.22)	1.80	.08	.47
	WL	-.46 (5.21)			
Mindfulness (CAMS-R) T1-T2	ACT	-1.47 (3.*89*)	-.35	.72	.08
	WL	-1.11 (4.*61*)			
Mindfulness (CAMS-R) T1-T3	ACT	-1.29 (3.74)	-1.12	.26	.29
	WL	-.26 (3.19)			

Note 1. Effect sizes were assessed using Cohen's *d* as follow: *d* = 0.2 (small effect), *d* = 0.5 (medium effect), and *d* = 0.8 (large effect; Cohen, 1988).

Table S2: *Results from Mediation Analyses with Disability and its Subscales as Outcome variables (HDI; T1-T2 Change Scores)*

							Bootstrap results for indirect effects: bias corrected & accelerated confidence internals (BCa), (95% CI)[2]	
Mediators Change Scores (T1-T2)		Paths	Coefficient	SE	*t* [1]	*p*	Lower	Upper
			General Disability (HDI)					
CPAQ	Pain Acceptance	*a*	3.11	1.27	2.44	<.0001		
		b	-1.20	.42	-2.82	.0062		
		Total (*c*)	-12.20	4.70	-2.59	.0115		
		Direct (*c'*)	-8.44	4.66	-1.80	.0748		
		a * *b*					-7.51	-.55
PIPS-Avoid.	Avoidance of pain	*a*	-5.17	2.18	-2.36	.0209		
		b	.58	.27	2.17	.0338		
		Total (*c*)	-11.89	4.89	-2.43	.0178		
		Direct (*c'*)	-8.86	4.95	-1.78	.0786		
		a * *b*					-7.68	-.011
PIPS-Fus.	Fusion with pain	*a*	-2.42	1.01	-2.38	.0198		
		b	1.21	.55	2.20	.0311		
		Total (c)	-12.93	4.60	-2.74	.0077		
		Direct (*c'*)	-9.99	4.76	-2.06	.0399		
		a * *b*					-8.01	.048
CAQ	Committed Actions	*a*	.73	1.08	-1.60	.1145		
		b	-.03	.38	-.08	.9325		
		Total (c)	-12.02	4.76	-2.52	.0140		
		Direct (*c'*)	-11.99	4.80	-2.49	.0151		
		a * *b*					-.92	2.42
VQ-Pr.	Values Progress	*a*	.76	1.32	.58	.5655		

		b	-.50	.43	-1.14	.2547		
		Total (c)	-12.01	4.76	-2.52	.0140		
		Direct (*c'*)	-11.63	4.76	-2.44	.0173		
		a * *b*					-2.16	1.25
VQ-Ob.	Values Obstruction	*a*	-3.39	1.51	-2.42	.0283		
		b	.34	.38	.92	.0270		
		Total (c)	-12.20	4.70	-2.60	.0115		
		Direct (*c'*)	-11.02	4.87	-2.26	.0270		
		a * *b*					-.22	.09
CAMS-R	Mindfulness	*a*	.35	1.02	.35	.7266		
		b	-.36	.55	-.65	.5170		
		Total (c)	-12.20	4.69	-2.59	.0115		
		Direct (*c'*)	-12.07	4.72	-2.55	.0129		
		a * *b*					-1.65	1.40
		Functional Disability (HDI-Func)						
G-CPAQ	Pain Acceptance	*a*	3.11	1.27	2.44	.0170		
		b	-.63	.20	-3.06	.0031		
		Total (c)	-6.90	2.31	-2.98	.0039		
		Direct (*c'*)	-4.92	2.27	-2.16	.0340		
		a * *b*					-.42	-.32
G-PIPS-Av.	Avoidance of Pain	*a*	-5.17	2.18	-2.36	.0209		
		b	.28	.13	2.02	.0472		
		Total (c)	-6.74	2.41	-2.79	.0068		
		Direct (*c'*)	-5.34	2.45	-2.18	.0332		
		a * *b*					-3.43	-.06
G-PIPS-Fus.	Fusion with Pain	*a*	-2.42	1.01	-2.38	.0198		
		b	.45	.27	1.67	.0984		
		Total (c)	-7.41	2.28	-3.24	.0018		
		Direct (*c'*)	-6.31	2.35	-2.68	.0091		
		a * *b*					-3.03	.20
CAQ	Committed Actions	*a*	.73	1.52	.48	.6310		

