Acceptance and Commitment Therapy for long-term conditions; and Pain acceptance clustering in a population with persistent pain

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Pernille Frisvoll

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The University of Edinburgh

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Thesis Abstract

Background and aims: Acceptance and Commitment Therapy (ACT) is increasingly used in the management of long-term conditions and is thought to reduce psychological distress and improve quality of life. The first systematic review of ACT in long term conditions was published in 2016. Given the rapid evolution of ACT in long-term conditions, we aimed to update this review and systematically review the evidence base in the past seven years (Chapter 1). Specifically, we aimed to comment on the effectiveness of ACT in reducing psychological distress and improving quality of life in these contexts and assess the methodological quality of the studies. In Chapter 2 we consider persistent pain, which is a distressing and disabling condition. Pain Management programmes reduce distress and disability associated with persistent pain, but treatment response is uneven among completers. Group composition may affect outcomes, but grouping people based on pain condition or demographic variables has shown limited utility. Research has suggested that grouping people based on their scores on the Chronic Pain Acceptance Questionnaire (CPAQ-8) may be clinically useful. Previous research indicated four clusters with different profiles based on the Activity Engagement and Pain Willingness subscales. We sought to explore CPAQ-clustering in an English-speaking sample and identify whether different clusters have different profiles of functioning and distress, which may indicate differing treatment needs.

Methods: In Chapter 1, we systematically review the evidence base for ACT in long-term conditions. Relevant databases were systematically searched for ACT intervention studies from 2015 to the present, and applications in mental health and conditions that have already been reviewed were excluded. In Chapter 2, we describe the results of an online survey exploring CPAQ clustering in a population with persistent pain. This study recruited 213 people with persistent pain through social media and specialist pain clinics, who responded to questionnaires on pain and functioning. They were divided into four clusters based on CPAQ-8 cut-off scores.

Results: Our systematic search (Chapter 1) identified 12 relevant studies, two of which were randomised controlled trials (RCTs), two were case studies/series, and eight used a pre-post design. Their methodological quality was appraised, and half were rated by a second reviewer. ACT has been applied in a wide range of conditions since 2015 (e.g. cystic fibrosis, myocardial infarction, systemic lupus), many of which have not been subject of much psychological research previously. ACT showed some effect in reducing distress. Evidence was lacking for quality of life, psychological flexibility and health indices. In Chapter 2, MANOVAs revealed cluster differences on measures of functioning (pain interference, self-efficacy, and valued living) and distress (anxiety and depression).

Discussion: Chapter 1 results indicate that ACT may improve distress across long-term conditions. Small sample sizes and lack of RCTs limit the methodological quality of the evidence base, and we offer suggestions for how future ACT intervention studies may be improved. The findings in Chapter 2 indicate that people who present to specialist pain clinics may be meaningfully grouped based on their CPAQ-8 profile. The differences between these clusters are discussed and suggestions offered for how this may inform triage and intervention in specialist pain clinics. Future research will indicate whether this in turn may improve treatment response.

Lay Summary

Living with a long-term condition often causes distress, disability and reduces quality of life. Acceptance and Commitment Therapy (ACT) is a psychological treatment that aims to help people live better with their condition and reduce the distress they experience. Previous reviews have already showed that ACT can be helpful for people with persistent pain, type 2 diabetes, neurological conditions, and cancer. In Chapter 1 we have compiled the available research on ACT for people with other long-term conditions that have been studied less. We assessed how well it works to reduce distress and improve quality of life in these contexts. The quality of these studies was generally poor, and we offered suggestions for how methodology may be improved in future studies. We found that ACT has been somewhat helpful to reduce distress in various conditions, such as cystic fibrosis, inflammatory bowel disease, systemic lupus and heart disease. There was little evidence that it helped to improve quality of life or health.

Persistent pain is a distressing and disabling condition. We know that Pain Management Programmes work very well to reduce distress and disability for some people with pain, but not all. We do not know why it works so well for some people and not others, but we have reason to think that it is important that groups are cohesive and share commonalities. The research to date shows that grouping people by age, pain site, or pain condition does not improve outcomes. Some research has shown that grouping people based on how much they accept their pain may be more useful. The Chronic Pain Acceptance Questionnaire (CPAQ) is an 8-item questionnaire that assesses how willing people are to tolerate pain (Pain Willingness), and how much they engage in daily activities despite pain (Activity Engagement). We wanted to explore whether grouping people based on their CPAQ scores would give us groups that differed in terms of their pain, levels of functioning and wellbeing. We recruited 213 people with pain via social media who took part in an online survey. We divided this sample into clusters based on their CPAQ scores and found that groups differed in pain severity, pain interference, anxiety, depression, pain self-efficacy, and valued living. This suggests that people with different levels

of pain acceptance may have different needs. We believe that grouping people in this way may be useful for pain management programmes, and we have made suggestions for how pain clinics may use this information.

Chapter 1: Systematic Review

The effectiveness of Acceptance and Commitment Therapy in reducing psychological distress and improving quality of life in long-term conditions

Pernille Frisvoll [ab], Siri Hartmann [a], and David Gillanders [a]

[a] Clinical and Health Psychology, School of Health and Social Science, University of Edinburgh, EH8 9AG

[b] NHS Lothian Pain Management Programme, Astley Ainslie Hospital, Edinburgh, EH9 2HL

Corresponding author: Pernille Frisvoll, NHS Lothian Pain Management Programme, Astley Ainslie Hospital, Edinburgh, EH9 2HL

Email:

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Abstract

Acceptance and Commitment Therapy (ACT) is increasingly used in the management of long-term conditions and is thought to reduce psychological distress and improve quality of life. The first systematic review of ACT in long-term conditions was published in 2016. Given the rapid evolution of ACT in long-term conditions, we aimed to systematically review the evidence base from the last seven years. Specifically, we aimed to comment on the effectiveness of ACT in reducing psychological distress and improving quality of life, and assess how the methodological quality of the rese arch has evolved. Medline, EMBASE, PsycInfo and PsycArticles were systematically searched for ACT intervention studies from 2015 to the present, and applications in mental health and conditions that have already been reviewed were excluded. 12 studies were included, their methodological quality was appraised, and half were rated by a second reviewer. A wide range of conditions have been studied since 2015 (e.g. cystic fibrosis, myocardial infarction, systemic lupus), many of which have not been subject of much psychological intervention research. ACT consistently showed good effect in reducing distress. Evidence was mixed for quality of life, psychological flexibility, and health indices. Small sample sizes and lack of RCTs limit the methodological quality of the evidence base. Suggestions are offered for future researchers.

Keywords

Acceptance and Commitment Therapy; Long-Term Conditions; Psychological Flexibility; Health-Related Quality of Life; Chronic Illness; Systematic Review

Introduction

Long-term physical conditions, also called chronic diseases or illnesses, are conditions that are persistent in nature and require ongoing treatment and care (World Health Organisation, 2002, p.11). Such conditions differ by symptoms, visibility, treatment and management burden, and level of stigma (Joachim & Acorn, 2000). However, they present similar challenges for the individual around treatment adherence, lifestyle changes, condition monitoring and functional impairment (May, Montori, & Mair, 2009; Eton et al., 2013). Long-term conditions are associated with increased rates of anxiety and depression (Clark & Currie, 2009), and reduced quality of life (Megari, 2013). The relationship between psychological and physical symptoms is bidirectional: psychological distress is likely to exacerbate challenges with health management and lead to poorer physical outcomes, which in turn can reduce quality of life and increase distress (Evans et al., 2005).

Medical management of long-term conditions tends to focus on symptom reduction, however; symptom severity and level of disability is not necessarily directly associated with distress or quality of life (Robbins et al., 2001). It is therefore possible to improve distress and quality of life independent of symptom reduction, which is relevant for many long-term conditions where the latter is less feasible. Psychological treatments in healthcare settings aim to reduce health-related distress and promote adaptive health behaviours. A recent meta-analysis shows that such interventions are a cost-effective alternative to usual medical care across a range of long-term conditions (NHS Education for Scotland, 2021).

One psychological intervention that has gained popularity in healthcare settings in the past two decades is Acceptance and Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 2011). The ACT model posits that distress is exacerbated and maintained by efforts to avoid or eliminate unpleasant experiences, where such efforts come at the cost of leading a meaningful life (McCracken, 1998). This is particularly relevant in long-term conditions, where individuals can get caught up in

ineffective efforts at symptom reduction while neglecting valued behaviours (e.g. avoiding movement so as not to exacerbate pain), leading to increased hopelessness and reduction in mood. Another example may be where individuals wish to avoid reminders of their condition, leading to poor adherence to treatment and management strategies, which in turn increases symptom severity and risk of complications. Similarly, individuals may get stuck in ruminations about their condition and its future prognosis, which has a detrimental impact on mood, adaptive behaviour, and functioning. These responses are referred to in ACT as psychological inflexibility (McCracken & Morley, 2014), and is a common feature among those with long-term conditions and associated distress.

ACT aims to promote the opposite, namely psychological flexibility, which is made up of six interdependent and overlapping processes: acceptance (a willingness to accept experiences as they are), contact with the present moment (non-judgemental awareness of the present), cognitive defusion (seeing thoughts as mental phenomena rather than fact), self-as-context (ability to see things from multiple perspectives), values (being aware of what is personally meaningful) and committed action (acting in line with personal values) (McCracken & Morley, 2014). Psychological flexibility is associated with better psychological and physical health outcomes (Gloster, Meyer, & Lieb, 2017; Hulbert-Williams & Storey, 2016; Kashdan & Rottenberg, 2010). In the context of long-term conditions, ACT attempts to facilitate greater psychological flexibility through acceptance of the condition (including unpleasant thoughts and symptoms), encouraging valued behaviours and a non-judgemental awareness of the present, as well as changing the relationship to difficult thoughts. Evidence shows that this leads to better adjustment to and management of long-term conditions, reduced distress and improved quality of life (A-Tjak, Davis, Morina, Powers, Smits, & Emmelkamp, 2015; Gloster, Walder, Levin, Twohig, & Karekla, 2020).

Graham, Gouick, Krahé and Gillanders (2016) conducted a systematic review of the literature on ACT for long-term conditions, concluding their search in February 2015. As this was the first review of its kind, inclusion criteria were broad, which resulted in a heterogeneous collection of

studies for review. They spanned a wide range of different settings, including paediatric and adult populations and included both individual and group, and direct and indirect (carer-led), interventions. Promising effects of ACT were found for improvements in quality of life, distress, and management of physical symptoms across a range of conditions, including HIV, cancer, diabetes, cardiac and neurological conditions. Graham and colleagues reported that methodological quality generally was low and most studies non-controlled, limiting the extent to which positive outcomes could be attributed to ACT intervention. It was therefore concluded that ACT was not yet a well-established intervention for long-term conditions at that time.

In the seven years since Graham and colleagues' systematic search, the use of ACT in clinical practice has continued to flourish, as has the research literature on ACT in long-term conditions, with new applications in conditions such as inflammatory bowel disease (Hou et al., 2017; Wynne et al., 2019), muscle disorders (Graham et al., 2017), cystic fibrosis (O'Hayer, O'Loughlin, Nurse, Smith, & Stephen, 2021), and systemic lupus (Sahebari et al., 2019), to name a few. The research literature has expanded in conditions previously reviewed by Graham and colleagues to the point where condition-specific reviews have been possible. Recent systematic reviews on ACT have been conducted in adults with cancer (Mathew, Doorenbos, Jang, & Hershberger, 2021; Li, Li, Guo, Li, & Yang; 2021; Salari et al., 2021), breast cancer (Li, Wung, Ni, Zhang, Weng, & He, 2021), persistent pain (Hughes, Clark, Colclough, Dale, & McMillan, 2017; Trindade et al., 2021), neurological conditions (Robinson, Russell, & Dysch, 2019), type 2 diabetes (Ngan, Chong, Chien, 2021), and in family caregivers of children with long-term conditions (Jin, Wong, Li, Chen, Chong, & Bai, 2020). With the advance of online delivery of psychological interventions, Herbert et al. (2022) have systematically reviewed the evidence for technology-supported ACT in various long-term conditions. All these reviews found positive effects of ACT on anxiety, depression, and psychological distress, and highlighted a general lack of methodological robustness in the literature. With small sample sizes, a paucity of randomised

controlled trials (RCTs) and few studies employing active control conditions the authors have declared it premature to clearly attribute promising results to ACT intervention. A high degree of heterogeneity of intervention type and duration has also made it difficult to make specific recommendations for clinical practice.

The Present Review

We aimed to update the systematic review by Graham and colleagues from 2016 given the rapid evolution of ACT studies in the context of long-term conditions, excluding conditions that have already been reviewed and described above. Specifically, this review will assess the effectiveness of ACT interventions in reducing psychological distress and improving quality of life for those living with long-term conditions for which the evidence is sparser at present. Secondary aims are to review the impact of ACT on psychological flexibility and health outcomes in these populations, and to document the quality of research methodology in this field seven years after the review by Graham et al. (2016).

Methods

Search Strategy

The protocol for this systematic review was registered on PROSPERO 29th November 2021 with the registration CRD42021289019. The search strategy outlined by Graham et al. (2016) was used as a basis for the current review. Databases EMBASE, Medline, PsycArticles and PsycInfo were searched, and the search limited to publications between January 2015 and 12th October 2021. The search terms used were identical to those of Graham et al. (2016): 'Acceptance and Commitment Therapy' and 'Contextual Cognitive Behavio$', combined with 'OR'. The terms were deliberately broad with the aim of capturing all ACT studies published within this timeframe, leaving it to the researcher to exclude non-relevant studies through screening. The search was repeated on 17th February 2022 to capture any studies published since the original search.

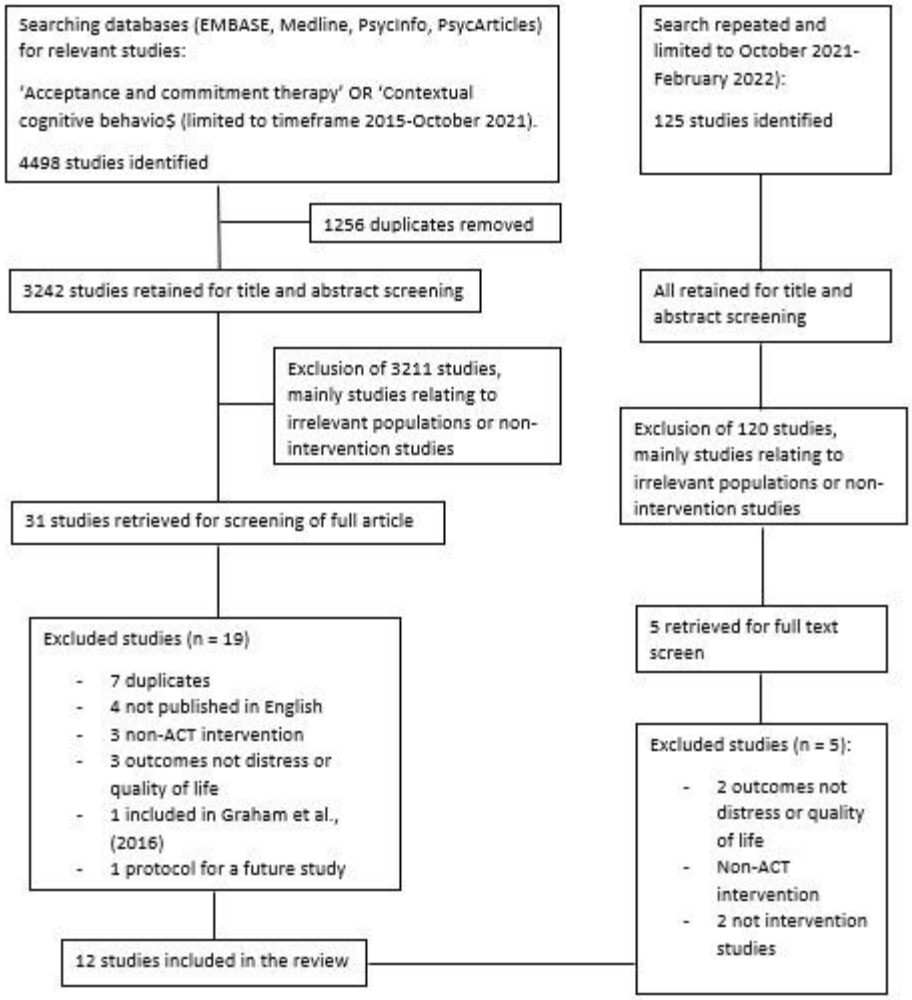
Papers were included if they described an original intervention study applying an ACT intervention in an adult population with a long-term condition, published in English, with outcomes related to psychological distress and/or quality of life. They were excluded if they related to an indirect intervention (e.g. parents or carers), targeted at a population where systematic review level evidence already exists for ACT (chronic pain, cancer, MS, neurological conditions, and diabetes type 2), a long-term condition where the biological pathology is unclear (e.g. functional neurological disorder, ME/CFS). Studies focusing primarily on illness prevention or treatment adherence were excluded, as were studies where there was no clear use of recognisable ACT techniques.

Titles were screened using the software Covidence (Covidence, 2021), and abstracts were read when the title indicated an intervention study using ACT in a clinical health sample. Potentially relevant papers were retrieved and reviewed in full, before finally being selected for inclusion in the

review if they met the criteria outlined above. This process was conducted by the lead author (PF). A random subset (50%) of full papers were screened by an additional member of the review team (SH), and there was 100% agreement in inclusion and exclusion. See Figure 1 for a PRISMA flow diagram of this process. The reference sections of the included studies were examined for any further studies for inclusion.

Figure 1

A PRISMA diagram of the systematic search and paper selection process.



Data Extraction

Information relating to sample characteristics, study design, intervention and statistical outcomes was extracted (See Table 1 for a summary of the included studies). Effect sizes (Cohen's d)

were calculated both within-groups (pre-post intervention) and, where relevant, between groups (post-intervention) using the means and standard deviations reported, along with the test-retest correlation score specific to each outcome measure. Where effect sizes were reported using a different effect size indicator, they were converted to Cohen's *d* to enable comparison (Cohen, 1988).

Quality Appraisal

The methodological quality of the included studies was evaluated using the Psychotherapy Outcome Study Methodology Rating Form (POMRF; Öst, 2008). The POMRF is a tool designed to measure the methodological quality of psychological intervention studies. It assesses various indicators of quality, such as representativeness of the sample, treatment fidelity, treatment assignment and presentation of results. Items are scored from 0-2, with higher scores indicating better quality. Two items were removed as they were not relevant to the current review (relating to psychiatric disorder and the reliability of its diagnosis), which left 20 items and a maximum total score of 40. See Appendix 2 for a POMRF template.

The quality of the included studies was appraised by the lead author (PF), with a random 50% of the papers being appraised by a second member of the review team (SH; see Appendix 3 for a table of ratings). Inter-rater reliability was moderate (72.5% and $k = 0.58$) (McHugh, 2012). Disagreements were discussed and resolved before all the papers were re-rated by PF.

Table 1

A Summary of the Methodology, Interventions and Outcomes of All the Included Studies in This Review.

