Developing and feasibility testing a self-management intervention for chronic pain in inflammatory bowel disease

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DEVELOPING AND FEASIBILITY TESTING A SELF-MANAGEMENT INTERVENTION FOR CHRONIC PAIN IN INFLAMMATORY BOWEL DISEASE

Louise Sweeney

Thesis incorporating publications submitted for the degree of Doctor of Philosophy

December 2019
Abstract

Background: Pain is a commonly reported and disabling symptom of inflammatory bowel disease (IBD) and has a significant impact on a patient’s quality of life, mood and functioning. While over two thirds will experience pain during active disease, a significant proportion (20-50%) of patients report pain in remission. A lack of clinical and endoscopic markers of active disease in the presence of pain is distressing for patients and challenging for clinicians. Preliminary research demonstrates that IBD-pain is a multifactorial construct, however further research is needed to better understand and effectively manage pain in IBD.

Aim: The aim of this thesis was to develop and feasibility test a self-management intervention for chronic pain in IBD.

Methods: The Medical Research Council (MRC) framework and Behavioural Inhibition System/Behavioural Activation System (BIS/BAS) theory of chronic pain were used to guide intervention development. A systematic review examined psychosocial factors associated with pain in IBD. A cross-sectional study evaluated the association between psychosocial factors identified in the review and other psychosocial factors. A qualitative study explored experiences, current management strategies and needs for an intervention for pain. Finally, a feasibility study assessed the feasibility and acceptability of a self-management intervention and gained preliminary estimates of efficacy on pain and psychosocial processes.

Results:

- The systematic review including 15 studies (paper 1) found cognitive, emotional and behavioural processes associated with pain, yet highlighted that further research was required using validated pain measures and to investigate psychosocial factors identified but not yet explored in IBD.

- The cross-sectional study (paper 2) (n=297) confirmed psychosocial factors identified in the review such as depression, anxiety and pain catastrophising. It also demonstrated cognitive and behavioural processes such as symptom focusing, avoidance resting behaviour and pain self-efficacy were associated with pain.
• The qualitative study (paper 3) (n = 14) identified three themes; i) vicious cycles ii) finding solutions and iii) attitudes. It found that pain is rarely experienced in isolation but with other symptoms of fatigue and urgency in IBD.

• Cognitive behaviour therapy techniques were used to target psychosocial processes in a BIS/BAS model of IBD-pain. Patient public involvement ensured that the intervention was tailored to people with IBD-pain. The intervention was delivered online with facilitator support over 9 weeks.

• A feasibility study (n=20) (paper 4 – submitted) demonstrated that the online intervention was acceptable, as participants understood the workings of the intervention and felt confident in their ability to complete sessions and tasks. Despite low recruitment rates, feasibility was demonstrated through usage and completion of the intervention and adequate provision of facilitator support. Scores improved for quality of life and reduced for negative affect and cognitive-behavioural processes. However, the study was not powered to detect significance in outcome measures, thus warranting further investigation in a randomised controlled trial.

**Discussion**: Overall, this thesis demonstrated the development, feasibility and acceptability of a CBT-based self-management intervention for IBD-pain and has enabled a better biopsychosocial understanding of pain in IBD. A large-scale randomised controlled trial is required to formally assess the long-term efficacy and cost-effectiveness of the intervention.
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Chapter 1 Introduction to Inflammatory Bowel Disease and Pain

1.1 Chapter overview

This chapter provides an introduction to inflammatory bowel disease (IBD), including symptoms, aetiology, diagnosis, epidemiology, treatment and the physical and psychological impact of IBD. The chapter describes in more depth the symptom of pain, clarifying the differences in aetiology between acute and chronic pain and the clinical challenges of pain management. The overlap between irritable bowel syndrome (IBS) and chronic pain in IBD is discussed and what we can learn from treatment approaches in IBS in the context of IBD-pain. A current conceptual model of IBD-pain is discussed, highlighting its strengths and limitations and the rationale for further research into this area of IBD.

1.2 Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic idiopathic autoimmune disease of the gastrointestinal tract, where a dysregulation in the innate and adaptive immune response results in overactive inflammation in the intestinal wall (Baumgart & Carding, 2007; Podolsky, 1991). The natural disease course is characterised by alternating periods of relapses and remission which occur unpredictably, and treatment of IBD aims to prolong remission and stall progression or complications associated with the disease.

The disease is categorised into two main sub-types, Crohn’s disease (CD) and ulcerative colitis (UC). In CD, the disease can occur at any region of the gastrointestinal tract from the oropharynx to the perianal area and is characterised by patchy, transmural inflammation, which can commonly result in abscesses, fistulas forming or sinus tracts (Hendrickson et al., 2012). Symptoms and clinical presentation in CD can vary dependent on the location, pattern, extent and severity of the disease (Van Assche et al., 2010). For example, CD can be manifested in gastroduodenal, upper gastrointestinal, diffuse small bowel, ileocolonic or terminal ileal regions. In UC, the inflammatory response is confined to the colon with differing extents of proximal extension; more extensive disease may refer to pancolitis (whole colon), extensive colitis (extending up to the hepatic flexure) or left-side colitis (Dignass et al., 2012), and an estimated 95% of patients have disease located in the rectum (Hendrickson et al., 2002). UC is characterised by mucosal inflammation, and clinical presentations of UC will differ by the severity of involvement of ulceration, oedema and haemorrhages. When clinical features are not clearly
characteristic of either UC or CD, or there is evidence of an overlap of the two, this is termed indeterminate colitis or IBD-unclassified (IBD-U) and is generally considered temporary until further confirmation of CD or UC diagnosis through capsule endoscopy, serology and genetic assessment (Mahdi, 2012; Silverberg et al., 2005).

1.2.1 Symptoms of IBD

Symptoms of IBD include loose stools, bloody diarrhoea, abdominal pain, urgency of defecation, fatigue and weight loss (Dignass et al., 2012). Symptoms can vary between patients depending on the location, extent and severity of the disease, such as early satiety, nausea and epigastric pain in the case of gastroduodenal CD or rapid weight loss in the case of extensive small bowel CD (Hendrickson et al., 2002). Disease-related complications may result in bowel obstruction, formation of strictures or fissures, in which case surgical intervention may be required (Baumgart & Carding, 2007, Cheung & Regueiro, 2003). Overall 20% and 80% of patients with UC and CD respectively will require surgery at least once in their life (Sica & Biancone, 2013). Surgical intervention is less common in UC patients, required in 15-35% including in an emergency context (Candido et al., 2019). For UC surgery may include subtotal colectomy (colon removed), panproctocolectomy (colon and rectum removed) to result in an ileostomy (stoma) or ileo-anal pouch. In CD, surgery may involve small bowel resection, subtotal colectomy or permanent ileostomy if necessary.

Extraintestinal manifestations (EIM) of IBD are common, seen in up to 50% of patients, with increasing risk correlating with disease duration (Bernstein et al., 2001; Harbord et al., 2016). EIMs can include delayed growth in younger diagnosed patients due to malnutrition, weight loss, dermatological issues (reported in 2-34% of patients such as erythema nodosum) (Tavarela Veloso, 2004) ocular manifestations in a smaller percentage of patients (0.3-5%) and arthritis/musculoskeletal manifestations (9-53%) (Bernstein et al., 2011; Isaacs, 2008; Levin, 2011). Some EIMs such as joint pain, skin or eye complications are more common in active disease, whereas others such as liver complications may occur independent of disease activity (Ardizzone et al., 2008; Harbord et al., 2016).

Despite the heterogeneity of symptoms experienced between individuals with IBD, the most frequently reported symptoms are pain, fatigue and incontinence (Farrell et al., 2015). In active disease, over 70% of patients report pain (Bielefeldt et al., 2009) and 44-86% experience fatigue (Czuber-Dochan et al., 2013a). Pooled prevalence of faecal incontinence has ranged in the literature due to differences in...
definitions and study samples, but is estimated between 24% (Gu et al., 2018) and 60% (Nigam et al., 2019). While pharmacological treatment in IBD aims to alleviate clinical symptoms as well as treat underlying disease, a significant proportion of patients continue to experience pain, fatigue and incontinence in remission (Bielefeldt et al., 2009; Czuber-Dochan et al., 2013; Nigam et al., 2019). Moreover, research priority setting exercises (Hart et al., 2017) and studies on IBD-burden and quality of life have reinforced the need for a better understanding, assessment and management of symptoms (Schirbel et al., 2010; Czuber-Dochan et al., 2013b; Norton et al., 2013; Lönnfors et al., 2014; Artom et al., 2016; Artom et al., 2017).

1.2.2 Aetiology and risk factors

Although the exact aetiology of IBD is still inconclusive, it is thought that IBD can be caused by a complex interplay of genetic, environmental, immunological and intestinal microbial influences. Environmental factors are suggested to trigger a genetically susceptible host (Kim & Cheon, 2017) resulting in a maintained abnormal immune response and altered functioning and regulation of the gut mucosa and gut layers (Tsianos et al., 2012). Genomic-wide studies have identified 201 loci on genetic variations, such as the NOD2 gene variants, which explain the increased heritability in IBD (27 gene loci identified specific for CD and 32 specific for UC) (Liu & Stappenbeck, 2016). Population-based studies have demonstrated a heightened genetic risk for IBD, presenting an 8 to 10-fold greater risk of developing IBD among relatives (Cho & Brant, 2011) and a concordance rate of 19% and 50% between monozygotic twins for UC and CD respectively (Orholm et al., 2003; Halfvarson et al., 2003) But gene variant susceptibility appears to only account for 7.5% of variance in UC and 15% in CD (Ellinghaus et al., 2015). Therefore, to understand the overarching pathogenesis of IBD we must take into consideration a combination of genetic variants as well as known environmental risk factors.

Suggested environmental causes of IBD have included smoking, diet, microbial exposure or pollution stress (Zhang & Li, 2014). Although smoking has shown to hold a protective element for UC (Mahid et al., 2006), it has been identified as a risk for onset and recurrence in CD (Silverstein et al., 1989; Highuchi et al., 2012). In general, meta-analyses have demonstrated an increased risk factor of between 1.5 and 2.0 (Linderbeg et al., 1992; Russel et al., 1998; Mahid et al., 2006) of CD from smoking, with a more pronounced association in Caucasian populations (Ng et al., 2013). Food antigens are believed to bring about an immunologic response, and studies have now suggested that a ‘Westernised’ diet of processed foods may increase an individual’s risk of developing CD and potentially UC.
(Tragnone et al., 1995; Riordan et al., 1998; Tjonneland et al., 2009; Jantchou et al., 2010). Other environmental risk factors that may trigger IBD in a genetically vulnerable host include changes in microbial composition, brought about by antibiotic or non-steroidal anti-inflammatory drug use or enteric infections (Ananthakrishnan, 2013; Abegunde et al. 2016). No clearly identified risk factor has been established between gender and IBD diagnoses, however one study found higher incidence in males for UC and females for CD, possibly due to the role of hormones in disease expression (Shivashankar et al., 2017). Jewish populations have a 2- to 4-fold increased risk of developing IBD, with several studies documenting a genetic mutation in Ashkenazi Jews compared to non-Jewish populations (Afzali & Cross, 2016). Currently, non-Hispanic whites have the highest reported incidence rates of IBD, however the rapid shift in epidemiologic data highlights the influence of environmental over ethnic risk factors (Sanots et al., 2018).

1.2.3 Epidemiology

The incidence and prevalence of IBD are increasing worldwide, with IBD emerging as a public health problem. Traditionally, epidemiology of IBD was believed to be isolated to Western regions; the highest prevalence of CD is in North America (20.2 per 100,000), and UC in Europe (24.3 per 100,000) (Ponder & Long, 2013). Approximately 1.5 million and 2 million people are diagnosed with IBD in Europe and North America, respectively (Burisch et al., 2013). For CD and UC, incidence rates in Europe are 505 and 322 per 100,000 per annum, respectively (Ng et al., 2017), and highest rates have been located in the UK and Scandinavia (Burisch et al., 2013). In the United Kingdom, approximately 300,000 people are diagnosed with IBD, with an annual incidence rate per 100,000 of 8.8 to 13.4 and 5.6 to 8.6 for UC and CD respectively (Bardhan et al., 2010). However, recently rates of IBD have been rapidly increasing in areas previously with low prevalence such as Asia, Africa, eastern Europe and South Africa (Ng et al., 2017), possibly due to lifestyle and environmental changes. Rising prevalence of IBD globally may alternatively be explained by earlier detection and diagnosis, greater awareness of the disease or improved referral pathways from general practitioners (van den Heuvel et al., 2017). A geographical environmental risk factor for IBD has been supported by migration studies, demonstrating an individual’s increased risk when moving from low prevalence to high prevalence regions (Pinsk et al., 2007). Clinically, IBD is most commonly presented during two peak age ranges, late adolescence into early adulthood (15-30 years) (Johnston & Logan, 2008) and a smaller second peak particularly for UC (50-
70 years) (Andres & Friedman, 1999). Approximately 10% of diagnoses occur under the age of 18 (Hanauer, 2006).

### 1.2.4 Diagnosing IBD

Diagnosing IBD can be a clinical challenge, as gastrointestinal symptoms can commonly occur without identifiable lesions or threshold inflammatory levels. Consequently, a significantly high proportion of patients with IBD will have been given a prior diagnosis of IBS. However, UC can commonly be diagnosed earlier after onset of symptoms compared to CD, due to the large amounts of blood identifiable in the stool from UC (Hendrickson et al., 2002). Other challenges to definitive diagnosis include delays in tertiary referrals or misdiagnoses of food intolerances (Mosli et al., 2014). There is no single diagnostic test for IBD, therefore a combination of clinical, histological, radiological and endoscopic investigations is recommended. For example, magnetic resonance imaging (MRI), computed tomographic (CT) scans, ultrasonography (US) and ileocolonoscopy are among imaging techniques used. Non-invasive techniques include taking samples from the blood (C-reactive protein) or stools (faecal calprotectin). C-reactive protein (CRP) is an acute phase protein rapidly produced by hepatocytes upon stimulation from pro-inflammatory cytokines (e.g. IL-6, TNF-alpha). It is a more robust indicator of active disease in CD than UC, possibly due to its short half-life or the greater production of serum IL-6 in CD (Vermeire et al., 2006). As it is a non-specific inflammatory marker, CRP can be highly influenced by bacterial infections, malignancies or extraintestinal disorders (Pepys & Hirschfield, 2003).

In contrast, faecal calprotectin is released into the intestinal lumen from activated neutrophils and has been shown to correlate with inflammation (Konikoff & Denison, 2006) and predict risk of relapse (Molander et al., 2014; Ferrerio-Iglesias et al., 2016). It is a National Institute for Health and Care Excellence (NICE, 2013) recommended test to differentiate IBD from other gastrointestinal problems such as IBS.

Multiple assessments are also recommended to monitor disease activity following diagnosis to facilitate a ‘treat to target’ approach (Siegel et al., 2016). Alongside objective measures of inflammation (e.g. CRP, FCP, markers of mucosal healing), this includes disease activity indices (DAIs). For UC, the most commonly used DAI’s are the Simple Clinical Colitis Activity Index (SCCAI) (Walmsley et al., 1998) and Mayo Score (Schroeder et al., 1987). For CD, clinical assessment through DAI’s include the Harvey Bradshaw Index (HBI) (Harvey & Bradshaw, 1980) and Crohn’s Disease Activity Index (CDAI) (Best et al., 1979). However, the correlation between DAI’s and endoscopic markers is poor, particularly in CD.
(Schoepfer et al., 2010; af Björkesten et al., 2012; Falvey et al., 2015). DAI’s rely on subjective reports and therefore may arguably be measuring symptom reporting behaviour than disease activity (Targownik et al., 2015; Gracie et al., 2016). A further limitation to DAI’s are they do not address key aspects of the patient experience, including impact of IBD on quality of life and functioning. Quality of life measures in IBD include the IBD-control which has been recommended for use in clinical practice and captures the patient’s assessment of disease control relevant to both UC and CD, and correlates with disease activity, global physician assessment and more extensive quality of life measures (Bodger et al., 2014). Therefore, assessment of disease activity in IBD is recommended to measure objective inflammation through imaging and histological reports, as well as clinical symptoms and quality of life measures (Walsh et al. 2016).

1.3 Treatment in IBD – pharmacological agents and stepwise strategies

While this thesis takes a great focus on psychological approaches in the context of IBD-pain, it is important to understand the overall patient’s clinical care, including the biomedical factors and pharmacological treatment used to manage the disease. The goal of pharmacological therapy in IBD is to prolong and maintain clinical remission while minimising adverse effects of treatment. Pharmacological agents are the main type of recommended treatment in IBD, and there is an array of treatment approaches following a stepwise hierarchy, which is dependent on a patient’s disease profile and response to treatment. Balance and choice of medication in IBD is also complicated by the ever-increasing development of new drugs, such as biologic agents. Medical therapy in IBD involves aminosalicylates, corticosteroids, immunosuppressants, antibiotics and biologics including anti-TNF agents. Step-up algorithms for treatment in IBD are subject to the extent and severity of disease in UC or CD, with more toxic drugs targeted for more aggressive disease or in the case of lack of treatment response.

1.3.1 Aminosalicylates

The first line of step-up therapy is aminosalicylates, which include mesalazine (5-ASA) or sulfasalazine. This is predominantly used and recommended as a first-line therapy for the maintenance of remission in mild to moderate UC. These drugs can be administered orally or by rectal delivery (enemas, suppositories) and act as a topical anti-inflammatory agent within the gastrointestinal tract, by inhibition
of inflammatory cytokines, cyclooxygenase and lipoxygenase. Dose-related adverse effects can include nausea, vomiting, folate deficiency, headache and arthralgia and occur in 10-45% of patients with UC on sulfazaline (Pithadia & Jain, 2011). Meta-analyses have demonstrated the efficacy of aminosalicylates compared to placebo in UC patients, whereas in CD, aminosalicylates appear to perform similarly to placebo (Lim et al., 2016).

1.3.2 Corticosteroids
Glucocorticosteroids, such as hydrocortisone, budesonide and prednisolone, can be used alone or in conjunction with other pharmacological agents. These are used to induce remission in both CD and UC, usually in the context of moderate to severe disease or non-response to aminosalicylates. However, steroids are ineffective at preventing the risk of relapse and long periods of use are associated with several risk factors such as bone disease, diabetes, osteopenia and infection (Steinhart et al., 2003; Ford et al., 2011; Dubois-Camacho et al., 2017). Due to their rapid acting mechanism on symptom reduction, many patients become steroid-dependent (Schiro & Stein, 2015) and so it is important that steroids are recommended for short periods followed by maintenance drugs which are more effective and safer at preventing relapse. Generally, patients will fall within one of the categories steroid-dependent (30-40% or partially responsive), steroid-responsive (40% of patients) or steroid unresponsive (15-20%), and recognition of this requires careful monitoring and appropriate use of complimentary or steroid sparing agents to reduce risk of long-term use.

1.3.3 Immunosuppressants
Third-line therapy recommended for patients who have failed aminosalicylates, present chronic corticosteroid use and can be used an adjuvant therapy, are immunosuppressant drugs, known as thiopurines. These drugs work by inhibition of white blood cell production and are effective in maintaining remission for patients who have had repeated courses of steroids (Timmer et al., 2016). For example, 6-mecaptopurine or azathioprine are recommended for both UC and CD and are predominantly viewed as maintenance rather than drugs for induction of remission, due to their delayed response effects. Adverse effects of thiopurines are infection, bone marrow suppression, allergic reaction and pancreatitis. Treatment of IBD with thiopurines is also associated with a threefold increased relative risk in developing malignancy, non-melanoma skin cancer and lymphoma (Gómez-Garcia et al., 2013).
Methotrexate, another immunomodulatory drug, can be effective as a maintenance drug for CD patients who have not responded to azathioprine. It is a folic acid antagonist and has several anti-inflammatory properties including reducing generation of pro-inflammatory cytokines lymphocyte apoptosis (Pieri et al., 2006). Adverse effects of methotrexate include nausea, vomiting, pulmonary fibrosis, bone marrow suppression and hepatotoxicity, yet taking methotrexate with folic acid supplements can minimise risk.

1.3.4 Biologics

The development of biologics over the last two decades has been a landmark treatment approach in IBD and led to significant improvements in IBD care (Moss, 2015). Biologics work by blocking or neutralising key mediators central to the pathogenesis of IBD. These biological agents include anti-tumour necrosis factor strategies (TNF-α) (e.g. infliximab, adalimumab), anti-integrin/adhesion molecules (e.g. vedolizumab, natalizumab) and more recently anti-interleukin and anti-interferon (IFN) antibodies (e.g. ustekinumab). These drugs are generally considered after failure of corticosteroids or immunosuppressants, or both, although biologics may be considered the first-line agent with aggressive disease activity or perianal CD. TNF blockers are monoclonal antibodies that inhibit the pro-inflammatory effect of this cytokine by binding to it and are generally recommended for more severe disease or non-response to anti-inflammatory or immunosuppressant agents (Blonski et al., 2011).

Infliximab was the first Food and Drug Administration (FDA) approved anti-TNF approved drug used for CD and UC over 20 years ago and is administered intravenously in infusions. Other TNF blockers that have been approved subsequently include adalimumab and golimumab (for UC only), both of which are administered sub-cutaneously. These latter biologics may be more suitable for patients who do not respond or tolerate infliximab. Meta-analyses have shown greater efficacy of infliximab and adalimumab in inducing remission relative to placebo (Stidham et al., 2014). Induction of remission rates by Infliximab in a meta-analysis was 45.3% at weeks 10-12 and for Adalimumab was 24.2% at week 4 (Ford et al., 2011). However, anti-TNF is not effective in maintaining remission in all patients; a third of patients will be primary non-responders when anti-TNF is introduced and half of patients who do respond to the drug initially may present symptoms and loss of response within a small number of years (Gisbert & Panes, 2009; Billioud et al., 2011). Specifically, 44% of CD and 38% of UC patients have risk of relapse after discontinuing an anti-TNF biologic (Gisbert & Panes, 2009). Common side effects to anti-TNF drugs are dry skin reactions, increased risk of infection or melanoma skin cancer, arthralgia, tuberculosis and allergic reactions (Bongartz et al., 2006; Long et al., 2010; Singh et al., 2011;
Lichtenstein et al., 2012). Many of these risks can be alleviated by screening for tuberculosis and giving appropriate vaccinations prior to starting an immunosuppressant drug (Rahier et al., 2014).

An increasing understanding of IBD pathophysiology has led to the development of new biologics approved by the FDA. These are drugs which target cellular adhesion molecules and integrins such as natalizumab and vedolizumab. Natazilizumab inhibits alpha-4-beta-7 integrin to receptors within the endothelial cells of the gut lining, thereby acting as an antagonist for further inflammation. It also binds to other integrins expressed in the brain, bone marrow and skin, increasing the risk of progressive multifocal leukoencephalopathy (PML) and therefore is only recommended to patients with severe CD who have not responded to other biologics. Vedolizumab acts by targeting leukocyte trafficking, inhibiting alpha-4-beta 7 specifically and therefore is regarded as safer and more widely used in both refractory UC and CD. This is administered via intravenous infusion and has shown more prolonged efficacy in comparison to anti-TNF drugs. A key clinical trial of vedolizumab (GEMINI) demonstrated clinical response at 6 weeks and remission by one year (Feagen et al., 2013; Sandborn et al., 2013). Ustkinumab is a more recently approved drug, a monoclonal antibody against IL-12/23 in CD following phase III favourable clinical trial data. It is recommended for the treatment of moderate to severe CD and patients who have failed treatment response in other therapies.

A key aim when implementing biologics into an individual’s treatment regime is to ensure that antibody response to the drugs is not elevated. Over time a loss of response to a biologic may occur as a result of gradual antibody formation and therefore leading to symptom flares while on the drug. Clinicians may combat this by reducing dose intervals, increase the overall dose, changing to a biologic with a different mechanism of action (e.g. anti-TNF drug to vedolizumab) or introducing an immunosuppressive drug (Papay et al., 2013; Peyrin-Biroulet & Lémann, 2011). Therapeutic drug monitoring through serum trough levels can be used to predict non-response to biologics and attenuate risk of symptom flares (Strik et al., 2016). Alternatively, to circumvent issues arising around immunogenicity, combination therapy has been recommended, where a biologic is taken with an immunosuppressant drug, which has shown reduced antidrug antibody formations and more concentrated drug effects (Vermeire et al., 2007; Hayes et al., 2014). This has been demonstrated predominantly in infliximab in combination with azathioprine in a number of clinical trials.
In CD, a more recent debate has proposed that a top-down approach may be more effective in treating the disease (Spurio et al., 2012). This is not only in the context of inducing remission but also stalling the progression of disease, as it has been proposed that prolonged use of milder drugs can result in worse prognosis in some cases (Khanna et al., 2015; Colombel & Madahaven, 2017). Conversely, a top-down strategy for patients can risk overtreatment and greater harm from biologic agents, as an estimated 20% of patients have indolent disease without need for drugs to induce or maintain remission (Jess et al., 2007; Solberg et al., 2007). Consequently, choice of biologics requires individualised and calculated decision-making, acknowledging the drug’s efficacy and safety profile in different contexts of disease phenotype, extent and severity, patient preferences, cost effectiveness, route of administration as well as other important factors regarding disease prognosis (Danese et al., 2015; Colombel et al., 2017).