		b	.10	.19	.54	.5881		
		Total (c)	-6.95	2.35	-2.98	.0041		
		Direct (*c'*)	-7.02	2.36	-2.97	.0041		
		a * *b*					-.03	.14
VQ- Pr.	Value Progress	*a*	.76	1.32	.58	.5655		
		b	-.18	.21	-.84	.3991		
		Total (c)	-6.95	2.35	-2.96	.0042		
		Direct (*c'*)	-6.81	2.35	-2.89	.0052		
		a * *b*					-.93	.52
VQ-Ob.	Value Obstruction	*a*	-3.39	1.52	-2.24	.0283		
		b	.20	.18	1.07	.2870		
		Total (c)	-6.91	2.31	-2.98	.0039		
		Direct (*c'*)	-6.23	2.39	-2.61	0.113		
		a * *b*					-2.55	.98
CAMS-R	Mindfulness	*a*	.36	1.02	.35	.7266		
		b	-.16	.27	-.57	.5683		
		Total (c)	-6.90	2.31	-2.98	.0039		
		Direct (*c'*)	-6.85	2.32	-2.94	.0044		
		a * *b*					-.78	.72
Emotional Disability (HDI-Em)								
G-CPAQ	Pain Acceptance	*a*	3.12	1.27	2.44	.0170		
		b	-.53	.24	-2.19	.0318		
		Total (c)	-4.75	2.65	-1.79	.0776		
		Direct (*c'*)	-3.07	2.69	-1.14	.2577		
		a * *b*					-3.69	-.10
G-PIPS- Avoid.	Avoidance of Pain	*a*	-5.17	2.18	-2.38	.0209		
		b	.03	.15	2.12	.0372		
		Total (c)	-4.65	2.75	-1.68	.0960		
		Direct (*c'*)	-.298	2.80	-1.06	.2912		
		a * *b*					-4.63	.01
G-PIPS-Fus.	Fusion with pain	*a*	-2.42	1.01	-2.38	.0198		

		b	.69	.31	2.21	.0304		
		Total (c)	-4.92	2.68	-1.84	.0707		
		Direct (*c'*)	-3.24	2.71	-1.19	.2365		
		a * *b*					-4.79	.05
CAQ	Committed Actions	*a*	.73	1.52	.48	.6310		
		b	-.12	.22	-.58	.5607		
		Total (c)	-4.52	2.68	-1.69	.0956		
		Direct (*c'*)	-4.43	2.69	-1.65	.1048		
		a * *b*					-.73	1.07
VQ-Prog.	Values Progress	*a*	.76	1.32	.58	.5655		
		b	-.31	.24	-1.28	.2059		
		Total (c)	-4.42	2.67	-1.69	.0956		
		Direct (*c'*)	-4.29	2.67	-1.60	.1135		
		a * *b*					-1.32	.66
VQ-Obstr.	Values Obstruction	*a*	-3.39	1.41	-2.24	.0283		
		b	.17	.21	.83	.4135		
		Total (c)	-4.75	2.65	-1.79	.0776		
		Direct (*c'*)	-4.15	2.75	-1.50	.1359		
		a * *b*					-2.33	.75
CAMS-R	Mindfulness	*a*	.35	1.02	.35	.7266		
		b	-.14	.31	-.45	.6519		
		Total (c)	-4.75	2.65	-1.79	.0776		
		Direct (*c'*)	-4.70	2.66	-1.76	.0829		
		a * *b*					-.92	.71

Note 1: T1-T2 = pre to post treatment change scores
Note 2: Bootstrap distribution in adjusted for bias and skewness at ninety-five percentage confidence interval equates $p < .05$ (BCa; 95% CI).