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
Brassington et al. (2016)	Pre-post	21	Adults with long term conditions (transdiagnostic)	To develop and evaluate the effectiveness of a transdiagnostic ACT group in reducing psychological distress and increasing psychological flexibility in a population with long term conditions	Group	6 intervention + 2 follow-up (15+5)	33 (72%)	-	Participants used as their own control condition during wait time for group	HADS Anxiety HADS Depression Health-related quality of life (SF-36) Illness perceptions (BIPQ) Psychological inflexibility (AAQ-II) Valued living (VQ)	Significant (d = 0.74) Significant (d = 0.69) Significantly improved domains: Physical limitations, Emotional limitations and Fatigue (d = 0.48) No significant change Significant (d = 1.08) Significant improvement in both subscales: Progress (d = 0.66), Obstruction (d = 0.57)	Significant (d = 1.16) Domains significantly different: physical limitations, emotional limitations, fatigue (d = 0.37) Not significant Significant (d = 0.43) Significant difference in both subscales: Progress (d = 0.80), Obstructions (d = 0.42)	Anxiety and Depression both maintained (3 months) Physical and Emotional limits maintained; Fatigue not maintained Reductions maintained but change not significant Not maintained Maintained

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
Carvalho et al. (2021)	RCT	22	Adults with an existing diagnosis of chronic illness (transdiagnostic)	To compare the effectiveness and acceptability of digitally delivered ACT vs. CFT	Online self-directed content	4 (1.3)	13 (52%)	8 (33%)	4 sessions of online self-directed CFT content	Anxiety and depression (HADS) Illness shame (CISS) Illness-specific cognitive fusion (CFQ-CI) Psychological flexibility (CompACT) Self-compassion (SCS)	Neither Anxiety nor Depression significant Not significant Not significant Not significant Not significant	Not significant (d = 0.36) Not significant Not significant Not significant Not significant	No change from baseline (3 and 6 months) Statistically significant improvement from baseline Improved (6 months) Improved (6 months) Uncompassionate self-responding improved (6 months)
Faezipour et al. (2018)	Pre-post with control	11	Adults with HIV/AIDS scoring above 14 on the BDI-II	To determine the effectiveness of ACT in reducing depression among adults with HIV/AIDS	Group	8 (8)	12 (100%)	12 (100%)	Wait list	Depression (BDI-II)	Significant (d = 2.30)	Significant (d = 1.11)	No follow-up
Ghahnaviyeh et al. (2020)	Pre-post test with control	12	Adults with history of at least one MI	To evaluate the effect of an ACT intervention on quality of life in MI patients	Group	8 (12)	30 (100%)	30 (100%)	TAU + 3 training sessions	Physical and psychological quality of life (MLHFQ)	Significant (d = 2.42)	Significant (d = 1.64)	Maintained (d = 2.02, 6 months)
Hashemvarzi et al. (2021)	Pre-post test with control	9	Adults with colostomy	To determine the effectiveness of ACT on psychological distress and rumination in colostomy patients	Group	8 (16)	25 (100%)	25 (100%)	Unclear but presumed TAU	Psychological distress (KPDS) Rumination (RRS)	Significant (d = 1.30) Significant (d = 2.03)	Significant (d = 1.07) Significant (d = 1.31)	Maintained (6 weeks) Maintained (6 weeks)

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
Hoefnagels et al. (2021)	Pre-post study	13	Male adults with haemophilia on prophylactic treatment	To evaluate the effect of a tailored ACT intervention for patients with haemophilia	Group	8 +1 (16+2)	23 (96%)	-	-	Adherence (VERITAS-Pro) Quality of life (SF-36)	Total not significant, but domains 'time' and 'remember' sig. improved Significantly improved domains: general health (*d* = 0.61), role physical (*d* = 0.89)	-	Significant improved from baseline (12 months) Not maintained (12 months) but domain 'social functioning' significantly improved from baseline social functioning (*d* = 0.53),
Hou et al. (2017)	Pre-post feasibility study	11	Adults with IBD for >3 months and symptoms of anxiety or depression	To determine the feasibility of a 1-day ACT workshop for patients with IBD and depression or anxiety	Group	1 (5)	20 (100%)	-	-	Anxiety and depression (DASS-21) IBD status (HBICD) Health-related quality of life (SIBDQ)	Stress and Depression not significant, Anxiety significant (*d* = 0.85) Not significant Not significant	-	Post-scores collected at 3 months, no follow-up beyond this

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
O'Hayer et al. (2021)	Pre-post feasibility study	15	Adults with cystic fibrosis and symptoms of anxiety or depression	To develop and test the efficacy of an online and in-person ACT intervention in reducing anxiety and depression in people with cystic fibrosis	Group (videoconferencing or in-person)	6 (5)	27 (96%)	-	-	Anxiety (GAD-7, BAI) Depression (PHQ-9, BDI-II) Cognitive Fusion (CFQ-13)	GAD-7 not significant (*d* = 0.69), BAI significant *d* = 1.07) PHQ-9 not significant (*d* = 0.11), BDI-II significant (*d* = 0.94) Improvements strongly correlated with improvements in depression and anxiety (*r* = 0.67)	-	No improvements significantly maintained, but somewhat reduced from baseline (3 months)
Sahebari et al. (2019)	Pre-post study	9	Women with lupus	To evaluate the efficacy of ACT in reducing disappointment, psychological distress and psychasthenia in women with lupus	Group	8 (12)	12 (100%)	12 (100%)	Usual lupus medical care	Depression (BDI) Psychological distress (KPDS) Fatigue (KFSS)	Significant (*d* = 8.22) Significant (*d* = 5.82) Significant (*d* = 5.37)	Significant (*d* = 4.02) Significant (*d* = 4.05) Significant (*d* = 2.55)	No follow-up

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
Wynne et al. (2019)	RCT	26	Adults with mild or inactive inflammatory bowel disease and psychological distress	To evaluate the impact of an ACT intervention (vs usual IBD medical care) on stress in patients with inflammatory bowel diseases	Group	8 (12)	37 (61%)	42 (69%)	Usual IBD medical care	Psychological distress (DASS-21) Perceived stress (VAS) Psychological flexibility (AAQ-II) IBD-related quality of life (SHS) Disease activity (CDAI, Mayo score, bloods)	Stress significant (*d* = 3.09), Anxiety not significant (*d* = 1.32), Depression significant (*d* = 2.85) Significant (*d* = 3.76) Improvements strongly *correlated* with stress (*r* = -0.52) 28% improvement, not significant No significant differences	Stress significant (*d* = 1.96), Anxiety significant (*d* = 1.09), Depression significant (*d* = 1.39) Significant (*d* = 2.16) Not measured Significantly different from treatment group No difference between groups	All domains maintained (3 months) Maintained (3 months) Maintained (3 months) No effect No effect
Fellows et al. (2015)	Case study	N/A	Adult with difficult-to-treat asthma	To detail the formulation, ACT intervention and outcome in a case with difficult-to-treat asthma	Individual	12 (12)	1 (100%)	-	-	Depression (PHQ-9) Anxiety (GAD-7) Illness Beliefs	From 'severe' to 'mild' From 'severe' to 'mild' Improvement on all scales	-	-

Author/year	Design	POMRF score (0-40)	Population	Main objective	Format of intervention	No. of sessions (total hours)	No. of completers (%)	No. of people in the control group (%)	Control	Outcomes	Within-participant improvement post-intervention (ES)	Improvement compared to control (ES)	Maintained at follow-up (time)
Graham et al. (2017)	Case series	N/A	Adults with muscle disorders	To test the effectiveness of a brief self-guided ACT intervention in improving QoL, depression and anxiety in people with muscle disorders, and assess the acceptability of the intervention	Self-help with telephone calls from a therapist	3 (4-6)	7 (100%)	-	-	Quality of life (VAS QoL) Anxiety and depression (HADS) Psychological inflexibility (AAQ-II) Disability (HAQ-DI)	4 out of 7 improved 4 out of 7 improved 2 out of 7 improved 4 out of 7 improved	-	-

AAQ-II = Acceptance and Action Questionnaire II; ACT = Acceptance and Commitment Therapy; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; BIPQ = Brief Illness Perception Questionnaire; CFT = Compassion Focused Therapy; CFQ-13 = Cognitive Fusion Questionnaire; CFQ-CI = Cognitive Fusion Questionnaire – Chronic Illness; CISS = Chronic Illness-related Shame Scale; CompACT = Comprehensive assessment of Acceptance and Commitment Therapy processes; DASS-21 = Depression Anxiety and Stress Scale; ES = Effect size; GAD-7 = Generalised Anxiety Disorder 7; HADS = Hospital Anxiety and Depression Scale; HAQ-DI = Stanford Health Assessment Questionnaire Disability Index; HBICD = Harvey Bradshaw Index for patients with Crohn's Disease; IBD = inflammatory bowel disease; KFSS = Krupp Fatigue Severity Scale; KPDS = Kessler Psychological Distress Scale; MLHFQ = Minnesota Living with Heart Failure Questionnaire; MI = myocardial infarction; PHQ-9 = Patient Health Questionnaire 9; POMRF = Psychotherapy Outcome study Methodology Rating Form; RCT = Randomised Controlled Trial; RRS = Ruminative Responses Scale; SCS = Self-Compassion Scale; SF-36 = Short Form 36 Health Survey; SHS = Short Health Scale; SIBDQ = Short Inflammatory Bowel Disease Questionnaire; TAU = treatment as usual; VAS = Visual Analogue Scale; VAS QoL = Visual Analogue Scale Quality of Life; VERITAS-Pro = Validated Haemophilia Regimen Treatment Adherence Scale; VQ = Valuing Questionnaire.

Results

The search returned 4498 studies, of which 1256 were identified by Covidence as duplicates and removed. Following title and abstract screening of the remaining 3242 studies, 31 were retrieved and read in full. 19 of these were excluded as they did not meet the criteria for inclusion. The second search on 17th February returned 125 new studies, of which 5 were downloaded for full screen review following screening. None met the criteria for inclusion (See Figure 1 for a PRISMA diagram of the process). A total of 12 studies met all criteria and were included in the current systematic review.

Description of the Included Studies

Data was extracted from the 12 included studies (see Table 1). Of the included studies, two were case studies/series (Fellows et al., 2015; Graham et al., 2017), two were randomised controlled trials (RCTs; Carvalho et al., 2021; Wynne et al., 2019), four used a pre/post study design with a control condition Faezipour, Ghanbaripanah, Seyedalinaghi, Hajiabdolbaghi, & Voltarelli, 2018; Ghahnaviyeh, Bagherian, Feizi, Afshari, & Darani, 2020; Hashemvarzi, Abbasi, & Hosseini, 2021; Sahebari, Ebrahimabad, Shoraketokanlo, Sharbaf, & Khodashahi, 2019), one used a within-participant wait list control (Brassington et al., 2016) and three used a pre/post study design with no control condition (Hoefnagels, Fischer, Bos, Driessens, & Schrijvers, 2021; Hou et al., 2017; O'Hayer et al., 2021;).

The case series investigated the effectiveness of ACT in treating psychological distress in an adult with difficult-to-treat asthma (Fellows et al., 2015) and seven adults with muscle disorders (Graham et al., 2017), conditions which have not been subject to much psychological intervention research. The RCTs and pre/post studies applied ACT interventions in populations with HIV (Faezipour et al., 2018), myocardial infarction (MI; Ghahnaviyeh et al., 2020), colostomy (Hashemvarzi et al., 2021), haemophilia (Hoefnagels et al., 2021), inflammatory bowel disease (IBD; Hou et al., 2017, Wynne et al., 2019), cystic fibrosis (CF; O'Hayer et al., 2021), systemic lupus (Sahebari et al.,

2019), and two studied transdiagnostic populations with diverse chronic illnesses (Brassington et al., 2016; Carvalho et al., 2021).

Nine studies described delivering group intervention (Brassington et al., 2016; Faezipour et al., 2018; Ghahnaviyeh et al., 2020; Hashemvarzi et al., 2021; Hoefnagels et al., 2021; Hou et al., 2017, O'Hayer et al., 2021; Sahebari et al., 2019; Wynne et al., 2019). The average number of group sessions was 6.8 (range 1-8) and the average total intervention time was 11.2 hours (range 5-16). One study tested the efficacy of a single, five-hour group session (Hou et al., 2017), and two studies included at least one follow-up group session (Brassington et al., 2016; Hoefnagels et al., 2021). One study described a group intervention delivered online using live video-conferencing technology (O'Hayer et al., 2021). Only one study described an intervention delivered individually (Fellows et al., 2015) with individuals receiving 12 1-hour sessions. Two studies outlined a self-directed learning intervention: Carvalho et al. (2021) delivered four brief online modules without therapist guidance, and Graham et al. (2017) delivered 3 brief online modules with follow-up telephone calls from a therapist.

The total number of participants in the included studies was 406, with 241 (M = 20.1, range 2-37) completing an ACT intervention and 165 (M = 13.75, range 0-42) in control conditions. Of the seven studies including a control condition, only one was an active treatment (self-directed online Compassion-Focused Therapy modules; Carvalho et al., 2021). One utilised a waiting list-control (Faezipour et al., 2018), one utilised a within-subjects waiting list control (Brassington et al., 2016) and three used a treatment-as-usual approach (Ghahnaviyeh et al., 2020; Sahebari et al., 2019; Wynne et al., 2019), which included usual medical care for their specific conditions. Hashemvarzi et al. (2021) did not explicitly state the nature of their control condition, but this was assumed to be treatment-as-usual for colostomy.

An average of 90.5% of those who received an ACT intervention completed treatment (range 52-100%), with seven studies reporting a 100% completion rate (Fellows et al., 2015; Faezipour et

al., 2019; Graham et al., 2017; Ghahnavijeh et al., 2020; Hashemvarzi et al., 2021; Hou et al., 2017; Sahebari et al., 2019). The average completion rate in control conditions was 82%. These figures suggest good acceptability of ACT interventions.

Table 2

Methodological quality ratings of all RCT or pre-post studies using the POMRF.

POMRF items	Brassington et al., 2016	Carvalho et al., 2021	Faezipour et al., 2018	Ghahnaviyeh et al. 2020	Hashemvarzi et al. 2021	Hoefnagels et al., 2021	Hou et al., 2021	O'Hayer et al., 2021	Sahebari et al., 2019	Wynne et al., 2019
1.Clarity of sample description	2	2	1	1	1	1	2	1	0	2
2.Representativeness of sample	2	2	1	1	2	1	1	2	1	0
3.Specificity of outcome measures	2	2	1	1	1	2	2	1	1	2
4.Reliability/validity of outcome measures	2	2	2	2	1	1	1	2	1	1
5.Use of blind evaluators	0	1	0	1	0	0	0	0	0	2
6.Assessor training	0	0	0	0	0	0	0	0	0	1
7.Assignment to treatment	0	2	1	0	0	0	0	0	0	1
8.Design	0	2	0	0	0	0	0	0	1	0
9.Power analysis	1	2	0	0	0	0	0	0	0	2
10.Assessment points	1	1	0	1	1	2	0	1	0	1
11.Manualised/replicable/specific treatment	2	1	1	1	0	1	0	1	1	2
12.Number of therapists	1	0	0	0	0	1	0	1	0	0
13.Therapist training/experience	2	0	0	0	0	1	0	0	0	2
14.Checks for treatment adherence	1	0	0	0	0	0	0	0	0	2
15.Checks for therapist competence	2	0	0	0	0	0	0	1	0	2
16.Control of concomitant treatments	0	1	0	0	0	0	1	0	0	2
17.Handling of attrition	2	2	2	2	2	1	0	1	2	2
18.Statistical analyses and presentation of results	2	2	2	2	2	1	2	2	2	2
19.Clinical significance	0	2	0	0	0	1	0	1	0	0
20.Equality of therapy hours	0	2	0	0	0	0	0	0	0	0
Total scores	**22**	**26**	**11**	**12**	**10**	**13**	**9**	**14**	**9**	**26**

Methodological Quality of Studies Using Group-Based Statistics

The methodological quality of the 10 studies using a pre-post or RCT design was assessed using the POMFR (see Table 2). On average scores were low (M=15.2, SD=6.81), with a range of 9-26 out of 40. Only three of 11 studies scored above 20 (Brassington et al., 2016; Carvalho et al., 2021; Wynne et al., 2019), with 22, 26, and 26 points, respectively.

A strength was that most studies recruited their sample from a clinical setting, with inclusion and exclusion criteria that were neither too strict to capture a representative sample, nor too broad. Only one study used online recruitment where people self-selected for treatment (Carvalho et al., 2021). Two studies (Hou et al., 2017; Wynne et al., 2019) used very strict criteria which allowed for better control over outcomes but reduced the representativeness of their sample. Only a few studies controlled for concomitant treatments by for example requesting medications to be kept stable (Hou et al., 2017), by excluding those receiving psychological treatments (Carvalho et al., 2021), or both (Wynne et al., 2019).

Another methodological strength of most papers were the outcome measures, which were generally well-established, reliable and valid measures of distress in the context of health conditions. Most studies also utilised measures that captured each of the symptom clusters relevant to their population, including measures of distress, health-related quality of life, illness-specific and ACT-specific measures. One study (Sahebari et al., 2019) was an exception, using measures that did not seem to fit with their hypotheses. For example, they used the Beck Depression Inventory to measure 'disappointment', and a measure of fatigue to measure 'psychasthenia'.

ACT interventions were generally well described and based on established ACT treatments, with adaptations to the specific health condition. However, only two studies had made their treatment manual and materials publicly available, enhancing replicability (Brassington et al., 2016; Wynne et al., 2019). Two studies provided minimal detail on the intervention beyond the session number and format (Carvalho et al., 2021; Hashemvarzi et al., 2021).

Statistical analyses were appropriate and well-presented across studies. An exception was the study by Hoefnagels et al. (2021) where results were presented graphically without reporting means and standard deviations for all outcomes; this made it difficult to interpret results and impossible to calculate effect sizes. However, the lead author provided the means and standard deviations on request. There was a tendency across papers to focus solely on statistical significance, and only two studies reported effect sizes (Brassington et al., 2016; O'Hayer et al., 2021). One study used a somewhat arbitrary cut-off to signify clinical significance (Hoefnagels et al., 2021), and one study used reliable change indicators for each measure (Carvalho et al., 2021). Most did not mention clinical significance.

Attrition and its handling were methodological strengths; seven studies reported a remarkable 0-4% attrition rate among those receiving an ACT intervention (Faezipour et al., 2018; Ghahnaviyeh et al., 2020; Hashemvarzi et al., 2021; Hoefnagels et al., 2021; Hou et al., 2017; O'Hayer et al., 2021; Sahebari et al., 2019). The remaining studies reported drop-out rates between 28-48% and used intention-to-treat analyses to limit attrition bias (Brassington et al., 2016; Carvalho et al., 21; Wynne et al., 2019).

A problem across studies was small sample sizes. Only three studies (Brassington et al., 2016; Carvalho et al., 2021; Wynne et al., 2019) reported an a-priori power calculation, and only one of these was adequately powered by their own calculations (Carvalho et al., 2021). Brassington and colleagues did not achieve the required number of completers but remedied this through intention-to-treat analyses with an adequate sample. Wynne et al. did not achieve an adequate sample by their own standard, despite having the biggest sample of completers (N=37) of the studies in this review. This is indicative of a general problem with lack of power in the included studies, increasing the risk of both type 1 and type 2 errors.

Most studies lost points for using a non-controlled design or treatment-as-usual control group. It was not always clear how participants were selected and assigned to conditions; two studies did not include any information about condition allocation, despite having control conditions (Hashemvarzi et al., 2021; Sahebari et al., 2019). Three studies utilised acceptable blinding procedures (Carvalho et al., 2021; Ghahnaviyeh et al., 2020; Wynne et al., 2019) and as the only study using an active control group, Carvalho and colleagues were alone in using a double-blind procedure.

Most studies were limited to a single therapist, conflating the effect of therapy and therapist. Some used at least two therapists, but did not analyse therapist outcomes (Brassington et al., 2016; Hoefnagels et al., 2021; O'Hayer et al., 2021). Only a few studies included checks for treatment fidelity and therapist competence (Brassington et al., 2016; Wynne et al., 2019). Where therapist experience was reported, interventions were delivered by a mixture of therapists in training (O'Hayer et al., 2021) and qualified staff with experience of the patient group, supervised by certified ACT trainers (Brassington et al., 2016; Hoefnagels et al., 2021; Wynne et al., 2019).

Effectiveness of ACT Interventions

The following section will outline the impact of ACT interventions on psychological distress, quality of life and psychological flexibility.

Psychological Distress

All but one study (Hoefnagels et al., 2021) evaluated the impact of an ACT intervention on at least one measure of psychological distress, most commonly depression. Six of those utilising a pre-post or RCT design found significant improvements in depression scores following ACT intervention (Brassington et al., 2016; Faezipour et al., 2018; Hashemvarzi et al., 2021; O'Hayer et al., 2021; Sahebari et al., 2019; Wynne et al., 2019) most reporting large effect sizes (range d = 0.85-8.22). All of these evaluated a group intervention. Of the five studies that measured anxiety, three reported significant improvements following intervention (Brassington et al., 2016; Hou et al., 2017; O'Hayer et

al., 2021). Again, these were group interventions and reported large effect sizes from pre to post intervention (*d* = 0.85-1.07). Interestingly, the O'Hayer study utilised two measures of both anxiety and depression, and reported conflicting findings whereby one showed improvement and one did not.\ Two studies used a general measure of psychological distress and found improvements following an 8-week group programme for people with colostomy and systemic lupus, respectively (Hashemvarzi et al., 2021; Sahebari et al., 2019). However, the latter had a very small sample size and so it is likely that their very large effect sizes represent an outlier.

The only study with an active control (Carvalho et al., 2021) found no significant changes in any measures of distress over time in either condition, despite being one of the highest rated studies in the review. However, this study had a small sample size, and evaluated brief online ACT and CFT self-help interventions without therapist involvement. Hou et al. (2017) were the only other study that found no significant improvements in depression and stress; this was measured 3 months after a single, 5-hour ACT group session for people with IBD. It may be that the dose of ACT intervention was insufficient in these studies.

Of the studies that utilised a wait list or TAU control group, all reported significant improvements in the ACT group relative to control (Brassington et al., 2016; Faezipour et al., 2018; Hashemvarzi et al., 2021; Sahebari et al., 2019; Wynne et al., 2019). Effect sizes were considered large and ranged from *d*= 1.09-4.05.

Four of the studies that reported significant improvements in distress collected follow-up data. One reported that improvements in distress were maintained at 6 weeks (Hashemvarzi et al., 2021) and two at 3 months (Brassington et al., 2016; Wynne et al., 2019). Where results were not maintained, they were still reduced from baseline at 3 months (O'Hayer et al., 2021).

In summary, improvements on some measures of psychological distress were reported in studies using an ACT group intervention. These improvements were not consistent. Where improvements were reported these were superior to wait list and TAU, which consisted of usual medical care.

Quality of Life

Six studies included some measure of quality of life; one of these used a simple visual analogue scale asking about general quality of life, where four out of seven significantly improved following intervention (Graham et al., 2017). Two studies that measured health-related quality of life in a population with IBD reported no significant changes following group intervention (Hou et al., 2017; Wynne et al., 2019). The other two studies measuring health-related quality of life found significant effects following group intervention in a few subscales, namely 'health', 'physical' (Hoefnagels et al., 2021), 'fatigue', 'emotional limitations' and 'physical limitations' (Brassington et al., 2016). Effect sizes ranged from medium to large (d = 0.48-0.89). Where compared to a wait list condition, these improvements were significantly different with a small effect (d = 0.37; Brassington et al., 2016). Only some gains were maintained at 3-month follow-up ('physical' and 'emotional' domains in Brassington et al., 2016). One study used a measure of psychological and physical quality of life and found significant gains with very large effect sizes following group intervention (d = 2.42) which were maintained at 6 months (Ghahnaviyeh et al., 2020). Improvements were significantly different from a control group which received treatment as usual plus three non-specified 'training sessions', again with large effect sizes when comparing the groups (d = 1.64).

In summary, the evidence for improvements in quality of life following ACT group intervention is inconsistent. Condition-specific quality of life indices did not show change over time, and health-related quality of life measures only showed improvements in a minority of subscales. Intervention conditions compared favourably to control conditions where these were included.

Health Outcomes

Six out of ten pre-post studies included a health-related outcome. One study found no impact of ACT on illness perception (Brassington et al., 2016); another found no impact on illness shame (Carvalho et al., 2021). Two studies found no impact of ACT on IBD disease activity (Hou et al., 2017; Wynne et al., 2019). One study used a measure of adherence to prophylactic medication in haemophilia (Hoefnagels et al., 2021) but found significant improvements in only two of six subscales following a group intervention. Interestingly, the total score reached significance at 12-month follow-up, suggesting a long-term effect of ACT on treatment adherence in this population. One study measured fatigue and found a significant and very large effect of an ACT group intervention (Sahebari et al., 2019; d = 5.37). The effect was significantly different from the TAU control group (d = 2.55).