Evidently, pharmacological treatment in IBD involves a complex balance between inducing and maintaining clinical remission with reducing risk of adverse events associated with powerful drugs. Moreover, there is significant heterogeneity in patient response and tolerance to drugs, as well as in disease phenotype and other co-morbidities. Medical management in IBD involves detailed clinical assessment, a key alliance between patient and clinician and a wealth of other important factors (family planning, co-morbidities, drug interactions, side effects, patient preference, phenotype and severity of the disease, funding, availability and efficacy of the drug). These accumulate to ensure that the patient has an effective treatment pathway and that patients are adherent and aware of the benefits and risks of their treatment. However, despite the multiple options of drug therapies in IBD, a significant proportion do not respond to drugs, or lose response over time, and consequently are not relieved of their symptoms. Equally, many patients that do respond to treatment and have controlled inflammation may still experience ongoing symptoms, such as pain.

1.4 Targeting the gut microbiome - antibiotics, probiotics, pre-biotics and faecal microbiota transplantation (FMT)

As an imbalance in gut microbiota is identified as an important factor in the aetiology and pathogenesis of IBD, other treatment therapies in IBD include use of antibiotics, pre- and probiotics. These may facilitate functioning of mucosa barrier and immune system. For example, antibiotics, such as metronidazole or ciprofloxin, may be an effective adjuvant treatment, such as in the context of acute
pouchitis or perianal fistula drainage. In active CD, a meta-analysis including 1,160 patients showed a significant difference in remission rates with antibiotics use compared to placebo (Khan et al., 2011). However, overuse of these drugs is not appropriate and increases risk of developing resistance or infections. There have been a handful of trials examining the effects of pre- and probiotics in IBD, however the clinical effectiveness is unproven to date (Rolfe et al., 2006; Looijer-van Langen & Dieleman, 2008). Evidence in IBD has shown the clinical effectiveness of probiotics in UC and pouchitis but less conclusive evidence for CD populations (Hedin et al., 2007; Isaacs & Herfarth, 2008). More recently, a developing novel therapy has included faecal microbial transplantation. This is a more radical form of treatment aiming to restore a normal gut microbiome and involves the transplant of faeces from a healthy individual to a patient with IBD. The transplant can be applied by endoscopy or nasogastric tubes, via enemas or capsules into the intestine. The treatment originated from patients with clostridium difficile infections (C-diff) but increasing studies are conducted in IBD, particularly in UC (Lopez & Grinspan, 2016; Naurla et al., 2017). Several studies have demonstrated its preliminary efficacy in UC patients, providing evidence of long-term remission. A recent systematic review including 277 patients with UC found a significant difference in the rate of remission between patients who had undergone FMT and a placebo, with similar effect sizes to those seen in trials with biologic agents (Narula et al., 2017).

Through similar mechanistic pathways, some dietary approaches can be recommended to patients to modify the balance of microbial species in the gut. The most commonly researched and recommended dietary treatment in IBD is the low fermentable oligosaccharides, disaccharides, monosaccharides and polyol (FODMAP) diet. This consists of a highly selective diet initially, eliminating food groups, and then reintroducing foods through a dietician-guided and systematic approach. Studies demonstrating the efficacy of the low FODMAP diet in IBD have been limited but demonstrate the effectiveness on reducing gastrointestinal symptoms in quiescent disease, including pain (Gibson, 2017; Zhan & Dai, 2018; Cox et al., 2019). However, risks of undernutrition resulting from restriction of diet can be compromising and therefore requires close monitoring from dieticians. Other nutritional-related issues in IBD may occur due to malabsorption and increased circulating cytokines (Bannerman et al., 2001; Cabré & Gassull, 2001). Enteral nutrition or a liquid diet may be recommended in these cases or may be suggested in the case of bowel obstruction or a drug-free alternative to steroid therapy in adults, however poor adherence to liquid food in adults has resulted in limited success rates (Mowat et al.,
Overall, there is insufficient evidence for dietary causes or treatment in the context of IBD, but interestingly studies demonstrate that 50% of patients believe that diet plays an important causal and exacerbating role in the disease, and thus implement some form of diet-restrictive approach to alleviate symptoms (Limdi, 2018). Aligning with this, it has been estimated that up to half of patients also utilise complementary or alternative forms of therapy. These may include herbal teas and dietary supplements, manipulation and body-based (e.g., acupuncture) interventions and have been summarised and critiqued in a recent review (Torres et al., 2019).

1.5 Impact of inflammatory bowel disease: economic and societal

IBD has a significant impact both on a societal and individual level. Lifetime costs have shown to be equivalent to other major diseases, including cancer and heart disease (Luces & Bodger, 2006). In 2010, the UK National Health Service IBD audit estimated costs of £1 billion to the UK, averaging £3000 annually per person (UK IBD Audit, 2012). In a more recent paper presenting a UK cost care model accounting for treatment, side effects, complications and proportion of patients with default input values, the annual cost of treating a UC and CD equated to £3084 and £6156, respectively (severe UC equated to £10,760 and severe CD £10,513) (Ghosh & Premchand, 2015). There has been a changing trend in management of IBD from surgical and hospitalisation towards evolving pharmacological therapies, such as anti-TNF medication (Mehta, 2016). With this comes changes in distribution of costing in IBD but better and more cost-effective long-term management of IBD. Rising rates of anti-TNF therapy in IBD has resulted in reduced acute care costs (e.g., hospitalisation and surgery) towards an increment in pharmacy costing (Park et al., 2019). From the COIN study, anti-TNF accounted for the greater proportion of costs (64% and 31% of the total costs for CD and UC, respectively). Hospitalisation and surgery accounted for 19% and <1% of costs in CD, respectively and 23% and 1% in UC. Aside from healthcare use and treatment costs, costs of IBD also include indirect healthcare costs such as a loss or impaired ability to do paid or voluntary work. In the COIN study, productivity loss including absenteeism were 16% in CD and 39% in UC. Disease course, surgery, depression, chronic back pain and joint manifestations in IBD were among predictors of work disability in the Dutch nationwide web-based study (van der Walk et al., 2014). Another systemic impact of IBD includes the effects of chronic illness on the family. Social support has been recognised as an important buffering mechanism in facilitating adjustment (Jordan et al., 2016) and reducing psychological distress and disease activity (Slonim-Nevio et al., 2018). However, research has also shown the impact, burnout and reduced quality
of life that caregivers of people with IBD experience (Parekh et al. 2017; Shukla et al., 2018), and the concerns and anxiety they have regarding disease prognosis and risks of treatment (Magro et al., 2009).

1.6 Impact of inflammatory bowel disease: psychological, emotional and quality of life

To the individual, the disease has profound psychological and social consequences, as well as a large impact on physical functioning, summarised in Figure 1 (page 27). As there is no curative treatment for IBD, from the point of diagnosis an individual must cope with multiple aspects of having the disease, adhering to and managing medication regimes and the aggressive nature of some treatments, the embarrassing nature of symptoms and impact of symptoms on work, social and physical abilities on a daily basis. These can all be disruptive on an individual’s achieving their goals, carrying out leisure or social activities or future employment aspirations (Kemp, Griffiths & Lovell, 2012). Studies have demonstrated that 48% of patients feel that IBD significantly impacts their life compared to people without IBD, including in periods of remission (Lönnfors, Vermeire & Avedano, 2014). Overall quality of life is significantly lower in CD (Ganz et al., 2016; Floyd et al., 2015) and UC compared to the general population (Irvine, 2007; Irvine et al., 2008). In a survey of IBD patients, issues surrounding sexual relationships, feeling dirty or smelly, work performance, unpleasant odours and faecal incontinence were among the most highly ranked concerns for both CD and UC (Drossman & Ringel, 2004; De Rooy et al, 2001). Lack of bowel control may lead to feeling lack of self-worth and being stigmatised (Cooper et al., 2010; Casati & Toner, 2000). In one study, 84% of participants reported perceived stigma (Taft et al., 2009) and several studies have demonstrated persons living with IBD have feelings of shame and being different to others and concerns about how others see them (Taft & Keefer, 2016). As IBD is a concealable illness, disclosure can be a pertinent issue for many, with some choosing to conceal their disease, feeling too embarrassed to disclose their symptoms or not feeling understood, and consequently withdrawing from social situations and feeling isolated (Daniel, 2002; Dibley et al., 2013; Saunders, 2014). Managing medication, sleep and being near a toilet can be disrupting to enjoyment and fulfilment of life daily (Devlen et al., 2014). Even during periods of remission, it can take several months for a patient to feel they have regained control of their symptoms to engage confidently in social situations.
There is a wide evidence base demonstrating the significant psychological and emotional impact of IBD. IBD patients have a twofold risk of developing depression in their lifetime, demonstrated in the Manitoba IBD study (Walker et al., 2008). Overall, anxiety and depression are experienced by a one-third and one-fifth of people with IBD respectively, and psychiatric disorders have been found in 30-50% of people with IBD with quiescent disease (Walker et al., 2008). The worldwide prevalence of anxiety disorders in patients with IBD is 20.5%, with a higher prevalence of anxiety during active phases (75.6%) compared to periods of remission. Pooled prevalence of depressive symptoms is 21.6% and depressive disorders is 15.2%. Overall estimates for depressive symptoms are higher in CD patients compared to UC, and in active disease compared to remission (Neuendorf et al., 2017). Psychological issues in IBD can in turn have a negative impact on coping with the disease, adhering to medication and health-related quality of life (Hyphantis et al., 2010) and are associated with an increased risk of disease relapse (Goodhand et al., 2011; Goodhand et al., 2012).

Psychological distress has been shown to not only be a consequence of disease burden and activity in IBD, but a contributing factor. Stress may play a role in the pathogenesis of IBD, and stressful life events may be a precipitating factor in the onset of the disease. Perceived stress has been shown to predict risk of relapse in quiescent UC (Bitton et al., 2003) and disease exacerbation in UC (Levenstein et al., 2000), and major depressive disorder has been identified as a risk of factor of failure to respond to anti-TNF medication in CD (Persoons et al., 2005). This may be explained by the negative effects of stress on immune function, resulting in a dysregulation of the hypothalamic pituitary adrenal (HPA) axis, which plays a key role in the inflammatory response and mast cell activity in the gut (Santos et al., 2001), leading to further intestinal permeability. More recent research has investigated further the co-association between inflammation and depression in IBD. The prevalence of comorbidity between IBD and psychiatric disorders is higher rather than other chronic conditions including diabetes or chronic hepatitis. It has been argued that depressive symptoms should not be viewed solely as a result of having the disease but rather be viewed as an extraintestinal manifestation in IBD, with shared underlying mechanisms in the gut-brain axis and immune-inflammatory reactions (including IL-6, IL-2, IL-7 and CRP), resulting in a vicious cycle of bi-directional inflammatory responses. For example, 'leaky gut' processes of circulating mediators may not only explain EIMs such as joint pain and arthralgia but mood disorders or 'inflammatory depression' (Moulton et al., 2019).
1.7 Psychological services in IBD

Despite the high prevalence of psychological distress and mood disorders evident in IBD, psychological services for people with IBD in the UK are limited. Only 24% of IBD services have a defined access to a psychologist with knowledge of IBD (IBD Standards Group, 2013) and only 12% of services met the standard for having an established referral care pathway for patients needing further support or counselling (RCP, 2014). Both qualitative and quantitative research has demonstrated patient need for more psychological support, from both patient (Schoultz, Macaden & Watson, 2016; Klag et al., 2017; Jordan et al., 2018) and healthcare professional perspectives (Mickocka-Walus et al., 2014). The majority of current UK IBD care pathways have psychological support independent from the biomedical care of patients, rather than having the physical and psychosocial aspects of the disease addressed together or within the same multi-disciplinary team (MDT). Preferably, having a psychologist within the IBD MDT can allow for more collaborative shared decision-making for a patient’s treatment pathway (Regueiro et al., 2016; Keefer, 2019). In the United States and Australia, more established and comprehensive embedded care models have been developed, for example the IBD-Home in Pittsburgh (Reguiero et al., 2016), which provides resources to patients around behavioural skills, social support and stress reduction training, involving a team of nurse specialists, dieticians, social workers and a health coach, and in Adelaide with the embedded involvement of clinical health psychologists (Sack et al., 2012). This facilitates a biopsychosocial approach to patient care and addresses both physical and psychological aspects of the disease. This is important not only because of the evident multiple impacts that IBD has, but because symptoms and pathophysiology of IBD is highly influenced by and frequently co-existent with psychological issues.
Pain is a common symptom of IBD; 70% of patients report pain at disease onset (Farrell et al., 2015) and up to 80% will have pain during acute flares (Szigethy, 2018). Acute pain can be caused by multiple factors in IBD; direct effects of inflammatory mediators (cytokines, chemokines) can stimulate sensory
afferent endings or disease-related complications such as partial bowel obstruction can lead to an inability to pass gas, a stool or lead to infection (Srinath et al., 2014). Abnormal intestinal motility can result in accumulation of trapped air or fluid, causing discomfort or painful symptoms (Srinath et al., 2014). In these cases, noxious stimuli are detected by specialised afferent neurons (nociceptors) in the intestinal wall and ascend along pain pathways to the spinal dorsal horn and key brain regions, such as the anterior cingulate cortex within the limbic system (Beyak & Vanner, 2005; Jones et al., 2006; Farrell et al., 2014). Other causes of pain can include extra intestinal inflammatory manifestations (EIMS). Musculoskeletal pain is the most common EIM of IBD, occurring in 9-53% of patients, and can arise from conditions such as arthritis, peripheral arthritis or spondylitis (Bernstein et al., 2001; Isaacs, 2008; Levin & Burakoff, 2011). Other painful EIMs include skin conditions (e.g. erythema nodosum) and ocular complications (e.g. episcleritis) (Levin & Burakoff, 2011). Pain is a key indicator of disease activity in IBD, in which case stepwise medication or surgery may be used to treat inflammation or associated complications in order to alleviate pain.

However, an estimated 30-50% of patients will experience persistent pain when defined to be in remission from objective clinical and endoscopic markers (Bielefeldt et al., 2009). Chronic pain is defined as pain lasting 3 months or intermittently for 6 months, and as ‘aberrant somatosensory processing in peripheral or central nervous system (CNS) that is sustained beyond the normally expected time course relative to a stimulus’ (Greene, 2010, pg. 1). In IBD, it is thought to be caused by a complex interaction of peripheral, central, neurobiological, genetic and psychosocial factors (Bielefeldt et al., 2009). For example, primary afferent neurons in the gastrointestinal tract can become hypersensitive as a result of recurrent mechanical and chemical changes, such as inflammatory mediators (IL-1β), gut motility and distension (Farrell et al., 2014; Li et al., 2008, Docherty et al., 2011, Akbar et al., 2010). The expression of TRPV1 ion channels has been recognised as a mediator of visceral hyperalgesia in IBD (Miranda et al., 2007; Farrell et al., 2014). Altered pain signalling may occur along higher order/secondary neurons, due to long lasting excitability or disinhibited pain modulation (Bleakman, 2006). Slow, diffuse and delocalised signals from visceral pain can also lead to ‘referred’ pain in other regions (skin, joints and muscle) when processed along the spinal cord dorsal pathway (Almedia et al., 2004). Dysregulated signalling may also occur in key brain regions (Long & Drossman, 2010). Bao and colleagues (2016) demonstrated differences between resting brain activity in remissive Crohn’s disease patients with abdominal pain compared to those without abdominal pain,
demonstrating that abnormal resting brain activity in the insula and middle cingulate cortex is associated with abdominal pain in remissive CD. This is also supported by chronic pain research, which has shown functional reorganisation of brain areas when pain becomes chronic (Apkarian et al., 2009).

As well as sensory signalling and processing of pain, psychological functioning such as emotional distress may modify pain perception, with cortical regions such as the limbic system responsible for processing of pain and emotional regulation (Villemure & Bushnell, 2002). Emotional distress and other psychological processes can affect pain indirectly through the brain-gut axis (Bonaz and Bernstein, 2013), stimulating the production of catecholamines from the autonomic nervous system and the stress hormone cortisol from the HPA axis. These chemical changes can disrupt gut microbiota function, intestinal motility and inflammatory processes and thereby exacerbate pain (Bonaz and Bernstein, 2013; Spiller and Major, 2016; Gracie et al., 2017). In support of this, research has demonstrated the overlap in risk factors associated with brain-gut dysregulation in IBD, including chronic abdominal pain, depression and anxiety (Jonefjall et al., 2016). Therefore, chronic pain in IBD is influenced by a range of complex and interacting neurobiological and psychological processes, alongside occult disease-related factors, making pain control a challenging endeavour.

1.8.1 Impact of pain in inflammatory bowel disease

Pain has been rated amongst the topmost burdensome symptoms for IBD patients (Solomon 2012). The association between pain and poor quality of life has been demonstrated in several studies to date (Simrén et al., 2002; Schirbel et al., 2010; Zeitz et al., 2016), including joint pain (Palm et al., 2005). For example, in a large Swiss cohort study of over 2000 patients, 49% and 55% of people with UC and CD, respectively, reported that pain was a long-term problem (>5 years) and quality of life was significantly lower in those with pain (Zeitz et al., 2016). Physical functioning and disability are also significantly affected by pain (Fretz et al., 2019); pain interference has been associated with less sexual interest and satisfaction in adults with IBD (Eluri et al., 2018) and more frequent and moderate/severe pain has shown to affect life satisfaction, work productivity and work attendance (van der Have et al., 2015; Odes et al., 2017). A recent qualitative study demonstrated patient’s perceived stigma associated with complaints of pain in IBD and their frustration at clinicians’ lack of understanding and knowledge regarding pain control (Bernhofer et al., 2017).
In paediatric patients with IBD, where a reported 70% of individuals experience abdominal pain regardless of disease status (Griffiths, 2004), pain has also been associated with poorer quality of life (Greeney et al., 2012). Familial or child-parent relationships and satisfaction have an important role in buffering the impact of pain intensity on health-related quality of life (Caes et al., 2019). School attendance, playing and functional impairment have also been impacted by pain in youth with IBD (Clarr et al., 2017).

1.8.2 Assessment of pain
Pain is routinely assessed in both clinical practice and clinical trials as an indicator of disease activity (Kim et al., 2017; de Jong et al., 2018). For example, abdominal pain severity is rated using a visual analogue or numerical rating scale and disease activity indices commonly assess the presence of pain related EIMs of IBD, such as joint or eye pain. However, solely assessing pain in IBD through DAIs can reinforce an over-medicalised approach and can distress patients when pain does not correlate with endoscopic or other clinical markers. Consequently, many patients will be given a concurrent diagnosis of irritable bowel syndrome (IBS) (Grover et al., 2009). However, this has been challenged by debate over threshold criteria for quiescent disease, as it is contended that low-grade inflammation may be a driving factor in IBD-chronic pain (Keohane et al., 2010). Rectal balloon distension studies have shown UC patients response pattern more like that of healthy controls than IBS patients (Mayer et al., 2005). On the other hand, classifying IBS and IBD on a continuum may facilitate a better understanding of functional symptoms in IBD and widen therapeutic options for patients (discussed in more detail in Chapter 1 Section 1.8.4).

1.8.3 Pain management in IBD
Pain management is complex in IBD clinical care; while clinicians are faced with a number of pharmacological options for pain management, it is important to recognise the risks associated with use of these in the context of IBD. This not only includes risk factors such as gut-related side effects and risk of relapse (Takeuchi et al., 2006), but also limited robust evidence for some strategies in chronic IBD-pain populations specifically, such as in the case of anti-depressant use or anticonvulsants. Non-steroidal antiinflammatory drugs (NSAIDS) are widely used for the treatment of other inflammatory conditions and for some EIMs in IBD. The association of relapse rates with the use of NSAIDS in several early studies (Takeuchi et al., 2006) has led to the recommendations of selective COX-2 inhibitors to
manage IBD pain (Docherty et al., 2011), but it may be that risks associated between NSAIDs and disease exacerbation are relevant only to sub-groups of patients in IBD or dose or timing effects (Kaufmann & Taubin, 1987; Long et al., 2016). However generally the long-term safety of NSAIDs for IBD is inconclusive (Docherty et al., 2011). Antispasmodics may be used in the context of pain associated with inflammation or partial obstruction, however side effects can include exacerbation of gut dysmotility in some individuals (Makharia, 2011, Srinath et al., 2012). Anticonvulsants such as diazepam and gabapentin are drugs used for the treatment of visceral pain in IBS but evidence is lacking for IBD-pain (Houghton et al., 2007; Gale & Houghton, 2011). Opiate medication is not recommended for long-term use for pain management in IBD, as evidence demonstrates the risks of developing narcotic bowel syndrome (Grunkemeier et al., 2007), visceral hyperalgesia (Locke et al., 2009) and other gastrointestinal complications (Edwards et al., 2001; Poitras et al., 2018). Acknowledging these risks and rising rates of opioid use in non-cancer populations, the British Medical Association has recommended safer prescribing and greater provision of support to patients on opiates (BMA, 2017).

More recently, studies have isolated specific areas of pain processing and shown promising developments in novel therapeutic methods for IBD. For example, randomised controlled trials (RCTs) of transcranial direct current stimulation have shown reductions in pain and changes in functional resting-state and increases in functional connectivity through MRI (Volz et al., 2016; Neeb et al., 2019). In animal models, genetic and pharmacological inhibition of calcium processing channels in visceral sensory neurons have suggested modifying effects on colonic hypersensitivity (Picard et al., 2019). However, these novel techniques are still in early stages of development, and cost and availability hinder widespread access. Other interventions for abdominal pain in IBD have included dietary studies, medical marijuana, nicotine patches, muscle relaxation and stress management, highlighting the lack of consensus around pain management in IBD (Norton et al., 2017). Strict dietary interventions such as the low FODMAP diet have shown some beneficial effects for functional symptoms in RCTs (Maagaard et al., 2016, Prince et al., 2016), however significant effects on reducing abdominal pain has not always been consistent (Cox et al., 2019). Moreover, long-term adherence rates to these restrictive dietary interventions may be challenging (Prince et al., 2016; Limdi et al., 2018). A recent study describing the profile of marijuana users in IBD demonstrated that despite reported positive beneficial effects of marijuana use, users also demonstrated greater depression, anxiety and pain-related interference, and lower social satisfaction compared to non-users (Kerlin et al., 2018).
Different pharmacological approaches may be used depending on the type of pain (visceral, joint, somatic) or associated symptoms (anxiety, insomnia). Sleep disturbance and anxiety occur in 53% and 45% respectively of patients with chronic pain (Attal et al., 2011). In IBD, pain intensity scores have been twofold in UC patients with substantial fatigue and a third higher in CD patients with substantial fatigue (Jelsness-Jørgensen et al., 2017). Psychotropics such as tetracyclic antidepressants and selective serotonin uptake inhibitors have been shown to help with symptoms of sleep disturbance and anxiety and depression, respectively, as well as pain in patients with functional gastrointestinal GI disorders (Srinath et al., 2012; Szigethy, 2018). They are also considered an ‘adjuvant analgesic’ with the aim of reducing risk of opioid dependence (Passik, 2009). However, it has been estimated in meta-analyses that only approximately half of patients respond to pharmacological therapies for chronic pain generally (Bjordal, et al., 2007; Finnerup et al., 2010; Machado et al., 2008; Machado et al., 2015). Meanwhile, reliance on analgesics and pharmacological agents such as opioids for pain control can have iatrogenic effects and risk worsening disease burden, quality of life and levels of distress for patients in IBD (Sanford et al., 2014). Conceptualising pain as a solely biomedical problem can further distress patients when they do not see a correlation between pain symptoms and disease activity, or a response to pharmacological agents.

A small body of evidence has researched the effects of non-pharmacological interventions on pain in IBD, including studies conducted specifically in paediatric populations (Yeh et al., 2017). In adults, psychological interventions have included coping skills training (Hauytin et al., 2011; McCormick et al., 2013), stress management (Garcia-Vega et al., 2004), relaxation exercises (Shaw & Ehlrich, 1987) or multi-component interventions (Schwarz & Blanchard, 1993) (reviewed in Norton et al., 2017). Despite some improvements in pain symptoms, these studies are limited by sample sizes and lack of theoretical grounding, limiting their generalisability and scientific rigour.

1.8.4 Chronic IBD-pain and overlap with irritable bowel syndrome

IBS is a functional gastrointestinal condition which shares many clinical and pathogenic characteristics with pain in IBD. Abdominal pain is a cardinal symptom of IBS as well as other symptoms of diarrhoea, constipation and bloating. Diagnosis requires pain or discomfort for 12 weeks consecutively within a year, which is relieved by defecation and accompanied with change in stool habit or appearance (Drossman, 2016; Drossman et al., 2016). It is the most common diagnosis made by gastroenterologists globally, and in the UK is estimated to be present in 23% of women and 11% of men (overall prevalence
The overall estimated pooled prevalence of people with IBD with IBS is around 40%, with likelihood of developing IBS fourfold in IBD compared to the general population (Halpin & Ford, 2012). Currently there are no universal or standardised guidelines for this cohort of patients, with ‘best practice’ expert reviews only emerging in recent years (Colombel et al., 2019). However, given the overlap in symptomatology and in an attempt to guide management and treatment options, patients are frequently diagnosed under the term ‘IBS-IBD’.