Table S3: Results from Mediation Analyses with Disability and its Sub-scales (HDI; T1-T3 change scores) as Outcome variables

Mediators Change Scores T1-T3		Paths	Coefficient	SE	t[1]	p	Bootstrap results for indirect effects: bias corrected & accelerated confidence internals (BCa) (95% CI)[2] Lower	Upper
		General Headache Disability (HDI)						
G-CPAQ	Pain Acceptance	*a*	*4.62*	1.67	2.76	.0077		
		b	-1.05	.32	-3.21	.0022		
		Total (*c*)	-15.27	4.46	-3.42	.0011		
		Direct (*c'*)	-10.41	4.40	-2.36	.0215		
		a * *b*					-9.59	-1.19
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.06	2.09	-2.42	.0194		
		b	.78	.29	2.69	.0095		
		Total (*c*)	-16.69	4.73	-3.52	.0009		
		Direct (*c'*)	-12.70	4.71	-2.69	.0095		
		a * *b*					-11.79	-.03
G-PIPS-Fus.	Fusion with pain	*a*	-3.77	1.30	-2.91	.0051		
		b	1.43	.42	3.34	.0015		
		Total (*c*)	-15.54	4.53	-3.43	.0012		
		Direct (*c'*)	-10.11	4.48	-2.26	.0279		
		a * *b*					-12.02	-.77
CAQ	Committed Actions	*a*	1.42	1.14	1.25	.2150		
		b	-.05	.52	-.11	.9145		
		Total (*c*)	-14.14	4.41	-3.21	.0022		
		Direct (*c'*)	-14.05	4.51	-3.12	.0029		
		a * *b*					-2.22	1.92
VQ-Prog.	Values Progress	*a*	-.01	1.38	-.01	.2535		
		b	-.16	.43	-.37	.7058		

		Total (*c*)	-15.28	4.47	-3.42	.0011		
		Direct (*c'*)	-15.28	4.49	-3.40	.0012		
		a * *b*					-1.50	1.28
VQ-Ob.	Values Obstruction	*a*	-2.72	1.51	-1.80	.0786		
		b	.83	.37	2.20	.0319		
		Total (*c*)	-15.27	4.46	-3.42	.0011		
		Direct (*c'*)	-13.01	4.43	-2.93	.0049	-5.94	.27
		a * *b*						
CAMS-R	Mindfulness	*a*	1.03	.92	1.11	.2677		
		b	-1.55	.63	-2.45	.0172		
		Total (*c*)	-15.17	4.54	-3.34	.0015		
		Direct (*c'*)	-13.58	4.40	-3.09	.0032		
		a * *b*					-5.88	.98
Functional Disability (HDI-Func.)								
G-CPAQ	Pain Acceptance	*a*	4.62	1.67	2.76	.0077		
		b	-.48	.16	-2.93	.0049		
		Total (*c*)	-8.61	2.25	-3.83	.0003		
		Direct (*c'*)	-6.40	2.25	-2.83	.0066		
		a * *b*					-4.84	-.33
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.06	2.10	-2.41	.0194		
		b	.32	.15	2.09	.0407		
		Total (*c*)	-9.23	2.39	-3.85	.0003		
		Direct (*c'*)	-7.61	2.44	-3.11	.0030		
		a * *b*					-5.41	.18
G-PIPS-Fus.	Fusion with pain	*a*	-3.78	1.29	-2.91	.0051		
		b	.54	.22	2.43	.0182		
		Total (*c*)	-8.82	2.28	-3.86	.0003		
		Direct (*c'*)	-6.75	2.35	-2.87	.0057		
		a * *b*					-11.45	-2.05
CAQ	Committed Actions	*a*	1.43	1.14	1.25	.2150		
		b	-.03	.26	-.13	.8957		

		Total (*c*)	-8.00	2.21	-3.61	.0006		
		Direct (*c'*)	-7.95	2.26	-3.51	.0009		
		a * *b*					-12.44	-3.56
VQ-Pr.	Value Progress	*a*	-.01	1.38	-.01	.9940		
		b	-.08	.22	-.37	.7095		
		Total (*c*)	-8.61	2.27	-3.80	.0004		
		Direct (*c'*)	-8.61	2.26	-3.80	.0004		
		a * *b*					-13.15	-4.08
VQ-Obs.	Values Obstruction	*a*	-7.12	2.17	-3.28	.0018		
		B	.54	.18	2.96	.0044		
		Total (*c*)	-8.61	2.25	-3.83	.0003		
		Direct (*c'*)	-7.12	2.16	-3.28	.0018		
		a * *b*					-3.96	.02
CAMS-R	Mindfulness	*a*	1.03	.92	1.11	.2677		
		b	-.71	.32	-2.21	.0307		
		Total (*c*)	-8.52	2.28	-3.73	.0005		
		Direct (*c'*)	-7.78	2.23	-3.48	.0010		
		a * *b*					-12.28	-3.30
Emotional Disability (HDI-Em.)								
G-CPAQ	Pain Acceptance	*a*	4.62	1.67	2.76	.0077		
		b	-.56	.19	-2.93	.0049		
		Total (*c*)	-6.67	2.58	-1.57	.1212		
		Direct (*c'*)	-4.07	.258	-1.58	.1212.		
		a * *b*					-4.89	-.67
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.06	2.10	-2.42	.0194		
		β	.47	.16	2.80	.0071		
		Total (*c*)	-7.47	2.72	-2.74	.0083		
		Direct (*c'*)	-5.08	2.69	-1.88	.0651		
		a * *b*					-6.59	-.04
G-PIPS-Fus.	Fusion with pain	*a*	-3.78	1.29	-2.91	.0051		