In conclusion, the evidence that ACT intervention directly affects health outcomes is sparse. However, this is in keeping with the ACT model which suggests that distress can reduce in the absence of change in symptom severity.

ACT-Specific Measures

A small number of studies investigated ACT-specific measures. One study (Brassington et al., 2016) reported large and significant improvements following an ACT group programme on a measure of psychological inflexibility (d = 1.08), this was significantly higher than in the wait-list condition (d = 0.43). These effects were not maintained at 3 months. They also found a significant improvement in valued living (d = 0.57-0.66) which was maintained at follow-up. Two studies found significant improvements in cognitive fusion and psychological flexibility after a group programme (O'Hayer et al., 2021; Wynne et al., 2019); these changes were moderately correlated with improvements in distress (r = 0.52-0.67,) and maintained at 3 months. Carvalho et al. (2021) found no impact of self-help on psychological flexibility, but this was consistent with their other measures which also showed no change. Again, this could be a dose-related issue.

In summary, only a few studies tracked changes in measures related to psychological flexibility (or inflexibility), which is thought to be a mechanism of change in ACT. These studies, while sparse, suggest that psychological flexibility is improved by ACT intervention.

Case Studies/Series

One case study and one case series were included in the review. The case study outlined an ACT intervention applied to a person with longstanding, difficult to treat asthma and related health complications (Fellows et al., 2015). The individual intervention focused on acceptance, values-consistent behaviour, and coping with asthma attacks. This intervention resulted in a reduction in anxiety and depression scores from 'severe' to 'mild', and qualitative reports suggested improved illness acceptance and self-efficacy. The patient reported a high satisfaction with the treatment. A case series detailed a self-help ACT intervention for seven people with muscle disorders, which included telephone calls with a therapist (Graham et al., 2017). Four out of seven participants showed improvements in anxiety, depression, and quality of life. Only two demonstrated improvements in psychological flexibility. All seven reported finding the intervention acceptable, and to some extent, helpful.

Discussion

Overview of ACT Applications

Since the original review by Graham et al. (2016) research into ACT in long-term conditions has developed rapidly, with some conditions (persistent pain, type 2 diabetes, neurological conditions, cancer being so well-researched as to warrant targeted reviews (Hughes et al., 2017; Li, Li, Guo, Li, & Yang, 2021; Li, Wung, Ni, Zhang, Weng, & He, 2021; Mathew et al., 2021; Ngan et al., 2021; Robinson et al., 2019; Salari et al., 2021; Trindade et al., 2021). In addition, ACT has been used in a wide range of conditions such as haemophilia (Hoefnagels et al., 2021), muscle disorders (Graham et al., 2017), HIV (Faezipour et al., 2018), myocardial infarction (Ghahnaviyeh et al., 2020), systemic lupus (Sahebari et al., 2019), asthma (Fellows et al., 2015), colostomy (Hashemvarzi et al., 2021), cystic fibrosis (O'Hayer et al., 2021), and inflammatory bowel disease (Hou et al., 2017; Wynne et al., 2019). It has also been used transdiagnostically for chronic illness (Brassington et al., 2016; Carvalho et al., 2021). These interventions have targeted psychological distress (Brassington et al., 2016; Carvalho et al., 2021; Faezipour et al., 2018; Fellows et al., 2015; Ghahnaviyeh et al., 2020; Graham et al., 2017; Hashemvarzi et al., 2021; Hou et al., 2017; O'Hayer et al., 2021; Sahebari et al., 2019; Wynne et al., 2019), quality of life (Brassington et al., 2016; Graham et al., 2017; Ghahnaviyeh et al., 2020; Hoefnagels et al., 2021; Hou et al., 2017; Wynne et al., 2019), psychological flexibility (Brassington et al., 2016; Carvalho et al., 2021; O'Hayer et al., 2021; Wynne et al., 2019), illness beliefs (Brassington et al., 2016; Carvalho et al., 2021; Fellows et al., 2015), treatment adherence in haemophilia (Hoefnagels et al., 2021) fatigue in systemic lupus (Sahebari et al., 2019), and measures of disease activity in inflammatory bowel disease (Hou et al., 2017; Wynne et al., 2019).

Graham et al. (2016) questioned whether the growing popularity of ACT was a therapeutic fad or reflective of the utility of ACT in long-term conditions. The continued use of ACT in areas such

as persistent pain and cancer, and the expanse of ACT into new areas of clinical practice and research, is indicative of the breadth and popularity of ACT in long-term conditions. The wealth of reviews published in the last year suggest that, more than 15 years since the publication of the first ACT intervention study in a long-term condition (Dahl, Wilson, & Nilsson, 2004), the appetite for ACT has continued to grow. The number of new applications suggests that, with small tweaks, ACT interventions may be adapted to suit rarer conditions, or conditions that are less subject to study but nevertheless present frequently in clinical practice. It is also indicative that ACT may be used transdiagnostically, targeting psychological processes that are shared between conditions. This is promising for primary care services and services in more rural areas where trans diagnostic interventions are the most practical option in dealing with long-term conditions. Furthermore, ACT may therefore be a viable option for the more than 50% who have more than one long-term health condition (Barnett et al., 2012).

State of the Evidence

Like Graham et al. (2016), the current review found some evidence that ACT interventions led to improvements in psychological distress compared to treatment as usual in populations with long-term conditions. However, due to the lack of active control conditions it is not yet possible to assert whether these improvements are due to ACT specifically, or simply due to an active psychological treatment.

Unlike Graham et al. (201), this review found inconsistent evidence for improvements to quality of life indices in long-term conditions following ACT intervention. Similarly, there were inconsistent improvements in health outcomes. The conditions involved in the current review involve many unpleasant symptoms and secondary suffering, including pain, fatigue, polypharmacy, and disability (May et al., 2009) that are less malleable to change; yet changes to distress are thought possible in the absence of changes to symptom severity (McCracken & Morley, 2014). These findings are therefore consistent with the ACT model.

The findings in the current review are consistent with findings from other systematic reviews recently conducted in other long-term conditions; improvements in psychological distress (anxiety, depression and stress) have been reported following ACT intervention in cancer (Mathew et al., 2021; Li, Li et al., 2021; Salari et al., 2021), breast cancer (Li, Wu et al., 2021), persistent pain (Hughes et al., 2017), neurological conditions (Robinson et al., 2019), type 2 diabetes (Ngan et al., 2021), and for parents of children with long-term conditions (Jin et al., 2020)

These findings must be considered in the context of generally low methodological quality and small sample sizes. The issue of sample size is significant both because it decreases the chances of detecting true effects of intervention (Type 2 error), but also because any significant effects need to be powerful to be detected (overestimation of effect due to sampling bias: Type 1 error). Thus, where extremely large effect sizes are reported this may create a skewed perception of the usefulness of an intervention. Similar methodological issues were highlighted in the other systematic reviews outlined above, which suggests a paucity of robust research methodology across the field of ACT in long-term conditions.

The methodological quality of the papers in the current review was poorer on average than those reviewed by Graham et al. (2016); the average POMRF score reported by them was 19.33, compared to 15.20 in ours. It is difficult to ascertain whether this reflects poor inter-rater reliability of the quality appraisal tool, or whether it is reflective of a decrease in methodological quality of ACT studies in recent years. One possible explanation is that the current review mainly included studies in conditions that are less subject to study. As a result, most studies were pilot or feasibility studies, which by their nature have less methodological rigour than is afforded in more well-established and well-funded areas of research.

Some welcome differences emerged in the recent papers compared to those reviewed by Graham and colleagues; there was a higher degree of homogeneity among studies with 75% utilising a group intervention. Interventions also consisted of more sessions; only one study offered less than

five group sessions (11%), versus 58% reported by Graham et al. (2016). Heterogeneity of intervention duration and type makes it difficult to make recommendations for clinical practice, but in these data, there did seem to be a pattern; individual and group interventions with six or more sessions generally yielded positive outcomes, in contrast with interventions that were self-directed or only consisted of a single session. This suggests that there may be a dose-effect whereby a minimum 'dose' of ACT intervention may be necessary for improvements; this has been found in the psychotherapy literature where more sessions are associated with better outcomes (Kopta, 2006). Similarly, some involvement or guidance by a therapist may be necessary for ACT intervention to be effective. This fits with previous research on self-help in mental health contexts, which shows that therapist guidance is associated with better outcomes (Baumeister, Reichler, Munzinger, & Lin, 2014; Thompson, Destree, Albertella, & Fontenelle, 2021).

Methodological Suggestions for Future ACT Intervention Studies

To enhance the evidence base for ACT in long-term conditions, we make the following suggestions to improve on methodological quality in future intervention studies:

1. Conduct a priori power calculations and recruit more than the minimum required sample by a good margin, given variable attrition rates in intervention studies.
2. Compare ACT to another active psychological treatment, or a treatment that controls for the non-specific effects of treatment. At present it is impossible to disentangle the effects of ACT from the effect of any active intervention. Such control conditions should be matched for duration and intention. Where treatment as usual is the only practical comparator, it should be made clear what treatment as usual entails for that population. Concomitant treatments are very likely in a population with long-term conditions and should be controlled for.

3. Studies should utilise adequate blinding procedures and be transparent about how participants are allocated to each condition; ideally this should be random and completed by someone not directly involved in delivering intervention.
4. At least two therapists should be involved in each condition to avoid confounding therapist and therapy effects.
5. Treatment fidelity and therapist competence should be assessed by trained ACT therapists.
6. To enhance transparency and aid replicability, detailed treatment manuals should be made available as supplementary material.
7. To understand the longer-term impact of ACT, a follow-up period of at least 12 months is recommended.
8. Provide some measure of clinical significance. Reporting statistical significance alone is limited and does not tell us of the magnitude or real-life significance of the effect. Ideally researchers should report effect sizes and measure outcomes against a pre-determined indicator of clinical significance.

Limitations of This Review

This review has several limitations. Firstly, it was chosen not to conduct a meta-analysis given the heterogeneity of interventions, populations, and outcome measures, and the paucity of RCTs. While a meta-analysis can provide a clearer estimate of treatment effects, the heterogeneity in the included studies was thought to reduce the accuracy of a quantitative synthesis. It is hoped that a meta-analytic review will soon be possible given the rapid development of the research field.

A second limitation concerns effect size calculations. Within-subjects effect sizes were computed based on available test-retest correlations of individual outcome measures in the literature, as

these were not reported in the studies. Furthermore, calculations rested on the assumption that between-subjects scores were similar at baseline, which may not have been the case.

Balancing practicality with good research practice, half of the data extraction and quality appraisal were completed by a second reviewer. It is possible that the decision to not have a second reviewer involved in 100% of the process has introduced researcher bias. However, no inconsistencies were revealed in the data extraction process and there was an acceptable level of agreement in the quality appraisal. Furthermore, all studies were re-rated following discussion to minimise researcher bias.

Conclusion

ACT has continued to be applied in a wide range of long-term health conditions and has been increasingly used in rarer conditions less subject to study. Most of the included studies had small sample sizes and low methodological quality, and there is a general lack of RCTs. This limits the conclusions we can draw about the effectiveness of ACT versus other psychological therapies in these conditions. However, ACT interventions show consistent effects in reducing distress compared to treatment as usual in these contexts. Inconsistent evidence was found for improvement of quality of life and health outcomes. When these findings are considered in the context of recent systematic reviews of more commonly researched long-term conditions, the effects of ACT look promising.

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Chapter 2: Empirical Study

Further Exploration of Chronic Pain Acceptance Questionnaire Clustering in a Population with Persistent Pain

Pernille Frisvoll [ab], Sarah Young [b], Linsay Brassington [b], and David Gillanders [a]

[a] Clinical and Health Psychology, School of Health and Social Science, University of Edinburgh, EH8 9AG

[b] NHS Lothian Pain Management Programme, Astley Ainslie Hospital, Edinburgh, EH9 2HL

Corresponding author: Pernille Frisvoll, NHS Lothian Pain Management Programme, Astley Ainslie Hospital, Edinburgh, EH9 2HL

Email: Pernille.Frisvoll@nhslothian.scot.nhs.uk

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Abstract

Pain management programmes reduce distress and disability associated with persistent pain, but treatment response is uneven among completers, with some benefitting more than others. Group composition may affect outcomes, but grouping people based on pain condition or demographic variables has shown limited utility. Research has suggested that grouping people based on their scores on the Chronic Pain Acceptance Questionnaire (CPAQ-8) may be clinically useful. Previous research has identified four distinct clusters based on the Activity Engagement and Pain Willingness subscales. We sought to explore whether these clusters also have different profiles of functioning and distress and therefore, different treatment needs. This study recruited 213 people with persistent pain through social media and specialist pain clinics. MANOVAs and ANOVAs revealed differences between clusters on functioning (pain interference, pain self-efficacy, valued living) and psychological distress (anxiety and depression). These differences are discussed and suggestions offered for how this may potentially inform triage and intervention in specialist pain clinics, which may in turn improve treatment responses.

Perspective

This article presents what may be an easy-to-use, quick, and clinically meaningful tool for grouping people with persistent pain based on pain acceptance. This has the potential to aid group cohesion in pain management programmes, and we offer suggestions for how pain interventions may be tailored to people at different stages of their pain acceptance journey.

Keywords

Chronic pain; Pain Acceptance; Chronic Pain Acceptance Questionnaire; Pain Rehabilitation; Pain Management

Introduction

There is a robust evidence base for interdisciplinary pain management programmes in helping to reduce pain-related distress and disability (e.g. Hann & McCracken, 2014; Pergolizzi et al., 2013; Scottish Intercollegiate Guidelines Network (SIGN) 2013; Stanos, 2012). Pain management programmes typically combine pain education and physical exercise with psychological interventions to r51ecognize and modify thoughts and actions that maintain pain-related distress (SIGN, 2013).

Despite this, effect sizes of outcomes such as disability and distress vary from low to medium and show uneven responsiveness among participants, with some benefitting more than others (Vlaeyen & Morley, 2005). Williams and Potts (2010) found bigger within-group than between-group effects on self-efficacy, walking distance and catastrophising in their sample of 3050 pain management programme completers, suggesting that outcomes are influenced by intra-group effects. However, most specialist services offer a one-size-fits-all approach, leading to groups of participants who may differ markedly in their psychological profile, level of disability, and degree of distress.

The wider literature on group therapy recognises group composition as important to outcomes (Burlingame, Fuhriman, & Mosier, 2003). Grouping patients based on shared characteristics improves group identification, cohesion and engagement (Leach et al., 2008), which lead to better outcomes in group therapy (Crowe & Grenyer, 2008). Perceived homogeneity is perhaps stronger where these shared characteristics are overt, for example age, gender or health condition (Wilson et al., 2018). However, research has shown that differences in treatment outcomes from a pain management programme are not moderated by age, gender, pain condition, pain duration or level of disability (Frisvoll, Dunbar, & Williams, 2016). Dividing patients into treatment groups based on these characteristics has not demonstrated usefulness (Morley, Williams & Eccleston, 2013). In their systematic review of psychological therapies for persistent pain, Williams, Fisher, Hearn and Eccleston

(2012) suggested that grouping patients based on psychological processes *may* be more clinically useful, lead to better group composition and outcomes.

One such grouping factor may be pain acceptance. Pain acceptance is predictive of reduced depression, anxiety, pain-related distress and disability, even when controlling for pain intensity (McCracken, 1998). It is rooted in the robust theoretical model of Psychological Flexibility, which underlies Acceptance and Commitment Therapy (ACT; Hayes & Duckworth, 2006). Pain acceptance is an important mediator of outcomes in pain management programmes, whether primarily based on Cognitive Behavioural Therapy (CBT), ACT, or Compassion Focused Therapy (CFT) (Åkerblom, Perrin, Fischer, & McCracken, 2015; Tin, 2019; Trompetter et al., 2015). The Chronic Pain Acceptance Questionnaire (CPAQ) is widely used in pain management settings to measure pain acceptance (McCracken, Vowles, and Eccleston, 2004; Fish et al., 2010). It consists of two distinct but correlated processes, namely pain willingness and activity engagement. Pain willingness (PW) refers to the extent to which respondents are open to experiencing pain without getting caught up in a struggle for pain relief. Activity engagement (AE) refers to the extent to which respondents continue engaging in usual activities whilst experiencing pain.

Rovner, Vowles, Gerdle, and Gillanders (2015) and Rovner, Johansson and Gillanders (2019) used latent class analysis to explore whether patients in a Swedish specialist pain clinic could be meaningfully grouped into different clusters based on their scores on long and short versions of the CPAQ. These studies revealed four distinct clusters: a group that scored highly on both activity engagement (AE) and pain willingness (PW), a group that scored low on both, and two middle groups: one with high PW and low AE, and one with low PW and high AE. CPAQ-8 was as robust as CPAQ-20 in clustering solution. Clusters had distinct psychological and behavioural profiles with differences in disability, anxiety, depression, quality of life and fear of movement. For example, the low-scoring cluster were the most distressed and disabled, in contrast with the high-scoring cluster which was the least distressed and highest functioning. The Low AE/High PW cluster showed a similar openness

to pain as the high-scoring cluster, but this did not translate into action, and they were still as functionally impaired as the low-scoring cluster. The cluster scoring highly on AE but not PW were functioning at the level of the high-scoring cluster but exhibited a high degree of anxiety and fear of movement. These findings suggest that CPAQ clusters have distinct profiles and treatment needs, and that pain acceptance scores may be a clinically useful grouping factor in this population. Rovner et al. (2019) hypothesised about how stepped treatment approaches may be adapted to suit the profile of these clusters, but this requires further study.

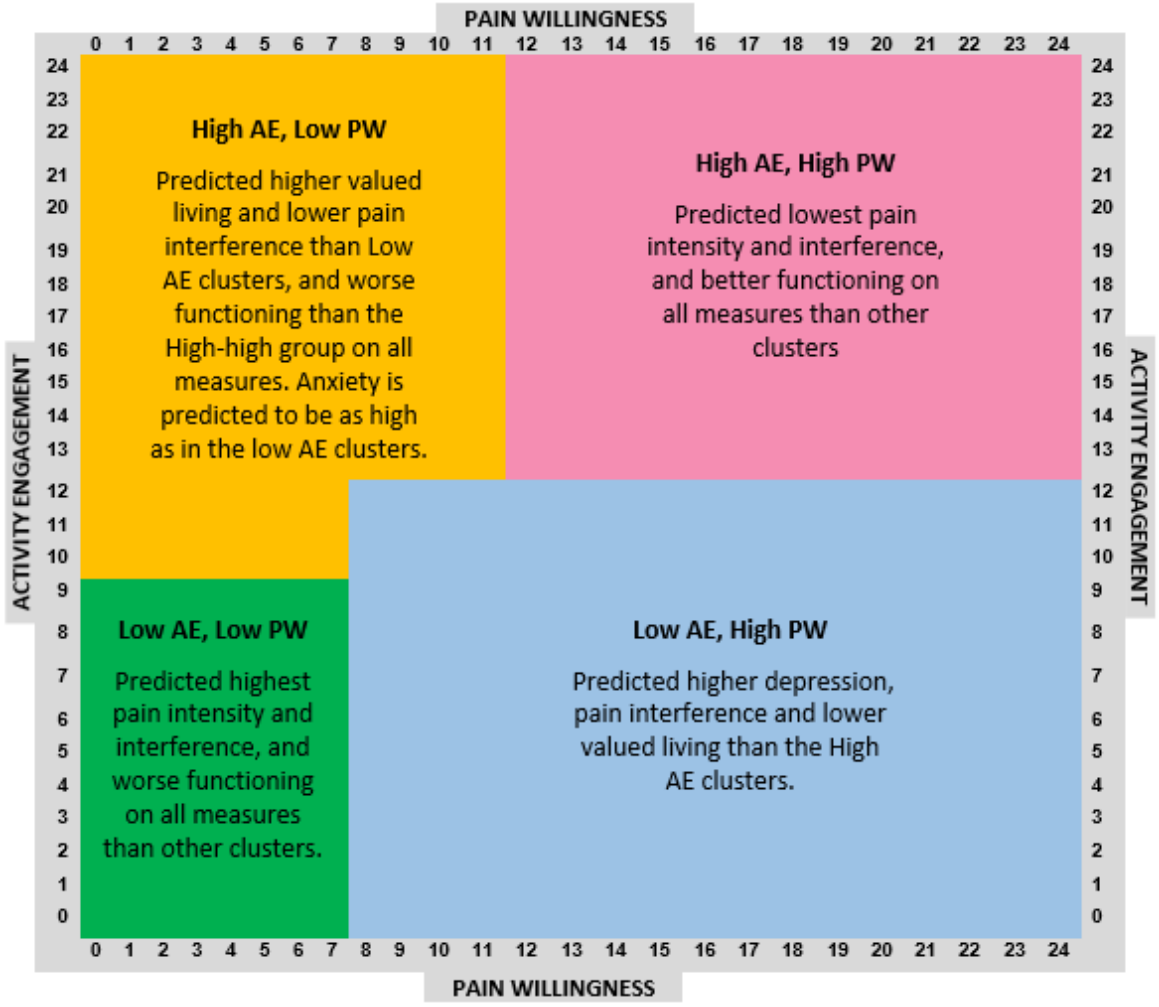
Aims

The aim of this study was to assess whether CPAQ-clustering in an English-speaking population with persistent pain would yield groups that meaningfully differ on variables related to functioning and psychological distress. Similarly to Rovner and colleagues, we have measured pain intensity, pain interference, anxiety, and depression. Furthermore, we have included measures of pain self-efficacy and valued living. It was hypothesised that cluster differences would follow a similar pattern to that found by Rovner et al. (2019; see Figure 2 for specific hypotheses), with lowest levels of functioning in the low-scoring cluster, and the highest levels of functioning in the higher-scoring cluster. A similar pattern is expected on measures of depression, with the lower-scoring clusters exhibiting higher levels of distress. The anxiety variable is expected to have a different pattern, with the High AE, Low PW group scoring as highly on anxiety as the two low AE clusters.