There is an increasing argument that IBS and IBD should be viewed on a functional continuum rather than classified and treated as distinct entities (Mearin, Perello & Balboa, 2009; Long & Drossman, 2010; Spiller & Major, 2016). Overlap in symptomatology and pathogenesis between chronic pain in IBD and IBS including occult inflammation, defects in the gut barrier and gut microbiome, visceral hypersensitivity, dysregulation of the central nervous system (CNS) and influence of psychological processes (van Tilburg et al., 2013, Hungin et al., 2015, Mayer et al., 2015; Quigley, 2016, Grover et al., 2009). Recently, the term ‘irritable inflammatory bowel syndrome’ (IIBS) has been suggested, arguing that the presence of functional symptoms in IBD may be due to a predisposition or underlying phenotype to develop IBS (Quigley, 2016). A number of IBS-associated triggers along the brain-gut axis could make an individual susceptible to “functional” symptoms and can be primed or upregulated by IBD activity. In this sense, it is argued that postinfectious IBS can be conceptualised in much the same way as post-flare pain in IBD in triggering these vulnerabilities (Spiller & Major, 2016). For example, pre-existing intestinal permeability, a large quantity of TRPV1 pain receptors or psychosocial factors may make an individual susceptible to ongoing pain symptoms during periods of IBD remission.

Treatment for IBS includes a range of pharmacological and non-pharmacological approaches, as well as dietary techniques. Pharmacological approaches will vary depending on sub-group of IBS phenotypes (Weinberg et al., 2014) and include antispasmodics, tricyclic antidepressants, selective serotonin reuptake inhibitors, peppermint oil, or bowel-specific interventions such as antibiotics, probiotics or bile salt sequestrants (Weaver et al., 2017). Non-pharmacological intervention in IBS is a rapidly evolving area, and systematic reviews have advocated the use of psychological approaches such as cognitive behavioural therapy, gut-directed hypnotherapy and dynamic psychotherapy (Ford et al., 2014; Hanlon et al., 2018; Colombel et al., 2019). It is advised that an individualised, multi-faceted biopsychosocial management approach is utilised in IBS, and thus, IBS-IBD patients (Mikocka-Walus
et al., 2012). Indeed, these approaches may be of value in providing symptom relief in the context of chronic IBD-pain specifically but testing on IBD-pain populations is critical before they can be recommended.

1.8.5 **Theoretical development of IBD-pain: a biopsychosocial model**

Recognising the need for a more biopsychosocial approach to pain in IBD, a conceptual model was proposed by Bielefeldt and colleagues (2009). This summarises key central and peripheral influencing factors in the maintenance of IBD-related pain (Figure 2). Inflammatory and disease-related processes result in sensitisation of visceral afferent neurons, increasing afferent input and thus greater perception of pain. Negative affect, worrying and psychological comorbidity influence cognitive processing and arousal, which can influence both ascending and descending pain signals and amplify sensory input (Bielefeldt et al., 2009). Emotional processes and hypervigilance are suggested to have a bi-directional influence with pain, as pain can trigger negative emotions and cognitive processing, which in turn can heighten sensitivity and distress associated with pain signals, exacerbating anxiety and hypervigilance (Lackner and Quigley, 2005).

The model by Bielefeldt et al. (2009) represents a significant step forward in a theoretical understanding of IBD-related pain. It encapsulates neurobiological, luminal and psychological processes contributing to the maintenance of pain in IBD. However, the model does not identify specific pain-related psychological processes that may be exacerbating or maintaining IBD-pain and which might be targeted through psychological interventions. Theoretical models of primary chronic pain (discussed in Chapter 2) argue that the types of behavioural, cognitive and emotional responses an individual has in response to pain and pain-related cues are fundamental to understanding the development of persistent pain (Vlaeyen and Linton, 2000). A more comprehensive model of IBD-related pain should acknowledge the interaction between disease-related neurobiological processes, CNS dysregulation such as the role of the hypothalamic pituitary adrenal (HPA) axis and pain-specific psychological processes.
1.9 Thesis rationale and overview

The aim of this thesis is to develop and feasibility test a self-management intervention for pain in IBD. The empirical studies carried out in this thesis provide a deeper understanding of some of the psychosocial processes in IBD-pain and inform the development of an intervention for people with IBD and pain, with the aim of reducing the severity and impact of pain and improving quality of life for patients.

To develop a comprehensive understanding of IBD-pain, this thesis is guided by the Medical Research Council (MRC) framework for developing complex health interventions. The MRC framework recommends selection of appropriate theory, identification of the evidence base and modelling processes and outcomes through both qualitative and quantitative means, culminating in a feasibility/testing stage (described in Chapter 3). Identification of appropriate theory is discussed and justified by reviewing current models of chronic pain in Chapter 2. In gaining a better understanding of the current evidence base, a systematic review was undertaken to identify psychosocial constructs previously identified to be associated with IBD-pain (Chapter 4) (published article, *Alimentary Pharmacology & Therapeutics*) (Sweeney et al., 2018). This is followed by two chapters which aimed
to build a theoretical model of IBD-pain; Chapter 5 presents a cross-sectional study to quantitatively explore sociodemographic, clinical and psychosocial factors associated with pain in IBD (published article European Journal of Gastroenterology & Hepatology) (Sweeney et al., in press). Chapter 6 presents a qualitative study to explore how people with IBD perceive and manage their pain and what their needs are for a pain management intervention. This uses thematic analysis to explore themes arising from the data (published article, British Journal of Pain) (Sweeney et al., 2019). Development of a theoretical model for IBD-pain, based on Chapters 4-6, and development of an online CBT-based self-management intervention is discussed in Chapter 7. Chapter 7 also describes in detail the intervention development process, including mapping intervention components based on the IBD-pain theoretical model, and the format and content of the intervention. Chapter 8 presents the findings of the feasibility study, testing the online interventions for acceptability, feasibility and preliminary estimates of efficacy on pain outcomes (severity and interference) and quality of life. Lastly, Chapter 9 presents a discussion of the thesis findings, limitations and future recommendations for clinical practice and research in this area.

1.10 Thesis in context of IBD-related research and programme development

The funding and approval for this PhD was developed by researchers at King’s College London, who had conducted previous work in other burdensome symptoms of IBD; fatigue (Czuber-Dochan et al., 2013a; Czuber-Dochan et al., 2014; Artom et al., 2016; Artom et al., 2017) and incontinence (Dibley et al., 2013; Norton et al., 2013; Norton et al., 2015). These researchers were informed by literature, research priority settings (Hart et al., 2017) and clinical practice that pain was a similarly poorly understood and managed symptom of IBD. A full-time three-year funded PhD was funded by Crohn’s and Colitis (UK) (https://www.crohnsandcolitis.org.uk/research/projects/pain-management-in-ibd) to add to this body of research and develop a better understanding of chronic pain in IBD and a feasibility test a self-management intervention. This aimed to draw from expertise from previous research in Health Psychology on symptom management in long-term conditions. Researchers at King’s College London (including the thesis author) published a systematic review on interventions for abdominal pain in IBD, which further highlighted the lack of theoretical understanding and management of pain (Norton et al., 2017).
Cumulatively, the work conducted in IBD-pain, fatigue and urgency/incontinence aimed to provide a background and rationale to apply for a National Health of Institute Research (NIHR) programme grant for the management of chronic pain, fatigue and urgency/incontinence in IBD. Therefore, my role as a researcher was to fill this gap in the literature on pain in IBD; developing a better understanding of pain in IBD to guide intervention development and inform the wider research field on chronic IBD-symptoms. This work has successfully led to the funding of the NIHR programme grant: ‘Living well with inflammatory bowel disease: optimising management of fatigue, pain and faecal urgency/incontinence via tailored online self-management’ (IBD-BOOST). BOOST will be described in more depth in Chapter 3 Section 3.5, clarifying how the work from this thesis guided intervention development in BOOST and what my role was in BOOST. Chapter 7 also describes in more detail how the work undertaken in this thesis and BOOST culminated in amalgamating the IBD-pain and BOOST interventions, given the significant overlap, therefore forming the intervention for this thesis.

1.11 Chapter 1 Summary

This chapter has provided an overview of IBD and demonstrated that pain, despite being a commonly experienced symptom in IBD, is an under-researched and poorly managed symptom in IBD. Pain significantly impacts an individual’s quality of life, including physical functioning, work productivity and life satisfaction. Pain in IBD can be caused by a multitude of factors, including peripheral, neurobiological, central and psychological processes. While a conceptual model previously developed (Bielefeldt et al., 2009) summarises the influence and interaction of processes in IBD-pain, there is a need to update and embellish the model using accumulating evidence from IBD, IBS and the chronic pain literature. This will facilitate a more comprehensive understanding of IBD-pain and the development of an effective pain management intervention. In supporting a conceptual understanding of IBD-pain, Chapter 2 will review current psychological approaches to chronic pain.
Chapter 2 Theoretical Approaches to Understanding Chronic Pain

2.1 Chapter overview

The previous chapter identified that pain is a significant problem and an under-researched area in IBD. A conceptual model of IBD-pain highlights that pain is a multifactorial construct influenced by peripheral and central processes, and that pain management requires a biopsychosocial approach. To further an understanding of psychological processes associated with IBD chronic-pain, it is important to review the literature on theoretical approaches to chronic pain, both in non-disease related, primary chronic pain and disease-related chronic pain, where biopsychosocial models of disease-specific pain have been developed to aid the development of tailored interventions. This chapter therefore provides a critical analysis of different theoretical approaches to understanding and treating chronic pain and presents the Behavioural Activation System/Behavioural Inhibition System (BIS/BAS) model.

2.2 Psychological approaches to understanding primary chronic pain

After a long standing dominant biomedical view of pain, Melzack and Wall’s (1965) Gate Control Theory shed light on the role of both physiological and psychological processes in pain, and more specifically the influence of emotional and cognitive processes on the transmission of nociceptive signals. This sparked a wave of research exploring key psychological mechanisms that may be operating in the context of chronic pain. Over the last 50 years of research, comprehensive models have been developed to aid our understanding of chronic pain. These include operant models of behavioural reinforcement and a number of cognitive behavioural theories, including the fear-avoidance model and ‘third wave’ approaches (Fordyce, 1976; Hayes, 1999; Vlaeyen & Linton, 2000). The development of these theories has broadened our understanding of pain and identified key mechanisms in the aetiology and prognosis of chronic pain. However, such models have a number of limitations and shortcomings in evidence-based research. The Behavioural Inhibition System and Behavioural Activation System (BIS/BAS) model of chronic pain (Jensen et al., 2016) provides a comprehensive conceptual understanding of how chronic pain develops and is maintained, and importantly, how psychological interventions, such as cognitive behavioural therapy (CBT), operate. These ‘first’, ‘second’ and ‘third wave’ psychological approaches to understanding and treating chronic pain are discussed below,
highlighting their strengths and limitations, and the rationale for the use of the BIS/BAS framework for the context of this thesis is presented.

2.2.1 Psychological approaches to understanding and treating chronic pain

Originating from research carried out by Fordyce (1976), the operant theory of chronic pain argues that environmental responses to particular behaviours will either lead to increases or decreases of that behaviour, based on perceived reward or punishment, respectively. For example, illness behaviours that are reinforced (such as increased social support or decrease in tasks or responsibilities) will result in further illness behaviours. However, if they are ignored or different behaviours are reinforced, such as wellness behaviours of exercise or active coping, then this will in turn lead to a decrease in illness behaviours. In this regard, the development of chronic pain can arise from consistently reinforced pain behaviours leading to deconditioning and the maintenance of pain. It is suggested that psychological interventions involving analysis of environmental factors that reinforce maladaptive behaviours and identifying those that reinforce adaptive ones, termed ‘contingency management’, may be beneficial. For example, the involvement of significant others in interventions can have an impact on pain and pain-associated disability through reinforcement of adaptive behaviours (Fordyce et al., 1968). Despite operant models marking significant progress in chronic pain research, their main limitations include a narrow focus on pain behaviours as the sole mechanism in chronic pain, the overestimation of social contingencies and the underestimation of cognitive processes (Turk, 1996; Williams & Daniel, 2012; McCracken, 2014).

Conversely, the cognitive behavioural approach to chronic pain (Turk et al., 1983) contends that individuals are active agents in processing of information and over time have built up a ‘cognitive schema’ through learned experience. This content is formulated about the sense of self and the world and the future (Beck, 1991). When the individual is placed in unfamiliar circumstances, predetermined cognitive schema are activated to facilitate beliefs, expectations and processing of novel situations. Resultant emotions and behaviours occur from these cognitive processes can in turn lead to the maintenance of pain. Cognitive behavioural therapy (CBT) operates by allowing individuals to identify unhelpful beliefs around pain and form new associations, through procedural learning and cognitive re-structuring (Turk et al., 1983) (a more detailed description of CBT is provided in Chapter 7).
Embedded within a cognitive behavioural approach to chronic pain, the Fear-Avoidance model argues that an individual can perceive pain as threatening and harmful to the body and therefore engage in catastrophising thoughts around pain (Lethem et al., 1983; Asmundson et al., 2004). These cognitive processes may subsequently lead to fear of activity, which in turn affects inhibitory processes such as behavioural avoidance and inactivity which can exacerbate the pain experience. Hypervigilance and hypersensitivity are important recognised constructs in the Fear Avoidance model, as the individual may have heightened attention to threat-related cues, and inactivity over time makes the individual susceptible to further mental and physical harm and therefore making them more vulnerable to pain, suffering, disability and physical deconditioning. The model suggests a unidirectional and cyclical relationship between cognitive, emotional and behavioural factors (Figure 3). There is a wide body of evidence in support of the Fear Avoidance model (Leeuw et al., 2007), including the association between pain-related cognitive factors (e.g. fear avoidance, catastrophising) and disability, however association with pain intensity is less consistent (Crombez et al., 2012). In addition, the model fails to acknowledge the influences of an individual’s motivations and value-based goals or provide an explanation as to which individuals can recover or function in the presence of pain (Crombez et al., 2012). Despite support for the model in cross-sectional studies, prospective longitudinal studies have failed to support the sequential format of the model (Amundson et al., 2012).

![Fear avoidance model of chronic pain](image)

Figure 3 Fear avoidance model of chronic pain (Vlayen & Linton, 2000, pg. 329)

The Avoidance Endurance model (Hasenbring & Verbunt, 2010) shares many similarities with the Fear Avoidance model, however its extension concerns two discrete paths that may lead to pain-related
disability as a result of pain-related fear and anxiety. These are the distress endurance response and the eustress endurance response. The former describes attempts to suppress pain with initial arousal of anxiety and depression and then task persistence, which ultimately results in burnout and exacerbation of symptoms (otherwise termed ‘all or nothing’ or ‘boom and bust’). The latter response describes the use of distraction techniques followed by task persistence, which can initially result in positive mood. Despite both these approaches having an acute period of pain cessation, both are hypothesised to exacerbate pain in the long term (Hasenbring et al., 2014). Similarly to the Fear Avoidance model, an underlying limitation of the Avoidance Endurance model is that it fails to acknowledge motivations and goals or provide an alternative route by which individuals can recover or function through pain (McCracken & Morley, 2014).

‘Third wave’ approaches to chronic pain include techniques such as mindfulness and acceptance and commitment therapy (ACT). Relational Frame Theory, central to ACT, argues that although we cannot unlearn our preformed associations, through ‘psychological flexibility’ and other techniques (acceptance, cognitive defusion, observer stance) we can make wider and more flexible associations between links (Hayes et al., 2006). Through psychological intervention, individuals are encouraged not to identify what thoughts and emotions they have but to modify the context in which those thoughts and emotion function, and how they identify themselves with them (McCracken & Vowles, 2014). ACT encourages an individual to detach themselves from these associations and their meaning and to engage in activities that reflect their goals. For example, rather than holding an association between fearful beliefs and avoidant behaviours, an individual may be taught to recognise and make contact with those beliefs whilst continuing with actions that facilitate the attainment of valued goals (McCracken & Morley, 2014). Support for ACT-based approaches has been demonstrated in meta-analyses (Veehof et al., 2016), demonstrating its superiority over mindfulness-based interventions. For example, ACT compared to relaxation or multi-disciplinary interventions demonstrate moderate to large effects on outcomes of depression, disability, pain and pain-interference. However, CBT treatments have been shown to be more effective in comparison to acceptance and mindfulness-based interventions on similar outcomes (Veehof et al., 2016). In addition, the model of psychological flexibility largely ignores the interacting influences of biological, emotional and social factors in the maintenance of pain (Lumley et al., 2011).
More recently, chronic pain theories have moved away from a sole focus on exacerbating negative factors and looked towards resilience and positive psychology as a potential useful avenue for pain interventions. For example, the dual factor model (Sturgeon & Zautra, 2010) identifies both ‘vulnerability’ and ‘resilience mechanisms’ to understand the development of chronic pain and related disability, and why some individuals continue to function (and indeed flourish) in the face of adversity (Figure 4). Resilience mechanisms such as pain self-efficacy and positive affect can serve as modifiable factors through positive psychological interventions, which allow an individual to reorient their attention away from an ongoing attempt to reduce or control the pain towards meaningful goals, recovery and sustainability (Goubert & Trompetter, 2017). Supporting evidence has shown the beneficial effects of positive psychological interventions on outcomes such as subjective well-being and pain self-efficacy in a review of chronic non-cancer pain (Iddon et al., 2016). In IBD research, a recent longitudinal study showed that greater illness acceptance, coping efficacy and social support were associated with positive adjustment, namely resilience (return to pre-illness functioning) or thriving (personal growth), in individuals with IBD (Sirois and Hirsch, 2017). Moreover, emotional regulation has shown beneficial effects on psychological and physical functioning in another recent longitudinal study in IBD (Trindade et al., 2018). The growing number of two factor model approaches to chronic pain can help inform interventions to recognise and target negative and positive psychological outcomes and targets for treatment.

Figure 4 Dual factor model of vulnerability and resilience mechanisms in chronic pain (Sturgeon & Zautra, 2010, pg. 107)
2.2.2 The BIS/BAS model of chronic pain

The BIS (behavioural inhibition system) and BAS (behavioural activation system) (Figure 5) are two independent neurophysiological systems that are suggested to underlie an individual’s behaviour, emotion and motivation (Carver & White; 1994). Based on Gray’s Reinforcement Sensitivity Theory (Gray, 1987; Gray; 1994), the BIS and BAS represent approach and avoidance behaviours in response to cues indicating potential reward or punishment, respectively. These systems operate automatically and are generated from (and constantly influenced by) associative and experiential learning. These learned associations and formed connections give rise to BIS/BAS related content and appraisal processes which bear similarities to the cognitive network or ‘schema’ posited in cognitive behavioural models. Whether the BIS or BAS is activated depends on the individual and their learning history, focus of attention and genetic predisposition. The BIS/BAS model of chronic pain, developed by Jensen and colleagues (2016), provides a way of understanding the interaction between psychosocial and neurobiological processes in the maintenance of pain, as well as providing a mechanism by which psychosocial treatments operate (Jensen et al., 2016).

In the context of chronic pain, the BIS/BAS model hypothesises that the experience of pain and pain-related cues can activate BIS-associated cognitions, emotions and behaviours. These in turn will aim to maximise the likelihood of avoiding or reducing the pain experience and cause the individual to ‘stop, look and listen’ (Gray, 1991). For example, BIS-related behaviours may include withdrawal, avoidant behaviours and illness-focused coping (guarding, resting). BIS-related cognitions and emotions may occur as a result of these behavioural responses. However, they may also allow the individual to shift their attention and become sensitive to pain-related cues (anxiety, hypervigilance). BIS-related processes are adaptive for the individual by decreasing the likelihood of being in a situation of threat or danger (such as pain). BIS-related emotions such as fear and depressive symptoms, although ultimately unpleasant, facilitate behavioural inhibition. Over time these processes are likely to contribute to the ongoing experience of pain, either through heightened attention (hypervigilance) or heightened sensation (hypersensitivity) via a number of neurobiological and physiological pathways.

In what context, then, would BAS be activated when an individual is experiencing pain? As discussed, the activation of BIS or BAS in the presence of pain depends on their learning history, attentional focus, physiological state and predispositions (Jensen et al., 2016). For example, as a result of personal, social and environmental factors, an individual may have the necessary resources to adapt and function in
the presence of pain. BAS-related processes, such as self-efficacy, perceived social support and optimism, may be pertinent as a result of these factors. The strength of this BAS-content may then override BIS activation when an individual experiences pain. In this case, the individual is more likely to achieve value-based goals or an eventual state of psychological well-being despite pain. BAS-associated processes in turn are suggested to attenuate the perception of pain and the extent to which pain interferes with an individual’s life. An overactive BAS can also explain the endurance of ‘all or nothing’ behaviours seen in some individuals, as inactivity will be perceived as an aversive state (Jensen et al., 2016). The BAS system is hypothesised to reduce the input of pain perception. This may either be through attentional resources being diverted away from pain and towards achieving value-based goals (reward-seeking) or attenuating the levels of emotional arousal that could otherwise act to amplify pain signals.

Both BIS and BAS activation involves emotional, cognitive and behavioural processes that either lead to the increased likelihood of avoiding aversive states or reinforcement of rewards, respectively. Rather than a unidirectional relationship between these cognitive, emotional and behavioural processes, the model suggests a mutual causation and interacting relationship among these processes (Figure 5). Any one of them may occur primarily, however the occurrence of one is likely to have an influential effect on other BIS/BAS-related processes. Therefore, emotions, cognitions and behaviours may not only operate as causal agents in chronic pain but serve as outcomes i.e. negative affect can be an outcome of having chronic pain or engaging in withdrawal behaviours, but can also be seen as a causal factor for BIS-related cognitions (pain catastrophising) and behaviours (withdrawal). Although the BIS/BAS systems are independent systems, they can also interact, as BIS activation may indirectly have an inhibitory effect on BAS. However, there can be instances where both are activated. For example, an individual may think and feel in two minds about something (wanting to be able to exercise, but feeling afraid to, because of pain), however whichever system prevails will reflect the goals the individual has and thus how they will ultimately act.
2.2.3 The BIS/BAS approach and understanding psychological interventions

The BIS/BAS model of chronic pain also provides an explanation as to how psychological interventions may operate. A central characteristic of the BIS/BAS model is its automaticity. Through an individual’s learned associations, experiences and predispositions, how one appraises and behaviourally responds to a situation relies on a ‘reflexive’ and ‘associative’ system (Lieberman et al., 2002; Kahneman, 2003). Although this serves an adaptive purpose as it does not require executive control, thereby freeing up attentional resources, it also means that these systems can be vulnerable as they can occur outside of deliberate control.

In terms of how the BIS/BAS systems might be modified, Jensen et al. (2016) argue that psychological interventions operate by reducing the effect of this automaticity through learning to respond less automatically. Through new experiences and behaviour, the individual can form new associations and begin to make conscious evaluations to create new cognitive content, such as through techniques used in CBT. In the context of pain, this might involve encouraging an individual to think more consciously about their decisions on activity. For example, an individual can learn an association that taking the stairs or going for a walk at lunchtime once a day may not exacerbate pain and therefore, in the future,
will no longer be considered as a cue to activate the BIS system. In CBT, individuals are encouraged to identify unhelpful thoughts they may have and develop new ways of thinking that are more in tune with achieving their goals (Turk et al., 1983). This technique describes the increase of BAS-related content by forming new associations. CBT can take a range of approaches, such as aiming to strengthen an individual’s self-efficacy or reducing the frequency of catastrophising thoughts. The model hypothesises that whichever type of BIS or BAS related content it aims to target is most likely to see changes in those respective BIS or BAS-related processes. In addition, CBT can teach individuals to adopt a more detached approach to their thoughts, which addresses the way in which psychological interventions operate by encouraging the individual to think less automatically, as hypothesised by the BIS/BAS approach.

This ‘observer stance’ technique is also shared within the model of psychological flexibility. Techniques derived from this model, central to ACT, teach individuals to de-identify themselves with BIS-related content through tools such as cognitive defusion and acceptance, and thereby aim to break the cycle of BIS-processes. Thoughts, feelings or behaviours are identified as contents of experience and viewed separately rather than mutually interacting, and value-based goals are maintained (McCracken & Morley, 2014). In support, Hamill et al. (2015) argue that techniques such as acceptance and mindfulness (where one is non-judgmental to present events and feelings) may aim to reduce BIS sensitivity and promote emotional regulation. Indeed, the authors found that facets of mindfulness and acceptance significantly moderated the association between BIS sensitivity and psychological distress. In summary, the BIS/BAS model is not wedded to a single psychological approach and several therapeutic approaches may be applied in the aim of reducing BIS-related processes and increasing BAS activation.

2.2.4 Comparison of BIS/BAS model to current pain models

With regards to previous models of chronic pain, the BIS/BAS model addresses the key limitations of the Fear Avoidance and Avoidance Endurance models by involving aspects of motivation and goal-seeking based on whether environmental cues are perceived as reinforcing or punishing. The model suggests how BAS and BIS-related cognitions, emotions and behaviours facilitate approach and avoidant behaviours, which are recognised as fundamental mechanisms in chronic pain (Eccleston & Crombez, 1999; Vlayen & Linton, 2000). It also addresses the ‘cognitive schema’ from cognitive
behavioural approaches and parallels with ACT with regards to automatic forming of connections or ‘stimulus relations’.