		β	.88	.24	3.61	.0007		
		Total (*c*)	-6.72	2.63	-2.55	.0133		
		Direct (*c'*)	-3.37	2.56	-1.31	.1940		
		a * *b*					-7.61	-.66
CAQ	Committed Actions	*a*	1.43	1.14	1.25	.2150		
		b	-.02	.30	-.07	.9434		
		Total (*c*)	-6.13	2.58	-2.37	.0209		
		Direct (*c'*)	-6.10	2.64	-2.31	.0246		
		a * *b*					-1.13	1.26
VQ-Pr.	Value Progress	*a*	-.01	1.38	-.01	.2535		
		b	-.08	.25	-.33	.7433		
		Total (*c*)	-6.67	2.58	-2.58	.0125		
		Direct (*c'*)	-6.67	.260	-2.56	.0132		
		a * *b*					-.85	.71
VQ-Obs.	Values Obstruction	*a*	-2.25	1.04	2.17	.0342		
		β	.29	.22	1.26	.2118		
		Total (*c*)	-6.67	2.58	-2.58	.0125		
		Direct (*c'*)	-5.89	2.64	-2.22	.0298		
		a * *b*					-2.39	.44
CAMS-R	Mindfulness	*a*	1.03	.92	1.11	.2677		
		b	-.84	.36	-2.27	.0267		
		Total (*c*)	-6.65	2.63	-2.52	.0144		
		Direct (*c'*)	-5.78	2.56	-2.25	.0282		
		a * *b*					-3.42	.50

Note 1: T1-T3 = pre to three months follow-up change scores
Note 2: Bootstrap distribution in adjusted for bias and skewness at ninety-five percentage confidence interval equates p < .05 (BCa; 95% CI).

Table S4: Results from Mediation Analyses with Quality-of-Life Dimensions (MSQ; T1-T2 change scores) as Outcome Variables

							Bootstrap results for indirect effects: bias corrected & accelerated confidence internals (BCa) (95% CI)[2]	
Mediators Change Scores (T1-T2)		Paths	Coefficient	SE	t^1	*p*	Lower	Upper
			Role Restrictive (MSQ-RR)					
G-CPAQ	Pain Acceptance	*a*	3.11	1.27	2.45	.0170		
		b	1.33	.38	3.46	.0009		
		Total (*c*)	9.89	4.35	2.27	.0262		
		Direct (*c'*)	5.74	4.21	1.36	.1774		
		a * *b*					.68	8.43
G-PIPS-Avoid.	Avoidance of Pain	*a*	-5.17	2.18	-2.37	.0209		
		b	-.28	.25	-1.09	.2786		
		Total (*c*)	9.57	4.51	2.12	.0378		
		Direct (*c'*)	8/12	4.69	1.72	.0885		
		a * *b*					-.43	4.99
G-PIPS-Fus.	Fusion with pain	*a*	-2.42	1.01	-2.38	.0198		
		b	-.09	.52	-.17	.8649		
		Total (*c*)	10.85	4.30	2.52	.0141		
		Direct (*c'*)	10.62	4.51	2.35	.0216		
		a * *b*					-2.53	3.64
CAQ	Committed Actions	*a*	.73	1.52	.48	.6310		
		b	.15	.35	.44	.6626		
		Total (*c*)	9.21	4.35	2.11	.0383		
		Direct (*c'*)	9.10	4.39	2.07	.0422		
		a * *b*					-1.75	1.47