If clusters are found to have different profiles of functioning and distress, CPAQ-clustering could provide a useful and empirically based triage and treatment planning tool for specialist pain services.

Figure 2

CPAQ-8 clusters with hypotheses



Methods

Data Gathering

Participants were recruited through social media and online forums, and through two NHS Pain Management clinics, detailed below. Recruitment was undertaken between May and December 2021.

Online recruitment

The study was advertised using social media outlets such as Twitter, Facebook and Health Unlocked. Relevant third sector organisations, charities and professional networking groups were approached and asked to disseminate the research link to their audiences.

Clinical recruitment

NHS recruitment was conducted through the NHS Lothian and NHS Greater Glasgow & Clyde Pain Management Services. Both clinics delivered pain management programmes online due to restrictions posed by Covid-19. Staff informed the lead author (PF) of timings for the online groups, and PF briefly attended 13 different pain management programmes to advertise the opportunity to participate in this study. It was decided to attend at an early point to capture participants before anticipated change in psychological processes had occurred. In NHS Lothian the study link was also disseminated to patients invited for an initial appointment with the service, through a study flyer enclosed with their appointment letter (See Appendix 5).

Ethical approval

Ethical approval for this study was sought through the NHS Integrated Research Approval Service, and the Riverside Research Ethics Committee approved the application on 12th April 2021 (reference 21/PR/0448; Appendix 6). The School of Health in Social Science at University of Edin-

burgh approved the study on 6th May 2021 (See Appendix 7), and the Research & Development departments in NHS Greater Glasgow & Clyde and NHS Lothian gave local approval on 2nd June 2021 and 5th July 2021, respectively (Appendix 8 and 9).

Procedure

This cross-sectional questionnaire study used the software Qualtrics (2021) to set up an online survey which took approximately 20 minutes to complete. During the planning stage the survey, study protocol and materials were sent to a pain charity run by experts by experience for consultation, and they supported the study without amendments. The participant information sheet, consent form, debrief form and full study protocol can be found in Appendices 10-13.

All prospective participants were directed to the survey and first encountered a participant information sheet and a consent form. Having provided informed consent, participants were subject to an eligibility check and confirmed whether they met the criteria outlined above. Those who were eligible could complete the online survey which included a demographic questionnaire and several measures of pain and pain-related distress, detailed below.

Participants

Participants were eligible if they were over 18 and self-described as having had pain (not cancer-related) lasting more than 3 months and with an impact on functioning (e.g. work, social life, housework, carer responsibilities). Participants had to be fluent in English and were excluded if they had a self-reported diagnosis of intellectual disability or dementia.

A total of 213 participants completed the survey. Of these, 175 (83%) were recruited through online advertisement, 191 (89.7%) were women, 196 (91%) had been given a specific pain-causing diagnosis, and 137 (64.3%) had attended a pain clinic. The average number of pain locations was 5.7 (mode = 4) and the average pain duration was 13.8 years. See Table 3 for a full demographic overview.

Table 3

Demographic Variables By CPAQ-8 Cluster.

	CLUSTER MEMBERSHIP				
	TOTAL (N=213)	**Stuck (N=70)**	**Passive accepting (N=52)**	**Active avoidant (N=64)**	**Engaged (N=27)**
Descriptive variables (N)	*Mean (SD) or %*	*Mean (SD) or %*	*Mean (SD) or %*	*Mean (SD) or %*	*Mean (SD) or %*
Age (152)	45.86 (14.98)	46.60 (12.75)	49.13 (13.05)	42.11 (17.24)	46.24 (17.01)
Gender					
Women (191)	89.7%	88.6%	86.5%	90.6%	96.3%
Men (19)	8.9%	11.4%	13.5%	7.8%	0.0%
Other (2)	0.9%	0.0%	0.0%	1.6%	3.7%
Pain duration in years (211)	13.77 (10.94)	15.19 (12.73)	13.19 (8.84)	12.65 (9.16)	13.81 (13.45)
Ever attended a pain clinic (137)	64.3%	91.4%	65.4%	50.0%	59.3%
Been given a diagnosis related to pain (196)	91.0%	91.4%	94.2%	92.2%	88.9%
Number of pain location 0-12 (213)	5.67 (3.61)	6.04 (3.59)	6.00 (3.71)	5.27 (3.48)	4.93 (3.71)
Pain location					
Head (60)	28.2%	2.9%	34.6%	26.6%	4.7%
Face (35)	16.4%	21.4%	19.2%	9.4%	14.8%
Neck (112)	52.6%	60.0%	51.9%	43.8%	55.6%
Shoulders/upper limbs (128)	60.1%	67.1%	63.5%	50.0%	59.3%
Chest (42)	19.7%	21.4%	21.2%	15.6%	22.2%
Abdomen (58)	27.2%	28.6%	26.9%	26.6%	25.9%
Groin (39)	18.3%	20.0%	21.2%	17.2%	11.1%
Upper back (79)	37.1%	37.1%	36.5%	37.5%	37.0%
Lower back (132)	62.0%	70%	65.4%	56.3%	48.1%
Hips (120)	56.3%	57.1%	51.9%	59.4%	55.6%
Legs/lower limbs (140)	65.7%	65.7%	76.9%	64.1%	48.1%
Joints (124)	58.2%	54.3%	63.5%	59.4%	55.6%
Widespread pain (114)	53.5%	60%	55.8%	46.9%	48.1%
Other (23)	10.8%	10.0%	13.5%	14.1%	0.0%
Occupation					

Working full-time (47)	22.1%	5.7%	19.2%	34.4%	40.7%
Working part-time (20)	9.4%	2.9%	7.7%	14.1%	18.5%
Working reduced hours due to pain (23)	10.8%	12.9%	9.6%	10.9%	7.4%
Not working due to pain (70)	32.9%	60.0%	30.8%	17.2%	3.7%
Not working for other reasons (8)	3.8%	2.9%	5.8%	3.1%	3.7%
Home-maker (2)	0.9%	0%	3.8%	3.1%	0.0%
On long term sick-leave (6)	2.8%	2.9%	7.7%	0.0%	0.0%
Student (8)	3.8%	2.9%	3.8%	4.7%	3.7%
Retired (28)	13.1%	8.6%	11.5%	15.6%	22.2%
Recruited through					
A healthcare appointment (30)	14.2%	15.7%	17.3%	15.6%	0.0%
Online/social media advertisement (176)	83.0%	80%	78.8%	82.8%	100.0%
Pain clinic appointment letter (6)	2.8%	4.3%	3.8%	1.6%	0.0%

Measures

Outcomes were chosen in concurrence with the IMMPACT study, which put forward recommendations for core outcomes in chronic pain clinical trials (Dworkin et al., 2005), including pain severity and type, and physical and emotional functioning. Due to the number of dependent variables and to avoid responding fatigue (which is particularly likely in this population), brief measures were chosen wherever possible. It was also important that measures were free to use and could be easily translated to an online survey format.

Demographic questionnaire

The demographic questionnaire asked about age, gender, occupation, pain sites, pain diagnosis and duration, how they had first come across the study, whether they had ever attended a specialist pain clinic and if so, which professionals they had seen.

Chronic Pain Acceptance Questionnaire-8 (CPAQ-8)

The CPAQ-8 is an 8-item questionnaire that measures acceptance of chronic pain (Fish et al., 2010). It consists of two subscales with robust factor structures: activity engagement and pain willingness, each ranging from 0-24. Activity engagement refers to continued engagement in activities with chronic pain, and pain willingness refers to the openness of an individual to experiencing pain. CPAQ-8 has a near perfect correlation with the original 20-item questionnaire and has been validated in mixed chronic pain populations (Fish et al. 2010, Baranoff et al., 2014; Rovner et al., 2014). It shows good psychometric properties and sensitivity to rehabilitation processes (Reneman et al., 2010). The short version was chosen to minimise item burden, and because Rovner et al. (2019) demonstrated that it is equally valid for the purposes of clustering. In this sample the Cronbach's alpha was .86 for the AE subscale and .74 for the PW subscale.

Brief Pain Inventory (BPI) – Short Form

This measure assessed subjective pain severity and interference of the reported pain with day-to-day activities, such as social relations and sleep (Cleeland & Ryan, 1994). It relies on numerical rating scales ranging from 0-10 and has been validated for assessment of chronic pain both in research and clinical settings (Tan, Jensen, Thornby, & Shanti, 2004). In this study the pain intensity subscale was used to measure subjective pain severity and the pain interference subscale was used to measure pain-related disability. This fits with the IMMPACT study's recommendations of measuring pain-related functional impairment separately from pain intensity as the two do not correlate (Dworkin et al., 2005). The BPI has excellent psychometric properties for use in different populations with persistent pain, with internal consistency ranging from .82-.95, excellent test-retest reliability (ICC = .83-96), and good construct validity; the interference subscale has a good correlation with other measures of physical disability (r= .69-.82). The short form version was used in this study as it omits qualitative and pictorial items that are not relevant to the study aims. In this sample the Cronbach's alpha was .87 for the Pain Severity subscale and .89 for the Pain Interference subscale.

The Generalised Anxiety Disorder Assessment-7 (GAD-7)

This 7-item questionnaire with total scores ranging from 0-21 is based on criteria for Generalised Anxiety Disorder. A score of 10 yields 89% sensitivity and 82% specificity for probable clinically significant anxiety symptoms (Spitzer, Kroenke, Williams, & Löwe, 2006). It is also sensitive to other anxiety disorders such as panic disorder (74%), social anxiety (72%) and post-traumatic stress disorder (66%). It has been validated in a sample of people with migraines and has excellent internal consistency with Cronbach's alpha of .91 (Seo & Park, 2015a). The Cronbach's alpha in our sample was also .91. The GAD-7 was chosen over other measures of anxiety as it is short, free to use and widely used in research and clinical practice.

The Patient Health Questionnaire-9 (PHQ-9)

This 9-item questionnaire with total scores ranging from 0-27 is based directly on diagnostic criteria for major depression, and a score of 10 or more yields 88% sensitivity and 88% specificity for clinically significant major depression (Kroenke, Spitzer & Williams, 2001). It has been validated across a range of medical settings (Gilbody et al., 2007), and in a population suffering from migraines it yielded a Cronbach's alpha of .89 (Seo & Park, 2015b). In our sample the Cronbach's alpha was .87. It was chosen over other measures of depression as it is short, free to use and widely used in research and clinical practice.

Pain Self-Efficacy Questionnaire (PSEQ)

Pain self-efficacy is an individual's sense of efficacy in managing their daily lives with chronic pain. A meta-analysis has demonstrated the relationship between pain self-efficacy and other outcomes such as pain severity, distress and disability (Jackson, Wang, Wang, & Fan, 2014), making this a key target for PAIN MANAGEMENT PROGRAMME intervention. The PSEQ is a 10-item questionnaire (scores ranging from 0-60) measuring this construct, with higher score indicates higher pain self-efficacy (Nicholas, 2007). It is easy to administer and is made for use across pain sites and conditions. It has good internal consistency (Cronbach's alpha of .92), test-retest reliability, and correlates

with measures of pain-related disability and general self-efficacy (Nicholas, 2007). The Cronbach's alpha in the current sample was .92.

Valuing Questionnaire (VQ)

The VQ consists of 10 items and assesses the extent to which an individual lives according to their values (Smout, Davies, Burns, & Christie, 2014). Unlike other scales of valued living, it measures two constructs: 'progress' with and 'obstruction' to values-consistent behaviour. Both are measured on a scale of 0-30, where a high score indicates higher degree of values-consistent living on the 'progress' subscale and a high degree of barriers on the 'obstruction' subscale. The VQ has established good construct validity and concurrent validity when compared to other measures of valued living and has been validated in populations with persistent pain (Carvalho et al., 2018; Rickardsson, 2019). Additionally, it is brief and lends itself to online administration. In the current sample the Cronbach's alpha was .86 for the Progress subscale and .76 for the Obstruction subscale.

Statistical Analysis Strategy

Statistical analyses were conducted using SPSS for Windows version 25 (IBM, 2017). Participants were allocated to cluster membership based on Rovner and colleagues' clinical cut-off scores for AE and PW on the CPAQ-8. Cluster membership formed the independent variable with four levels. The cut-off scores for clustering as defined by Rovner et al. (2019), are detailed in Table 4.

One-way MANOVAs were used to test whether the clusters (the independent variable) differ on a linear combination of measures of functioning (pain interference, pain self-efficacy, and two subscales of valued living), and a combination of measures of psychological distress (anxiety and depression). MANOVA was chosen over ANOVA in this instance because a MANOVA takes account of the relationship between the dependent variables and has greater power to detect true cluster differences, and because it better controls for the increased chance of type 1 errors when making multiple comparisons.

Planned multivariate contrasts with Bonferroni corrections were used in the event of a significant result to identify which clusters significantly differ from each other.

To understand differences in pain and functioning between clusters at a univariate level, one-way ANOVAs were conducted for each of the dependent variables with cluster as a grouping factor. Where significant these were followed up by Gabriel's post-hoc tests.

Table 4

Clinical cut-off Scores on the CPAQ-8 for Clustering, identified by Rovner et al. (2019)

Cluster	**AE**	**PW**
Low	0-9	0-7
Low AE, High PW	0-12	8-24
High AE, Low PW	10-12 OR 13-24	0-7 0-11
High	13-24	12-24

Power Analysis

A power analysis to estimate sample size was conducted using G*Power (Faul, Erdfelder, Buchner, & Lang, 2009). This was based on the study by Rovner et al. (2019), who examined the differences between CPAQ clusters on anxiety and depression measures using a MANOVA. They had a sample size of 1775 and used an alpha level of 0.05. The effect sizes were not reported in the paper but were calculated using an online tool (Lenhard & Lenhard, 2016). This revealed Cohen's d ranging from 0.44-1.54 on the anxiety variable, which equates to medium to very large effect sizes according to Cohen's classification (1988). For the depression variable the effect sizes ranged from 0.06-1.265 on the between-cluster comparisons, or from very small to very large.

An a priori power analysis was conducted to determine the required sample size to detect a statistically significant effect in a MANOVA with one independent variable (cluster membership) and nine independent variables (pain intensity, pain interfe rence, anxiety, depression, pain self-efficacy, emotion regulation, self-compassion, valued living, alexithymia), with significance level 0.05. Given the variability in effect sizes between different clusters in the Rovner study, it was decided to adopt a conservative estimate and assume a medium effect size of 0.5. The power was set to .80 and alpha level of .05 in accordance with recommendations from Fritz & MacKinnon (2007). With these parameters the minimum required sample size is 164. Cluster sizes are likely to be uneven, and analyses require at least as many people in each cluster as there are dependent variables (Tabachnick, Fidell, & Ullman, 2007), in this instance nine. The final number of variables included in the study were seven (due to the removal of some that were deemed less relevant to study aims), which would have somewhat reduced the target number of participants. It was decided that a repeat power analysis was not needed.

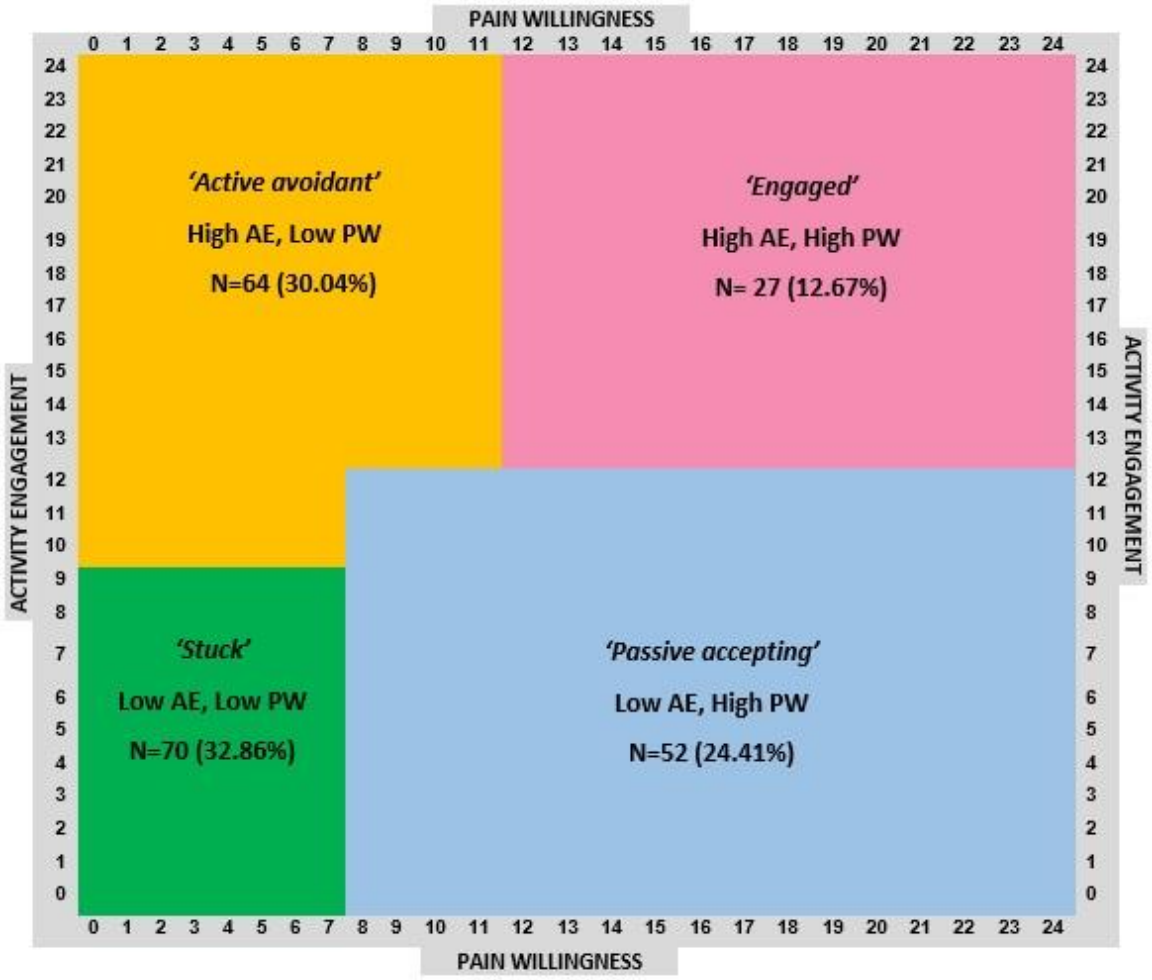
Results

Cluster Membership

Participants were divided into clusters using the clinical cut-off scores for AE and PW on CPAQ-8. Proportions of participants categorised into each cluster is outlined in Figure 3.

Figure 3

Proportions of Participants in Each CPAQ-8 Cluster.



Cluster Labels

To aid clarity and enhance readability of our results, it was decided to create descriptive labels for the clusters. These are not intended to be reductive or pejorative, but an attempt to reflect the behavioural patterns inferred by CPAQ-8 scores. The Low cluster, who are low in both AE and

PW will be described as the 'Stuck' cluster due to their low willingness and engagement in activity. The cluster who is high in PW but low in AE will be described as the 'Passive accepting' cluster as their level of PW has not yet translated into action. The high AE/low PW cluster will henceforth be called the 'Active avoidant' cluster, due to their high activity levels and low willingness to tolerate pain. The cluster that is high in both AE and PW will be called the 'Engaged' cluster throughout due to their high levels of acceptance and activity engagement. It is important to note that we think of these clusters as malleable response styles rather than fixed patterns of behaviour.

Data Screening

Histograms were examined, and Z-scores were calculated for the skewness and kurtosis of each dependent variable, which confirmed that the assumption of univariate normality was met. The data was then divided by cluster; the Shapiro-Wilk test was significant for all dependent variables, meaning that the assumption of multivariate normality was violated. One outlier was identified as exceeding the critical value for Mahalonobis distance and was therefore excluded from further analysis. Correlations between the dependent variables were all small to moderate, and thus there was no multicollinearity. Box's test of equality of variance was non-significant, as were Levene's tests for all dependent variables. The data therefore met the assumption of homogeneity of variance. In conclusion, the data met all the assumptions of MANOVA other than multivariate normality; MANOVA is robust against this, and the Pillai's trace test statistic was chosen as this is the most robust to the combination of this violation and unequal sample sizes, given that Box's test was non-significant.

Multivariate Analyses

To test the hypothesis that the clusters differ on a combination of dependent variables, two one-way MANOVAs were performed. Both used cluster membership as the independent variable with four levels. The first was a 'functioning' MANOVA with pain interference, pain self-efficacy, and two sub-

scales of valued living (progress and obstruction) as dependent variables. The second was a 'psychological distress' MANOVA with anxiety and depression as dependent variables. Due to unequal sample sizes and not meeting all the assumptions, it was decided to use the Pillai's trace test statistic which is robust against parametric violations.

The 'functioning' MANOVA revealed a significant test statistic (Pillai's trace $F(12, 621) = 11.36$, $p < 0.001$, meaning that there was a significant difference between at least two of the clusters on measures of functioning.

The 'psychological distress' MANOVA also showed a significant test statistic (Pillai's trace $F(6, 416) = 8.93$, $p < 0.001$, meaning that there was a significant difference between at least two of the clusters on psychological measures.

These cluster differences were investigated through multivariate pairwise comparisons with Bonferroni corrections (see Table 5). This revealed that all clusters significantly differed from each other on the combination of variables related to functioning. On the combination of variables related to psychological distress, all clusters differed from each other except the Stuck and Passive Accepting, and the Passive Accepting and Active Avoidant.

Table 5

Test Statistics for the Multivariate Between-Cluster Differences.