Recognising that an individual’s emotional, cognitive and behavioural processes play a significant role in chronic pain, the BIS/BAS model addresses two cognitive-behavioural cycles. However, it presents, on a wider perspective, how these cognitions, emotions and behaviours are initiated (by anticipation of reward or punishment) and operate (automatically through associative learning). The inclusion of two separate operating cognitive-behavioural processes reflects the dynamic and multifaceted aspects of pain. At times, based on attentional resources, physiological states (such as particularly severe pain or active disease in IBD) and external factors, the BIS-related content may be more prominent and therefore override BAS-content. Furthermore, a BIS-BAS model of IBD-related chronic pain would contend that BIS or BAS processes may be still present but vary as to whether they are operating in the background or foreground of decision-making. Thus, the model is particularly relevant to disease-related pain where contextual influences such as symptom severity can vary.

Overall, the key advantages in the BIS/BAS model include:

1. It provides a model which involves mutually influencing factors rather than a unidirectional process in the maintenance of chronic pain.
2. It suggests that two cognitive behavioural processes can be present in an individual but based on a range of factors (attentional resources, physiological state, social environment), BIS or BAS-related content will override and ultimately guide decision making in response to pain.
3. It proposes a dynamic and multifaceted theory for disease-specific pain, in which symptoms are recurrent and fluctuating in severity and therefore may have a more significant influence in activating BIS or BAS-related content.
4. It suggests a mechanism by which psychological interventions (including CBT) may operate for individuals with chronic pain.

2.2.5 Limitations of the BIS/BAS

Despite these recognised strengths of the BIS/BAS framework, a limitation of the model is that it does not fully address social processes such as social support and reinforcement. Rather, social factors are
conceptualised within the external network of ‘environmental influences’ that can influence both BIS and BAS processes. The social environment is highly influential over one’s psychological functioning and behaviours. Moreover, the inclusion of significant others in interventions such as educational or coping skills training has been recommended and is commonly included in pain management programmes (Fardyce, 1976; Loeser & Egan, 1989; Sanders, 1996) including for disease-related pain populations such as arthritis (Radojevic et al., 1992; Keefe et al., 1996).

The original BIS/BAS theory (Carver & White, 1994) has been extensively investigated, such as investigation of reward or threat sensitivity in healthy adult and paediatric populations or mood disorders, and the BIS/BAS scale developed by Carver & White (1994; 2013) has been cited over 2000 times (Pagliaccio et al., 2016). However, in chronic pain populations, compared to other psychological models of chronic pain, the BIS/BAS theory has received less empirical support, and to the thesis author’s knowledge has not yet been tested in an intervention. Yet one could argue that limited prior empirical support does not reduce the validity and application of a theoretical model for developing a complex health intervention. For example, the trans theoretical model (TTM) (Prochaska & DiClemente, 1983; Prochaska et al., 1992) has received criticism and limited empirical support (Sutton, 2000), however the TTM has been widely used in various intervention studies including smoking cessation and sexual health behaviours (Harlow et al., 1999; Sutton, 2000). The BIS/BAS framework unifies several pre-established theories, including cognitive behavioural theories, fear avoidance model and dual processing models in chronic pain, taking into account possible ‘resilience mechanisms’ as proposed by Sturgeon & Zatura (2010). Furthermore, interventional research provides an opportunity to test a theory, widening knowledge and understanding. To date, no research has applied or tested the BIS/BAS model in the context of chronic IBD pain. However, recently the BIS/BAS model has been recognised as a potentially helpful approach to understanding chronic pain in IBD (Reguiero et al., 2017) and has been applied to studies of emotional regulation in chronic musculoskeletal pain (Serrano-Ibanez et al., 2018).

### 2.3 Disease-specific biopsychosocial models of chronic pain

The development of theoretical models is key for conceptualising suggested psychological processes in chronic pain. However, in the context of disease-related persistent pain, one cannot ignore the role of physiological and neurobiological processes. As a result, disease-specific biopsychosocial models of
pain have been developed, including in multiple sclerosis (MS) (Kerns et al., 2002; Harrison et al., 2015a; Harrison et al., 2015b), sickle cell disease (Taylor et al., 2013) and HIV (Marcus et al., 2000). For example, Harrison et al. (Harrison et al., 2015a) identified cognitive, emotional, behavioural and biological factors that may be contributing to MS-related chronic pain, such as primary lesions or central nervous system processing. Similarly, a systematic review on HIV-chronic pain identified psychological processes (emotional distress, illness perceptions), as well as biological/medical (lower CD4+ counts, intravenous drug users) and sociodemographic factors (gender, age) associated with pain (Parker et al., 2014). These sociodemographic and biological factors are important to acknowledge in specific disease populations, as it is integral to address these aspects in tailored self-management interventions to achieve optimal outcomes. Indeed, development of these biopsychosocial models has led to multimodal assessment and management of disease-related chronic pain (Marcus et al., 2000; Michalski et al., 2011; Amatya et al., 2018; Merlin et al., 2018; Arewasikporn et al., 2019).

2.3.1 Conceptual model of IBS

Recurrent abdominal pain is a key symptom and diagnostic criterion for IBS (Lacy et al., 2016) and a wealth of research has investigated biopsychosocial models of IBS, including predisposing, precipitating and perpetuating factors (Hauser et al., 2014). Psychosocial factors have been identified as a key mechanism in IBS aetiology, including the role of personality, stress and coping styles (van Tilburg et al., 2013). The effects of psychological stress include both early life stressors, predisposing individuals to show greater reactivity to stress (Qin et al., 2014), and acute stressors on the gut-brain axis. A biopsychosocial model of IBS was first suggested by Drossman (1998) and has been developed since (Tanaka et al., 2011; Van Oudenhove et al., 2016), which emphasises the interaction of IBS biology (genetics, microbiome, dysmotility), the environment (trauma, life events) and cognitive-behavioural processes. These processes include catastrophising, somatisation (van Tilburg et al., 2013), symptom focusing, coping skills, and anxiety (Windgassen et al., 2019a), and have given rise to CBT being an effective and predominantly used psychotherapeutic approach in IBS (Kinsinger, 2017). Specifically, a cognitive behavioural model of IBS posits that an interaction of gastrointestinal-specific thoughts, negative affect and unhelpful behaviours perpetuate IBS symptoms and impact on quality of life (Blanchard et al., 1992, Hutton, 2005; Kennedy et al., 2005; Spence & Moss-Morris, 2007; Windgassen et al., 2019b). CBT-based interventions for IBS include psychoeducation, stress management and cognitive and behavioural techniques to improve bowel habits, facilitate stable eating
patterns and reduce symptom focusing. The evidence base for CBT in IBS is well-supported (Li et al., 2014; Ballou & Keefer, 2017); and a recent large RCT showed that both web-based and telephone-supported CBT led to reductions in IBS symptom severity and improved quality of life, which was sustained at one and two-year follow up (Everitt et al., 2019a; Everitt et al., 2019b).

Further work in IBS has sought to investigate psychosocial processes in the context of specific IBS-symptoms or sub-types. For example, Windgassen and colleagues (2019b) identified that specific cognitive-behavioural processes are more pertinent within sub-types of IBS, such as avoidance and control behaviours in the context of diarrheal and constipation-predominant IBS, respectively. In chronic abdominal pain in IBS, suggested psychological mechanisms include (trait and/or state) emotional or cognitive factors which may have a mediating effect on visceral hyperalgesia, alongside other existing disturbances along the gut-brain axis (Figure 6) (Elsenbruch et al., 2011). Neuroimaging studies have elegantly demonstrated the effects of cognitive and emotional processing in anticipation of or response to visceral stimulation (Lorenz et al., 2003; Elsenbruch et al., 2010a; Elsenbruch et al., 2010b). One study induced visceral stimuli in either a high-anxiety or low-anxiety condition, compared to a neutral condition, and found that individuals with IBS showed reduced activation in the dorsolateral prefrontal cortex (DLPFC) (Elsenbruch et al., 2010a), which is thought to be a key region involved in pain control (Bunge et al., 2001; Lorenz et al., 2003). Meanwhile, greater activation was observed in the insula and ventrolateral prefrontal cortex (VLPFC), the latter of which is thought to be involved in cognitive modulation of pain, such as processes of anticipation, expectation and conditioning. The study demonstrates the important influence of behavioural and central responses in pain processing and perception in IBS-chronic abdominal pain (Lieberman et al., 2004; Lu et al., 2010). These findings highlight that particular psychosocial processes may be significant not only in biopsychosocial models of long-term conditions but for specific sub-types or symptoms within conditions.
Chapter 2 Summary

This chapter has presented different theoretical approaches to understanding chronic pain. Many psychological models have been developed to aid our understanding of chronic pain, and selection of appropriate theory entails a detailed and sophisticated understanding of the evidence-base and relevance to the intervention in question (Michie et al., 2005). Each psychological model that has been presented holds its own strengths and limitations. The BIS/BAS model of chronic pain (Jensen et al.,...
2016) draws on the limitations of previous models and presents a sophisticated conceptual framework of how chronic pain may develop and be maintained over time. It suggests how psychological interventions operate, by forming of new adaptive associations and learning to respond less automatically. It therefore suggests, in the context of this thesis, that both approach and inhibitory-related processes may be important to investigate in IBD-chronic pain. However, importantly, the development of a theoretical model of IBD-pain must unify a conceptual understanding of chronic pain with disease-related processes. Developing this in-depth biopsychosocial understanding of IBD-pain will aid the identification of specific psychosocial factors to target within an intervention, as has been developed in biopsychosocial models of other long-term conditions (MS, HIV and IBS).
Chapter 3 Methodology

3.1 Chapter overview

The preceding chapters presented an overview of IBD, pain and psychological approaches to understanding chronic pain. Chapter 1 highlighted the gaps in the literature and the need to better understand biopsychosocial factors in the context of IBD-pain to aid the development of an effective self-management intervention. Chapter 2 explored current psychological approaches to chronic pain and presented the BIS/BAS model which proposes that approach and inhibitory-related processes operate in the context of pain, and how psychological interventions operate to target these distinct but interacting systems. This chapter discusses methodological approaches for developing complex interventions in health. The chapter reviews a taxonomy of intervention development approaches and provides a rationale for the application of the Medical Research Council (MRC) framework to the intervention developed in this thesis. Each stage of the MRC framework is discussed, and how the work undertaken in this thesis aligns with these stages to contribute to the development of an intervention for IBD-pain. The chapter also briefly discusses how findings contributed to a National Institute of Health Research (NIHR) programme grant study titled ‘BOOST’, and how intervention development in this thesis was later informed by BOOST.

3.2 Developing complex interventions in health

Complex interventions are defined as interventions which have several components that interact and influence the impact between intervention and outcomes (Craig et al., 2008). Interventions may be defined as complex for several reasons; they may target a range of possible outcomes including a specific sub-population of individuals or behavioural processes, involve interacting components that work together to produce an effect, vary in degree of tailoring to the individual or be highly influenced by the local context. Developing and assessing complex interventions is a challenging endeavour, and to optimise effect much rigour is needed in conception, design, planning and execution. However, an estimated 85% of research activity has been described as ‘research waste’ in healthcare (Chalmers & Glasziou, 2009). This can include research that has lacked an identified research question or theoretical basis, has weaknesses in design, conduct or analysis or is insufficiently powered or reported (Ioannidis et al., 2015; Chalmers & Glasziou, 2009). This has led to a lack of dissemination and an impact on
clinical care (Chalmers, et al., 2014; Glasziou et al., 2008) and public health policy (Ahmad et al., 2010). Moreover, poor reporting and describing of interventions results in an inability to replicate (Dromboski et al., 2007; Glasziou et al., 2008), and efficacy in intervention trials does not always translate to effectiveness in real-world settings (Glasgow et al., 2012). Reviews of just under 1000 intervention studies of behaviour change have demonstrated that only 5-30% provide sufficient detail for replication (Moncher & Prinz, 1991; Gresham et al., 1993; Dane & Schneider, 1998). To optimise translation of research into practice, researchers have therefore highlighted the need for more established guidance on development and reporting of interventions in healthcare (Glasziou et al., 2010; 2014; Hoffman et al., 2014).

3.2.1 Taxonomy of intervention development approaches

Over recent years, several approaches have been published to guide development and reporting of interventions. A recent systematic review sought to synthesise these intervention development approaches, culminating in a taxonomy of eight approaches (O’Cathain et al., 2019). These are listed as follows:

- Partnership – decision-making and intervention co-developed with users
- Target population-centered – intervention based on views and actions of users
- Theory and evidence-centered – combining evidence and theory
- Implementation-based – will the intervention be effective in the real world
- Efficiency-based – experimental designs used to test and determine active components
- Stepped or phase-based – emphasis on systematic set of processes in development
- Intervention-specific – constructed for a specific sub-population
- Combination – existing approaches combined to aid development

The taxonomy highlights the wealth of approaches developed in recent years, with different approaches having more emphasis on certain phases within the intervention development and evaluation process. However, there is also overlap of core actions which are ubiquitously carried across approaches. Summarising these distinct and overlapping actions, seven domains of actions were formed, composed of 18 ‘key actions’ documented in total (O’Cathain et al., 2019). These seven domains were conception, planning, designing, creating, refining, documenting and planning for future evaluation.
Conception refers to transparency about where the research question originated from and identifying the need from a clear evidence base. Planning involves a multitude of aspects, including clarity around members in the intervention development team, identifying active components to target in an intervention, planning of the design, format and mode of delivery of an intervention and tailoring it to the needs and specific processes within the target population. Designing and creating require the use of pre-defined theory to guide intervention components, and the involvement of multiple stakeholders to ensure that the intervention is targeted to the population in question. Refining, documenting and planning for future evaluation refers to the feasibility/piloting stage of an intervention, and how early studies on small samples can help in the iterative process of ensuring that an intervention is effective in a context particular to the target population, and to optimise implementation and efficacy on key outcomes of the intervention. While some approaches recommend a sequential element to the process, generally it is now understood that actions occur in an iterative or cyclical fashion rather than linear, or indeed concurrently, despite early versions of some approaches describing a linear approach (Campbell et al., 2000).

Understanding which intervention development approach is suitable for researchers seeking to develop a complex health intervention can be challenging. Each approach holds its own strengths and weaknesses and may be more relevant depending on the context of the intervention (e.g. local service development, digital health intervention, population health interventions). Some approaches may be more centred around development phases, ensuring that the target population are included in decision-making around intervention creation and design, while others may emphasise optimising effectiveness in the real-world setting or provision of a discrete checklist of actions for intervention development. For example, a partnership approach of experience-based co-design (EBCD) entails a rigorous method of drawing on the narrative of multiple stakeholders including patients and staff to guide intervention development, and has shown improvements in service delivery (Robert, 2013). However, the data collection process in EBCD can be time consuming, weighted heavily in qualitative research and findings may be more relevant in a local service context but less generalisable for wider dissemination (Locock et al., 2014). Alternatively, implementation-based approaches, such as the RE-AIM planning tool, provides a checklist within its guidance to optimise effectiveness of intervention in real-world settings, such as ensuring that the intervention is maintained by individuals and settings over time (RE-AIM, 2013). However, this framework lacks detail in the intervention development process. Combination
approaches ensure that multiple phases in the intervention development process are accounted for, such as the Participatory Action Research process which combines theories of Behaviour Change with Persuasive technology (PAR-BCP) (Janols & Lindgren, 2017). This unifies partnership and theory-based approaches, however, fails to provide a detailed stepwise approach on actions to be taken within the framework. Nonetheless, across different complex health intervention approaches, the use of theory in design and evaluation of interventions is considered a pivotal aspect and ‘best practice’ in the development and evaluation process (Rimer & Glanz, 2005; Craig et al., 2008).

3.2.2 Role of theory in complex health interventions

Critically, complex health interventions must not only seek to understand whether they are effective but how they operationalise and why they work (De Silva et al., 2014). Theory is defined as a systematic way of understanding ideas or events, through a set of definitions and concepts that organises or explains a phenomenon (Rimer & Glanz, 2005). Generated through accumulation of evidence, theory provides a conceptual basis to an intervention by identifying key causal mechanisms to be targeted and tested (Michie & Abraham, 2004). Acknowledging the complexity of interacting and multiple components within an intervention, theory aids an understanding of the selection and pathway of intervention techniques on desired outcomes (Wingood & DiClemente, 1996; Michie et al., 2008;), and the identification of ‘active components’ in bringing about behaviour change (Eccles et al., 2005). Concerning interventions for specific stakeholders or behavioural processes, theory allows for intervention techniques to be tailored and refined (Noar, Benac & Harris, 2007). Theory is a core aspect of both the development and evaluation of an intervention (Hardeman et al., 2005; Michie et al., 2005), while testing of an intervention strengthens or builds on a theoretical model of what works and in what context, thus widening the evidence base (Johnson & Dixon, 2008; Jamal et al., 2015). Interventions that lack theory are subject to implicit bias, are less likely to be generalisable and are limited in an understanding of their effect (Michie & Abraham, 2004).

However, the association between use of theory and demonstrated effectiveness of intervention is not consistent and clear in the literature. This may be explained by poor reporting of use of theory in interventions. For example, while some reviews demonstrate a positive association between reported use of theory and greater efficacy of an intervention (Hardeman et al., 2002; Glanz & Bishop, 2010; Webb et al., 2010), others have found either a small or no association between theory and effectiveness (Roe et al., 1997; Stephensen, Imrie & Sutton, 2000). To account for this, coding manuals and schemes
have since been developed to standardise and improve comprehensive reporting of theory in interventions (Painter et al., 2008; Michie & Prestwich, 2010). Alternatively, comprehensive use and reporting of theory can be facilitated by use of theory-centred approaches, which emphasise a systematic approach to identification of theory and evidence to guide intervention development and evaluation.

3.2.3 Use of the Medical Research Council (MRC) framework in developing complex health interventions

A widely cited evidence-based approach to intervention development is the Medical Research Council (MRC) framework (Craig et al., 2008). This provides a set of guidelines for the development, evaluation and implementation of complex interventions in health, using a ‘develop-test-implement-evaluate’ approach (Richards, 2015). It is a widely used framework in healthcare, social care and public health research and the most cited framework for developing complex health interventions (Corry et al., 2013). Its widespread use in intervention development may be attributed to the provision of practical, theoretical and methodological considerations recommended within its guidelines. The original MRC framework was published by Campbell et al. (2000) and has been updated (Craig et al., 2008), with subsequent additional guidance published on specific aspects on intervention development (Bleijenberg et al., 2018) and process evaluation (Moore et al., 2015).

The original MRC framework suggested a stepwise linear approach, involving a pre-clinical phase and four subsequent phases of modelling, testing and implementing an intervention (Figure 7) (Campbell et al., 2000). The pre-clinical phase involves reviewing empirical evidence and theory to identify active ingredients and possible confounders of an intervention. Phase I of modelling describes defining relevant components to be tested in an intervention, which can be achieved by use of qualitative and quantitative data collection. An exploratory phase in phase II consists of a feasibility/piloting stage to test components and recruitment procedures, to then be followed by a larger RCT to formally test intervention components and their effects (Phase III). Finally, the evaluation phase considers long-term implementation and whether effects are maintained for desired outcomes in different contexts. Notwithstanding the merit of this original framework, it invites several criticisms and has limitations. Its linear structure does not reflect the complex, multi-factorial and interacting nature of intervention development, and many aspects of intervention development may occur in parallel (Massoud et al., 2016). It is limited in its scope in development and piloting phases, and lacks integration between
processes and outcomes and the consideration of political, social or geographical factors and overarching complexity of adaptive systems (Campbell et al., 2007). The 2000 MRC framework is confined to RCT-based trialling of interventions, failing to consider whether intervention outcomes would be effective and translate to other contexts (Blackwood et al., 2010).

Acknowledging these limitations, an updated version of the MRC framework was presented by Craig and colleagues (2008). This retained key aspects of the original framework but presents a more flexible and iterative model, which provides greater weighting on intervention development and evaluation phases. This includes a development phase, feasibility and piloting, evaluation and implementation phases (Figure 8). Moreover, reporting and implementation of interventions was embedded within the development and evaluating stage, reinforcing that each stage is crucial and influential in the overall process of intervention development. Despite this newly defined relationship, a ‘best practice’ series of stages is still recommended by this framework of systematic identification of evidence and theory, testing of components through modelling of outcomes followed by a piloting phase to assess intervention effectiveness and testing procedures to lead to dissemination and implementation requiring further research to monitor process of effects long-term and in other settings (Craig et al., 2008).
updated framework also provided a more comprehensive definition of ‘complex’ in interventions to guide researchers, such as the number of interacting components, difficulty of behaviours required by those delivering or receiving the intervention, number of groups or levels to be targeted, variability and number of outcomes and extent of tailoring or flexibility within the intervention.

The development phase of intervention development is more detailed in this updated framework, consisting of i) identifying the evidence base ii) identifying/developing appropriate theory and iii) modelling processes and outcomes. This stage predominantly aims to identify the causal mechanisms and pathways between treatment aspects and desired outcomes and identification of ‘active ingredients’ within an intervention. Feasibility and piloting stages are key for determining the acceptability of an intervention, such as assessing recruitment and retention rates and sample sizes and may include a combination of qualitative and quantitative data collection. Evaluation of a complex intervention considers a range of approaches, including randomised and non-randomised experimental designs, to assess the effectiveness of an intervention, and recommends that whichever approach is used is relevant to certain characteristics of the study in question. Evaluation requires careful consideration of key outcomes given the theoretical underpinning and evidence-base identified in the development phase, understanding process evaluation and contextual factors, and assessing cost-effectiveness. Finally, the implementation stage entails involving key stakeholders to optimise long-term efficacy and effectiveness of intervention, thorough understanding of benefits, harms and costs in decision-making in a given context, and monitoring and surveillance of long-term implementation such as inclusion of long-term follow up of outcomes and impact.
Since the 2008 updated publication of the MRC framework, further research has identified gaps in this framework, including the need for further detail and refinement in the development phase (Bleijenberg et al., 2018). Bleijenberg and colleagues (2018) argued for four additional aspects to the intervention development phase within the MRC framework. These were i) problem-identification and definition ii) determine the needs iii) examine current practice and contexts and iv) intervention design (Figure 9). These additional factors sought to provide more depth to identifying the evidence base and considering local context, which were not acknowledged in the 2008 version of the MRC framework.

*Problem identification and definition* provides greater emphasis on operationalising and having an in-depth understanding of the original problem in question (Conn et al., 2001; van Meijel et al., 2004), proposed as the essential starting point to any intervention (Aranda, 2008). This can be explored by means of qualitative interviews, focus groups, surveys or other means to identify the problem in the specific context and provide insight into key aspects of the problem and from different perspectives. Similarly, qualitative methods can be used in the *determine the needs* phase of intervention development, which provides further opportunity to optimise effectiveness and address the specific needs of various stakeholders involved. It provides for a better understanding of which aspects of the intervention are most likely to be adopted and maintained over time by stakeholders and aid decision-making in the level of dose, intensity and content of the intervention. *Examine practice* is embedded within aspects of considering context and evidence base, by understanding in more detail existing intervention practice and the barriers and facilitators perceived among both recipients and providers to be involved in the intervention. This resonates with Normalisation Process Theory (NPT) (May et al.,
2009; May et al., 2013) which aims to understand individual and organisational systems to ensure interventions can be implemented into routine care. Finally, intervention design is closely interrelated with modelling of outcomes, and examines decision-making in more depth around intensity, dose and duration (Conn et al., 2001). Reporting of this aspect of the intervention design is crucial for replication and clearer understanding of the success or failure of the intervention (Bleijenberg et al., 2018).

3.3 Identifying an intervention development approach

In determining which intervention development approach is most applicable and relevant, O’Cathain and colleagues (2019a) recommend a set of key questions (Table 1). In the context of this thesis, considerations include i) targeting modifiable factors associated with pain through behaviour change to improve quality of life and reduce the severity and impact of pain in people with IBD ii) the complexity and multi-factorial nature of pain and the role of self-management iii) the use of theory, evidence-base and service user input to guide intervention development iv) synthesising knowledge and understanding of IBD, psychological models of chronic pain and similar interventions in other long-term conditions v)
current evidence base for guidance on complex interventions in health guided by theory vi) capitalising on an intervention development team and other resources available.