VQ-Pr	Values Progress	*a*	.76	1.32	.58	.5655		
		b	.36	.40	.91	.3620		
		Total (*c*)	9.21	4.35	2.11	.0383		
		Direct (*c'*)	8.92	4.37	2.04	.0452		
		*a * b*					-1.18	1.66
VQ-Ob.	Values Obstruction	*a*	-3.39	1.52	-2.24	.0283		
		b	-.17	.35	-.49	.6263		
		Total (*c*)	9.89	4.35	2.27	.0262		
		Direct (*c'*)	9.31	4.53	2.05	.0440		
		*a * b*					-3.74	5.40
CAMS-R	Mindfulness	*a*	.35	1.02	.35	.73		
		b	.17	.52	2.24	.0283		
		Total (*c*)	9.89	4.36	2.27	.0262		
		Direct (*c'*)	9.83	4.38	2.24	.0283		
		*a * b*					1.08	18.59
			Role Preventive (MSQ-RP)					
G-CPAQ	Pain Acceptance	*a*	3.11	1.27	2.45	.0170		
		b	1.19	.45	2.59	.0118		
		Total (*c*)	8.94	5.02	1.78	.0795		
		Direct (*c'*)	5.23	5.03	1.04	.3020		
		*a * b*					-4.81	15.29
G-PIPS-Fus.	Fusion with pain	*a*	-2.42	1.01	-2.38	.0198		
		b	-.16	.61	-.27	.7884		
		Total (*c*)	9.58	5.05	1.89	.0623		
		Direct (*c'*)	9.18	5.30	1.73	.0880		
		*a * b*					-1.40	19.77
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.17	2.18	-2.36	.0209		
		b	-.46	.28	-1.61	.1121		
		Total (*c*)	7.34	5.09	1.44	.1545		
		Direct (*c'*)	4.96	5.24	.9450	.3482		
		*a * b*					-5.52	15.44
CAQ	Committed Actions	*a*	.73	1.52	.48	.6310		

		b	.23	.40	.58	.5595		
		Total (*c*)	8.17	5.03	1.62	.1091		
		Direct (*c'*)	7.99	5.06	1.57	.1192		
		a * *b*					-2.11	18.11
VQ-Pr.	Values Progress	*a*	.76	1.32	.57	.5655		
		b	.54	.46	1.18	.2426		
		Total (*c*)	8.17	5.03	1.62	.1091		
		Direct (*c'*)	7.75	5.03	1.54	.1279		
		a * *b*					-1.17	2.73
VQ-Ob.	Values Obstruction	*a*	-3.38	1.51	-2.24	.0283		
		b	-.52	.40	-1.29	.2014		
		Total (*c*)	8.94	5.02	1.78	.0795		
		Direct (*c'*)	7.19	5.18	1.38	.1697		
		a * *b*					-1.05	7.26
CAMS-R	Mindfulness	*a*	.35	1.02	.35	.7266		
		b	.32	.59	.54	.5883		
		Total (*c*)	8.94	5.02	1.78	.0795		
		Direct (*c'*)	8.83	5.05	1.75	.0853		
		a * *b*					-1.26	18.92
				Emotional Role (MSQ-EM)				
G-CPAQ	Pain Acceptance	*a*	3.20	1.28	2.48	.0155		
		b	1.10	.51	2.13	.0368		
		Total (*c*)	7.37	5.59	1.31	.1920		
		Direct (*c'*)	3.85	5.70	.67	.5020		
		a * *b*					-7.53	15.23
G-PIPS-Fus.	Fusion with pain	*a*	-2.467	1.02	-2.40	.0191		
		b	-.94	.67	-1.40	.1651		
		Total (*c*)	7.45	5.68	1.31	.1942		
		Direct (*c'*)	5.11	5.88	.86	.3880		
		a * *b*					-1.08	7.64
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.15	2.21	-2.32	.0233		
		b	-.44	.32	-1.34	.1838		