Cluster comparisons	Functioning (F-statistic, p-level)	Psychological distress (F-statistic, p-level)
Stuck		
Vs Passive accepting	F = 13.94, p < .001*	F = 1.41, p = .236
Active avoidant	F = 95.78, p < .001*	F = 9.6, p = .02*
Engaged	F = 150.34, p < .001*	F = 38.23, p < .001*
Passive accepting		
Active avoidant	F = 29.43, p < .001*	F = 2.93, p = .088
Engaged	F = 78.20, p < .001*	F = 24.97, p < .001*
Active avoidant		
Engaged	F = 22.35, p < .001*	F = 14.23, p < .001*

**significant at Bonferroni-adjusted significance level .0083*

Univariate analyses

To understand the mean differences between clusters on measures of functioning at a univariate level, one-way ANOVAs were conducted on each of the seven dependent variables (pain intensity, pain severity, anxiety, depression, pain self-efficacy, valued living and barriers to valued living) with cluster as a grouping factor. Significant results were followed up by Gabriel's post hoc tests to account for unequal sample sizes. See Table 6 for mean scores across clusters, and Figure 4 for box plots of each outcome measure.

Significant differences were found between clusters on all dependent variables (all $p \leq .003$). These differences followed an expected pattern where the Stuck cluster scored worse on all measures of functioning and psychological distress, and the Engaged cluster scored the highest.

Table 6

Mean Scores on Outcome Variables Across Clusters.

	CLUSTER MEMBERSHIP				
	TOTAL (N=212)	**Stuck (N=69)**	**Passive accept-ing (N=52)**	**Active avoidant (N=64)**	**Engaged (N=27)**
Descriptive variables (range)	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
BPI Pain Severity 0-10	5.53 (1.69)	6.11 (1.45)	5.80 (1.58)	5.24 (1.62)	4.22 (1.88)
BPI Pain Interference 0-10	5.99 (2.27)	7.07 (1.64)	6.74 (1.85)	5.35 (2.20)	3.30 (1.87)
GAD-7 Anxiety 0-21	9.75 (5.82)	11.09 (5.49)	9.56 (5.33)	10.63 (6.13)	4.63 (3.90)
PHQ-9 Depression 0-27	13.99 (6.45)	16.33 (5.93)	15.04 (5.54)	13.14 (6.69)	8.00 (4.69)
PSEQ Pain self-efficacy 0-60	23.65 (12.16)	14.49 (7.81)	20.56 (10.45)	29.52 (8.59)	39.11 (8.59)
VQ Valued living					
Progress 0-30	13.07 (7.05)	9.55 (5.29)	11.77 (7.09)	16.02 (6.75)	17.59 (6.46)
Obstruction 0-30	14.34 (6.30)	16.28 (6.26)	14.88 (5.67)	13.48 (6.05)	10.41 (6.24)

Table 7

Post-Hoc Comparisons Between Clusters for Each of the Outcome Measures.

Cluster comparisons	Pain severity	Pain interference	Anxiety	Depression	Pain self-efficacy	VQ Progress	VQ Obstruction
Stuck							
Vs Passive accepting	.869	.924	.562	.797	.001*	.301	.757
Active avoidant	.011*	<.001*	.997	.013*	<.001*	<.001*	.050*
Engaged	<.001*	<.001*	<.001*	<.001*	<.001*	<.001*	<.001*
Passive accepting							
Active avoidant	.309	.002*	.878	.422	<.001*	.003*	.765
Engaged	<.001*	<.001*	<.001*	<.001*	<.001*	.001*	.011*
Active avoidant							
Engaged	.028*	<.001*	<.001*	.001*	<.001*	.847	.138

**Indicates statistical significance at p-level .05*

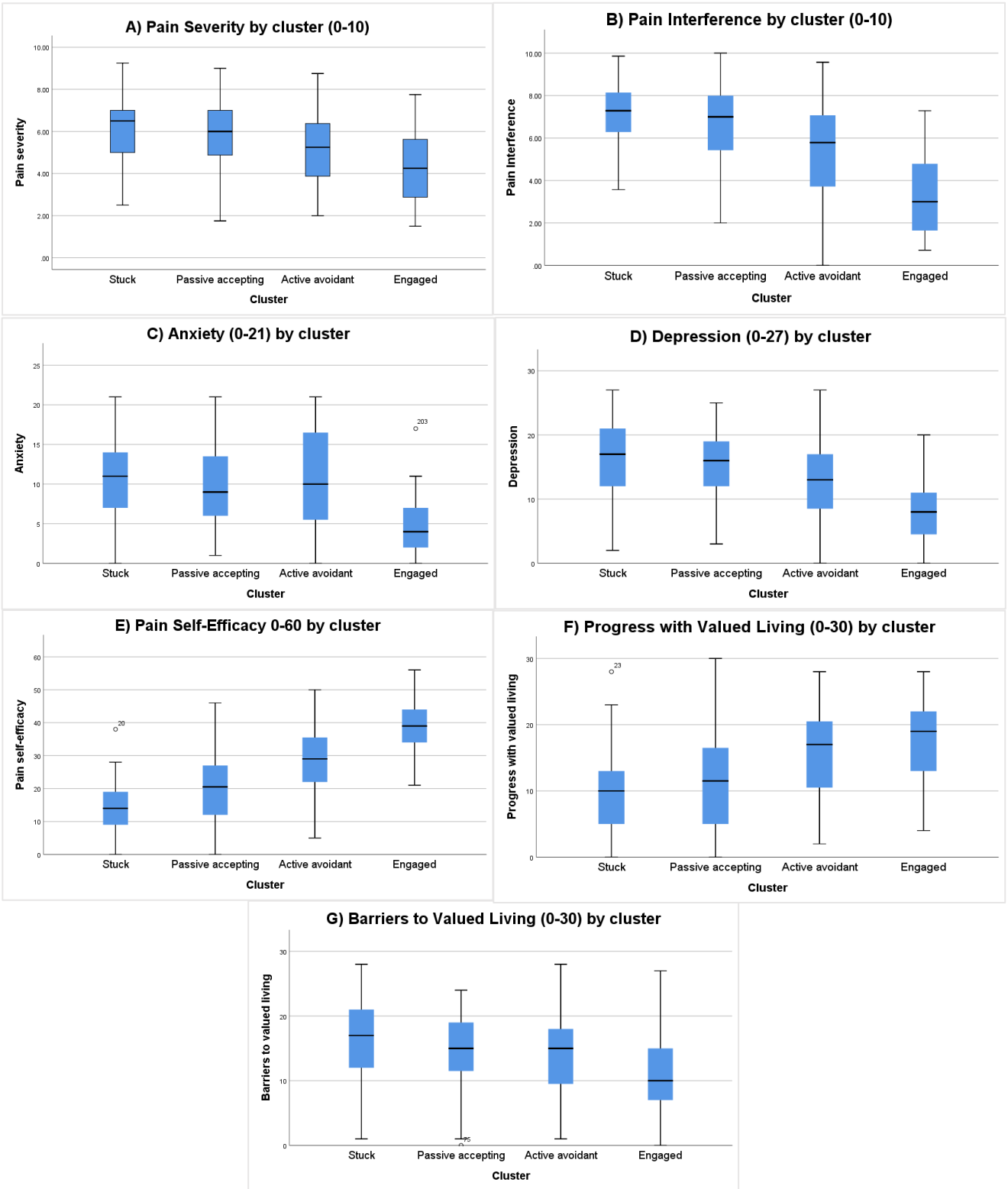
Post-hoc tests revealed that the Stuck cluster displayed significantly lower functioning and higher distress than the Active avoidant and the Engaged group, but only significantly differed from the Passive accepting group in pain self-efficacy.

The Passive accepting cluster scored significantly lower than the Active avoidant cluster only on pain interference, pain self-efficacy, and progress with valued living. The Passive accepting cluster scored significantly worse on all measures compared to the Engaged group.

The Active avoidant displayed significantly worse scores than the Engaged group on pain severity, pain interference, anxiety, depression, and pain self-efficacy, but not on valued living.

Figure 4

Box Plots For Each Outcome Measure By Cluster.



A. The Stuck cluster reported significantly higher pain severity than the Active avoidant and Engaged clusters. The Engaged cluster had significantly lower pain severity than all other clusters.

B. All clusters significantly differed from one another on pain interference, except the Stuck and the Passive accepting clusters.

C. The Engaged cluster had significantly lower levels of anxiety than the other three clusters; no other clusters significantly differed from each other.

D. The Engaged cluster reported significantly lower levels of depression than the other three clusters. The Stuck group also significantly differed from the Active avoidant group.

E. All clusters significantly differed from each other on pain self-efficacy, with the Stuck cluster reporting the lowest, and the Engaged group reporting the highest levels.

F. The Stuck and the Passive accepting cluster did not significantly differ from each other on progress with valued living, but both significantly differed from the Active avoidant and Engaged clusters.

G. The Stuck cluster reported significantly more obstruction to valued living than the Active avoidant and the Engaged clusters. The Passive accepting cluster also significantly differed from the Engaged cluster.

Discussion

This study aimed to assess whether CPAQ-clustering in an English-speaking sample of people with persistent pain would yield groups that meaningfully differ on variables related to functioning and psychological distress. Clusters were labelled according to the behaviour patterns implied by their CPAQ scores: the Low cluster was labelled the 'Stuck' group, the Low AE/High PW cluster was labelled 'Passive accepting', the High AE/Low PW group was named the 'Active avoidant' and the High cluster the 'Engaged' group.

Our findings demonstrated significantly different profiles between all these clusters on a combination of measures of functioning, which comprised pain interference, pain self-efficacy, and progress with/barriers to valued living. With regards to psychological distress, significant differences existed between the Stuck cluster and the Active Avoidant and Engaged clusters, between the Passive Accepting and the Engaged cluster, and between the Active Avoidant and Engaged clusters. No significant differences were evident between the Stuck and Passive Accepting, or the Passive Accepting and Active Avoidant clusters. This is likely to be related to the anxiety variable, which does not conform with a linear pattern of difference between clusters.

Outcomes mostly varied between clusters in a linear, expected pattern; the Stuck cluster exhibited the highest level of pain and distress and the lowest level of functioning on all measures, and the opposite was found in the Engaged cluster. The scores of the middle clusters fell in between, with the Passive accepting group scoring worse than the Active avoidant group. These findings were in line with our hypotheses and previous findings (Rovner et al., 2015; 2019). As expected, the anxiety variable diverged from this linear pattern as the Active avoidant cluster scored as highly on anxiety as the two Low AE clusters. This was in line with our hypothesis and suggests that this is a group whose high activity levels may be associated with high levels of anxiety. Rovner et al. (2019) speculated that this group may be "compulsively overdoing" in an effort to avoid pain, reflective of their

low willingness to experience pain (PW). This group, by definition, have a similar level of activity engagement as the Engaged group. In addition, we found that they engaged in similar levels of valued living as the Engaged group, while functioning significantly worse on all other measures. We may therefore speculate that the PW component of pain acceptance may be particularly important to functioning and wellbeing in persistent pain. However, the Passive accepting and Engaged clusters have similar PW levels; yet they significantly differed on all measures of distress and functioning. This is therefore not supported.

We also expected that the Passive accepting cluster would function significantly better than the Stuck cluster on all measures. In our sample the only significant difference between the two were pain self-efficacy, where the Passive accepting group scored higher. This lack of distinction between the two clusters was surprising, given that previous studies had found significant differences on pain intensity, quality of life, fear of movement and all measures of functioning except physical activity (Rovner et al., 2015; 2019).

The Passive accepting cluster did significantly differ from the next cluster (the Active avoidant) on pain interference, self-efficacy and progress with valued living. The Stuck cluster differed from the Active avoidant group on all measures, except anxiety. These findings suggest that differences in functioning may not just be a function of pain acceptance; there appears to be a distinction in functioning based on AE, whereby the high AE clusters function significantly better than the low AE clusters. We may therefore speculate that higher engagement in activity and valued living may be protective of mood, pain interference and self-efficacy. This fits with behavioural approaches to persistent pain intervention. Research into mechanisms of change in PAIN MANAGEMENT PROGRAMMEs highlight the importance of behavioural activation, and particularly, "adopting an early action attitude" in improving outcomes (Burns et al., 2015). Similarly, Miró et al. (2018) found that changes in AE, but not PW, were associated with improvements in disability during a pain management programme.

Rovner et al. (2019) hypothesised that the High AE/Low PW, or the Active avoidant cluster, may benefit from a treatment approach that focuses on slowing down and improving self-compassion. This implies that this cluster would display low levels of self-compassion, and we therefore included this variable to test this hypothesis. The Active avoidant group did not display lower levels of self-compassion than the other clusters; instead, we saw a pattern where the low AE clusters scored lower than the high AE clusters. This suggests that the low AE clusters may be the ones that could benefit from increasing self-compassion.

There was, expectedly, an unequal distribution of participants in each cluster, with the Engaged group being the smallest. Rovner et al. (2019) hypothesised that few people fell into the High AE/PW group as their sample was recruited from a pain clinic. We found a similar distribution with only 12% falling into the Engaged cluster, and a more evenly distributed split of the other three clusters, with proportions ranging from 24-33%, compared to 19-42% in Rovner's sample. While our sample was largely recruited from the community, a majority (64%) of our sample reported having attended a Pain Clinic. It may be that a truly community-based sample would have a different cluster distribution with more people in the Engaged group.

Implications of Clustering

These findings indicate that participants in different CPAQ-clusters differ on clinically meaningful variables which may influence the response to pain management programmes. Our results indicate meaningful differences between the four CPAQ-clusters on functioning, and to some degree on psychological distress. It could therefore be useful in triage and treatment planning in specialist pain clinics. A first step may be to evaluate the use of CPAQ-clustering to improve group cohesion in standard pain management programmes. Furthermore, the different profiles may be an indication of different treatment needs. A future aim may be to move away from the one-size-fits-all approach to pain management programmes and move towards a more tailored approach where clustering informs different treatment options based on the different clusters' profiles of functioning.

Based on our findings we may hypothesise that the Engaged group may need only a low-intensity intervention such as pain education and self-help materials, building on their existing strengths. Conversely, the Stuck and Passive accepting groups may need the longest and highest intensity interventions with interdisciplinary support. Our findings suggest that these clusters would benefit particularly from graded exposure to activity, re-engagement with valued activities, and enhancing their self-efficacy in managing pain. Pain education and anxiety management will be important adjuncts to reduce fear associated with increasing activity.

We may also hypothesise that the Active avoidant group may benefit from a less intensive intervention that focuses on reducing overactivity and anxiety, while enhancing their willingness to experience pain. This may be achieved for example through activity pacing combined with mindful awareness and relaxation.

Limitations

There are some limitations to the current study. While care was taken to reduce the item burden by selecting short measures, there is a chance that participants will have been affected by fatigue due to the high number of items. This may have resulted in response bias such as answering all questions in a similar way, or choosing neutral options more often. More likely people affected by fatigue may have dropped out of the study altogether before submitting their responses, which may have led to a sample that are less affected by fatigue, or who are more prone to 'pushing through' their symptoms.

As with all studies using self-report measures the results rely on, and may be limited by, the respondents' understanding and interpretation of these measures. This survey was set to 'force' respondents to respond to each item, and the online administration means that there was limited opportunity for participants to clarify item meanings unless they contacted the lead researcher via email. In clinical practice such clarifications are sometimes sought due to the physical presence of a clinician, but no one contacted the lead researcher in this instance. This may be an indication that no

questions arose or that participants responded at random in order to progress with the survey in these instances.

Another limitation is that the sample largely consisted of women. This is consistent with Rovner et al. (2015; 2019) and is commensurate with the common gender gap typically seen in specialist pain services. However, this predominance of women may have impacted on the patterns of responses found in these clusters. We cannot guarantee that these findings extend to men.

A degree of sampling bias is present in this study as it consisted of a self-selected sample of people interested in participating. Participation also necessitated some level of digital competence and access, and thus excluded participants affected by digital poverty. It is difficult to say how this might have impacted on the current findings and limits how well these may generalise to the population of people presenting to specialist pain clinics.

Future Research

Future research could test the replicability of these findings in non-Western contexts and make efforts to include more men in their samples. The next steps in this field would be to test the clinical utility of these clusters in specialist pain clinics. A first step would be to use CPAQ clustering at the triaging stage and assess how this grouping variable would impact response to standard pain management programmes. A further research goal would be to tailor interventions to the identified treatment needs of different clusters and assess the effect this has on treatment response and the efficiency of treatment pathways.

Conclusion

Our findings supported differences in measures of functioning and distress between CPAQ-clusters in an English-speaking sample of people with persistent pain. Like previous studies we identified cluster differences in terms of pain intensity, pain interference, anxiety, and depression. In addition, we found differences in valued living and pain self-efficacy. Importantly, cluster differences

were not just associated with pain acceptance but differed based on both AE and PW. In the future CPAQ clustering may present a quick, easy-to-use, and clinically meaningful tool for specialist pain clinics, whereby they may use only eight items to triage patients into tailored interventions. Future research will identify whether this may lead to better group cohesion, effectivity of treatment pathways and a more even treatment response among people who present to specialist pain clinics.

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List of Appendices

Appendix 1: Clinical Psychology Review Author Guidelines

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[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T. (2015). *Mortality data for Japanese oak wilt disease and surrounding forest compositions.* Mendeley Data, v1. http://dx.doi.org/10.17632/xwj98nb39r.1

Appendix 2: Psychotherapy Outcome Study Methodology Rating Form

Psychotherapy outcome study methodology rating form

Note: If not enough information is given regarding a specific item a rating of 0 is given.

1.Clarity of sample description

0 *Poor*. Vague description of sample (e.g. only mentioned whether patients were diagnosed with the disorder).

1 *Fair*. Fair description of sample (e.g. mentioned inclusion/exclusion criteria, demographics, etc.).

2 *Good*. Good description of sample (e.g. mentioned inclusion/exclusion criteria, demographics, and the prevalence of comorbid disorders).

Comment:

2. Representativeness of the sample

0 *Poor*. Sample is very different from patients seeking treatment for the disorder (e.g. there are excessively strict exclusion criteria).
1 *Fair*. Sample is somewhat representative of patients seeking treatment for the disorder (e.g. patients were only excluded if they met criteria for other major disorders).
2 *Good*. Sample is very representative of patients seeking treatment for the disorder (e.g. authors made efforts to ensure representativeness of sample).
Comment:

3.Specificity of outcome measures

0 *Poor*. Very broad outcome measures, not specific to the disorder (e.g. SCL-90R total score).

1 *Fair*. Moderately specific outcome measures.

2 *Good*. Specific outcome measures, such as a measure for each symptom cluster.

Comment:

4. Reliability and validity of outcome measures

0 *Poor*. Measures have unknown psychometric properties, or properties that fail to meet current standards of acceptability.

1 *Fair*. Some, but not all measures have known or adequate psychometric properties.

2 *Good*. All measures have good psychometric properties. The outcome measures are the best available for the authors' purpose.

Comment:

5. Use of blind evaluators

0 *Poor*. Blind assessor was not used (e.g. assessor was the therapist, assessor was not blind to treatment condition, or the authors do not specify).

1 *Fair*. Blind assessor was used, but no checks were used to assess the blind.

2 *Good*. Blind assessor was used in correct fashion. Checks were used to assess whether the assessor was aware of treatment condition.

Comment:

6. Assessor training

0 *Poor*. Assessor training and accuracy are not specified, or are unacceptable.
1 *Fair*. Minimum criterion for assessor training is specified (e.g. assessor has had specific training in the use of the outcome measure), but accuracy is not monitored or reported.
2 *Good*. Minimum criterion of assessor training is specified. Inter-rater reliability was checked, and/or assessment procedures were calibrated during the study to prevent evaluator drift.
Comment:

7. Assignment to treatment

0 *Poor*. Biased assignment, e.g. patients selected their own therapy or were assigned in another non-random fashion, or there is only one group.
1 *Fair*. Random or stratified assignment. There may be some systematic bias but not enough to pose a serious threat to internal validity. There may be therapist by treatment confounds. *N* may be too small to protect against bias.
2 *Good*. Random or stratified assignment, and patients are randomly assigned to therapists within condition. When theoretically different treatments are used, each treatment is provided by a large enough number of different therapists. *N* is large enough to protect against bias.
Comment:

8. Design

0 *Poor*. Active treatment vs. WLC, or briefly described TAU.

1 *Fair*. Active treatment vs. TAU with good description, or placebo condition.
2 *Good*. Active treatment vs. another previously empirically documented active treatment.
Comment:

9. Power analysis
0 *Poor*. No power analysis was made prior to the initiation of the study.
1 *Fair*. A power analysis based on an estimated effect size was used.
2 *Good*. A data-informed power analysis was made and the sample size was decided accordingly.
Comment:

10. Assessment points
0 *Poor*. Only pre- and post-treatment, or pre- and follow-up.
1 *Fair*. Pre-, post-, and follow-up <1 year.
2 *Good*. Pre-, post-, and follow-up ⩾1 year.
Comment:

11. Manualized, replicable, specific treatment programs
0 *Poor*. Description of treatment procedure is unclear, and treatment is not based on a publicly available, detailed treatment manual. Patients may be receiving multiple forms of treatment at once in an uncontrolled manner.
1 *Fair*. Treatment is not designed for the disorder, or description of the treatment is generally clear and based on a publicly available, detailed treatment manual, but there are some ambiguities about the procedure. Patients may have received additional forms of treatment, but this is balanced between groups or otherwise controlled.
2 *Good*. Treatment is designed for the disorder. A detailed treatment manual is available, and/or treatment is explained in sufficient detail for replication. No ambiguities about the treatment procedure. Patients receive only the treatment in question.
Comment:

12. Number of therapists
0 *Poor*. Only one therapist, i.e. complete confounding between therapy and therapist.
1 *Fair*. At least two therapists, but the effect of therapist on outcome is not analyzed.
2 *Good*. Three, or more therapists, and the effect of therapist on outcome is analyzed.
Comment:

13. Therapist training/experience
0 *Poor*. Very limited clinical experience of the treatment and/or disorder (e.g. students).
1 *Fair*. Some clinical experience of the treatment and/or disorder.
2 *Good*. Long clinical experience of the treatment and the disorder (e.g. practicing therapists).