Table 1 Questions recommended by O’Cathain et al (2019a) to guide choice of intervention development approaches from taxonomy

<table>
<thead>
<tr>
<th>Guidance question</th>
<th>Considerations in context of current thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is the intention of the intervention?</strong></td>
<td>Reduce pain (severity, impact) and improve quality of life in adults with IBD</td>
</tr>
<tr>
<td><strong>What is the context of the intervention?</strong></td>
<td>Self-management, pain management, behaviour change, sub-population of IBD, under-research and limited understanding of biopsychosocial factors in IBD-pain, complex symptom with multifactorial aetiology, limitations in resources for face to face psychological services and support for digital health</td>
</tr>
<tr>
<td><strong>What values inform the intervention development?</strong></td>
<td>Theory (chronic pain, IBD-pain), patient public involvement (PPI), evidence-base in IBD and autoimmune/long-term conditions (IBS, MS, RA)</td>
</tr>
<tr>
<td><strong>What skills and experience does the team bring?</strong></td>
<td>Health psychology, IBD, nursing, self-management interventions in other long-term conditions (MS, IBS, CFS)</td>
</tr>
<tr>
<td><strong>Which approaches have resulted in interventions shown to be effective?</strong></td>
<td>Theory-based approaches - MRC framework (Craig et al., 2008) – widely cited (Corry et al., 2013; Levati et al., 2016) and applied for similar complex health interventions</td>
</tr>
<tr>
<td><strong>What resources are available for intervention development?</strong></td>
<td>Online web agency, intervention development team (BOOST), PPI (patients and IBD clinical team)</td>
</tr>
</tbody>
</table>


3.4 **Rationale for guidance from the MRC framework**

Given the emphasis on theory and behaviour change relevant to this thesis, and the comprehensive guidance on development and feasibility phases provided by the MRC framework, the MRC framework was selected as the guidance for intervention development. The MRC framework has been consistently applied and reported for a wide range of complex health interventions, including chronic pain management (Carnes et al., 2013), public health (Gray et al., 2013), older adults (Booth et al., 2019)
and interventions for several long-term conditions (Levati et al., 2016). The strength of the MRC framework lies in the emphasis on theory and modelling of outcomes to identify active components to target and tailor for a specific population, and the iterative and interacting nature of its phases to optimise the development and feasibility, and therefore efficacy, of an intervention. Furthermore, it provides a detailed set of guidelines and supporting techniques with practical examples, including the use of a systematic review and a logic model to facilitate identifying the evidence base and causal mechanisms within an intervention, respectively. A logic model is a graphical display of the pathway of the intervention and underlying assumptions, providing a visual representation of the process from problem identification, to intervention components, to desired outcomes (Rehfuess et al., 2018).

Overall, the MRC framework provides a robust systematic approach to developing a complex health intervention. Incorporating the MRC framework by Craig et al. (2008) with additional recommendations from Bleijenbeg et al., (2018) and Moore et al., (2015) allows for crucial aspects in the intervention development and feasibility stages to be considered in this thesis, such as contextual factors and understanding the needs of the target population. As such, each phase of the MRC framework will be discussed in turn, including the additional four phases by Bleijenbery et al. (2018), and how these map onto the output and undertakings of this thesis. This is summarised in Table 2. Full results of each phase will not be presented here but in relevant subsequent chapters. However, some chapter findings may be discussed here in the context of their role in guiding intervention development.

The intervention development phase was informed by work undertaken in BOOST. Therefore, the contributions made from the output from this thesis and BOOST will first be discussed.
Table 2 MRC framework phases incorporating additional recommendations by Bleijenberg et al. (2018) and how these map onto intervention development ‘actions’ and work undertaken in thesis.

<table>
<thead>
<tr>
<th>MRC framework phase</th>
<th>Action (number) (O’Cathain et al., 2018)</th>
<th>Chapter</th>
<th>Results</th>
<th>Implications for thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problem identification and definition</td>
<td>(3) Planning - understand the problems or issues to be addressed</td>
<td>1</td>
<td>Pain is a prevalent and poorly understood symptom of IBD. Little consensus and inconclusive evidence on pain management.</td>
<td>Provides rationale for thesis and development of biopsychosocial model and intervention for IBD pain</td>
</tr>
<tr>
<td>Identifying the evidence base</td>
<td></td>
<td>4</td>
<td>Reveals positive and negative psychosocial factors associated with IBD-pain. Many previous studies limited by lack of comprehensive pain assessment</td>
<td>Identification of positive and negative factors associated with pain supports BIS/BAS model as theoretical underpinning and suggests components to be modelled in mixed methods study</td>
</tr>
<tr>
<td>Identifying or developing theory</td>
<td>(5) Planning - identifying possible ways of making changes to address problems</td>
<td>2, 7</td>
<td>Reviewing theoretical approaches to chronic pain and justification for use of BIS/BAS model in understanding and treating IBD-chronic pain</td>
<td>Provides conceptual basis for mechanisms, i.e. modifiable psychosocial processes to be targeted in intervention (reducing BIS-related processes/associations, increasing BAS-related process/associations, reducing automaticity)</td>
</tr>
<tr>
<td>Determine the needs</td>
<td>(7) Planning – consider real-world-issues on cost and effectiveness (10) Designing – re-visit decisions about where to intervene</td>
<td>5, 6, 7</td>
<td>Qualitative study explored experiences of people with IBD and pain and needs for a self-management intervention. Intervention development included PPI involvement on content, format and delivery of intervention</td>
<td>Results guided content of self-management intervention, for example ensuring content in activity and exercise session acknowledged other IBD symptoms in hindering ability to undertake certain exercise e.g. fatigue, incontinence. Feedback on dietary advice led to inclusion in session</td>
</tr>
<tr>
<td>Examine practice</td>
<td></td>
<td>1, 7</td>
<td>Review of previous interventions in IBD (Norton et al., 2017) and current context on resources for psychological support in IBD. Discussions between PPI and intervention development team involved both patients with IBD and healthcare professionals.</td>
<td>Previous interventions and current context argued for rationale for online intervention with therapist support (to account for limited resources in face to face services but high attrition in lack of therapist support in online format). PPI and intervention development team discussions facilitated decision over number of telephone sessions versus in-site messages.</td>
</tr>
<tr>
<td>Modelling process and outcomes</td>
<td>(8) Planning – consideration of continuation</td>
<td>5, 6</td>
<td>Confirmed positive and negative psychosocial processes associated with pain including constructs not yet investigated in IBD-pain (self-efficacy, cognitive and behavioural responses to symptoms). Qualitative study provided further insight into experiences of pain in IBD, including the role of mood/attitudes, vicious cycles and management strategies</td>
<td>Results build on BIS/BAS model of pain in IBD and confirms constructs to target within session content of intervention, e.g. fear avoidance and graded activity exercises, managing stress and coping with emotions, identifying catastrophising thoughts and coming up with alternatives.</td>
</tr>
<tr>
<td>Intervention design</td>
<td>(9) Designing – generate ideas about solutions, components and features of an intervention (10) Documenting - document the intervention</td>
<td>7</td>
<td>Extensive involvement with PPI and multiple intervention development team meetings, making iterative changes to session design and content based on user testing and feedback from patients.</td>
<td>Led to refined intervention, tailored for people with IBD and based on mixed methods findings, to optimise acceptability and feasibility of intervention, as well as improving outcomes on pain (interference and severity) and quality of life.</td>
</tr>
<tr>
<td>Feasibility and testing phase</td>
<td></td>
<td>8</td>
<td>Online intervention feasible and acceptable for people with IBD and chronic pain. CBT-based self-management intervention reduced psychological distress and self-reports of disease activity and improved quality of life and pain self-efficacy. Smaller changes on pain outcomes.</td>
<td>Online intervention led to reductions in BIS-related processes and some improvements in BAS-related processes. Smaller changes on pain outcomes suggests disease-related factors may be overriding relationship between BIS/BAS and pain perception. Further research warranted in larger sample sizes and with follow-up data collection.</td>
</tr>
</tbody>
</table>
3.5 IBD-BOOST

Alongside pain, fatigue and urgency/incontinence are common and burdensome symptoms of IBD, are poorly managed in clinical practice and have a significant impact on patient’s quality of life (Farrell et al., 2015). Collectively, previous research in IBD-fatigue and urgency/incontinence, and the output from this thesis led to the development of the study; ‘Living well with inflammatory bowel disease: optimising management of fatigue, pain and faecal urgency/incontinence via tailored online self-management’ (IBD-BOOST) (Figure 10). This is a National Health Institute of Research (NIHR) randomised controlled trial to test the efficacy of an IBD nurse-supported online self-management intervention for pain, fatigue and urgency in IBD.

The development of the intervention for this thesis and BOOST occurred in parallel and, due to overlap of content and research being undertaken in this area, the author of this thesis was embedded within the BOOST research team. While output from this thesis contributed to BOOST, work was undertaken within BOOST that guided the pain intervention content and design. For example, BOOST output included extensive patient public involvement (PPI), including focus groups and individual interviews with multiple stakeholders (nurses, gastroenterologists, IBD patients) to optimise content and delivery of the intervention. As presented in Chapter 7 Section 7.3.1, it became clear in the intervention development process that there was significant overlap and parallels between the BOOST treatment manual and the intervention manual developed for IBD-pain specifically from findings arising within this thesis. Integrating PPI feedback, specific output from this thesis and research in IBD-fatigue and urgency resulted in seven core online treatment sessions (to be completed across symptoms) and four symptom-specific sessions (two pain-specific, one fatigue-specific and one urgency-specific). As such, it was decided that the core sessions and pain-specific sessions were to be used as the intervention for this thesis. For clarity, Figure 10 summaries the pre-BOOST and BOOST intervention development phases and i) the contributions from this thesis on IBD-pain ii) previous work carried out on fatigue and urgency iii) the work undertaken in BOOST separately to this thesis iv) the output from the BOOST intervention development team in which the author of this thesis was embedded.
<table>
<thead>
<tr>
<th>Pain (thesis output)</th>
<th>Pre-BOOST Intervention Development Phase</th>
<th>BOOST Intervention Development Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thesis chapter 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>(Artom et al., 2016)</td>
<td>(Artom et al., 2017a)</td>
</tr>
<tr>
<td>Urgency/incontinence</td>
<td>(Proudfoot et al., 2018)</td>
<td>(Norton et al., 2013)</td>
</tr>
<tr>
<td>BOOST</td>
<td></td>
<td>Interviews, focus groups, PPI meetings</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BOOST including thesis author</td>
<td>Nurse focus groups and PPI meetings</td>
<td>BOOST meetings; thesis author wrote Session 2, 6 &amp; pain-specific</td>
</tr>
</tbody>
</table>

Figure 10 Pre-BOOST and BOOST intervention development phases - demonstrating output from this thesis and the author’s involvement in BOOST for different research output stages. NB – grey rows indicate work the thesis author was not involved in.
3.6 Development phase

3.6.1 Step 1: Problem-identification & definition
The initial aspect of the development phase refers to having a clear understanding of the problem to be targeted and maps on to the O’Cathain et al. (2019a) action of ‘planning’ 3) *understand the problems or issued to be addressed*. Chapter 1 identified that pain is a burdensome and widely experienced symptom of IBD and that a significant proportion of patients continue to experience pain in remission. Moreover, there is much heterogeneity in pain management techniques, exemplifying a lack of clear understanding and consensus on how to support patients with IBD and this symptom. Although an initial conceptual model of IBD-pain has been proposed (Bielefeldt et al., 2009), further work since its publication demonstrates the need for a systematic search of the literature to further understand psychosocial factors associated with pain, and thus modifiable factors associated with pain to be targeted in an intervention.

3.6.2 Step 2: Identifying the evidence base – rationale for systematic review
After identifying the problem in question, the next stage in development required a systematic search of the evidence base, in order to help identify possible causal mechanisms and contextual factors within IBD-pain. In this step, it is critical to review previous research conducted. Previously, a systematic review identified the variety of interventions for abdominal pain management in IBD researched to date (Norton et al., 2017). The review revealed that many of the previous non-pharmacological interventions for IBD-pain lacked reporting of a theoretical underpinning and methodological rigour, including sample size. To gain a better insight into psychosocial processes in the context of pain, a systematic review was undertaken as recommended by the MRC framework (Craig et al., 2008) to understand modifiable factors to be mapped on intervention techniques. This provides the rationale for Chapter 4 (and publication): *Systematic Review: psychosocial factors associated with pain in inflammatory bowel disease*.

3.6.3 Step 3: Identifying appropriate theory
In identifying relevant theory to guide intervention development, it is important to acknowledge risks associated with previous use and application of theory. It has been argued that some researchers oversimplify the process of identifying appropriate theory and utilise ‘off the shelf’ theories to adhere to recommendations within guidelines (Sniehotta et al., 2014). Many intervention studies recycle widely
used theories in the assumption that they explain intervention effects, but at closer examination demonstrate limited clinical applicability in enhancing or explaining outcomes (Prestwich et al., 2014; Moore & Evans, 2017). Re-using older, more commonly used theories may confine and restrict processes and ignore others which may be occurring outside of a theory’s remit. Given these risks in identifying inappropriate or irrelevant theory for an intervention, Moore & Evans (2017) provide three recommendations on theory selection. Firstly, adequate theory conceptualises how a problem is created and maintained over time. Secondly, the authors highlight the value in moving away from individual-psychological theories of human behaviour towards conceptualising human behaviour as a multifactorial construct, and thus consider theories that integrate potential mechanisms across disciplines, such as the role of social, political or neurobiological influences in human behaviour. Finally, theory must not be ‘discrete packages’ described in isolation but rather account for the complexity of systems and differing contexts, which can be achieved through multiple stakeholder input along the process of developing complex interventions. The authors of the MRC framework recommend that selection of appropriate theory requires careful consideration and extensive research of the literature to select a theory which accumulates empirical support with relevant and modifiable processes to promote behaviour change (Craig et al., 2008).

In consulting the relevant literature for selection of theory in this thesis, it is important to have a comprehensive understanding of psychological approaches to chronic pain. This includes weighing up the strengths, limitations and applicability of theories. Chapter 2 reviewed the current evidence on psychological theories of chronic pain and provided the rationale for the use of the BIS/BAS framework as the basis of the intervention of this thesis. The BIS/BAS model of chronic pain (Jensen et al., 2016) synthesises theory from psychological models of chronic pain, while acknowledging neuropsychological factors in pain processing and behaviour, such as automaticity, learned associations and attentional biases. Importantly, it provides an understanding as to which psychological interventions may target processes encompassed within the model, such as learning to ‘respond less automatically’ and forming new learned associations that facilitate adaptive psychological processes in the context of pain. Chapter 7 provides a section on theoretical development, taking into consideration the findings of the systematic review, cross-sectional and qualitative studies in Chapters 4, 5 and 6, respectively, to update the BIS/BAS model adapted to chronic IBD-pain. This section of the MRC framework comes under the
action of ‘Planning’ 5) identifying possible ways of making changes to address problems (O’Cathain et al., 2019a).

3.6.4 Step 4 – Determine the needs – rationale for qualitative study

This recently incorporated phase of MRC framework stage refers to having a thorough understanding of the needs, preference and capacities of stakeholders involved in the intervention, including the recipients and deliverers of the intervention (van Meijel et al., 2004). This aspect provides a crucial contribution not only to ensuring that the intervention is tailored to the target population but that the intervention is effective and feasible. Understanding what people with IBD-pain need from an intervention, and how they perceive that intervention to be implemented, is crucial to understanding which content to include and which aspects of an intervention are most likely to be adopted (O’Cathain et al., 2019a). Collection of this information can be achieved through qualitative means and can include understanding both barriers and facilitators in an intervention. A qualitative study is presented in Chapter 5, in which the aims were to develop a better understanding around i) the nature of pain in IBD, ii) what pain management strategies people with IBD use for their pain and iii) the needs and preferences for an intervention for individuals with IBD-pain. Although the needs of people with IBD for a future intervention did not arise as a main theme in the qualitative study’s findings presented in Chapter 5, the results confirmed important areas to target in the intervention, as well as supporting findings from the cross-sectional study. Furthermore, supporting qualitative research (e.g. patient and nurse focus groups) and patient public involvement (PPI) during intervention development in the BOOST study (Figure 10) provided further guidance on patient’s needs and preferences. People with IBD were included within the intervention development team, who provided iterative feedback on the format, content and delivery of the intervention. Additionally, healthcare professionals were also included to provide feedback on content. Therefore, multiple stakeholders were included in the intervention development process, so that the content was tailored to the needs of people with IBD. The contribution of complementary findings from BOOST is described in more detail in the intervention development section of Chapter 7 Section 7.3.1. This stage of the intervention development process maps onto the action of ‘Planning’ 7) consider real-world issues around cost and delivery of intervention and ‘Designing’ action 10) re-visit decision about where to intervene.
3.6.5  **Step 5 - Examination of current practice and context**

Awareness and understanding of the relevant context to which an intervention may be implemented is vital in ensuring it can be effectively implemented and sustained in the long term. Indeed, a failure to consult stakeholders in the intervention development process can result in challenges to implementation, uptake or change in clinical practice (Perkins et al., 2007). Examining the current context of psychological services for people with IBD, Chapter 1 (Section 1.7) highlighted that, due to limited resources and funding in the NHS, availability and accessibility to face to face psychological support in IBD is limited. Therefore, developing a face to face psychological intervention to be delivered by trained psychologists, although it might potentially lead to improved outcomes in an RCT, may not necessarily be feasible in a wider context of implementation in the NHS. Therefore, consideration of the current practice and context described in Chapter 1 provided the rationale for alternative means of intervention delivery and modality (discussed more in Chapter 7 on intervention development). As well as understanding the current practice within the field of IBD, it was equally important to consult supporting literature on psychosocial interventions in similar long-term and auto-immune conditions, and previously in IBD. This included reviewing the wide evidence base of interventions tested in IBS, as well as autoimmune conditions such as MS. These are considered in Chapter 1 and Chapter 7. For example, the intervention was designed and created based on similar CBT-based interventions in IBS (Moss-Morris et al., 2014), fatigue in IBD (Artom et al., 2017b), MS (van Kessel et al., 2004) and primary chronic pain (Cole et al., 2012). Intervention development also importantly acknowledged previous challenges and limitations in interventions for IBD (Mikocka-Walus et al., 2015; 2017; McCombie et al., 2016).

3.6.6  **Step 6 - Modelling processes and outcomes**

Findings from the systematic review on psychosocial factors associated with IBD-pain (Chapter 4) and guidance from the BIS/BAS model suggested components to be modelled and tested in a cross-sectional study. Moreover, psychosocial factors identified in other areas of pain research, such as IBS, primary chronic pain and pain related to other long-term autoimmune conditions, were informative for other potential psychosocial processes to be investigated. Thus, the cross-sectional study presented in Chapter 5 tested the potential association of psychosocial factors and confirmed that emotional, cognitive and behavioural factors were associated with pain, including both negative risk factors and protective positive factors, supporting the BIS/BAS framework and targets for treatment in the
development of an intervention for IBD-pain. The qualitative study, as well as allowing for the needs of people to be explored and understood for intervention development, also allowed for a greater exploration of the experiences and management strategies in IBD-pain. This study also built on an understanding of components to be targeted within the intervention and aligned with findings from the cross-sectional study. Chapter 7 presents a logic model (Section 7.2.8), which provides a visual summary of how treatment targets, based in cognitive behavioural therapy principles, were included in the intervention to map on to BIS and BAS processes. Therefore, the building of a theoretical model of IBD-pain through quantitative and qualitative means and summarising psychosocial processes and treatment targets in a logic model supported the continuation to a feasibility, piloting stage, mapping onto the action of ‘Planning’ 8) consideration of continuation.

3.6.6.1 Rationale for and challenges of a mixed methods approach

A combination of quantitative and qualitative data collection methods was used to guide intervention development, as recommended by the MRC framework (Craig et al., 2008). However, some have argued around the epistemological challenges of mixed methods research in producing ‘knowledge’ (Yardley & Bishop, 2015), otherwise known as the incompatibility hypothesis. Quantitative research represents a positive and realist position where research is a tool to collect objective and precise measures, while qualitative research emerges from a constructivist interpretation where research is gathered by means of collecting rich and novel findings which are governed by socio-cultural contexts and other factors. The increasing popularity and advantages to utilising both methods of research together have led to a pragmatist approach (Cornish & Gillespie, 2009; Yardley & Bishop, 2007). This allows the strengths and weakness of both respective approaches to complement and address each other (Johnson & Onwuegbuzie, 2004). Quantitative research is dominant in health research and its strengths lie in testing out an a priori hypothesis, ability to generalise findings through use of valid and reliable measures and develop an understanding of causal mechanisms and associations between constructs. Yet qualitative research holds merit in providing an insight into individual experiences and views around a topic without reducing these to measurable constructs which may be limited in socio-cultural applicability. Qualitative research can also generate robust theoretical understanding and questionnaire development. In the context of developing an intervention, a mixed-methods approach lends itself when addressing multi-faceted, broad and complex research questions (Tariq & Woodman, 2013), such as living with a chronic illness (Nicca et al., 2012) or health service interventions (Raven et
For example, quantitative measures can test the effects of the intervention, while qualitative data can provide an in-depth understanding of the experiences of an intervention, such as facilitators and barriers to uptake or adherence (Campbell et al., 2000; Campbell et al., 2007). Techniques of integrating mixed methods research have been discussed (O’Cathain, 2010a;2010b), such as use of ‘triangulation’, where convergence, complementarity or discrepancy between findings can be drawn, or a ‘mixed methods matrix’, where both quantitative and qualitative data gave been collected on the same cases.

For this thesis, an explanatory design (Creswell et al., 2003) was implemented, using a quantitative study first to test psychosocial constructs, followed by in-depth exploration of IBD-pain by qualitative interviews. This was to allow for in-depth exploration of patient experiences and concepts that have emerged from the quantitative findings (Rossman & Wilson, 1985; Tashakkori & Teddie 1998; Creswell et al., 2003). Participants who had taken part in the cross-sectional survey and consented to take part in a follow-up interview could be selected for the qualitative study. This approach allowed for a range of participants from different sociodemographic backgrounds and psychological profiles to be selected, to explore in more depth the different ways individuals cope and manage pain in IBD and the role of positive (protective) and negative (risk) psychosocial factors in the context of IBD-pain. An explanatory design in mixed methods research has been extensively used, it is practical to administer and its sequential nature facilitates implementation and reporting (Ivankova & Creswell, 2006). Equal weighting within the thesis was given to quantitative and qualitative studies, whereby results from both studies were implemented and integrated into intervention development and content.

### 3.6.7 Intervention design

This phase of the development process aligns closely with modelling of processes and outcomes but focuses more on decision-making around and formation of content, intensity and dose (Conn et al., 2001). Firstly, findings arising from quantitative and qualitative studies aimed to provide greater clarity on mechanisms to target within the intervention. Furthermore, extensive PPI involvement in intervention development conducted in BOOST was thought to be of great value in receiving feedback on content and design, ensuring that content of intervention sessions was tailored to people with IBD and that the interface of the intervention was user-friendly and easy to navigate. This PPI input included both people with IBD and IBD clinicians to guide decision-making on the level of therapist input that was necessary and feasible to optimise engagement and adherence to the intervention. This phase of development
maps on to the action of ‘designing’ 9) generate ideas about solutions, components and features of an intervention. Although the intervention was administered online, intervention design also entailed producing a paper version so that the intervention was formally documented, as well as documenting the various rounds of feedback and iterations provided by PPI feedback. This therefore maps on to the action plan of ‘documenting’ 17) document the intervention. Intervention design and iterations are described in more detail in Chapter 7 Section 7.3.4.

3.7 Feasibility and piloting stage

When determining whether an intervention works, this not only concerns whether it will have the desired effect on key outcomes (i.e. behaviour change), but it is acceptable and feasible. The feasibility and piloting stage of the MRC framework allows for the procedures of the intervention to be tested; to assess aspects of recruitment, retention and sample size in preparation for the larger full scale RCT undertaken at the next stage of the process. Acceptability, compliance and the delivery of the intervention are often overlooked in the evaluation stage (Craig et al., 2008). A feasibility study can encompass both quantitative and qualitative aspects, such as testing preliminary efficacy of the intervention on desired outcomes (alongside acceptability and feasibility) and collecting feedback on the intervention through semi-structured interviews. It is important that feedback is collected from both intervention deliverers and recipients, as this may lead to changes in the dose, content or other aspects of delivery. A pilot study can allow for key uncertainties from the intervention development work to be addressed (Craig & Petticrew, 2013), once feasibility has been demonstrated. As such, the final stage in this thesis was to carry out a feasibility study to assess the feasibility and acceptability of the intervention, as well as obtain preliminary estimates of efficacy. This is presented in Chapter 8, which also integrates qualitative feedback from participants and the intervention facilitator, to guide further intervention development in preparation for piloting and full-scale RCT stages (outside of the PhD).

3.8 Evaluation and implementation stages

Although the evaluation and implementation stages of the MRC framework were not carried out and mapped to an output within this thesis, they are nevertheless integral stages to the intervention development process. Evaluation involves selecting a suitable design to assess the efficacy and effectiveness of an intervention. This can include experimental study designs (e.g. individually randomised trials, cluster randomised trials or N-of-1 designs) where randomisation can occur to reduce
likelihood of selection bias, or non-experimental designs. Non-experimental designs may be more appropriate in the case of adverse or rare events, in which case a case-control method may be carried out in the evaluation stage. Crucial to the evaluation stage is choice of outcome measures which can be facilitated by use of robust theory and logic models to guide choice of measures. Other aspects of decision-making on outcomes include time of change, follow-up length and an overall understanding of the rate or pattern of change brought about by the intervention. The evaluation stage also encompasses process evaluation and cost-effectiveness; process evaluation looks in more depth at aspects of fidelity, quality of implementation, causal mechanisms and contextual influences on outcomes of an intervention (Craig et al., 2008). The MRC framework has since provided more detail on key stages and aspects of process evaluation within an intervention (Moore et al., 2015).