		Total (*c*)	7.07	5.82	1.21	.2295		
		Direct (*c'*)	4.81	6.03	.79	.4283		
		a * *b*					-1.29	7.35
CAQ	Committed Actions	*a*	.88	1.54	.57	.5683		
		b	.49	.44	1.11	.2669		
		Total (*c*)	6.07	5.52	1.10	.2749		
		Direct (*c'*)	5.64	5.52	1.02	.3108		
		a * *b*					-5.39	16.67
VQ-Ob.	Value Obstruction	*a*	-3.34	1.53	-2.18	.0327		
		b	.04	.44	.10	.9200		
		Total (*c*)	7.38	5.59	1.32	.1920		
		Direct (*c'*)	7.53	5.83	1.29	.2015		
		a * *b*					-4.12	19.19
VQ-Pr.	Value Progress	*a*	.79	1.34	.59	.5569		
		b	.25	.50	.50	.6152		
		Total (*c*)	6.07	5.56	1.05	.2952		
		Direct (*c'*)	5.87	5.56	1.05	.2952		
		a * *b*					-1.09	1.68
CAMS-R	Mindfulness	*a*	.27	1.03	.26	.7944		
		b	-1.08	.65	-1.66	.1012		
		Total (*c*)	7.38	5.59	1.31	.1920		
		Direct (*c'*)	7.67	5.53	1.38	.1699		
		a * *b*					-3.36	2.50

Note 1: T1-T2 = pre to post treatment change scores
Note 2: Bootstrap distribution in adjusted for bias and skewness at ninety-five percentage confidence interval equates $p < .05$ (BCa; 95% CI).

Table S5: Results from Mediation Analyses with Quality-of-Life Dimensions (MSQ; T1-T3 change scores) as Outcomes

							Bootstrap results for indirect effects: bias corrected & accelerated confidence internals (BCa) (95% CI)[2]	
Mediators Change Scores (T1-T3)		Paths	Coefficient	SE	*t*	*p*	Lower	Upper
			Role Restrictive Dimension (RR-MSQ)					
G-CPAQ	Pain Acceptance	*a*	4.62	1.67	2.76	.0077		
		b	.55	.33	1.62	.1100		
		Total (*c*)	14.45	4.32	3.31	.0016		
		Direct (*c'*)	11.90	4.57	2.60	.0118		
		a * *b*					.17	6.40
G-PIPS- Av.	Avoidance of Pain	*a*	-5.06	2.09	-2.41	.0149		
		b	-.25	.30	-.81	.4199		
		Total (*c*)	14.78	4.65	3.17	.0025		
		Direct (*c'*)	13.52	4.92	2.74	.0083		
		a * *b*					-.98	5.53
G-PIPS-Fus.	Pain Fusion	*a*	-3.78	1.29	-2.91	.0051		
		b	-.17	.45	-.38	.7056		
		Total (*c*)	14.86	4.41	3.36	.0014		
		Direct (*c'*)	14.21	4.78	2.93	.0044		
		a * *b*					-3.16	5.08
CAQ	Committed Actions	*a*	1.43	1.14	1.25	.2150		
		b	.79	.51	1.54	.1278		
		Total (*c*)	14.12	4.42	3.19	.0023		
		Direct (*c'*)	12.99	4.43	2.93	.0049		
		a * *b*					-.92	5.09
VQ-Pr.	Values Progress	*a*	-.01	1.38	-.01	.9940		
		b	.45	.41	1.08	.2841		
		Total (*c*)	14.45	4.35	3.31	.0016		

		Direct (*c'*)	14.45	4.39	3.32	.0016		
		a * *b*					-1.84	1.65
VQ-Ob.	Values Obstructions	*a*	-2.72	1.51	-1.80	.0768		
		b	-.80	.37	-2.15	.0356		
		Total (*c*)	14.45	4.35	3.31	.0016		
		Direct (*c'*)	12.28	4.39	2.82	.0065		
		a * *b*					-1.68	7.93
CAMS-R	Mindfulness	*a*	1.03	.92	1.11	.2677		
		b	1.34	.62	2.16	.0352		
		Total (*c*)	14.33	4.43	3.23	.0021		
		Direct (*c'*)	12.94	4.34	2.97	.0042		
		a * *b*					-1.19	4.11
Role Preventive Dimension (RP-MSQ)								
G-CPAQ	Pain Acceptance	*a*	4.63	1.67	2.76	.0077		
		b	.55	.40	1.41	.1621		
		Total (*c*)	15.44	5.02	3.07	.0033		
		Direct (*c'*)	12.86	5.31	2.42	.0186		
		a * *b*					-.21	5.92
G-PIPS-Fus.	Pain Fusion	*a*	-3.78	1.29	-2.91	.0051		
		b	-.28	.52	-.54	.5931		
		Total (*c*)	15.99	5.09	3.14	.0027		
		Direct (*c'*)	14.91	5.50	2.71	.0089		
		a * *b*					-3.48	5.63
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.06	2.09	-2.41	.0194		
		b	-.27	.35	-.77	.4456		
		Total (*c*)	15.66	5.40	2.90	.0055		
		Direct (*c'*)	14.28	5.72	2.50	.0157		
		a * *b*					-1.64	5.93
CAQ	Committed Actions	*a*	1.43	1.14	1.25	.2150		
		b	-.05	.60	-.09	.9297		
		Total (*c*)	14.88	5.09	2.92	.0050		
		Direct (*c'*)	14.95	5.21	2.87	.0058		