Comment:

14. Checks for treatment adherence

0 *Poor*. No checks were made to assure that the intervention was consistent with protocol.
1 *Fair*. Some checks were made (e.g. assessed a proportion of therapy tapes).
2 *Good*. Frequent checks were made (e.g. weekly supervision of each session using a detailed rating form).
Comment:

15. Checks for therapist competence

0 *Poor*. No checks were made to assure that the intervention was delivered competently.
1 *Fair*. Some checks were made (e.g. assessed a proportion of therapy tapes).
2 *Good*. Frequent checks were made (e.g. weekly supervision of each session using a detailed rating form).
Comment:

16. Control of concomitant treatments (e.g. medications)

0 *Poor*. No attempt to control for concomitant treatments, or no information about concomitant treatments provided. Patients may have been receiving other forms of treatment in addition to the study treatment.

1 *Fair*. Asked patients to keep medications stable and/or to discontinue other psychological therapies during the treatment.

2 *Good*. Ensured that patients did not receive any other treatments (medical or psychological) during the study.

Comment:

17. Handling of attrition

0 *Poor*. Proportions of attrition are not described, or described but no dropout analysis is performed.
1 *Fair*. Proportions of attrition are described, and dropout analysis or intent-to-treat analysis is performed.
2 *Good*. No attrition, or proportions of attrition are described, dropout analysis is performed, and results are presented as intent-to-treat analysis.
Comment:

18. Statistical analyses and presentation of results

0 *Poor*. Inadequate statistical methods are used and/or data are not fully presented.

1 *Fair*. Adequate statistical methods are used but data are not fully presented.
2 *Good*. Adequate statistical methods are used and data are presented with *M* and SD.
Comment:

19. Clinical significance

0 *Poor*. No presentation of clinical significance was done.

1 *Fair*. An arbitrary criterion for clinical significance was used and the conditions were compared regarding percent clinically improved.

2 *Good*. Jacobson's criteria for clinical significance were used and presented for a selection (or all) of the outcome measures, and conditions were compared regarding percent clinically improved.

Comment:

20. Equality of therapy hours (for non-WLC designs only)
0 *Poor*. Conditions differ markedly (⩾20% difference in therapy hours).
1 *Fair*. Conditions differ somewhat (10–19% difference in therapy hours).
2 *Good*. Conditions do not differ (<10% difference in therapy hours).
Comment:

Total score:

Additional comments:

Appendix 3: POMRF Ratings by Both Reviewers

Items	Brassington et al. 2016			Carvalho et al. 2021			Hashemvarzi et al. 2021			Hou et al. 2017			O'Hayer et al. 2021			Wynne et al., 2019		
	P rating	S rating	New rating	P rating	S rating	New rating	P rating	S rating	New rating	P rating	S rating	New rating	P rating	S rating	New rating	P rating	S rating	New rating
1.Clarity of sample description	2	2	2	1	2	2	1	1	1	2	1	2	1	1	1	2	1	2
2.Representativeness of sample	2	2	2	1	2	2	1	2	2	1	2	1	2	2	2	0	2	0
3.Specificity of outcome measures	2	2	2	2	2	2	1	1	1	1	2	2	1	2	1	1	2	2
4.Reliability/validity of outcomes	2	2	2	2	2	2	1	1	1	1	0	1	2	2	2	1	1	1
5.Use of blind evaluators	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	2	1	2
6.Assessor training	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
7.Assignment to treatment	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	2	1	1
8.Design	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
9.Power analysis	1	1	1	1	2	2	0	0	0	0	0	0	0	0	0	2	2	2
10.Assessment points	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1
11.Manualised/replicable/specific treatments	2	2	2	0	2	1	0	0	0	1	0	0	1	2	1	2	0	2
12.Number of therapists	1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
13.Therapist training/experience	1	2	2	0	0	0	0	0	0	0	0	0	1	0	0	2	2	2
14.Checks for treatment adherence	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	2	0	2
15.Checks for therapist competence	2	1	2	0	0	0	0	0	0	0	0	0	1	1	1	2	2	2
16.Control of concomitant treatments	0	1	0	1	1	1	0	0	0	1	0	1	0	0	0	2	1	2
17.Handling of attrition	2	2	2	2	2	2	2	0	2	1	0	0	1	0	1	2	2	2
18.Statistical analyses and presentation	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
19.Clinical significance	0	2	0	2	2	2	0	0	0	0	0	0	1	1	1	0	2	0
20.Equality of therapy hours	0	0	0	2	2	2	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	21	24	22	22	26	26	9	10	10	11	8	9	15	16	14	26	22	26
Number of discrepancies	20.00%	4	0	25.00%	5		10.00%	2		40.00%	8		20.00%	4		50%	10	
Number changed			1			4			1			4			2			2
Number agreed	80.00%	16		75.00%	15		90.00%	18		60.00%	12		80.00%	16		50.00%	10	

Appendix 4: The Journal of Pain Author Guidelines

NEW SUBMISSIONS

References

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.

Divide the article into clearly defined sections.

Please ensure the text of your paper is double-spaced and includes page numbers - this is an essential peer review requirement.

Figures and tables embedded in text

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.

Peer review

This journal operates a single anonymized review process. All contributions will be initially assessed by the editor for suitability for the journal. Papers deemed suitable are then typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final. Editors are not involved in decisions about papers which they have written themselves or have been written by family members or colleagues or which relate to products or services in which the editor has an interest. Any such submission is subject to all of the journal's usual procedures, with peer review handled independently of the relevant editor and their research groups. More information on types of peer review.

REVISED SUBMISSIONS

Use of word processing software

Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

Pages must be numbered consecutively, beginning with the title page. Manuscripts without numbered pages will be returned to authors for correction. Materials should be presented in this order:

5 Cover letter

6 Manuscript (as a single file that contains the following): title page (include all authors' names and affiliations and disclosures), abstract, perspective, key words, text, acknowledgments (optional), references, figure legends

7 Figures

8 Tables

9 Checklist (see more information)

Cover letter

A cover letter must be presented and must include contact information for the corresponding author; this contact information must also be presented on the title page and must match the corresponding author designated in the Elsevier Editorial System upon upload. (When such information differs, manuscripts will be returned to authors for correction.) Any conflicts of interest should be noted, and if no conflicts are present, this should be explicitly stated. Include a statement that all authors are listed and that all have contributed substantially to the manuscript. Authors must state whether manuscripts from the same study were submitted or published. Authors are asked to suggest the names of three potential reviewers; please include contact information.

Title page (page 1)

The title should be a concise and informative description of the study and should indicate animal species if the research was conducted on nonhuman animals subjects. Within the title, use nonproprietary names for drugs, and descriptions for devices. Brand name may be mentioned only once within the text (upon first reference), unless essential to the study. The title page should include the authors' names, department(s), institution where the work was done, and institutional affiliations of authors. The corresponding author must be clearly identified and phone/fax/e-mail information must be provided. The corresponding author noted on the manuscript's title page must be the same person designated as corresponding author within the Elsevier Editorial System. The title page should include a short running title (45 characters, excluding spaces).

Disclosures

This required section must appear on the title page. **Research funding** sources must be acknowledged, including corporate, grant, institutional, or departmental funds. If this does not apply, authors must state that no funding sources were provided. In this section, all authors must disclose any potential **conflicts of interest** and must include a declaration statement if no conflicts exist. Conflicts include honoraria, travel to conferences, consultancies, stock ownership (excluding publicly owned mutual funds), equity interests, and patent-licensing arrangements (particularly if a commercial product is noted in the article).

Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Abstract (page 2)
An abstract of 200 words or less should describe concisely the purpose of the study, the main findings, and conclusions, all in one paragraph without subheadings. References may not be included in the abstract.
Trial registration
The Journal will only consider for publication randomized clinical trials that were registered with an appropriate registration agency (such as clinicaltrials.gov) before the first subject was recruited. Registration information must be included at the end of the Abstract.

These guidelines apply to studies that involve both pharmacological and non-pharmacological interventions. The online registry information should appear at the end of the abstract.

Perspective
This item, limited to 50 words, should appear at the end of the abstract. The perspective presents a synopsis of the work to facilitate understanding of its significance. Authors of basic science reports should highlight the potential clinical relevance of their results for the benefit of clinical readers. Authors of clinical science reports should highlight the underlying mechanisms for the results, for the benefit of clinical scientists and basic scientists. Example: "Perspective: This article presents the psychometric properties of a new measure of spouse responses to patient chronic pain and well behavior. This measure could potentially help clinicians who seek to assess how spouse responses may contribute to patient pain and disability." References should not be included in the Perspective.
Key words
Five key words should be provided following the Perspective.
Text
Text headings should be as follows:
Introduction: State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.
Methods: Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference; only relevant modifcations should be described.
Results: Results should be clear and concise.
Discussion: This should explore the significance of the results of the work, not repeat them. Avoid extensive citations and discussion of published literature.
Subheadings in the *Methods, Results,* and *Discussion* sections should be used as necessary to aid organization and presentation, but subheadings and sections should not be numbered. All sections should be written concisely. Limit the *Introduction* to 600 words and the *Discussion* to 1500 words. Note that section labels may not apply to some article types, including Focus Articles and Critical Review Articles.
Footnotes are not permitted in the text. Information must be cited parenthetically, or within the *References* section.
Essential title page information

• ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.
• ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.
• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to**

date by the corresponding author.
• ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Highlights

Highlights are optional yet highly encouraged for this journal, as they increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any). Please have a look at the examples here: example Highlights.

Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

Graphical abstract

Although a graphical abstract is optional, its use is encouraged as it draws more attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.

Authors can make use of Elsevier's Illustration Services to ensure the best presentation of their images and in accordance with all technical requirements.

Acknowledgments

Collate acknowledgments in a separate section at the end of the article before the references; do not include them on the title page, as a footnote to the title, or otherwise. List here those individuals who provided help during the research (eg, providing language help, writing assistance, or proofreading the article). The Acknowledgments section is optional.

Footnotes

Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors build footnotes into the text, and this feature may be used. Should this not be the case, indicate the position of footnotes in the text and present the footnotes themselves separately at the end of the article.

Artwork

All figures must be cited in the text; figures must be cited in consecutive order (this also applies to individual panels within figures). Computer-generated figures should use solid fills or cross-hatching, not tonal shading. Color figures may be accepted but any cost related to print production is the responsibility of the author. However, authors who are members of the American Pain Society may qualify for complimentary production of essential color figures. Also, color figures may be published in the electronic version of *The Journal* at no cost to the authors. Within figures, patients' eyes must be masked unless authors receive patient permission. For a consent form, contact the Editorial Office at jpain@jpain.us.

TIFF and EPS are the preferred formats for artwork. All type fonts used in studio-created artwork must be either "embedded" in the file or supplied separately. All graphic files supplied as bitmap format (not vector format) in TIFF, JPEG, or GIF must be submitted in sufficiently high resolution (240-300 dpi for grayscale or color images and 600-1000 dpi for line art) to allow for printing. See Elseviers website for guidelines for

preparing electronic artwork: https://www.elsevier.com/authors/author-schemas/artwork-and-media-instructions.

Electronic artwork

General points

• Make sure you use uniform lettering and sizing of your original artwork.
• Preferred fonts: Arial (or Helvetica), Times New Roman (or Times), Symbol, Courier.
• Number the illustrations according to their sequence in the text.
• Use a logical naming convention for your artwork files.
• Indicate per figure if it is a single, 1.5 or 2-column fitting image.
• For Word submissions only, you may still provide figures and their captions, and tables within a single file at the revision stage.
• Please note that individual figure files larger than 10 MB must be provided in separate source files.

A detailed guide on electronic artwork is available.

You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

Regardless of the application used, when your electronic artwork is finalized, please 'save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.
TIFF (or JPG): Color or grayscale photographs (halftones): always use a minimum of 300 dpi.
TIFF (or JPG): Bitmapped line drawings: use a minimum of 1000 dpi.
TIFF (or JPG): Combinations bitmapped line/half-tone (color or grayscale): a minimum of 500 dpi is required.

Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); the resolution is too low.
• Supply files that are too low in resolution.
• Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. **For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article**. Please indicate your preference for color: in print or online only. Further information on the preparation of electronic artwork.

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Figure Legends

A legend must be provided for each figure. Figure legends should be brief and not repetitive of description in the text. Legends should be placed in numerical order after the list of references.

Tables

All tables must be cited in the text in consecutive order. Tables should be comprehensive without reference

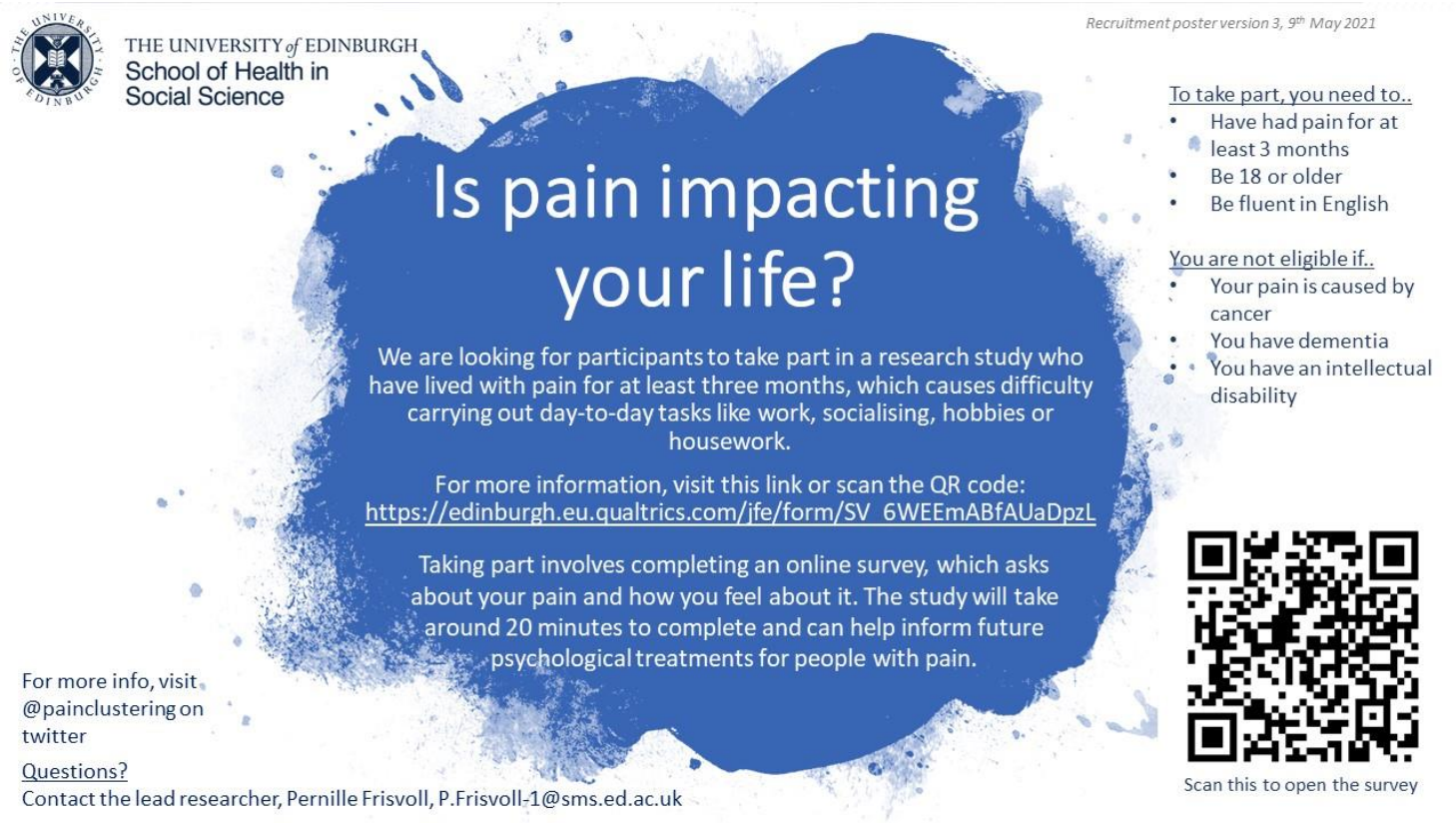
to the text and should not be repetitive of descriptions in the text. Every table should consist of two or more columns; tables with only one column will be treated as lists and incorporated into the text. Each column must have a column heading. Explanatory matter and source notations for borrowed or adapted tables should be placed in a table footnote, not in the title or table body.

References

Reference formatting

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Appendix 5: Study Flyer



Appendix 6: Ethical Approval by NHS Integrated Research Approval Service

London - Riverside Research Ethics Committee

Ground Floor
Temple Quay House

2 The Square

Bristol
BS1 6PN

Telephone: 02071048199

12 April 2021

Dr David Gillanders

Room 2.12, Doorway 6, Medical Quad
Teviot Place

Edinburgh
EH8 9AG

Dear Dr Gillanders

Study title:	**Further exploration of the validity of Chronic Pain Acceptance Questionnaire clustering in a persistent pain population**
REC reference:	**21/PR/0448**
Protocol number:	**CAHSS2012/06**
IRAS project ID:	**289748**

The Proportionate Review Sub-committee of the London - Riverside Research Ethics Committee reviewed the above application on 01 April 2021.

Ethical opinion

On behalf of the Research Ethics Committee (REC), the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

- registering research studies
- reporting results
- informing participants
- sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host

organisations.

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2.

Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral:

https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

If you have not already included registration details in your IRAS application form, you should notify the REC of the registration details as soon as possible.

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit:

https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-sum maries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion").

Approved documents

The documents reviewed and approved were:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [PL confirmation]	1	03 July 2020
IRAS Application Form [IRAS_Form_23032021]		23 March 2021
IRAS Application Form XML file [IRAS_Form_23032021]		23 March 2021
IRAS Checklist XML [Checklist_23032021]		23 March 2021
Letters of invitation to participant [Poster/flyer]	1	08 March 2021
Non-validated questionnaire [Demographic questionnaire]	1	08 March 2021
Organisation Information Document [Organisation information document]	1	19 March 2021
Other [PI confirmation]	1	04 August 2020
Other [EL cert]	1	01 August 2020
Other [CT confirmation]	1	04 August 2020
Participant consent form [consent form]	1	08 March 2021
Participant information sheet (PIS) [Participant information sheet]	1	08 March 2021

Participant information sheet (PIS) [Blurb to those who are not eligible for the study]	1	08 March 2021
Research protocol or project proposal [Research protocol]	1	08 March 2021
Schedule of Events or SoECAT [Schedule of Events]	1	25 February 2021
Summary CV for Chief Investigator (CI) [David Gillanders CV]	1	04 March 2021
Summary CV for student [Pernille Frisvoll CV]	1	11 December 2020
Validated questionnaire [CPAQ 8]		
Validated questionnaire [BPI]		
Validated questionnaire [GAD7]		
Validated questionnaire [PHQ9]		
Validated questionnaire [PSEQ]		
Validated questionnaire [VQ]		
Validated questionnaire [ERQ]		
Validated questionnaire [PAQ]		
Validated questionnaire [SCS]		

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known

please use the feedback form available on the HRA website:

http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at:

https://www.hra.nhs.uk/planning-and-improving-research/learning/

With the Committee's best wishes for the success of this project.

IRAS project ID: 289748	**Please quote this number on all correspondence**

Yours sincerelv

pp

Dr Marga-ret Jones Chair

Email: riverside.rec@hra.nhs.uk

Enclosures: List of names and professions of members who took part in the review

"After ethical review – guidance for researchers"

Copy to: Ms Charlotte Smith

Lead Nation
gram.nrspcc@nhs.scot

Health Research Authority

London - Riverside Research Ethics Committee

Attendance at PRS Sub-Committee of the REC meeting on 01 April 2021.

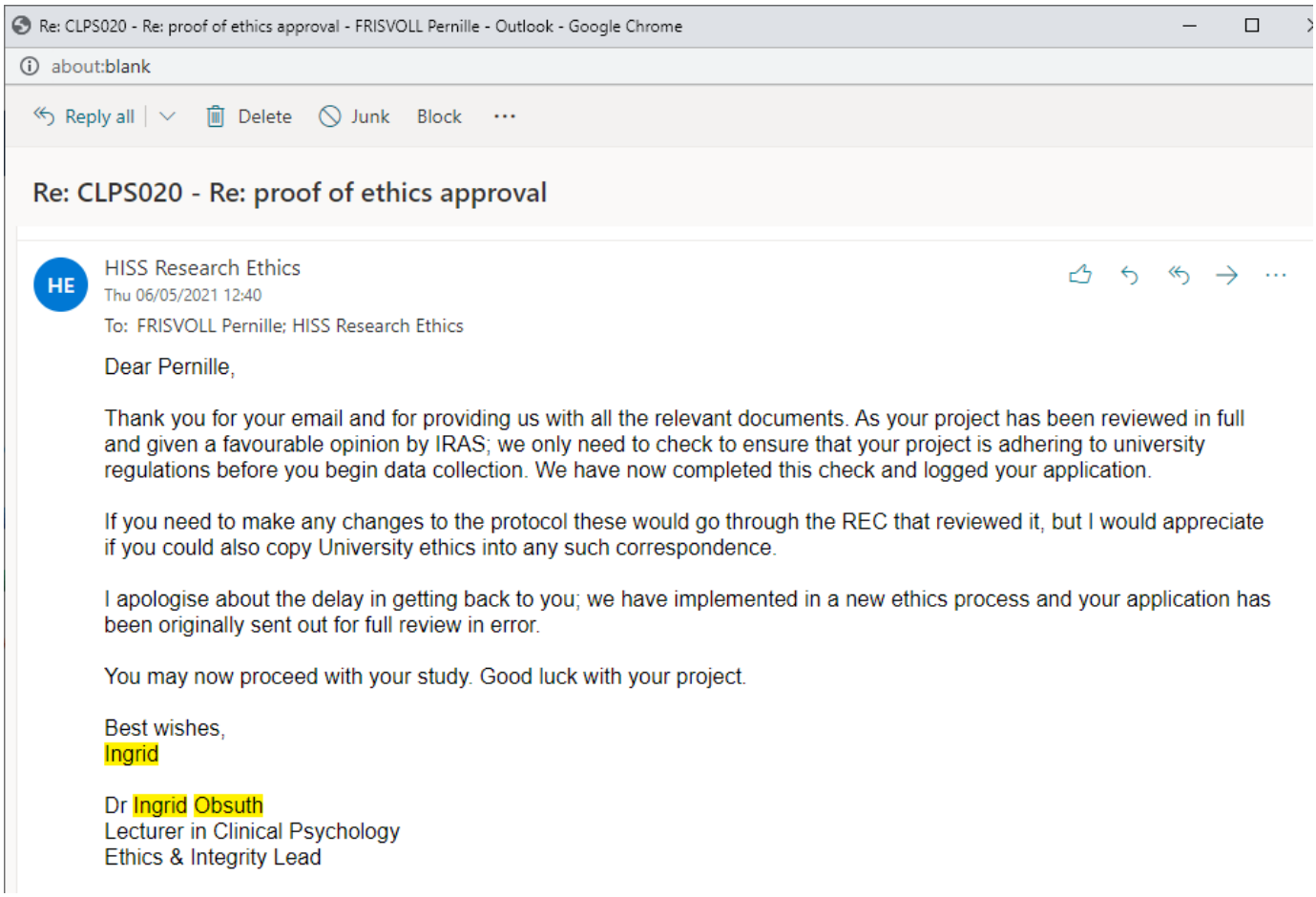
Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Nuria Gonzalez-Cinca	Clinical Study Manager	Yes	
Dr Margaret Jones	Retired General Practitioner	Yes	Chaired the meeting.
Dr Lorraine Murphy	Pharmaceutical Consultant	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Mia Cooper	Approvals Administrator

Appendix 7: Approval from School of Health in Social Sciences at University of Edinburgh



Re: CLPS020 - Re: proof of ethics approval - FRISVOLL Pernille - Outlook - Google Chrome

about:blank

Reply all | Delete | Junk | Block | ...