Fundamental to the evaluation phase for researchers to consider is whether the evaluation of an intervention has been sufficiently reported, to optimise transparency and accuracy in dissemination and publication (Craig et al., 2008). To overcome the inconsistencies or shortfalls in previous inadequate reporting of interventions, a bank of checklist guidelines has been developed in reporting interventions for researchers to select and adhere to (EQUATOR study) (Moher et al., 2009). Widely utilised checklists for randomised controlled trials include the Consolidated Standards of Reporting Trials (CONSORT) (Moher et al., 2001), or more recently the Template for Intervention Description and Replication (TIDieR) checklist (Hoffman et al., 2014) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (Chan et al., 2013). Yet the reporting of intervention outcomes continues in many cases to be of a poor standard and guidelines are not consistently implemented (Shamseer et al., 2016). Publishing of study protocols or detailed accounts of intervention development are other options to address issues around poor reporting and transparency. A protocol was not published for this current thesis as time and resources spent on intervention development and set up of the feasibility study took priority over preparation of study protocol for publication.

Implementation is the final and critical stage of the MRC framework to ensure that the intervention can be repeated and maintained over time. Within this stage are the challenges of ensuring that fidelity of the intervention is maintained while the intervention is applied in different populations and contexts. This involves adequate dissemination of the intervention through publication and ensuring that findings and intervention methods are available and accessible to key stakeholders for the intervention to be sufficiently implemented and maintained, such as through provision of educational talks or workshops.
Implementation also requires acknowledgment that effects may not be as large in different settings and over time, which can be addressed by long-term follow up in the trial phase, if possible (Craig et al., 2008). Although details around implementation were not included within this thesis, consideration of clinical implications of the feasibility study (and overall thesis) findings is presented in Chapter 9 Section 9.7.

### 3.9 Limitations of the MRC framework

While the MRC is widely used and a relevant framework for this thesis, it is important to acknowledge outstanding limitations of this guidance. Despite iterations, the MRC framework by Craig et al. (2008) fails to account for contextually sensitive factors (Moore et al., 2019). It is argued that interventions are inherently ‘events within systems’ (Hawe et al., 2009) and it is critical that intervention development guidance recognises health interventions within complex social systems rather than being decontextualised components. In this regard, relying on an understanding of the individual-level system may be limited when changes at higher system levels are influential on health outcomes (Moore & Evans, 2017). Therefore, one could argue that changing behaviour in the context of IBD-pain is not only isolated to individual behaviour but takes place within a wider system of individuals’ ever-changing and interacting biological, social and environmental contexts. Acknowledging this limitation, the updated MRC framework recently published (after completion of empirical work in this thesis) (O’Cathain et al., 2019b) includes a strong emphasis on a systems perspectives and context. As this updated guidance was published towards the end this thesis, this was not applied and discussed in this methodology chapter but is discussed in Chapter 9. Nonetheless, as stated, incorporating recommendations by Bleijenberg et al. (2018) ensured that consideration of contextual factors (e.g. limitations in face to face psychological services in IBD and implications for long term implementation) was included in the intervention development process (Section 3.6.5).

Alternative intervention development frameworks which have a strong emphasis on theory and evidence-base include the Behavioural Change Wheel (BCW) (Michie et al. 2014) and Intervention Mapping (IM) (Bartholomew-Eldredge et al., 2016). The BCW is a thorough framework considering how outcomes of behaviour change can be mapped onto intervention components. It provides clear explanation and guidance on actions to take, by specifying target behaviours and identifying what intervention components and functions will bring about desired outcomes through use of the COM-B
model or Theoretical Domains Framework. However, the BCW does not specify which stakeholders should be involved and at which stage in the intervention development process, and PPI involvement was a key aspect of intervention development for IBD-pain. Heavy reliance on behaviour change may arguably neglect other important aspects of the intervention such as disease-related factors within the target population, local settings and implementation. In the case of IBD-pain, other important areas to target in an intervention include the role of emotions and pain-related thoughts that may precede behaviour. The IM framework is a similarly comprehensive approach which integrates theory, systematic reviewing of the evidence and collecting information from the target population, as well as important environmental factors. This is comprised of six steps including a needs assessment, use of a logic model to provide guidance on how processes lead to desired outcomes and designing, producing and evaluating stages. However, its rigour can be time-costly and resource-intensive (Pittson & Wallace, 2011) and has predominantly been used in the context of unidimensional behaviour change interventions, such as weight loss and primary care prevention programmes (Kwak et al., 2007; van Oostrom et al., 2007). As such, it was not deemed appropriate for the use of a more complex interventions in the case of IBD-pain management.

3.10 Chapter 3 Summary

This chapter has discussed the importance of methodological rigour when developing complex health interventions and the use the MRC framework to guide structure and output of the thesis. The role of theory is a pivotal aspect and considered ‘best practice’ when developing complex interventions in health (Craig et al., 2008). The MRC framework is a widely applied and, despite acknowledgement of its limitations, a well-regarded intervention development framework, which provides a comprehensive set of guidelines on the use of theory, systematic reviewing of the evidence and a mixed-methods approach, as well as the guidance around stages of evaluation and implementation (Craig et al., 2008). Subsequent iterations to the 2008 MRC framework development (Bleijemberg et al., 2018) and evaluation (Moore et al., 2015) stages have strengthened its rigor and clarity. Consequently, the MRC framework’s applicability and relevance to the context of this thesis have been argued, and how these stages have been mapped onto the undertakings and output within this thesis.
Chapter 4 Systematic review

4.1 Chapter overview

Preceding chapters outlined the need to better understand psychosocial factors associated with pain, with the aim of guiding intervention development. As recommended by the MRC framework for developing complex health interventions, a systematic review of the literature is key to synthesising the literature and critiquing existing evidence. This chapter presents the publication of the systematic review: psychosocial factors associated with pain in inflammatory bowel disease (Sweeney et al., 2018). Supplementary Tables 1 & 2 are presented in Appendix A. The chapter provides additional description of methods used, including rationale for the databases and search terms that were used. To assess the literature for any further studies examining psychosocial factors associated with pain in IBD since the publication of the systematic review, an updated search was conducted using the same databases and search terms. Findings are presented and summarised at the end of this chapter.

The study presented in this chapter is presented in the following article:


All study documents are included in Appendix A.
4.2 Published article

**Title:** Systematic review: psychosocial factors associated with pain in inflammatory bowel disease

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**Conflicts of Interest:** None
Abstract

**Background** Pain is a frequently reported symptom of inflammatory bowel disease (IBD) experienced by patients in active disease and remission. Psychological factors play a significant role in pain, but have not been systematically reviewed in IBD.

**Aim** To review psychosocial factors associated with pain in adults diagnosed with IBD.

**Methods** Electronic (PsycInfo, MEDLINE, EMBASE, Cochrane Library, CINAHL, Web of Science) and hand-searching were conducted February-May 2017. Two authors carried out screening and data extraction.

**Results** Fifteen studies including 5539 IBD patients were identified. Emotional, cognitive-behavioural and personality factors were associated with IBD-pain. Depression and anxiety were the most commonly explored constructs, followed by perceived stress and pain catastrophising, all of which were positively associated with greater pain. Greater abdominal pain was associated with a concurrent mood disorder over fivefold (OR 5.76, 95% CI 1.39, 23.89). Coping strategies and pain fear avoidance correlated with pain levels. Perceived social support ($r = .26$) and internal locus of control ($r = .33$) correlated with less pain. Patients reporting pain in IBD remission more frequently had an existing diagnosis of a mood disorder, a chronic pain disorder and irritable bowel syndrome. Six studies controlled for disease activity, of which 4 found that psychosocial factors significantly predicted pain. The majority of studies (n=10) were of high quality.

**Conclusion** Psychosocial factors appear to play a significant role in IBD-pain. Further research is required to explore psychosocial constructs in relation to IBD-pain, with use of validated pain measures, large sample sizes and clearer characterisation of disease activity.

**Key words:** inflammatory bowel disease, Crohn’s disease, ulcerative colitis, pain, psychosocial, psychological factors, systematic review

**Short title:** Psychosocial factors and pain in IBD
**Introduction**

Abdominal pain is a commonly experienced and debilitating symptom of IBD, with up to 70% of patients experiencing pain when the disease is active\(^1-3\). Common causes of IBD-related abdominal pain include acute inflammation, strictures, adhesions, small-bowel obstruction and bowel dysmotility\(^4\). Reducing abdominal pain is a key therapeutic target for IBD therapy, however pain severity does not always correlate with endoscopic and clinical biomarkers, and a significant proportion of patients (20-50%) report ongoing pain during periods of remission\(^3, 5-7\). Bodily pain, cramps and extra intestinal manifestations of IBD such as arthralgia are also reported by patients\(^3, 8\). In an IBD population-based cohort, peripheral arthritis and non-inflammatory joint pain were reported by 0.4% and 16% of patients, respectively\(^9\). The prevalence of chronic widespread pain or fibromyalgia has ranged between 3.5-30% in adults with IBD\(^10, 11\). Suggested causes of extra intestinal manifestations of pain in IBD include genetic predisposition, such as polymorphisms of the NOD2 gene involved in the transcription of proinflammatory cytokines and chemokines, or the migration of gut lymphocytes\(^9, 12\). Research has shown the capacity of activated intestinal lymphocytes to enter the joints and adhere to inflamed synovial vessels\(^13\). Such processes within the ‘joint-gut axis’ are suggested to explain the high co-occurrence of IBD and arthropathies, however research into this area of IBD-pain has received much less attention.

Chronic pain in IBD is a complex phenomenon driven by a range of peripheral and central nervous system (CNS) processes. In the case of acute pain, noxious signalling is processed by sensory afferent nerves that innervate the gut wall and send signals from the lower gastrointestinal tract to the CNS via the dorsal spinal horn\(^14\). However, recurrent inflammation and release of mucosal signalling molecules (e.g. nerve growth factor, glial cell-lined derived neurotrophic factor and ion channel expression TRPV1/TRPA1) in the context of chronic IBD can result in visceral hypersensitivity\(^1, 14\). In CNS processing, recurrent visceral stimulation can lead to the activation of the N-methyl-D-aspartate receptor and influx of calcium in higher/second-order sensory neurons, resulting in long-lasting neuronal excitability in the absence of inflammation\(^15\). Central processing within the brain such as stress and arousal may also have a role in pain perception and aetiology of chronic IBD-pain, such as
via mechanisms along the ‘brain-gut’ axis. Stress can exacerbate IBD symptoms by the production of cortisol and catecholamines from the hypothalamic-pituitary-adrenal and sympathetic-adrenal-medullary axis and thereby the release of circulating inflammatory cytokines (e.g IL-6)\textsuperscript{16, 17}. Emotional and cognitive processes can also amplify perception of incoming visceral signals by modulating descending inhibitory processes\textsuperscript{18}. Similar mechanisms have been recognised in irritable bowel syndrome (IBS), and functional symptoms in quiescent IBD are frequently entangled with a diagnosis of IBS\textsuperscript{19, 20}. However, there is mixed support as to whether conceptualising symptoms in quiescent IBD as IBS is useful.

Current treatments for pain management in IBD carry a number of risks and limitations. Escalating pharmacotherapy or exploratory surgery for pain in the absence of inflammation can have iatrogenic side effects, potentially exacerbating disease activity, psychological distress and worsening quality of life for patients. Alternative options such as antispasmodics, anticonvulsants, tricyclic antidepressants and cyclooxygenase-2 (COX-2) inhibitors may provide pain relief, yet their long-term use can exacerbate gut symptoms and bowel dysmotility\textsuperscript{17}. A significant number of patients use opioids or marijuana for pain control despite psychological and disease-related risks\textsuperscript{21-24}. In a European IBD cohort (n = 2831), 21.5% and 14.7% of patients were reported to take antidepressant or opioid medication, respectively\textsuperscript{25}. Norton et al.\textsuperscript{26} recently reviewed abdominal pain management interventions in IBD and found promising evidence for psychological approaches for IBD pain. For example, self-directed and therapist-led stress management\textsuperscript{27}, coping skills\textsuperscript{28} and disease anxiety-related cognitive behavioural therapy (CBT)\textsuperscript{29}, all appear to attenuate abdominal pain symptoms, albeit in predominantly small samples. Adjuvant psychological therapy may be particularly effective for individuals with IBD in pain, at risk of psychological distress and who are experiencing ongoing symptoms in the absence of active disease\textsuperscript{30}. Yet the review highlighted the need for evidence-based theory to aid the development of effective psychosocial interventions for IBD-pain.

Bielefeldt et al have proposed a biopsychosocial model of IBD-pain\textsuperscript{1}. This identifies two key processes of hypersensitivity and hypervigilance in the aetiology of chronic pain, summarising the role of inflammation and visceral hypersensitivity in increasing central processing of pain, and the influence of emotional responses and mood disorders that can act to amplify the pain experience by disinhibition of descending signals\textsuperscript{1} (Figure 1). The model has provided a useful insight into the possible mechanisms of chronic IBD-pain, however it is yet to be thoroughly investigated.
Two distinct processes of hypervigilance and hypersensitivity are suggested to underlie greater pain. Recurrent inflammatory activity can lead to hypersensitivity of visceral neurons, resulting in increased central input of pain signals. Emotional reactivity to the affective dimension of pain (valence) can cause an individual to become hypervigilant, leading to disinhibition of descending pathways and further increase of sensory input.

Despite pain being rated as one of patients’ most bothersome symptoms in IBD, this remains an area of limited research. In addition to the disease, the symptom of pain specifically has a profound impact on the quality of life and functioning of IBD patients. To date, systematic reviews in IBD have explored the role of psychosocial factors on the course of IBD and associated psychotherapeutic approaches, psychosocial correlates of adjustment in IBD and pain management interventions in IBD. However, a systematic review of psychosocial factors in IBD-pain specifically is lacking. A comprehensive profile of psychological and social factors associated with pain in IBD will provide a basis for developing a theory of IBD pain to underpin a psychosocial intervention, as has been applied in other conditions such as multiple sclerosis and paediatric chronic fatigue syndrome.
Specific study aims are:

I) To systematically review psychological and social factors associated with pain in adults diagnosed with IBD.

II) To assess the association of pain and clinical and sociodemographic factors within included studies of psychosocial investigations.

Methods

The protocol for this review was prospectively registered on 23/03/2017 (PROSPERO 42016052479).

Eligibility criteria

Studies were eligible if they reported on pain in an adult IBD population and measured at least one psychosocial factor. Studies including paediatric populations were not included, as it was contended that psychological processes compared to adult IBD-pain were likely to be different, for example the role of parent-child dyads. A focus on adult IBD-pain would therefore yield greater clarity in identifying key targets for a self-management intervention. Pain measures included any pain measure such as pain intensity, severity, diagnosis of chronic pain (> 3 months), pain-associated disability or interference. Inclusion and exclusion criteria for this review are presented in Table 1.
### Table 1. Inclusion and exclusion criteria for studies

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<td><strong>Population</strong></td>
<td>Adults ≥18 years with IBD</td>
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<td>Active and inactive disease</td>
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<td>Patients &lt; 18 years</td>
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<td>Adults without a diagnosis of IBD</td>
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<td><strong>Exposure/correlate</strong></td>
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<td><strong>Control/comparison</strong></td>
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<td>Chronic pain associated with another condition</td>
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<td></td>
<td>Bodily pain</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td>Joint/musculoskeletal pain</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Prospective, longitudinal and experimental studies (if reporting baseline associations)</td>
</tr>
<tr>
<td></td>
<td>Non-empirical, qualitative or review papers</td>
</tr>
<tr>
<td></td>
<td>Studies not published in English</td>
</tr>
</tbody>
</table>

**Information sources, search and study selection**

Studies were identified through multiple online database and hand searching. Online searches were conducted in January and February 2017, and a final search was conducted on 24 May 2017.

Databases included EMBASE (1974 to 2017 Week 2), Medline (1946 to 2017 Week 2) PsycInfo (1806 to 2017 Week 1), Web of Science, CINAHL and the Cochrane Library. Additional articles were identified manually by the first author through reference lists. Authors of abstracts and those known to be working in the field of IBD pain were contacted directly for any unpublished data. Search terms
were tailored for each database and included terms for ‘inflammatory bowel disease’, ‘pain’ and ‘psychosocial factors’ and combined using the set operators OR and AND (Table 2). MeSH and explode terms were utilised to maximise search results. Cross-sectional, prospective, longitudinal and experimental studies (reporting a baseline association of psychosocial factors and pain) were included. Only studies presented in English were selected (no scope for translation) however no restrictions were applied with regards to publication date due to the limited number of studies on psychosocial factors and pain in IBD. L.S. and L.M. independently carried out abstract and full-text screening using predetermined criteria. Any disagreements between reviewers were resolved through discussion utilising inclusion criteria.

Table 2. Search terms entered into databases

<table>
<thead>
<tr>
<th>IBD terms</th>
<th>AND</th>
<th>Pain terms</th>
<th>AND</th>
<th>Psychosocial factors terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease</td>
<td></td>
<td>Pain (OR)</td>
<td>AND</td>
<td>Psycholog* (OR)</td>
</tr>
<tr>
<td>IBD (OR)</td>
<td></td>
<td>Chronic pain (OR)</td>
<td></td>
<td>Psychosocial* (OR)</td>
</tr>
<tr>
<td>Ulcerative Colitis (OR)</td>
<td></td>
<td>Chronic abdominal pain (OR)</td>
<td></td>
<td>Social* (OR)</td>
</tr>
<tr>
<td>UC (OR)</td>
<td></td>
<td>Abdominal pain (OR)</td>
<td></td>
<td>Illness beliefs (OR)</td>
</tr>
<tr>
<td>Crohn’s Disease (OR)</td>
<td></td>
<td>Persistent pain (OR)</td>
<td></td>
<td>Catastrophising (OR)</td>
</tr>
<tr>
<td>CD (OR)</td>
<td></td>
<td>Pain interference (OR)</td>
<td></td>
<td>Anxi* (OR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pain-related* (OR)</td>
<td></td>
<td>Depress* (OR)</td>
</tr>
</tbody>
</table>


Data collection

Predefined data extraction criteria were used by two authors (L.S. and L.M.) to extract relevant data. Any discrepancies were again resolved by consensus or inclusion of a third author (C.N). Extracted information from each study included (1) study design (2) number of participants, (3) characteristics of patient sample (age, IBD diagnosis), (4) comparator group (if applicable) (5) recruitment source (6) type of (correlate) psychosocial measure, (7) type of (outcome) pain measure, (8) key findings (9) key quantitative data (10) additional clinical/demographic correlates with pain. Due to variety in pain and psychosocial measures used, meta-analyses were not possible and so a narrative review was conducted.

Quality assessment

Methodological quality of studies was assessed using the Critical Appraisal Skills Programme (CASP) guidelines, selected by the specific methodological design of included studies\textsuperscript{37}. The same criteria have been applied in previous reviews on IBD populations\textsuperscript{38, 39}. Studies were assessed by L.S. and L.M. and points were deducted for a lack of defined objectives and hypothesis; non-validated measurement tools; inappropriateness or limited data regarding methodological design and statistical analysis; selective reporting of results and limitations not addressed. Assessment of studies yielded a low, medium or high quality rating. Any disagreement between reviewers was resolved through consensus or inclusion of C.N. Studies were classified as High (n =10), Medium (n=4) and Low quality (n=1) (see Supplementary Table 1). As all papers were considered to contribute to the topic of interest, no studies were excluded on the basis of quality.

Results

Study characteristics

Combined database and manual searches identified 3336 references. After removing duplicates and undertaking title and abstract screening, full-texts of 65 studies were assessed by L.S and L.M. Fifteen studies reported in 16 papers were included (Figure 2). Studies excluded at the full-text screening stage, with reasons, are provided in Table S2.
**Results of individual studies**

The 15 studies included a total of 5539 IBD participants (including indeterminate colitis) and 993 non-IBD participants. A wide variety of pain measures were used in studies, with a significant proportion of studies relying on single-item questions or sub-scores to assess pain. Moreover, there was wide variability in study design and methodology. Eight studies were cohort studies and seven were case-control studies. One study was reported in 2 papers (Tripp DA, Hayley D, et al, Queen’s University, Kingston, ON, Canada, unpublished result and Tripp DA, Walker S, et al, Queen’s University, Kingston, ON, Canada, unpublished details). Three studies compared IBD with healthy controls (Tripp DA, Hayley D, et al, unpublished result and Tripp DA, Walker S, et al, unpublished result) and 4 studies involved other patient groups including back pain, IBS, arthritis and gastro-oesophageal reflux.
disease.\textsuperscript{42-45} One study was longitudinal and 14 studies were cross-sectional design, of which one was baseline data from an intervention study\textsuperscript{46} and 2 were national cohort survey studies.\textsuperscript{47,48} A summary of included studies is provided in Table 3, with detailed results of each included study presented in Table S1.

Twenty-five psychosocial factors in relation to pain were identified, including emotional, cognitive, behavioural and personality factors. Ten and 5 studies conducted univariate and multivariate analyses respectively (Table 4). A variety of pain presentations were investigated and different pain measures were used by the studies (Table 5). Two papers explored different pain presentations (Tripp DA, Walker S, et al, unpublished details),\textsuperscript{49} including joint pain, chronic pain with a neuropathic component and migraine.\textsuperscript{49} Prevalence of probable migraine and chronic pain were significantly higher in the IBD cohort compared to the general population.\textsuperscript{49} Prevalence of patients with IBD with chronic pain in studies ranged from 11.3\% to 38\%.\textsuperscript{2,49} Percent-ages of patients experiencing pain of at least moderate intensity at the time of study, or who had experienced pain within the last 3 months, ranged from 21\% to 82.5\% across studies. The 25 psychosocial factors identified were grouped into 3 broad categories; emotional, cognitive-behavioural and personality factors, and are reviewed below.

Addressing the second aim of the review, clinical and sociodemographic factors associated with pain identified within the reviewed studies are then reported.