		a * *b*					-3.86	2.16
VQ-Pr.	Value Progress	*a*	-.01	1.38	-.01	.9940		
		b	.27	.48	.55	.5801		
		Total (*c*)	15.44	5.02	3.07	.0033		
		Direct (*c'*)	15.45	5.06	3.05	.0034		
		a * *b*					-1.17	1.83
VQ-Ob.	Value Obstructions	*a*	-2.72	1.51	-1.80	.0768		
		b	-.97	.45	-2.26	.0271		
		Total (*c*)	15.44	5.03	3.07	.0033		
		Direct (*c'*)	12.82	4.10	2.56	.0129	-.69	8.68
		a * *b*						
CAMS-R	Mindfulness	*a*	1.03	.92	1.12	.2677		
		b	.97	.73	1.31	.1943		
		Total (*c*)	15.43	5.12	3.01	.0039		
		Direct (*c'*)	14.43	5.15	2.80	.0069		
		a * *b*					-.67	4.01
			Emotional Role (MSQ-EM)					
G-CPAQ	Pain Acceptance	*a*	4.63	1.67	2.76	.0077		
		b	1.40	.53	2.65	.0104		
		Total (*c*)	14.14	7.05	2.01	.0496		
		Direct (*c'*)	7.64	7.14	1.07	.2889		
		a * *b*					-1.16	15.62
G-PIPS-Avoid.	Avoidance of pain	*a*	-5.06	2.09	-2.41	.0194		
		b	-1.09	.47	-2.30	.0252		
		Total (*c*)	14.75	7.54	1.95	.0557		
		Direct (*c'*)	9.21	7.64	1.20	.2332		
		a * *b*					-.80	15.83
G-PIPS-Fus.	Fusion with pain	*a*	-3.78	1.29	-2.91	.0051		
		b	-1.10	.72	-1.51	.1366		
		Total (*c*)	14.87	7.15	2.07	.0422		
		Direct (*c'*)	10.71	7.59	1.41	.1635		
		a * *b*					-1.66	13.98

CAQ	Committed Action	*a*	1.43	1.14	1.25	.2150		
		b	.45	.77	.58	.5628		
		Total (*c*)	11.17	6.58	1.69	.1228		
		Direct (*c'*)	10.52	6.71	1.56	.1228		
		a * *b*					-3.40	3.92
VQ-Ob.	Values Obstruction	*a*	-2.72	1.51	-1.80	.0768		
		b	.02	.62	.02	.9795		
		Total (*c*)	14.15	7.05	2.01	.0496		
		Direct (*c'*)	14.19	7.31	1.94	.0575		
		a * *b*					-5.25	5.19
VQ-Pr.	Values Progress	*a*	-.01	1.38	-.01	.9940		
		b	-.75	.67	-1.10	.2741		
		Total (*c*)	14.14	7.05	2.01	.0496		
		Direct (*c'*)	14.14	7.04	2.01	.0494		
		a * *b*					-2.50	4.11
CAMS-R	Mindfulness	*a*	1.03	.92	1.12	.2677		
		b	-.19	1.05	-.18	.8593		
		Total (*c*)	14.13	7.18	1.95	.0557		
		Direct (*c'*)	14.33	7.32	1.95	.0557		
		a * *b*					-3.61	2.23

Note 1: T1-T3 = pre to three months follow-up change scores

Note 2: Bootstrap distribution in adjusted for bias and skewness at ninety-five percentage confidence interval equates $p < .05$ (BCa; 95% CI).

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located ** Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	Page 1	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	Pages 3 & 4	
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	Pages 7-9	
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	Pages 5 & 6	
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	Page 6	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	Pages 4 & 6	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	Page 4	

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	Page 6	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.		N/A
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).		N/A
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.		n/a
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.		n/a

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).