Re: CLPS020 - Re: proof of ethics approval

HE

HISS Research Ethics
Thu 06/05/2021 12:40

To: FRISVOLL Pernille; HISS Research Ethics

Dear Pernille,

Thank you for your email and for providing us with all the relevant documents. As your project has been reviewed in full and given a favourable opinion by IRAS; we only need to check to ensure that your project is adhering to university regulations before you begin data collection. We have now completed this check and logged your application.

If you need to make any changes to the protocol these would go through the REC that reviewed it, but I would appreciate if you could also copy University ethics into any such correspondence.

I apologise about the delay in getting back to you; we have implemented in a new ethics process and your application has been originally sent out for full review in error.

You may now proceed with your study. Good luck with your project.

Best wishes,
Ingrid

Dr Ingrid Obsuth
Lecturer in Clinical Psychology
Ethics & Integrity Lead

Appendix 8: Approval from NHS Greater Glasgow & Clyde Research & Development Department

Administrator: Mr Scott Broadley Telephone Number: 0141 314 4001

E-Mail: Scott.Broadley@ggc.scot.nhs.uk

Website: https://www.nhsggc.org.uk/about-us/professional- support-sites/research-development/

Research & Innovation Dykebar Hospital, Ward 11

Grahamston Road Paisley, PA2 7DE Scotland, UK

02 June 2021

Dr Anna Graham

Glasgow Pain Management Programme
Building 3, Floor 2, Templeton Business Centre 62 Templeton Street

Glasgow, G40 2DA

NHS GG&C Board Approval

Dear Dr Graham,

Study Title:	Further exploration of the validity of Chronic Pain Acceptance Questionnaire clustering in a persistent pain population
Principal Investigator:	Dr Anna Graham
GG&C HB site	Greater Glasgow & Clyde Pain Management Programme, Templeton Business Centre
Sponsor	University of Edinburgh & NHS Lothian
R&I reference:	GN21MH146
REC reference:	21/PR/0448
Protocol no: (including version and date)	Version 1, 08/03/2021

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

- **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004

    - During the life span of the study GGHB requires the following information relating to this site
        - Notification of any potential serious breaches.
        - Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

- **For all studies** the following information is required during their lifespan.
    - First study participant should be recruited within 30 days of approval date.
    - Recruitment Numbers on a monthly basis.
    - Any change to local research team staff should be notified to R&I team
    - Any amendments – Substantial or Non Substantial
    - Notification of Trial/study end including final recruitment figures
    - Final Report & Copies of Publications/Abstracts
    - You must work in accordance with the current NHS GG&C COVID19 guidelines and principles.

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database. I wish you every success with this research study

Yours sincerely,

Mr Scott Broadley

Senior Research Administrator

Appendix 9: Approval from NHS Lothian Research & Development Department

Queen's Medical Research Institute

47 Little France Crescent, Edinburgh, EH16 4TJ

Research & Development Room E1.16

Tel: 0131 242 3330

Email: accord@nhslothian.scot.nhs.uk

Director: Professor Alasdair Gra

FM/LD/approval 05

July 2021

Dr Sarah Young

NHS Lothian

Pain Management service Astley Ainslie Hospital
133 Grange Loan
Edinburgh

EH9 2HL

Dear Dr Young

Lothian R&D Project No: 2021/0098 **REC No:** 21/PR/0448

Title of Research: Further exploration of the validity of Chronic Pain Acceptance Questionnaire clustering in a persistent pain population

Participant Information Sheet:
Version 1.0, dated 8 March 2021

Consent Form:
Version 1.0, dated 8 March 2021

Protocol: Version 1.0, dated 8 March 2021

Approved Location(s) within NHS Lothian: Astley Ainslie Hospital

I am pleased to inform you this letter provides Site Specific approval for NHS Lothian for the above study and you may proceed with your research, subject to the conditions below.

Please be aware that ACCORD has issued COVID-19 Clinical Research Plan

and Guidance that includes instructions for restarting/commencing non-COVID-19 clinical research, and also advice on what to do if there is a requirement to halt recruitment of new participants to an active study, what to do if the study design needs to be amended or if there is a resource issue within the study team in light of the ongoing COVID-19 pandemic.

The ACCORD guidance is available on the ACCORD website;

http://www.accord.scot/about-accord/accord-news/covid19-planning-and-guidance-research-0

The guidance detailed here applies to research projects Sponsored by NHS Lothian and/or the University of Edinburgh and to NHS Lothian hosted studies until further notice.

Please note that the NHS Lothian R&D Office must be informed of any changes to the study such as amendments to the protocol, funding, recruitment, personnel or resource input required of NHS Lothian.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Data controllers and processors have a legal obligation to hold a register of all its information assets (e.g. personal information (data) and/or special categories of personal data held in paper or electronic format for the purpose of clinical research). This R&D management approval is given on the understanding that you, as a potential information asset owner, will register any information assets associated with this research project with your employing organisation (where the data is held) in accordance the Data Protection Act 2018.

Please keep this office informed of the following study information, **which is a condition of NHS Lothian R&D Management Approval**:

- Date you are ready to begin recruitment, date of the recruitment of the first participant and the monthly recruitment figures thereafter.
- Date the final participant is recruited and the final recruitment figures.
- Date your study / trial is completed within NHS Lothian.

I wish you every success

with your study. Yours sin-

cerely

Fiona McArdle (Jul 5, 2021 15:30 GMT+1)

Ms Fiona
McArdle
Deputy
R&D Di-
rector

cc Dr David Gillanders, Chief Investigator, UoE

Ms Pernille Frisvoll, Trainee Clinical Psychologist, UoE

Ms Sheena Muir, Hospital & Hosted Services Manager, Astley Ainslie Hospital

Appendix 10: Participant Information Sheet

THE UNIVERSITY of EDINBURGH
School of Health in Social Science

NHS Lothian

Further exploration of the validity of Chronic Pain Acceptance Questionnaire Clustering in a persistent pain population

Information Sheet for Participants

You are being invited to take part in a research project. Before you decide if you would like to take part, we would like you to understand why we are doing this research and what it involves.

Please take the time to read the following information carefully and decide whether or not you want to take part. Once you have read this information sheet, you can close this window and return to the survey later using the same link or QR code as before. This information sheet tells you the purpose of the research, what will happen if you agree to take part and how it will be carried out. If there is anything that is not clear, or if you would like more information, please contact the lead researcher (contact details at the end of this information sheet).

What is the purpose of the research?

This research explores how people think and feel about their pain. We know that treatments such as pain management programmes help many people manage their pain better and improve quality of life, but we don't know why it works so well for some people and not so well for others. We think it is because people with pain are all so different and need different things from their clinicians. We think that an important way in which people differ, is in how they relate to their pain. Previous research has found that people can be placed into distinct groups based on how they deal with their pain. It is very likely that people in different groups need different things from their clinicians. If we knew more about what people need, and if we could group them according to what they need, we may be able to offer treatment that is more specific and potentially more effective for them.

Who can take part?

We are looking for people who have lived with pain for at least 3 months, and who experience some kind of difficulty in carrying out day-to-day activities like socialising, working or housework, because of pain. You have to be over 18 and fluent in English to take part. Unfortunately you cannot take part if you have a diagnosis of learning disability or dementia, or if your pain has been caused by cancer.

Do I have to take part?

No – it is entirely up to you. If you do decide to take part, you are still free to withdraw at any time and without giving a reason; you can do so by closing the browser window, which will delete your responses. Deciding not to take part or withdrawing from the study will not affect your healthcare. Please note that as your responses are anonymous, once you submit the survey it will not be possible to withdraw your data as we will not be able to identify it.

What will happen if I take part?

Once you have read this information sheet, you will see some questions further down the page which asks you to give your consent to take part by ticking 'yes' to a number of statements. You will then be asked some questions about yourself to check that you are eligible to take part. If you do not meet the inclusion/exclusion criteria, the survey will be closed and you will be taken to a separate information sheet which thanks you for your willingness to take part, and signposts you to relevant resources. In this case the information you have already given will be deleted.

If you are eligible, you will then be asked to complete a series of online questionnaires that ask you about your pain, your day-to-day activities, your mood, and how you feel about yourself and your pain. The whole process will take approximately 20 minutes to complete. We ask you to please answer every question in the study.

What are the possible benefits of taking part?

There are no direct benefits to you, but the information we gain will help us to understand how different people deal with their pain, which may help us to understand what people with pain need from their healthcare providers. By doing so, we hope that treatments for persistent pain will develop to be better tailored to the individual. You may get some satisfaction from being a part of this process.

What are the possible disadvantages or risks of taking part?

It is unlikely that you will experience any negative effects from taking part in this research. There is a small chance that you may find some of the questionnaires upsetting. If this happens, further support can be accessed through Breathing Space (0800 83 85 87) or The Samaritans (116 123). You are also free to stop taking part at any time, simply by closing the browser window.

Will my information be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage.

You do not have to leave any information that can identify you as an individual. This means that your responses will be anonymous and cannot be traced back to you. We will ask information that may be considered personal, such as your gender and pain diagnosis (if you have any), but you can choose to not leave this information if you prefer not to. All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage.

Your data will be processed in accordance with Data Protection Law. All information collected about you will be kept strictly confidential. As your data is anonymous, and it will be referred to by a unique participant number rather than by name. Your data will only be viewed by the researcher/research team. All electronic data will be stored on a password-protected computer file.

What are your choices about how your information is used?

- You can stop taking part in the study at any time, without giving a reason, simply by closing the browser window. This means that the data you have already provided will be deleted.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

The University of Edinburgh is the sponsor for this study based in the United Kingdom. We will be using the information you provide in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Edinburgh will keep this anonymised information about you for 10 years after the study has finished and this may be used in future ethically approved research.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from [www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team

For general information about how we use your data go to:

https://www.ed.ac.uk/records-management/privacy-notice-research

What will happen to the results of the research?

The results of this research will be written up as a doctoral thesis submitted to the University of Edinburgh. This will also take the form of an article submitted to a peer-reviewed journal and may be presented at academic conferences. If you would like to access the results of this study, you can follow @painclustering on Twitter for updates.

Who is organising the research and why?

The research is sponsored by the University of Edinburgh and NHS Lothian. It has been organised by the researcher as part of their doctoral thesis.

Who has reviewed the research?

The study proposal has been reviewed within the research team and independently by two members of staff in Clinical & Health Psychology and the University of Edinburgh.

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from London Riverside Research Ethics Committee. NHS Management Approval has also been given.

Researcher Contact Details

If you have any questions that you would like to ask about any aspect of the research, please contact Pernille Frisvoll (student researcher) at P.Frisvoll-1@sms.ed.ac.uk.

Independent Contact Details

If you would like to talk to someone who is independent of the research team, please contact Dr Angus MacBeth, Research Director, Doctorate in Clinical Psychology, University of Edinburgh: Angus.Macbeth@ed.ac.uk.

Complaints

If you would like to make a complaint about any aspect of this research, please contact:

NHS Lothian Patient Experience Team

2 – 4 Waterloo Place, Edinburgh, EH1 3EG

feedback@nhslothian.scot.nhs.uk

0131 536 3370

OR

The UoE Research Governance team at cahss.res.ethics@ed.ac.uk

Appendix 11: Consent Form

Further exploration of the validity of Chronic Pain Acceptance Questionnaire clustering in a persistent pain population

Consent form

	Please tick
I have read and understood the information sheet (Version 2, 19.Feb.21) for this study and have had the opportunity to consider the information, and contact the researcher to ask questions.	☐
I understand that my participation is voluntary and I am free to withdraw at any time without giving a reason and without my medical care or legal rights being affected.	☐
I understand that my anonymous data will be stored for a minimum of 10 years and may be used in future ethically approved research.	☐
I understand that relevant sections of my data collected during the study may be looked at by individuals from the Sponsors (University of Edinburgh and NHS Lothian) or from the NHS board, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.	☐

I confirm that I agree to take part in the above study.

Eligibility check:

We will ask you the following questions to ensure you are eligible to take part:

I have had pain for at least three months. ☐

My pain has made it harder for me to do everyday tasks, such as work, socialising, hobbies, housework or caring responsibilities. ☐

I am 18 years of age, or older. ☐

I am fluent in English. ☐

My pain is *not* caused by cancer. ☐

I do not have an intellectual disability. ☐

I do not have dementia. ☐

Appendix 12: Debrief Form

Exploring the validity of clustering people with persistent pain

Participant debrief form

Thank you!

Many thanks for your participation in this study; your responses have been recorded and are greatly appreciated. This research intends to understand more about the treatment needs of people with persistent pain, with the hope of making pain management programmes as relevant as possible to those who access them.

Keep informed of results

If you would like to keep informed of the results of this study, you can follow the Twitter page @painclustering for updates.

In case of distress

We acknowledge that some of the questions asked may have been upsetting to some or may have brought up difficult thoughts and feelings. If this is the case for you, we recommend that you look after yourself and discuss it with someone. You may wish to contact the lead researcher, Pernille Frisvoll (Trainee Clinical Psychologist), p.frisvoll-1@sms.ed.ac.uk if you wish to discuss any aspect of the research and how it may be affecting you. Please do not use this as an emergency contact as we cannot guarantee a speedy response. If you require more immediate support, you should contact your GP, or access any of the crisis lines below:

Breathing Space offers a confidential phone line for anyone in Scotland above the age of 16 who is feeling distressed. Their phone number is **0800 83 85 87**, and the line is open from Monday-Thursday 6pm-2am, and on the weekend from Friday 6pm-Monday 6am.
Their website is https://breathingspace.scot/

Samaritans offer a free, confidential phone line for anyone struggling to cope for any reason. Their phone number is **116 123**, and the phone line is open 24 hours a day, 365 days a year. You can also contact them via email, via jo@samaritans.org , where you will receive a response within 24 hours.
Their website is https://www.samaritans.org/

Further resources for managing pain

Pain Concern is a charitable organisation working to support people suffering from persistent pain in the UK, their family and healthcare staff. The website offers helpful information and resources: https://painconcern.org.uk/

Reconnect 2 Life is an interactive programme to help you look at your pain and how it affects you. It consists of a number of different modules which can be completed in any order you please: https://www.torbayandsouthdevon.nhs.uk/services/pain-service/reconnect2life/

Pain UK is an umbrella-organisation that supports UK charities for people living with pain. Visit their website for an overview of UK charities with links to their respective websites. You may find resources that are specific to your pain condition: https://painuk.org/members/charities/

Further questions, independent advice and complaints

If you would like to talk to someone who is independent of the research team prior to making a decision, please contact Dr Angus MacBeth, Research Director, Doctorate in Clinical Psychology, University of Edinburgh:

If you would like to make a complaint about any aspect of this research, please contact

- NHS Lothian Patient Experience team via email: feedback@nhslothian.scot.nhs.uk or by telephone: 0131 536 3370 if you were told about the study through while accessing NHS Lothian healthcare services.
- NHS Greater Glasgow and Clyde complaints team via email: complaints@ggc.scot.nhs.uk or by telephone 0141 201 4500 if you were told about the study through while accessing NHS Greater Glasgow & Clyde healthcare services.
- The UoE Research Governance team at cahss.res.ethics@ed.ac.uk if you accessed this study through an online platform.

Appendix 13: Study Protocol

Non-CTIMP Study Protocol

Further exploration of Chronic Pain Acceptance Questionnaire clustering in a persistent pain population

	The University of Edinburgh and Lothian Health Board ACCORD The Queen's Medical Research Institute 47 Little France Crescent Edinburgh EH16 4TJ
Protocol authors	**Pernille Frisvoll**
Chief Investigator	**Dr David Gillanders**
Sponsor number	CAHSS2012/06
REC Number	21/PR/0448
Version Number and Date	**Version 1, 8th March 2021**

CONTENTS

To update the table of contents, highlight the existing table of contents; right click "update fields" and OK

LIST OF ABBREVIATIONS

ACCORD	Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
PI	Principal Investigator
QA	Quality Assurance
REC	Research Ethics Committee
SOP	Standard Operating Procedure
PAIN MAN-AGE-MENT PRO-GRAMME	Pain Management Programme
CPAQ	Chronic Pain Acceptance Questionnaire
PW	Pain willingness
AE	Activity engagement
CBT	Cognitive Behavioural Therapy
ACT	Acceptance and Commitment Therapy

1 INTRODUCTION

2 BACKGROUND

Persistent, or, chronic pain is defined as any pain lasting longer than three months, the origins of which can be multifactorial (International Association for the Study of Pain, 2011). It is estimated that around 18% of European adults suffer from persistent pain that is moderate or severe (Breivik et al., 2006). Living with pain can be distressing and is associated with high prevalence of anxiety disorders, depression, disability, and unemployment (Asmundsson & Katz, 2009; Fishbain, Cutler, Rosomoff, & Rosomoff, 1997). These effects incur not only a personal and emotional cost, but an economic cost to society through hospital and community care, benefits, and sick pay (Maniadakis & Gray, 2000; Reginster, 2002). It is recognised that pain-related fear and distress can be as debilitating as the pain condition itself; a longitudinal study by Fisher and Johnston (1998) found no relationship between pain and disability, but instead found that disability was mediated by pain-related distress. Additionally, anxiety and depression in pain is associated with worse functional outcomes and increased disability (Arnow et al., 2006; Lerman et al., 2015; Vowles, Zvolensky, Gross, & Sperry, 2004). While there is no 'cure' for persistent pain, there is a rationale for treatments aiming to reduce distress and improve physical functioning alongside medical management. This calls for a multidisciplinary or interdisciplinary approach to treatment (Pergolizzi et al., 2013).

Many who struggle with the impact of persistent pain are offered pain management within specialist secondary care settings in the NHS. National government guidelines recommend that interdisciplinary pain management intervention is delivered in group format, often called pain management programmes or PAIN MANAGEMENT PROGRAMMEs (Scottish Intercollegiate Guidelines Network (SIGN) 2013). The group format allows for the sharing of experiences and social learning, which facilitates connection as opposed to the social isolation and shame often experienced by people with persistent pain (Rose, 1994). PAIN MANAGEMENT PROGRAMMEs have a focus on pain education and activity management, and uses psychological models to help patients identify thinking patterns and behaviours that maintain pain-related distress (SIGN, 2013). Initially PAIN MANAGEMENT PROGRAMMEs were based on the cognitive behavioural (CBT) model of pain, which focuses on graded exposure to exercise and challenging unhelpful thinking (e.g. Sharp, 2001). The last decade has seen a shift towards an Acceptance and Commitment Therapy (ACT) model of pain. The ACT model focuses on increasing engagement with valued living and adopting a non-judging mindful awareness to all aspects of one's experience, including pain (McCracken & Vowles, 2014). There is a robust evidence base for PAIN MANAGEMENT PROGRAMMEs whether based on CBT or ACT principles in helping to reduce pain-related distress and disability (e.g. Hann & McCracken, 2014; Stanos, 2012).

While PAIN MANAGEMENT PROGRAMMEs have a robust evidence base, effect sizes vary from low to medium and show uneven responsiveness among participants (Vlaeyen & Morley, 2005). From the wider literature on group therapy, it is recognised that group composition is an important aspect of treatment (Burlingame, Fuhriman, & Mosier, 2003). Grouping patients based on shared characteristics can be helpful in aiding group cohesion and engagement, which are important predictors of outcomes (Crowe & Grenyer, 2008). The persistent pain population who present for treatment in specialist settings are heterogeneous both demographically and psychologically, which may be a reason for uneven responses to group treatment. Differences in treatment outcomes from a PAIN MANAGEMENT PROGRAMME are not attributable to pain condition, pain duration, level of disability or demographic variables (Frisvoll, Dunbar, & Williams, 2016), and dividing patients into treatment groups on this basis has not demonstrated usefulness (Morley, Williams, and Eccleston, 2013). Thus, most services offer a one-

size-fits-all approach whereby everyone eligible for a PAIN MANAGEMENT PROGRAMME undergoes the same treatment, and group composition is random. Based on their systematic review of psychological therapies for persistent pain, de C Williams, Eccleston and Morley (2012) suggested that grouping patients based on psychological processes may be more clinically useful. As such, grouping patients based on psychological processes that are known to influence treatment response might allow for more meaningful and effective group treatment.