**Emotional factors**

One study investigated the presence of a mood disorder (by physician diagnosis) in relation to pain\textsuperscript{50}. From multivariate analyses, a co-existing mood disorder increased the odds of pain frequency and pain severity fivefold (OR 5.76, 95\% CI 1.39, 23.89).
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Psychosocial factor investigated</th>
<th>Pain measure</th>
<th>Key findings</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boye 2008⁴⁶</td>
<td>Cross-sectional</td>
<td>BussPerry Aggression Eysenck Personality Questionnaire Multidimensional Health Locus of Control Scale Toronto Alexithymia Scale</td>
<td>Short Form-36&lt;br&gt; <em>Bodily pain</em></td>
<td>High internal locus of control associated with higher pain-related quality of life in CD.</td>
<td>High</td>
</tr>
<tr>
<td>Boyle, unpublished</td>
<td>Cross-sectional</td>
<td>Stress - Anxiety -Depression (21 score) Crohn’s and Colitis Knowledge</td>
<td>Brief Pain Inventory&lt;br&gt; <em>Abdominal pain</em></td>
<td>Mean scores in the SAD-21 for anxiety, depression and stress were significantly greater in pain reporters.</td>
<td>Medium</td>
</tr>
<tr>
<td>Coates 2013⁵⁰</td>
<td>Cross-sectional</td>
<td>Mood disorder</td>
<td>SIBDQ Pain Score Modified ulcerative colitis disease activity index survey&lt;br&gt; <em>Abdominal pain</em></td>
<td>Patients with higher pain more frequently carried a concurrent diagnosis of a mood disorder. (OR 5.76, 95% CI 1.39–23.89)</td>
<td>High</td>
</tr>
<tr>
<td>Deberry 2014⁴¹</td>
<td>Cross-sectional</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>VAS&lt;br&gt;McGill Short Form Questionnaire&lt;br&gt; <em>Abdominal pain</em></td>
<td>Patients with UC with pain had significantly higher HADS when compared with controls and patients with UC without pain - UC with pain. Higher depression scores independently predicted pain in UC patients (r &gt; 0.5)</td>
<td>High</td>
</tr>
<tr>
<td>Edman 2017⁴⁴</td>
<td>Cross-sectional</td>
<td>Perceived Stress Scale</td>
<td>Self-report numerical rating scale of pain&lt;br&gt; <em>Unspecified location</em></td>
<td>Perceived stress significantly positively correlated with average pain (r = 0.32, p &lt;.0001) and worst pain (r = 0.35, p &lt;.01) in the IBD group.</td>
<td>High</td>
</tr>
<tr>
<td>Esteve 2013⁴³</td>
<td>Cross-sectional</td>
<td>Acceptance and Action Questionnaire</td>
<td>SF-36 bodily pain&lt;br&gt;Pain intensity scale&lt;br&gt; <em>Chronic pain&lt;br&gt;Bodily pain</em></td>
<td>Across all three groups, pain intensity (and experiential avoidance) correlated with pain fear avoidance (beta = .19, p &lt;.05)</td>
<td>High</td>
</tr>
<tr>
<td>Study</td>
<td>Study Type</td>
<td>Measure/Assessment</td>
<td>Findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>---------------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fuller-Thompson &amp; Sulman 2006</strong></td>
<td>Cross-sectional</td>
<td>Depression (Kessler and Mroczek scale)</td>
<td>Respondents whose activities were limited by pain (depressed = 35.1% vs non-depressed = 58.4%, p &lt; .001) and who were in severe pain were much more likely to be depressed. Those who reported that activities were prevented by pain were significantly more depressed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fuller-Thompson 2015</strong></td>
<td>Cross-sectional</td>
<td>Generalised anxiety disorder</td>
<td>Anxiety was predicted by chronic pain (OR 2.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Goodhand 2012</strong></td>
<td>Cross-sectional</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>Chi-squared analyses showed a significant association between abdominal pain and HADS-A scores in CD patients.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moisset 2015</strong></td>
<td>Cross-sectional</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>Depression significantly associated with probable migraine. HAD anxiety was significantly associated with arthralgia/joint pain. HAD anxiety was significantly associated with overall pain.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Morrison 2015</strong></td>
<td>Cross-sectional</td>
<td>Survey of Pain Attitudes Coping Strategies Questionnaire Hospital Anxiety and Depression Scale</td>
<td>Independent and significant associations with moderate-severe pain were catastrophising tendency (OR 34.69), depression (OR 1.8), medication beliefs (OR 1.05) and active disease (OR 48.54).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Measured Outcomes</td>
<td>Findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
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<td>----------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odes</td>
<td>Cross-sectional</td>
<td>Brief Symptom Inventory, Brief COPE Inventory, Family Assessment Device, Satisfaction with Life Scale, Work Productivity and Activity Impairment, Harvey Bradshaw Index Short Inflammatory Bowel Disease Questionnaire (SiBDQ) SF-36 bodily pain Abdominal pain Bodily pain</td>
<td>Higher pain scores significantly correlated with psychological stress, dysfunctional coping strategies, poor family relationships, work abstinence, presenteeism, productivity loss and activity impairments and all WPAI sub-measures.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schwarz</td>
<td>Cross-sectional</td>
<td>Beck Depression Inventory State-Trait Anxiety Psychosomatic Symptom Checklist Daily symptom diary (0-4 scale) Abdominal pain</td>
<td>Pain/tenderness significantly correlated with all psychological measures excluding STAI-trait.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sirois &amp; Wood</td>
<td>Longitudinal</td>
<td>Gratitude (Q-6) Depression Scale Perceived Stress Scale Duke-UNC Functional Social Support questionnaire Bowel Symptoms sub-scale (Inflammatory Bowel Disease Questionnaire) Abdominal pain</td>
<td>T1 pain significantly positively correlated with T2 depressive symptoms, T2 pain, perceived stress and helplessness, and negatively correlated with T1 self-rated health measured by SF-36 (all p &lt; .01). T2 pain significantly correlated with T1 pain and perceived stress (all p &lt; .01)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tripp (paper 1), unpublished</td>
<td>Cross-sectional</td>
<td>Pain Catastrophising Scale Depression (PHQ-9) Short Inflammatory Bowel Disease Questionnaire Short Form McGill Pain Questionnaire Pain body Diagram Abdominal pain 1, 2, &gt;3 locations</td>
<td>All IBD pain phenotype groups reported more pain catastrophising and depressive symptoms than controls. Patients with IBD abdominal pain reported significantly less pain catastrophising (p &lt; .01) and depressive symptoms (p &lt; .001) than IBD patients with 1-2/3+ pain locations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tripp (paper 2), unpublished</td>
<td>Cross-sectional</td>
<td>Chronic Pain Coping Inventory Pain Catastrophizing Scale Depression (PHQ-9) Multidimensional Scale of Perceived Social Support Bowel Disease Questionnaire Short Form McGill Pain Questionnaire Pain body Diagram Unspecified location</td>
<td>Pain associated with illness-focused coping (r = .7), pain catastrophising (r = .52), wellness-focused coping (r = .35), depressive symptoms (r = .68) and perceived social support -.26.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Depression**

Ten of the 15 included studies explored depression in relation to pain, of which 9 found that depression/depressive symptoms were significantly positively associated with higher pain intensity (Tripp DA, Hay-ley D, et al, unpublished result; Tripp DA, Walker S, et al, unpublished details and Boyle et al, University College Dublin, Dublin, Ireland, unpublished details),\(^{40-42,45,49}\) more locations of pain (Tripp DA, Walker S, et al, unpublished details) and reports that pain prevented and/or restricted activities.\(^{48}\) All but one of these studies was cross-sectional in design. Assessing different pain presentations, 1 study found that higher Hospital Anxiety Depression (HAD) depression scores (4th quartile vs 1st quartile) were associated with a 3.44 increased risk of probable migraine, but were not found to correlate with joint pain, abdominal pain or chronic pain with a neuropathic component.\(^{49}\) In the only longitudinal study identified in this review, pain at baseline correlated with depressive symptoms at baseline and 6 months.\(^{45}\) Five of these studies used the hospital anxiety depression score (HADS) questionnaire. Two of these studies included a comparison group, namely IBS\(^{42}\) and patients with arthritis.\(^{49}\)

One study investigating depression stratified participants who had active and inactive disease, defined by colonoscopy and histological reports\(^{41}\). Mucosal inflammation did not show a significant association with pain rating. Depression scores remained the only significant predictor of greater pain ratings in multivariate analyses, after controlling for age, growth factors levels (neurturin NRTN) and ion channel density (transient receptor potential Ankyrin TRPA1) in the colonic mucosa.

**Anxiety**

Of the 7 included studies that explored anxiety and pain, all found a significant positive association between these variables in cross sectional analysis\(^{2,41,42,47,49}\). One study found that state but not trait anxiety significantly correlated with increased abdominal pain/tenderness, however this was deemed a low quality study\(^{42}\). Exploring the association between anxiety and different pain presentations, HAD anxiety scores significantly correlated with joint and overall pain severity and probable migraine in an IBD cohort, but not abdominal or chronic pain with a neuropathic component in one longitudinal study\(^{49}\).
The HADS questionnaire was used in one study to assess factors associated with mood disorders in IBD\(^4\), and found that abdominal pain was significantly associated with HAD anxiety in CD. Active disease (SCCAI/endoscopic active disease Baron’s score >1) and perceived stress independently predicted anxiety and depression scores in UC. Being an inpatient also predicted higher HAD depression scores.

**Table 4. Factors associated with pain identified in included studies**

<table>
<thead>
<tr>
<th>Factor associated with pain</th>
<th>Study - univariate/multivariate analysis (U/M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychosocial</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>+***</td>
</tr>
<tr>
<td>Anxiety</td>
<td>+*** NS</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>+***</td>
</tr>
<tr>
<td>Stress</td>
<td>+*** +***</td>
</tr>
<tr>
<td>Somatisation</td>
<td></td>
</tr>
<tr>
<td>Pain catastrophising</td>
<td></td>
</tr>
<tr>
<td>Helplessness</td>
<td></td>
</tr>
<tr>
<td>Medication beliefs</td>
<td></td>
</tr>
<tr>
<td>IBD knowledge</td>
<td>NS</td>
</tr>
<tr>
<td>Dysfunctional coping</td>
<td>+*</td>
</tr>
<tr>
<td>Problem focused coping</td>
<td>-*</td>
</tr>
<tr>
<td>Emotion focused coping</td>
<td>+</td>
</tr>
<tr>
<td>Illness focused coping</td>
<td>+**</td>
</tr>
<tr>
<td>Wellness focused coping</td>
<td></td>
</tr>
<tr>
<td>Pain fear avoidance</td>
<td>+</td>
</tr>
<tr>
<td>Internal locus of control</td>
<td></td>
</tr>
<tr>
<td>Neuroticism</td>
<td>NS</td>
</tr>
<tr>
<td>Hostility/aggression</td>
<td>NS</td>
</tr>
<tr>
<td>Alexithymia</td>
<td>NS</td>
</tr>
<tr>
<td>Conventionality</td>
<td>NS</td>
</tr>
<tr>
<td>Perceived Social Support</td>
<td></td>
</tr>
<tr>
<td>Benefit Finding</td>
<td>NS</td>
</tr>
<tr>
<td>Illness Acceptance</td>
<td>NS</td>
</tr>
<tr>
<td>Gratatitude</td>
<td>NS</td>
</tr>
<tr>
<td>Thriving</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical/demographic</td>
<td></td>
</tr>
<tr>
<td>Disease activity index</td>
<td>+* +*</td>
</tr>
<tr>
<td>Disease duration</td>
<td>NS +*</td>
</tr>
<tr>
<td>Female gender</td>
<td>+**</td>
</tr>
<tr>
<td>Age</td>
<td>NS +**</td>
</tr>
<tr>
<td>Inflammatory markers</td>
<td>+*</td>
</tr>
<tr>
<td>ESR/CRP/calpro/endosc</td>
<td>NS</td>
</tr>
<tr>
<td>TRPV1/TRPVA1</td>
<td>NS</td>
</tr>
<tr>
<td>Opioid use</td>
<td>+**</td>
</tr>
<tr>
<td>Antidepressant use</td>
<td>+*</td>
</tr>
<tr>
<td>Units of alcohol p/week</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic pain syndrome</td>
<td>+*</td>
</tr>
</tbody>
</table>

If provided, \( p \leq 0.05 \), \( p \leq 0.01 \), \( p \leq 0.001 \). NB inflammatory markers include histology, endoscopy, calprotectin, C-reactive protein. TRPV1/TRPVA1 = transient receptor potential cation channel subfamily V1/ankyrin 1. +/− indicate positive or negative associations.
Stress

Four studies assessed levels of psychological stress, including perceived stress, in relation to pain (Boyle et al, unpublished details). 44,45,51. All of these studies found significant and positive correlations between stress and pain intensity (Boyle et al, unpublished details), 44,45,51 pain-related interference (Boyle et al, unpublished details) and bodily pain.51 In regression analyses, odds ratio for psychological stress (OR lowest 2.26, highest 12.17) and female gender (OR highest 3.19) increased with greater pain using three pain sub-scores51. Three out of four studies were cross-sectional in design, however one longitudinal study found only baseline pain scores correlated with baseline perceived stress45.

Table 5. List of pain presentations and pain measures in reviewed studies

<table>
<thead>
<tr>
<th>Type of pain</th>
<th>Pain measure</th>
<th>No. of studies/reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>Short inflammatory bowel disease questionnaire pain item</td>
<td>2 50, 51</td>
</tr>
<tr>
<td></td>
<td>Modified UC disease activity index</td>
<td>1 50</td>
</tr>
<tr>
<td></td>
<td>Harvey Bradshaw Index pain item</td>
<td>2 40, 51</td>
</tr>
<tr>
<td></td>
<td>Daily symptom diary</td>
<td>1 42</td>
</tr>
<tr>
<td></td>
<td>Bowel Symptoms sub-scale (IBDQ)</td>
<td>1 45</td>
</tr>
<tr>
<td></td>
<td>Visual analogue score</td>
<td>1 41</td>
</tr>
<tr>
<td></td>
<td>Short Form McGill Questionnaire</td>
<td>1 41</td>
</tr>
<tr>
<td>Unspecified location of pain</td>
<td>Brief Pain Inventory</td>
<td>1 (Boyle et al, unpublished details)</td>
</tr>
<tr>
<td></td>
<td>Self-report numerical rating scale</td>
<td>1 44</td>
</tr>
<tr>
<td></td>
<td>Pain intensity scale</td>
<td>1 43</td>
</tr>
<tr>
<td></td>
<td>Single pain survey item</td>
<td>2 47, 48</td>
</tr>
<tr>
<td></td>
<td>Von Korff Pain intensity and Disability</td>
<td>1 2</td>
</tr>
<tr>
<td></td>
<td>Short Form McGill Questionnaire</td>
<td>2 (Tripp et al., unpublished papers)</td>
</tr>
<tr>
<td>Bodily pain/ pain-related</td>
<td>SF-36</td>
<td>3</td>
</tr>
<tr>
<td>quality of life</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Cognitive-behavioural factors

Pain catastrophising

Three studies investigated pain catastrophising, which refers to an exaggerated negative cognitive and affective interpretation of actual pain or an expected pain experience. It includes magnifying potential negative factors associated with pain, feelings of helplessness and an inability to disengage from pain-related thoughts. All 3 cross-sectional studies found that pain catastrophising was associated with greater pain reporting in IBD (Tripp DA, Hayley D, et al, unpublished result; and, Tripp DA, Walker S, et al, unpublished details). Participants who reported more than 1 location of pain also were found to catastrophise more about pain in 1 study that looked at pain phenotyping (Tripp DA, Walker S, et al, unpublished details). Phenotype 1, 2 and 3 represented abdominal pain, 1-2 locations (e.g. abdominal and lower back) and 3+ locations, respectively. In univariate analyses, all pain phenotype participants with IBD showed significantly higher scores for pain catastrophising compared to healthy controls. However, phenotype 1 showed significantly lower scores for these 2 psychosocial measures compared to phenotype 2 and 3, with no significant difference between the latter phenotypes (Tripp DA, Walker S, et al, unpublished details). One high-quality study found that a tendency to catastrophise was a significant predictor of moderate to severe pain after controlling for active disease, measured by the Harvey-Bradshaw index (HBI) or SCCAI.
Coping

Coping is an important construct in the context of chronic illness, and refers to an individual's efforts to tolerate and resolve stressors that exceed his or her resources. Three cross-sectional studies assessed the association between pain and coping, using a variety of measures. As measured by the Coping Strategies Questionnaire, one study found that having a catastrophising tendency predicted moderate to severe pain in multivariate analyses, as aforementioned. However, in univariate analyses, ignoring sensations, praying and hoping, cognitive coping/suppression, helplessness and diverting attention/praying were all found to be significantly correlated to greater pain intensity and associated disability. In this study, chronic pain was present in 38% of patients, of which chronic abdominal pain was the most frequently reported (91%) followed by joint pain (33%), back pain (33%) and chronic headache (33%). Moderate to severe pain was also associated with active disease according to the HBI or SCCAI. Excluding disease activity, there were no differences in other disease characteristics (medication, disease duration) between moderate-severe and mild pain reporters.

Coping strategies were investigated in one study, which assessed pain in participants recruited online and in clinics, through pain sub-scales in the HBI, Short Inflammatory Bowel Disease Questionnaire and Short-Form 36. These included emotion-focused coping (e.g. acceptance, humour, and emotional support use), problem-focused coping (e.g. active coping and planning) and unhelpful or 'dysfunctional' coping (e.g. self-blame, denial and substance use). For the whole cohort, use of 'dysfunctional' strategies was the only coping strategy that significantly correlated with severe pain across all three pain-sub scores (p < .001). In logistic regression analyses, dysfunctional coping showed significant increased odd ratios with mild pain (OR 1.06 in HBI and SF-36) and moderate pain (OR 1.07 in SIBDQ) (both p < .05). From the SIBDQ pain sub-score, use of problem-focused coping was associated with a 15% reduced risk of experiencing severe pain (p < .05). Emotion-focused coping showed no significant association with pain across pain sub-scores. Both illness-focused (guarding, resting behaviours) and wellness-focused coping (task persistence, relaxation) were positively associated with pain in one high quality study (Tripp DA, Hayley D, et al, unpublished result) (Pearson r = 7.2 and 3.5 respectively).
Knowledge and beliefs, perceived social support

One study assessed participants’ knowledge of IBD and found no association with pain levels (Boyle et al, unpublished details). Most (70.6%) pain reporters said their doctor ‘did not understand their pain symptoms’. Significantly more patients reporting pain had active disease (defined by physician assessment); however, no significant associations were found between age, alcohol consumption or disease duration and pain (Boyle et al, unpublished details). Lower beliefs in the effectiveness of pain medication were found to be associated with greater pain in multivariate analyses in another study. In univariate analyses of this study, the extent to which participants believed that they were disabled by pain (disability score) significantly correlated with pain. A positive psychological factor, perceived social support, was significantly associated with less pain in 1 high-quality cross-sectional study (Tripp DA, Hayley D, et al, unpublished details); however, this was not supported in a prospective study which found no association with social support and pain levels.

Pain fear avoidance

Pain fear avoidance was investigated in IBD patients diagnosed with chronic pain, along with patients with back pain and heterogenous pain conditions (e.g. fibromyalgia and spinal pain syndromes). This construct explores individual’s beliefs of fearful or threatening situations, and is argued to exacerbate deconditioning and disability in the context of chronic pain. In a cross-sectional design, pain intensity correlated with pain fear avoidance across all three groups. No data were provided on disease activity.

Personality factors

Personality factors and bodily pain within a health-related quality of life (HRQoL) measure was investigated in one study. Patients were recruited on the basis of a disease activity index for CD or UC of >4 (active disease) and perceived stress questionnaire score of > 60. In CD patients only, greater scores on a bodily pain sub-scale (demonstrating better pain-related quality of life) was associated with internal locus of control (p = .04). In regression analyses, although the overall model (including control variables) was not found to be significant in explaining bodily pain, the personality variable of internal locus of control remained significant. Pain levels were not associated with positive personality traits of gratitude, benefit finding or thriving in the only included longitudinal study.
Clinical and sociodemographic factors

Addressing the second aim of this review, clinical or sociodemographic correlates of pain reported within included papers were extracted. Six out of 15 studies controlled for disease activity and/or clinical factors (Boyle et al, unpublished details).2,41,49,50 Within these, 4 found an association between active disease and pain (3 out of 4 measured by physician-reported disease activity index) (Boyle et al, unpublished details),2,46,49 and 1 found an association between an inflammatory marker (C-reactive protein) and pain.50 Abdominal pain showed no association with disease activity in 2 studies41,49 and active disease only predicted pain in UC but not CD patients in another study.46 Three studies found that psychosocial factors remained significant predictors of pain alongside active disease or markers of inflammation.2,41,49,50 One study found that depression remained the only significant predictor of pain ratings when controlling for clinical factors (r > .50).41 This study investigated the influence of ion channel density and neurotrophic factors on pain, which are upregulated as a result of inflammatory activity and can lead to visceral hypersensitivity.1 In univariate analyses, higher NRTN and lower TRPA1 levels in the mucosa correlated with higher pain ratings. Endoscopic findings and cytokine inflammatory markers (IL 1b, IL6, IL17) did not correlate with pain ratings.41 Disease duration was associated with probable migraine,49 but not found to be significantly associated with pain ratings in another study (Boyle et al, unpublished details). With regard to medication use, 2 studies found that no IBD-specific medications were associated with overall pain risk2,49 and 1 found that only use of NSAIDS was significantly greater in the abdominal pain group.50 As expected, opiate and paracetamol use increased in relation to pain severity groups in 22,50 and 3 studies respectively (Boyle et al, unpublished details).2,50

Seven studies assessed the relationship between gender and pain, and three found a significant association with pain and female gender49-51, including greater prevalence of migraine in females51. Younger age was associated with greater pain43,52 and probable migraine.49 In quiescent IBD, one study found that patients reporting frequent to constant levels of pain were significantly more likely to have a co-existing diagnosis of a mood disorder, a chronic pain syndrome, a diagnosis of IBS, were more likely to be female, be younger and have higher ESR (mm/hour) values.50
Discussion

This systematic review investigated psychosocial factors associated with pain in adults diagnosed with IBD. Emotional, cognitive-behavioural and personality factors were found to be associated with pain. The majority of studies were of high quality and had moderate to large sample sizes, lending weight to the conclusions of the review. Depression and anxiety were the most commonly explored psychosocial constructs in relation to IBD-pain. Findings indicate that higher levels of depression and anxiety are associated with greater pain severity/intensity. A recent systematic review identified prevalence rates of 15% and 20% for depression and anxiety in over 150,000 IBD patients, respectively. Prospective studies with IBD patients have demonstrated that depression and anxiety are associated with symptom exacerbation and onset of active disease. The current review suggests that pain may be one of the symptoms associated with these psychological factors. Higher levels of perceived stress were also a significant correlate of IBD-pain (Boyle et al, Ireland, unpublished details), which supports previous evidence demonstrating the effects of stress on symptom exacerbation via the gut-brain axis. Negative emotional arousal may exacerbate pain in IBD directly through amplification of descending pain signals in higher order processing or by exacerbating inflammation via the production of cortisol. Alternatively, greater negative affect may contribute to unhelpful behaviours such as withdrawal or poor medication adherence, which can affect pain levels. The negative emotional factors identified in this review have been recognised in the IBS literature and served as targets for therapeutic change in non-pharmacological interventions for patients with IBS, supporting the view that IBS and IBD may share some similar pain mechanisms.

Exacerbation of pain symptoms from emotional arousal may also link to cognitive-behavioural factors. Greater catastrophising was associated with pain across several studies, which has been recognised as a contributing factor to chronic pain in conditions such as multiple sclerosis and fibromyalgia. Moreover, research in IBS has shown a mediating role of pain catastrophising between depression and abdominal pain. A number of studies examined coping strategies in relation to pain levels (Tripp DA, Hayley D, et al, unpublished details). Greater use of behaviours such as self-distraction, behavioural disengagement, denial, venting and self-blame (labelled ‘dysfunctional’ coping) and less use of active coping and planning (labelled ‘problem-focused’ coping) were related to increased pain severity. Emotionally-focused coping strategies (acceptance, humour,
positive framing) showed no relation to pain levels. In another reviewed study, both ‘wellness’ and ‘illness’-focused coping were investigated. Wellness-focused coping addresses behaviours that aim to facilitate pain control, such as exercise/stretching, task persistence and relaxation, whereas illness-focused coping includes withdrawal behaviours and giving up on an attempt to control the pain, such as guarding, resting and asking for assistance. Both types of coping were positively associated with increased pain intensity. These conflicting results suggest that the relation of over-arching coping styles to IBD-pain is unclear. One could argue that the use of emotionally focused techniques, such as acceptance and humour, may be adaptive or ‘functional’ for an individual in a given context. In this regard, identifying specific unhelpful thoughts and behaviours in relation to pain, such as denial, self-blame and fear avoidance, may be more effective targets than overarching coping styles for intervention development.

A number of positive psychological factors were explored in studies identified in the current review. Perceived social support and problem-focused coping were negatively associated with pain (Tripp DA, Hayley D, et al, unpublished details). An internal locus of control, namely the perception that one’s behaviour can control events and outcomes was associated with better pain-related quality of life. Research on chronic back pain has shown that individuals with an external locus of control are more likely to rely on maladaptive coping strategies such as low levels of activity and a lack of belief in recovery. This has been supported in research on IBD cohorts with back and joint pain. Perceived controllability of stressful life events has been investigated in individuals with functional gastrointestinal disorders, and has demonstrated that developing skills of coping flexibility, in particular learning to identify and respond adaptively to controllable versus uncontrollable stressors, may be a useful tool for patients with more complex symptoms. One study found that acceptance of pain significantly positively correlated with resilience and negatively correlated with low mood in IBD patients with chronic pain. This may suggest that targeting pain-related thoughts such as pain acceptance may indirectly reduce pain symptoms by improving mood. Positive psychological factors such as pain acceptance and resilience may be important avenues to explore with regards to pain adaptation, and as possible therapeutic mechanisms for future psychological interventions for IBD-related pain.
The review did not find a clear relationship between active disease/inflammation and pain. Previous studies have demonstrated an association between mucosal signalling molecules, such as an increase in pain nerve fibres TRPA1/TRPN1, and greater pain\(^{70, 71}\). However, this was not supported by one reviewed study\(^ {41}\). This demonstrates the complexity of identifying clinical factors related to pain in IBD and requires further clarification. The majority of studies that controlled for disease activity found that psychosocial factors remained significant predictors of pain levels regardless of disease activity. This supports the role of a biopsychosocial approach to IBD-pain and highlights the need to take an integrative approach when assessing patients’ symptoms and quality of life, in periods of both active and inactive disease.

The review identified that females and younger adults may be at particular risk of experiencing or reporting pain. \(^ {41, 49-51}\) However, no gender differences were noted for different types of pain presentations which has been highlighted in a study by Schirbel and colleagues, who found greater rates of arthralgia in females\(^ {3}\). This study by Schirbel et al. was not eligible for the review as no explicit psychosocial measure was included separate from HRQoL. However, in 400 IBD patients, 87.9% reported pain, 48.2% reported persistent pain and 38.3% of patients reported that pain was intensified by mental stress\(^ {3}\).

The current review confirms the role of emotional and cognitive factors in relation to pain in IBD, as proposed by Bielefeldt et al\(^ {1}\) in their model of IBD-pain. However, their model has a particular focus on anxiety and mood disorders, rather than addressing pain-specific emotions, cognitions and behaviours. This review has identified pain-specific psychosocial processes that may be important mechanisms of chronic pain in IBD, such as pain catastrophising and pain fear avoidance. In addition, results from the review suggest that positive psychological factors such as active coping, internal locus of control, resilience and pain acceptance may be buffering or ‘protective’ factors against more severe or chronic IBD-pain (Tripp DA, Hayley D, et al, unpublished details).\(^ {50, 51}\) Psychological therapies may therefore be beneficial to patients with chronic pain in IBD and particularly those with psychological distress and unhelpful thought processes. CBT has a large evidence-base for treatment in IBS and other functional gastrointestinal disorders\(^ {72-75}\), as well as positive outcomes for quality of life and coping skills in IBD populations\(^ {30, 62}\). Further research is required to confirm the role of negative psychological factors, including depression and anxiety, and pain-specific cognitive-
behavioural factors in relation to chronic pain in IBD. Additionally, the potential buffering effects of positive psychological factors on pain identified in the review warrants further investigation.