3 RATIONALE FOR STUDY

A potentially useful grouping factor may be pain acceptance. Pain acceptance is negatively associated with depression, anxiety, pain-related distress and disability. It is rooted in the robust theoretical model of psychological flexibility, which underlies ACT treatment developments in persistent pain. Pain acceptance is an important mediator of outcomes in PAIN MANAGEMENT PROGRAMMEs, whether primarily based on CBT, ACT, or compassion focused therapy (Åkerblom, Perrin, Fischer, & McCracken, 2015; Trompetter et al., 2015; Tin, 2019). The Chronic Pain Acceptance Questionnaire (CPAQ) is widely used in pain management settings to measure pain acceptance (McCracken, Vowles, and Eccleston, 2004). It consists of two distinct processes, namely pain willingness and activity engagement. Pain willingness refers to the extent to which respondents are open to experiencing pain without getting caught up in a struggle for pain relief. Activity engagement refers to the extent to which respondents continue engaging in activities whilst experiencing pain.

Rovner, Vowles, Gerdle, and Gillanders (2015) and Rovner, Johansson and Gillanders (2019) used latent class analysis to explore whether patients in a Swedish specialist pain management setting could be meaningfully grouped into different clusters based on their CPAQ scores. These studies revealed four distinct clusters: a group that scored highly for both activity engagement (AE) and pain willingness (PW), a group that scored low for both, a group that demonstrated high PW but low AE, and a group that demonstrated low PW but high AE. Cluster membership was also associated with differences in pain intensity, disability, anxiety and depression. This suggests that these clusters have different treatment needs, and that pain acceptance may be a useful process for grouping patients presenting for pain management treatment. The researchers created cut-off scores associated with each cluster, enabling clinicians to determine cluster membership quickly and reliably, with a high degree of sensitivity and specificity to replicate the statistically derived clusters.

The aim of this study is to further validate the usefulness of CPAQ-clustering in an English-speaking sample of people with persistent pain. Like Rovner, Johansson and Gillanders (2019), this study will explore differences in pain intensity, pain-related disability, anxiety and depression. In addition, it will explore whether clusters differ on other factors typically targeted in a PAIN MANAGEMENT PROGRAMME. This includes pain self-efficacy, emotion recognition and regulation, self-compassion, and valued living. This could further our understanding of differing treatment needs between clinically distinct groups of people with persistent pain, which in turn could inform future service development.

4 OBJECTIVES

5 Primary Objective

Can CPAQ-clustering provide clinically meaningful distinctions between different groups of people with persistent pain in a cross-sectional, English-speaking sample? Specifically, do they differ on

other important psychological processes typically targeted in a pain management programme, such as pain-related disability, mood, emotion recognition and regulation, self-compassion, and pain self-efficacy?

6 STUDY DESIGN

Design:

This is a cross-sectional, population-based, quantitative study which will be conducted via online and/or paper

questionnaires.

Sample:

This study will recruit people with persistent pain from the general, English-speaking population, and potentially from

a clinical setting within NHS Pain Management services. For the purposes of this study it is sufficient that people self-identify as having pain lasting longer than three months, with some associated impact on day-to-day functioning.

Recruitment:

Online recruitment will be done through relevant third sector organisations and charities, who can disseminate the survey link to their networks through forums, newsletters and magazines. Social media groups and forums for people with pain will also be approached and asked to share the link on their pages. The researcher and supervisors will also use their personal networks and social media platforms to recruit eligible participants.

Recruitment will also be done in a clinical setting in collaboration with certain Pain Management services in NHS Lothian and NHS Greater Glasgow & Clyde. This will be done in one of two ways: In some participating services, patients who are receiving pain management interventions digitally (e.g. via webinars or video platforms) will be approached by the researcher (student) at the end of their appointment and forwarded the survey link through the chat function for their consideration. In some participating services, patients who are due to attend an initial appointment will receive the study poster in the post along with their appointment letter.

Procedure:
The procedure will be similar whether the prospective participant has been recruited from their healthcare provider, a third party organisation or social media. The survey will be set up using Qualtrics. The study will be advertised as specified above. The advertisement will include a short blurb about the study, the inclusion/exclusion criteria, and a link to the online survey. Participants who click the link to the survey will first encounter a participant information sheet and consent form (see attached documents) which will outline the main aims of the study, what exactly is required of them, and the potential risks of taking part (possibly mild distress). Informed consent will be provided by ticking boxes to say that they have understood all of the information and agree to take part. Participants are also required to answer 'yes' to being over 18, being fluent in English, having had daily pain lasting longer than three

months, and 'yes' to this pain leading to some form of impact on activities of daily living (e.g. occupational, domestic, leisure and social activities). They have to answer 'no' to having an intellectual disability, dementia, and pain caused by cancer. If a prospective participant fails to meet either of these criteria, they will be redirected to a page that thanks them for their willingness to take part, and explains that they are not eligible. Participants who fulfil criteria proceed to the survey, which consists of demographic information and ten outcome measures, totalling 110 items. The process should take around 20 minutes to complete, and timing will be piloted by a small number of people to provide an accurate estimate in any advertising for the study. Patients will then be redirected to a debrief form which thanks them for their involvement, and signposts to relevant sources of support. Data handling and analysis Data collected through Qualtrics will be extracted directly to SPSS and the SPSS file will be saved to the researcher's encrypted NHS drive. No personal identifiers are needed as information is only collected at a single time point. Responses will therefore be labelled numerically and the data are completely anonymised. Analyses will be conducted in SPSS, and the dataset and outputs will be saved on an encrypted NHS drive.

7 STUDY POPULATION

8 NUMBER OF PARTICIPANTS

This study hopes to recruit a minimum of 164 participants living with persistent pain, recruited both through NHS sites and online sites/forums. The recruitment period is expected to last between 5-7 months depending on how quickly the target number of participants is reached.

9 INCLUSION CRITERIA

- Persistent pain for longer than 3 months
- Disruption to activities of daily living due to pain
- Fluent in English

10 EXCLUSION CRITERIA:

- Under the age of 18
- Having cancer pain
- Intellectual disability
- Dementia

11 PARTICIPANT SELECTION AND ENROLMENT

12 IDENTIFYING PARTICIPANTS

Participants recruited through some clinical settings will be approached by the researcher in conjunction with an online appointment (e.g. webinar, online pain management programme). The plan is for the researcher to attend at the very end of online group appointments, after being introduced by the clinicians. The researcher will inform the prospective participant(s) of the aims and purpose of the study,

what they may expect from taking part, and the risks and benefits involved. They will then be sent a study link in the chat function which they can access should they wish to take part. They will of course be informed that participation is entirely voluntary and their decision to take part (or not) will not impact on the healthcare they receive.

In some clinical settings a poster advertising the study will be sent out in the post to every new patient accessing the service with their initial appointment letter. Prospective participants will then be able to access the online survey on their own initiative should they wish to take part.

Potential participants from a non-clinical setting will come across the study on social media platforms they have chosen to be part of (e.g. Pain Concern's online forum, pain support groups on Facebook).

All participants will access the same survey link, and go through the same patient information summary and consent process.

13 CONSENTING PARTICIPANTS

Participants will get access to the patient information sheet and consent form when they click on the survey link. They can then take as long as they want to read the information before deciding whether or not to take part, with the opportunity to contact the researcher should they have any questions or concerns about the process. This study excludes participants who are considered vulnerable or unable to provide consent. Participants will be informed that their decision to take part is entirely voluntary, and will not impact on any healthcare they receive. Furthermore, they will be informed that no identifiable data will be collected, and their responses cannot be traced back to them as an individual. Consent will be sought via a tick box asking participants to confirm they have read the information sheet and that they agree to take part in the study.

14 Withdrawal of Study Participants

Participants are free to withdraw from the study at any point while answering the survey, simply by closing the browser window. As their responses are given at a single time point and are entirely anonymous, they are not able to withdraw their data once they have completed the study and submitted their responses.

15 STUDY ASSESSMENTS

16 STUDY ASSESSMENTS

This study will collect data at a single time point, which is when the individual participant chooses to access the survey. No further contact is required.

17 DATA COLLECTION

Data will be collected quantitatively through the survey software Qualtrics. Demographic and clinical

information will be collected, e.g. age, gender, ethnicity, occupation, pain site, pain duration, and past/current involvement with pain services. Additionally, the following measures will be used :

Chronic Pain Acceptance Questionnaire-8 (CPAQ-8)

The original 20-item version of the CPAQ was developed to measure pain acceptance in persistent pain, in line with Acceptance and Commitment Therapy processes (McCracken, Vowles, and Eccleston, 2004). It consists of two subscales with robust factor structures: pain willingness, which measures the extent to which respondents are open to experiencing pain without struggling for pain relief, and activity engagement, which measures the continued engagement in activities with pain. The CPAQ has adequate psychometric properties, is responsive to ACT treatment and correlates with a number of measures of distress (Reneman et al., 2010). A short version was developed which has near perfect correlation with the original, and has been validated in mixed chronic pain populations (Fish et al. 2010). The short form version has been chosen to minimise item load, and because Rovner et al. (2019) demonstrated that it is equally valid for clustering patients according to pain acceptance.

Brief Pain Inventory – Short form

This measure assesses subjective pain severity and interference of the reported pain with day to day activities, such as social relations and sleep (Cleeland & Ryan, 1994). It relies on numerical rating scales ranging from 0-10, and is widely used in assessment of pain both in research and clinical settings. In this study the pain intensity subscale will be used to measure subjective pain severity and the pain interference subscale will be used to measure pain-related disability. It has excellent psychometric properties for use in different populations with persistent pain, with internal consistency ranging from .82-.95, excellent test-retest reliability (ICC= .83-96), and a good construct validity; the interference subscale has a good correlation with other measures of physical disability (r= .69-.82). The short form version will be used in this study as it omits qualitative items that are not relevant to the study aims.

Anxiety – the Generalised Anxiety Disorder Assessment-7 (GAD-7)

This 7-item questionnaire is based on criteria for Generalised Anxiety Disorder and a score of 10 yields 89% sensitivity and 82% specificity (Spitzer, Kroenke, Williams, & Löwe, 2006). It is also sensitive to other anxiety disorders such as panic disorder (74%), social anxiety (72%) and post-traumatic stress disorder (66%). It has been validated in a sample of people with migraines and has excellent internal consistency with Cronbach's alpha of .91 (Seo & Park, 2015).

Depression – the Patient Health Questionnaire-9 (PHQ-9)

This 9-item questionnaire is based directly on diagnostic criteria for major depression, and a score of 10 or more yields 88% sensitivity and 88% specificity for depression (Kroenke, Spitzer & Williams, 2001). It has been validated across a range of medical settings (Gilbody et al., 2007), and in a population suffering from migraines it yielded a Cronbach's alpha of .89 (Seo & Park, 2015). It is widely used in research and clinical practice to measure depressive symptoms.

Pain Self Efficacy Questionnaire (PSEQ)

This is a 10-item questionnaire that measures an individual's sense of efficacy in managing their daily lives with pain (Nicholas, 2007). It is easy to administer and is made for use across pain sites and

conditions. It has good internal consistency (Cronbach's alpha of .92) and test-retest reliability. It correlates with measures of pain-related disability and general self-efficacy.

Valuing Questionnaire (VQ)

The VQ consists of 10 items, and assesses the extent to which an individual lives according to their values. It measures two constructs: 'progress' and 'obstruction' to values-consistent behaviour. The scale has established good construct validity and concurrent validity when compared to other scales measuring valued living. It has been validated for use in populations with persistent pain (Carvalho et al., 2018; Rickardsson, 2019).

Emotion Regulation Questionnaire (ERQ):

This 10-item scale measures two emotion regulation constructs: expressive suppression and cognitive reappraisal (Gross & John, 2003). Preece et al. (2019) validated the scale in large scale community samples and reported excellent internal consistency (α = .76-.90). Furthermore, they found that expressive suppression correlated positively with alexithymia and distress. Conversely, cognitive appraisal correlated negatively with alexithymia and distress. It has been supported for use in medical settings such as cardiology (Karademas et al., 2011) and bariatric surgery (Zijlstra et al., 2012).

Perth Alexithymia Questionnaire (PAQ)

This is a 24-item questionnaire assessing alexithymia, comprised of three constructs: difficulty identifying and describing feelings, and a tendency to focus attention externally. The PAQ includes 'positive' as well as 'negative' emotions, unlike similar scales like the Toronto Alexithymia Scale (TAS). The PAQ has been shown to have strong internal consistency, a robust factor structure and stronger facet-level structure than the TAS (Preece et al., 2018; 2020).

Self Compassion Scale – short form (SCS-sf)

This is a 12-item, shorter version of the 26-item Self Compassion Scale (Neff, 2003). The SCS-sf has been validated in both Dutch and English samples and has shown good internal consistency with a Cronbach's alpha of .86. It has a near perfect correlation (r = .97) with the full scale and has been recommended for research where the total self compassion construct is of higher importance than the subscales (Raes, Pommier, Neff & Van Gucht, 2011).

18 DATA MANAGEMENT

19 Personal Data

This study will not collect any data that may be considered to identify a person (e.g. name, chi number, address). The only data that may be considered personal is data relating to demographic variables such as age and gender.

Data will be stored by the student (PF) on Qualtrics and an encrypted drive, and will only be accessed by the research team.

Data will be stored for 10 years. At the end of this period, a review will be undertaken to decide

whether it is in public interest to continue storing the data. If it is decided that data storage will continue, this will be for a period of 5 years before another review is undertaken.

20 Data Information Flow

Data will be collected through Qualtrics. When the data collection period is complete, the data will be exported to an excel file which will be kept on the student's encrypted drive. It will then be deleted from Qualtrics and the survey will close to avoid unintentional collection of further data.

21 Transfer of Data

Data collected or generated by the study (including personal data) will not be transferred to any external individuals or organisations outside of the Sponsoring organisation(s).

22 Data Controller

A data controller is an organisation that determines the purposes for which, and the manner in which, any personal data are processed.

The University of Edinburgh and NHS Lothian are joint data controllers along with any other entities involved in delivering the study that may be a data controller in accordance with applicable laws (e.g. the site)

23 Data Breaches

Any data breaches will be reported to the University of Edinburgh and NHS Lothian Data Protection Officers who will onward report to the relevant authority according to the appropriate timelines if required.

24 STATISTICS AND DATA ANALYSIS

25 SAMPLE SIZE CALCULATION

Detail the sample size, precision or power calculation, dropout rates, relevant assumptions and justifications. Comment on an estimate of the recruitment period and justification that the required sample size will be achievable.

Power analysis:

A power analysis to estimate sample size was conducted using G*Power (Faul, Erdfelder, Buchner, & Lang, 2009). This was based on the study by Rovner et al. (2019), who examined the differences between CPAQ clusters on anxiety and depression measures using a MANOVA. They had a sample size of 1775 and used an alpha level of 0.5. The effect sizes were not reported in the paper but were calculated using an online tool (Lenhard & Lenhard, 2016). This revealed Cohen's d ranging from 0.44-1.54 on the anxiety variable, which equates to medium to very large effect sizes according to Cohen's classification (1988). For the depression variable the effect sizes ranged from 0.06-1.265 on the between-cluster comparisons, or from very small to very large. Similarly to Rovner et al., the current study will compare the differences on nine continuous variables based on cluster membership using a MANOVA. To determine the required sample size to detect a stastically significant effect, an apriori power analysis was conducted. Given the variability in effect sizes between different clusters in the Rovner study, it

was decided to go for a conservative estimate and assume a medium effect size of 0.5. The power was set to .80 and alpha level of .05 in accordance with recommendations from Fritz & MacKinnon (2007). With these parameters the minimum required sample size is 164. As the numbers in each cluster are likely to be uneven, it is important to note that the analyses require at least nine people in each cluster.

Justification that the required sample size will be achievable:

Up to a fifth of the adult population suffer from persistent pain, and the sampling criteria of this study exclude an exceedingly small proportion of these. This study will mainly recruit online through organisations, charities and online support groups. We are working on building relationships with Pain Concern and Pain UK, and plan to reach out to online support groups to help promote the survey. We have already been given permission by the national charity Pain Concern (conditional on ethical approval) to promote the survey on their online forum, which has a member base exceeding 28,000 people. If only 1% of forum members were to participate, we would have a sample of 280, exceeding our target. Additionally, Pain Management services in NHS Lothian and NHS GGC offer digital appointments to hundreds of people monthly. This opens up further opportunities not just to reach more prospective participants, but also to reach a more clinically relevant sample.

26 PROPOSED ANALYSES

Participants will be grouped into clusters based on the CPAQ-8. Cluster membership will form the independent variable and will have four levels.

A one-way MANOVA will be used to assess differences between the clusters on nine dependent variables: pain intensity, pain interference, anxiety, depression, valued living, pain self-efficacy, self-compassion, alexithymia, and emotion regulation. Post hoc comparisons will identify where potential differences lie. Based on Rovner et al (2019) It is hypothesized that the high group will score more positively on these measures, the low group will show the greatest dysfunction on these measures, and the two mixed groups will lie between these other group's scores.

27 RISKS

Informed consent

Prospective participants would be directed to the survey link, which would take them to a participant information form. They would be able to take as much time as they would like to read the information prior to deciding whether or not to take part. This would include a contact email address should they want to ask questions prior to making a decision.

Risk of distress

The survey will include questions about topics that may cause mild distress to some (e.g. questions about their pain condition, mood and attitudes to their pain). This will be explained in the participant information summary so that participants are prepared for this, and the debrief form will signpost to relevant helpline numbers and online resources, e.g. Breathing Space, Samaritans, Pain Concern.

28 OVERSIGHT ARRANGEMENTS

29 INSPECTION OF RECORDS

Investigators and institutions involved in the study will permit trial related monitoring and audits on behalf of the sponsor, REC review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

30 STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study and, if so, at what frequency.

Risk assessment, if required, will determine if audit by the ACCORD QA group is required. Should audit be required, details will be captured in an audit plan. Audit of Investigator sites, study management activities and study collaborative units, facilities and 3rd parties may be performed.

31 GOOD CLINICAL PRACTICE

32 ETHICAL CONDUCT

The study will be conducted in accordance with the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (ICH GCP).

Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met.

33 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for the overall conduct of the study at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

34 Informed Consent

The Investigator is responsible for ensuring informed consent is obtained before any protocol specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of what is involved.

Participants will get access to the patient information sheet and consent form when they click on the survey link. They can then take as long as they want to read the information before deciding whether or not to take part, with the opportunity to contact the researcher should they have any questions or

concerns about the process. This study excludes participants who are considered vulnerable or unable to provide consent. Participants will be informed that their decision to take part is entirely voluntary and will not impact on any healthcare they receive. Furthermore, they will be informed that no identifiable data will be collected, and their responses cannot be traced back to them as an individual.

35 Study Site Staff

The Investigator must be familiar with the protocol and the study requirements. It is the Investigator's responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their trial related duties.

36 Data Recording

The Principal Investigator is responsible for the quality of the data recorded in the CRF at each Investigator Site.

37 Investigator Documentation

- The Principal Investigator will ensure that the required documentation is available in local Investigator Site files ISFs.

38 GCP Training

For non-CTIMP (i.e. non-drug) studies all researchers are encouraged to undertake GCP training in order to understand the principles of GCP. However, this is not a mandatory requirement unless deemed so by the sponsor. GCP training status for all investigators should be indicated in their respective CVs.

39 Confidentiality

This study will not require any access to medical records or personal identifiers. The data collected cannot be traced back to any individual participant. Nevertheless, the data collected will be stored in a confidential manner on an encrypted drive, only accessible to the research team.

40 Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the General Data Protection Regulation and Data Protection Act) with regard to the collection, storage, processing and disclosure of personal information.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data and be of a form where individuals are not identified and re-identification is not likely to take place

STUDY CONDUCT RESPONSIBILITIES

41 PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, must be reviewed and approved by the Chief Investigator.

Amendments will be submitted to a sponsor representative for review and authorisation before being submitted in writing to the appropriate REC, and local R&D for approval prior to participants being enrolled into an amended protocol.

42 MANAGEMENT OF PROTOCOL NON COMPLIANCE

Prospective protocol deviations, i.e. protocol waivers, will not be approved by the sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC, and local R&D for review and approval if appropriate.

Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the sponsors every 3 months. Each protocol violation will be reported to the sponsor within 3 days of becoming aware of the violation. All protocol deviation logs and violation forms should be emailed to QA@accord.scot

Deviations and violations are non-compliance events discovered after the event has occurred. Deviation logs will be maintained for each site in multi-centre studies. An alternative frequency of deviation log submission to the sponsors may be agreed in writing with the sponsors.

43 SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the trial; or

(b) the scientific value of the trial.

If a potential serious breach is identified by the Chief investigator, Principal Investigator or delegates, the co-sponsors (seriousbreach@accord.scot) must be notified within 24 hours. It is the responsibility of the co-sponsors to assess the impact of the breach on the scientific value of the trial, to determine whether the incident constitutes a serious breach and report to research ethics committees as necessary.

44 STUDY RECORD RETENTION

All study documentation will be kept for a minimum of 10 years from the protocol defined end of study point. When the minimum retention period has elapsed, study documentation will not be destroyed without permission from the sponsor.

45 END OF STUDY

The end of study is defined as the last participant's last visit.

The Investigators or the co-sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the REC, and R+D Office(s) and co-sponsors within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow up is arranged for all participants involved. End of study notification will be reported to the co-sponsors via email to resgov@accord.scot

A summary report of the study will be provided to the REC within 1 year of the end of the study.

46 INSURANCE AND INDEMNITY

The co-sponsors are responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Chief Investigator and staff.

The following arrangements are in place to fulfil the co-sponsors' responsibilities:

- The Protocol has been designed by the Chief Investigator and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused by poor protocol design by the Chief Investigator and researchers employed by the University.
- Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The co-sponsors require individual sites participating in the study to arrange for their own insurance or indemnity in respect of these liabilities.
- Sites which are part of the United Kingdom's National Health Service will have the benefit of NHS Indemnity.
- Sites out with the United Kingdom will be responsible for arranging their own indemnity or insurance for their participation in the study, as well as for compliance with local law applicable to their participation in the study.

47 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

48 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team.

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