Limitations

Despite identification of key factors associated with pain in IBD, limitations must be acknowledged. Although a number of studies controlled for disease activity, only one stratified results based on patients with active and inactive disease\(^50\). Patients with active disease were included in the review as studies examining patients only in remission and fulfilling eligibility criteria were sparse in preliminary searches. Therefore, investigation of pain in patients in remission specifically was limited in this review. A substantial number of reviewed studies lacked the inclusion of a specific validated pain measure; eight out of 15 studies used either the pain sub-measure from HRQoL, disease activity index questionnaires or single items in questionnaire surveys\(^{47,48}\). The use of validated pain scales with broader profile of pain is recommended for pain assessment, including pain location, intensity/severity, pain interference and pain-related beliefs\(^{76,77}\). These constructs are also recommended as key outcome measures in pain clinical trials\(^78\).

Table 6. Recommendations for future observational and intervention studies

<table>
<thead>
<tr>
<th>Study type</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td><strong>Observational studies</strong></td>
<td>• Validated pain measure</td>
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<td></td>
<td>• Neuropathic pain measure</td>
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<td></td>
<td>• Long-term follow up</td>
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<td></td>
<td>• Objective marker of disease activity</td>
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<td></td>
<td>• Exploration of positive and negative psychosocial factors</td>
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<td></td>
<td>• Sample size power calculation</td>
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<tr>
<td><strong>Intervention studies</strong></td>
<td>• Intervention based on theoretical principles</td>
</tr>
<tr>
<td></td>
<td>• Validated pain measure</td>
</tr>
<tr>
<td></td>
<td>• Clear stratification of active and remission patients (or recruitment of remission patients only)</td>
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<tr>
<td></td>
<td>• Control group</td>
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Ongoing pain in IBD remission has been discussed in relation to IBS and conceptualised as IBS-IBD or more recently ‘irritable inflammatory bowel syndrome’\(^\text{79}\). In support, one study found that patients with quiescent UC but reporting frequent to constant levels of pain were more likely to have a diagnosis of IBS (and chronic pain syndromes), alongside a mood disorder\(^\text{50}\). As IBS and IBS-IBD were not the main focus of this review, these were not included in the search terms. In addition, it was felt by the authors that exploration of IBD-pain in isolation rather than the addition of IBS-IBD would have yielded a purer review on IBD pain, rather than with accompanying gastrointestinal or functional symptoms. At the screening stage, studies were not excluded if they involved IBS-IBD patients, but were excluded if pain was measured only within an IBD or IBS composite score. Therefore, although studies on IBS-IBD were considered for this review pending eligibility criteria, a large number of papers on IBS-IBD or functional symptoms in IBD may have provided a more comprehensive profile of psychosocial factors associated with pain in IBD. In addition, it may have yielded more studies examining IBD patients exclusively in remission.

All but one of the included studies were observational studies, therefore direction of causality cannot be determined. Future research would benefit from longitudinal studies to assess whether psychosocial factors can predict variation in pain ratings over time. Lastly, only one of the 15 included studies carried out a power calculation\(^\text{51}\). Further exploration of psychosocial factors and pain in IBD would be strengthened by prospective studies and use of statistical power analyses. Further recommendations for observational and intervention studies are summarised in Table 6.

**Clinical implications of key findings**

The review suggests a number of implications for clinical practice. A recent systematic review on chronic abdominal pain management in IBD presented promising findings for psychosocial interventions, including stress management techniques and coping skills training\(^\text{26}\). Results from this review support the application of a psychosocial intervention, alongside IBD medication, for pain management. In particular, the consistent association identified between depression and anxiety and
pain in the present review suggests that treatment of mood-related issues may improve pain levels and pain-related quality of life. Additionally, targeting pain-specific thoughts and behaviours such as pain catastrophising and fear avoidance may in turn show beneficial effects on mood as well as pain. The review also indicates that positive psychology may be an important avenue to explore in relation to treatment for pain. Active coping and perceptions of control and social support were associated with lower pain levels in this review. In addition, pain acceptance and resilience/psychological well-being may be useful targets for an intervention in buffering the impact of pain on patients with IBD. Further research is required to explore the role of negative ‘risk’ factors and positive ‘protective’ psychological factors in relation to IBD-pain, to aid the development of effective and disease-specific psychological treatment.

Conclusions and recommendations

This is the first review to systematically explore the role of psychosocial factors related to IBD-pain. The emotional, cognitive, behavioural and personality factors identified here are consistent with other systematic reviews on disease-specific pain and the chronic pain literature. In addition, the review has presented similarities between IBD and IBS pain, and supports the view that application of IBS-pain management approaches may be useful in the context of IBD, such as cognitive behavioural therapy. It is recommended that further research aims to confirm the importance of emotional factors and explore both negative and positive cognitive content and behavioural responses to pain. Further research in this area, with use of power calculation of sample sizes and validated pain measures, should help to build a more comprehensive understanding of IBD-related pain.
References


28. McCormick M, Reed-Knight B, Lewis JD, Gold BD, Blount RL. Coping Skills for Reducing Pain and in Adolescents with IBD. *Inflammatory Bowel Diseases* 2010;16(12):2148-2157.


47. Fuller-Thomson E, Lateef R, Sulman J. Robust Association Between Inflammatory Bowel Disease and Generalized Anxiety Disorder: Findings from a Nationally Representative Canadian Study. Inflammatory Bowel Diseases 2015;21(10):2341-2348.


4.3 Rationale for systematic review

A systematic review aims to “comprehensively identify, appraise and synthesise all the relevant studies on a given topic” (Petticrew & Roberts, 2006, pg. 19). It seeks to address a research question by accumulating large bodies of information to contribute to robust and broad conclusions and provide a stronger grounding of evidence than reliance on a single study. Systematic reviews take a methodical, reliable and transparent approach to identify relevant studies, using strict inclusion and exclusion criteria and pre-determined search terms. Systematic reviews are comprehensive and of high quality, and less likely to be prone to bias compared to other types of reviews (Siddaway et al., 2019). Reviewing the literature can provide invaluable information about a range of aspects within complex intervention development, such as effectiveness of previous similar interventions (Van Meijel et al., 2004), contextual variables or relevant outcome measures (Richards & Hallberg, 2015). Given the need to unpick psychosocial factors associated with pain in IBD, and to populate the BIS/BAS model, a systematic review was undertaken over another type of review (e.g. scoping review). A previous systematic review conducted by Norton and colleagues (2017) examined previous interventions for abdominal pain management. This demonstrated the heterogeneity and limitations in previous studies and advocated for future interventions to be guided by a theoretical basis.

4.4 Databases used

In selecting relevant databases for this review, it was important to consider not only the topic and research question but how the available databases compare; ensuring that gaps in the coverage of literature in databases are accounted for while minimising considerable overlap (McDonald et al., 1999). The databases selected for this review were EMBASE, Medline, PsycINFO, CINAHL, Web of Science and the Cochrane Library, as well as hand searching through article reference lists. EMBASE was selected as it includes a broad range of articles ranging from psychology to pharmacology, inclusive of English and non-English publications. Medline similarly provides a wide coverage of health and science literature, inclusive of nursing, medicine and clinical science. PsychINFO and CINAHL were selected as more focused databases concerning psychological and nursing/allied-healthcare professional research, respectively. Web of Science was also selected as it includes a multidisciplinary scope of research articles. Finally, the Cochrane Library was included as it a database of high-quality, evidence-based research for patients, healthcare providers and policy makers and covers topics such as...
registered clinical trials and other health interventions, systematic reviews and conference abstracts and proceedings. Collectively, these databases were anticipated to cover a broad range of articles and account for different healthcare professionals and researchers concerned with patient care and the patient experience in IBD.

4.5 Search terms

Selection of search terms needed to ensure that the correct condition, symptom and area of interest were located. This included accounting for acronyms of classifications of IBD (UC, CD) and relevant terms for pain and psychosocial factors. For pain, selection was guided by search terms used in systematic reviews in similar chronic pain research in long-term conditions, such as MS (Harrison et al. 2015a). This included use of both broad and specific pain terms (abdominal pain) and pain outcomes (pain interference). One challenge within this category was to decide whether to include IBS-IBD or irritable bowel syndrome in the search. Pain is a cardinal symptom of IBS, and many patients with chronic pain in IBD will frequently be labelled under a diagnosis of IBS-IBD (Grover et al., 2009). However, for the development of the intervention, it was important to isolate pain and psychosocial processes associated with this symptom rather than a broader set of symptoms. Symptoms of IBS also include diarrhoea, constipation and other functional gastrointestinal symptoms. Therefore, it would be more difficult to isolate psychosocial processes specifically relevant to pain. Furthermore, when running preliminary searches, it was apparent that including IBS in the search criteria would have resulted in a significantly greater number of hits that would be outside the scope of the review. Therefore, it was decided not to include IBS or IBS-IBD in the search criteria. Psychosocial search terms were guided by similar systematic reviews on psychosocial factors associated with symptoms (Artom et al., 2016; Carroll et al., 2016). It was also important to ensure that different aspects of psychosocial factor were accounted for, such as emotional, cognitive and behavioural processes.

4.6 Updated systematic review

4.6.1 Section overview

An updated systematic review was conducted to assess the literature for studies published since the review on psychosocial factors associated with pain in IBD. The same databases and search terms
were used relative to the original systematic review (Sweeney et al., 2018). Publication date was refined to January 2018 to October 2019.

4.6.2 Results of updated review

4.6.2.1 Study section
Databases initially yielded a total of 1,002 studies; Ovid (PsycInfo, Embase, Meldine) (n = 631). CINAHL (n = 0), Web of Science = (n=354), Cochrane Library (n= 17). 111 duplicates were identified and removed, resulting in 891 studies. From 891 full titles screened, 29 relevant abstracts were reviewed, of which 14 full texts were assessed. Four of these were not eligible and four reported papers from one database registry study, resulting in a final seven included studies. The flowchart of studies screened is summarised in Figure 11.

4.6.2.2 Study characteristics
Seven cross-sectional studies were included in the updated review (of which one also included longitudinal analysis), which investigated emotional, cognitive and behavioural factors associated with pain. Most studies included moderate to large sample sizes, ranging from 64-614 individuals with IBD, and ages ranged from 18-88. Five studies reported including a measure of disease activity and all included studies had a greater proportion of females. A summary of the included studies’ references and their key findings are presented in Table 3.

4.6.2.3 Main findings
Similar to the earlier systematic review, depression and anxiety were the most commonly explored constructs, investigated in six and four studies, respectively. Perceived stress, pain catastrophising and perceived social support were also similarly investigated and significantly associated with greater pain. However, in one study, longitudinal data found that only depressive symptoms (compared to perceived social support and pain catastrophising) significantly mediated the effects of pain on pain-related disability (Fretz et al., 2019). Psychosocial factors associated but not identified in the previous systematic review included suicidal ideation, anhedonia and diet-related perceptions and behaviours. Diet-related psychosocial processes associated with pain included negative perceptions of appetite, eating fewer meals, (Coates et al., 2018) and food avoidance (Marsh et al., 2019).
Identification: Online records (PsycInfo, MEDLINE, Embase, Web of Science, CINAHL & Cochrane Library: 1,003

Duplicates removed: 112

Screening: Titles screened: 891

Studies excluded at title: 862

Screening: Abstracts screened: 29

Studies excluded at abstract: 15

Screening: Full texts screened: 14

Studies excluded at full text: 4 (paediatric population n = 1, pain and psychosocial factor results not specified n = 2, IBD population not specified n = 1).

Included: Included in updated review: 7 (4 papers from one database study)

Figure 11 PRISMA flow chart of included studies in updated systematic review
<table>
<thead>
<tr>
<th>Study reference</th>
<th>Study design</th>
<th>Sample N (F/M) (CD/UC) Mean age (SD; range)</th>
<th>Pain measure</th>
<th>Psychosocial measures</th>
<th>Key findings</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Carpinelli et al. (2018)</td>
<td>Cross-sectional</td>
<td>120 IBS (n = 56) IBD (n = 64) (68/52) (34/30). 40.8 (14.5)</td>
<td>Abdominal pain VAS (0-100)</td>
<td>Anhedonia – Snaith Hamilton Pleasure Scale (SHAPS) Depression – Beck Depression Inventory-II</td>
<td>Multivariate regression analysis showed that the SHAPS score was significantly related to current abdominal pain (0-100 VAS) (adjusted B 0.007 (95% CI 0.001-0.14), P = 0.03) independent of gender and age. DAI measured - 69% inactive disease.</td>
<td>Small sample size.</td>
</tr>
<tr>
<td>2.* Coates et al. (2018)</td>
<td>Retrospective</td>
<td>614 (328/286) (420/187) NR</td>
<td>Short Inflammatory Bowel Disease Questionnaire</td>
<td>Survey items on diet Clinical and demographic characteristics collected</td>
<td>Patients with pain had greater negative perceptions of appetite (33 vs 4%) and were eating fewer meals compared to pain free individuals with IBD (p &lt; .001, chi-square). Lower abdominal pain perception were less likely to have anxiety or depression or use anti-depressants (20.9 vs. 63.6%, p&lt;0.01). DAI measured. Patients with pain were more likely to exhibit anxious or depressed states (37.0 vs 15.8%, p &lt; 0.0001). Patients with pain reported more reduction in appetite (25.4 vs.6.1%, p&lt;0.0001). DAI measured. Anxiety and depression were associated with abdominal pain in quiescent IBD and be more likely to use antidepressants. DAI measured.</td>
<td>Non-validated questionnaire to assess diet-related psychosocial processes Measurement of anxiety/depression not provided.</td>
</tr>
<tr>
<td>3. Enns et al. (2018)</td>
<td>Cross-sectional study</td>
<td>964 (IBD = 247, MS = 255, RA =154, Dep/Anx = 307). (729F/235M) 49.2 (14.2)</td>
<td>Medical Outcomes Study Pain Effects Scale (MOS-PES)</td>
<td>Hospital Anxiety Depression Scale Fatigue Impact Scale Work Impairment and Productivity Scale</td>
<td>Pain significantly correlated with fatigue (0.66), anxiety (0.48), depression (0.60), absenteeism (0.35), presenceeism (0.55) and general activity impairment (0.66).</td>
<td>DAI not measured.</td>
</tr>
<tr>
<td>4. Falling et al. (2019)</td>
<td>Cross-sectional online survey</td>
<td>305 (241/61) (201/104) 43.86 (14.76; 18-88)</td>
<td>Numerical Rating Scale PROMIS 4a Nociceptive Pain Quality 5a short forms Pain DETECT</td>
<td>Self-Administered Comorbidity Questionnaire</td>
<td>Identification of three pain sub-groups: mixed mechanism, central mechanism, regional and remission. Depression and anxiety significantly differed between latent class variable of pain phenotypes. Increased prevalence of anxiety and depression in class 1; mixed mechanism. DAI measured.</td>
<td></td>
</tr>
<tr>
<td>5. Fretz et al. (2019)</td>
<td>Cross-sectional (T1)</td>
<td>299 (175/124) (184/106)</td>
<td>McGill Pain Questionnaire</td>
<td>Patient Health Questionnaire PHQ-9</td>
<td>At baseline, pain was associated with catastrophizing (b=0.71, t(277)=10.34, p&lt;.001), depressive</td>
<td>DAI not measured.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>Demographics</td>
<td>Measures</td>
<td>Findings</td>
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<tr>
<td>Longitudinal (T2) (T3)</td>
<td>47.22 (16.27) (135/81) (128/75) (73/45) (76/37)</td>
<td>Pain Disability Index</td>
<td>Pain Catastrophising Scale</td>
<td>Perceived Social Support</td>
<td>Higher pain levels associated with increased odds of suicidal ideation. Multivariate logistic regression pain associated with SI based on PHQ-9 item (OR = 1.14 CI, 1.03, 1.25).</td>
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</table>

NB – NR = not reported. Data derived from Penn State IBD Natural History Registry.
4.7 Discussion

This updated systematic review on psychosocial factors associated with pain identified seven studies and reinforces the role of emotional, cognitive and behavioural factors in IBD-pain. It emphasises the association between pain and negative affect, as well as other negative psychosocial processes such as suicidal ideation, greater perceptions of stress and catastrophising thoughts about pain. The identification of a positive psychological factor, perceived social support, supports the role of protective psychological processes in pain, yet also highlights the limited research investigating positive psychosocial constructs in IBD-pain populations. A larger proportion of studies in the updated review reported a measure of disease activity compared to the previous systematic review. It is important to provide transparency over the disease status of patients to indicate clinical or disease-related factors which may be explaining pain symptoms. Two studies examined the relationship between IBD-pain and diet-related perceptions and behaviours, suggesting that pain has a significant impact on dietary behaviour and nutrition. This parallels with growing research in IBD demonstrating the impact on food-related quality of life (Czuber-Dochan et al., 2019a; Czuber-Dochan et al., 2019b). The predominant investigation around depression and anxiety, mirroring the previous systematic review, highlights the need to investigate more pain-specific emotional, cognitive and behavioural processes in IBD-pain populations to inform the development of a tailored and effective self-management intervention.

The pain outcomes utilised in included studies in the updated review ranged from IBD quality of life sub-measures or visual analogue scales to more comprehensive pain questionnaires, such as the McGill Questionnaire, PROMIS, pain DETECT and Medical Outcomes Study Pain Effects Scale (MOS-PES). While the MOS-PES has not been validated in IBD populations, use of more comprehensive and validated pain outcomes such as this are favoured to encapsulate and more thorough understanding of chronic or functional pain. For example, only measuring pain severity or intensity can risk erroneous prescribing of stronger pain medication or investigative and invasive surgical procedures. Understanding other key aspects around the pain experience, such as pain beliefs or pain-related impact, can guide assessment of psychological comorbidity or psychosocial issues which may be pertinent (Jensen al., 2018). The study by Fretz et al. (2019) demonstrates the key distinction between pain and pain-related disability, and the explanatory role that psychosocial factors (namely depressive symptoms) can have in explaining this relationship. This reinforces the need to target negative
psychosocial processes in an IBD-pain management intervention, to reduce the impact of pain on both emotional and physical functioning.

4.8 Chapter 4 Summary

Both the original and updated systematic review have presented emotional, cognitive and behavioural factors associated with pain in IBD. This includes negative affective processes such as depression, anxiety and stress, as well as pain-specific cognitive and behavioural responses, such as catastrophising thoughts and avoidance. The reviews present potentially protective psychosocial factors negatively associated with pain, which also warrant further investigation. These findings inform a BIS/BAS model of IBD-pain and exploration of psychosocial factors in further research. Limitations of included studies, such as measurements used to assess pain, provide a rationale for the need to better understand psychosocial factors associated with IBD-pain using comprehensive pain measures assessing pain severity and pain-related impact. Additionally, findings suggest the gaps in the literature of psychosocial processes which are yet to be examined in individuals with IBD and pain.
Chapter 5 Cross-sectional study

5.1 Chapter overview

The previous chapter provided a synthesis and critique of the current literature on psychosocial factors associated with pain in IBD. While presenting a number of psychosocial factors to be explored further, the review also highlighted psychosocial processes which have not been studied previously, which may also be important in the context of IBD-pain and can be targeted in an intervention. This chapter provides the manuscript publication for the cross-sectional study: “Developing a better biopsychosocial understanding of pain in inflammatory bowel disease: a cross-sectional study”. Following the manuscript, it provides a more detailed description and rationale for the study methods, including design and recruitment, and the strengths and limitations of these. It provides a rationale for the measures used, including the Brief Pain Inventory as the primary outcome and the selection of psychosocial outcomes to be measured.

The study presented in this chapter is presented in the following article:


All study documents are included in Appendix B.
5.2 Article in press

Title: Developing a biopsychosocial understanding of pain in inflammatory bowel disease: a cross-sectional study

Short title: Biopsychosocial understanding of pain in IBD

Authors: Sweeney, L.¹, Moss-Morris, R.², Czuber-Dochan, W¹, Murrells, T¹ & Norton, C¹.

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Key words: biopsychosocial; inflammatory bowel disease; pain

Conflicts of interest: None
Abstract

**Background:** Pain is frequently reported by patients with inflammatory bowel disease (IBD). Pain in IBD is not fully explained by disease activity or other clinical findings, and a recent systematic review suggested that psychosocial factors have an important role in IBD-pain. The aim of this study was to investigate psychosocial factors associated with pain in IBD.

**Methods:** 297 adults (>16 years) with IBD were recruited from outpatient clinics (n=114) and online (n=183). Participants completed validated questionnaires assessing pain and potential emotional, cognitive and behavioural correlates. Socio-demographic and clinical factors including disease activity were also recorded.

**Results:** 243 (81.8%) of participants reported pain. Of these 243, mean age was 36 years; 153 (63%) had Crohn’s disease (CD), 90 (37%) had ulcerative colitis (UC), and 165 (67.9%) were female. 62.6% reported mild, 31.6% moderate and 5.8% severe pain. 40.3% of participants with pain met established criteria for chronic pain and 18.5% reported opioid use. Female gender, smoking, surgery and steroid use were associated with greater pain severity. Psychosocial factors associated with pain-related interference included depression, catastrophising, fear avoidance, lower self-efficacy and worse mental well-being. Regression models explained 45.6% of the variance in pain severity and 49.7% of pain interference. Psychosocial factors explained 9.5% and 24% of this variance respectively when controlling for demographic and clinical variables.

**Conclusions:** Pain in IBD is significantly associated with cognitive and behavioural factors as well as low mood. This study contributes to a biopsychosocial understanding of pain in IBD and identifies important targets for future interventions.

**Key words:** Pain, IBD, biopsychosocial
Introduction

Pain is a common symptom in inflammatory bowel disease (IBD) and has a significant impact on quality of life. Attenuating pain is a primary target of IBD medical management; abdominal pain severity is routinely assessed in disease activity indices in clinical practice and serves as a key endpoint in IBD clinical trials. During active disease, over two thirds of patients report pain. However, 42-48% of patients will continue to experience pain, despite clinical and endoscopic evidence of quiescent disease. Abdominal pain is the most commonly reported type of pain in IBD, however extra-intestinal manifestations of pain in IBD can be present in the eyes, skin or joints. Pain that is not associated with inflammation, sub-acute obstruction or other disease-related complications in IBD is a clinical challenge, as conventional IBD medical therapy is inappropriate and patients report frustration that pain is not being adequately addressed.

Chronic abdominal pain in IBD is frequently categorised as irritable bowel syndrome (IBS)-type symptoms. Abdominal pain is a cardinal feature of IBS, with Rome IV criteria also including altered stool frequency or stool consistency. Thirty-six percent of people with ulcerative colitis (UC) and 46% with Crohn’s disease (CD) in remission meet the classification for IBS, and a biopsychosocial model of IBS and IBD places these conditions on a functional continuum of gut-brain interactions. However, there is limited evidence to confirm whether key processes and characteristics associated with chronic pain in IBS also apply to IBS-IBD populations. Many treatment approaches in IBS remain untested in the context of IBD-pain. Several key mechanisms identified in IBS and chronic pain research, including positive psychological factors and how individuals respond cognitively and behaviourally to symptoms, are yet to be explored in IBD-pain. While the primary focus of the present study was not IBS in IBD, the IBS literature informed our approach.

Causes of chronic pain in IBD involve both bottom-up (visceral and peripheral) and top-down (central, neurobiological and psychological) factors. Low-grade inflammation can result in the release of cytokines and other key mediators, leading to visceral hypersensitivity. Pain modulation in IBD is also influenced by central mechanisms; a recent small randomised controlled trial showed the ameliorating effects of transcranial direct current stimulation on several pain outcomes up to one week post treatment. Stress and other psychological processes may exacerbate pain by disrupting descending control mechanisms, gut-brain interactions or microbial regulation, or indirectly through adopting...
unhelpful coping behaviours. A recent systematic review showed a number of psychosocial factors associated with pain in IBD, including depression, anxiety and pain catastrophising, as well as protective psychosocial factors of perceptions of social support and control, which are associated with less pain. Coping styles and perceived stress correlated with pain in a large cohort of adults with CD.

Given this complex aetiology, adequate pain management in IBD can be challenging and there is much heterogeneity in interventions tested to date. Chronic opioid use has been shown to increase the risk of hyperalgesia and can lead to deleterious effects on the gastrointestinal tract, including narcotic bowel syndrome and opioid-induced constipation. Treating pain in IBD solely as a biomedical problem can limit therapeutic options and further distress patients. Adjunct psychological support with medical management in IBD can enable patients to manage symptoms and the emotional impact of the disease. Integrated care models in IBD encompassing psychological support have led to reductions in disease burden and healthcare costs.

Not enough is understood around potentially modifiable factors related to pain in adults with IBD. Preliminary research suggests that psychological processes have an important role in IBD-pain. Many previous studies are limited by study design, including limited pain measurement; measures of pain in quality of life or disease activity indices are frequently limited to one item on pain severity. Assessing the impact of pain and pain-specific beliefs, alongside severity, provides a better understanding of chronic or functional pain in IBD. A more detailed understanding of biopsychosocial factors associated with pain in IBD may aid the development of effective interventions. This has been demonstrated in other gastrointestinal and autoimmune diseases, including IBS and pain in multiple sclerosis (MS).

Given these considerations, the aims of this study were to i) identify the prevalence and severity of pain in adults with IBD ii) investigate the influence of sociodemographic, clinical and psychological factors in pain severity and pain-related interference in IBD. Psychosocial factors included positive and negative emotional, cognitive and behavioural factors, as well as constructs identified in chronic pain and IBS populations not yet assessed in IBD-pain.
Materials and Methods

Study design and population

An observational cross-sectional study design was used. Data collection took place January to June 2018. The primary outcomes were pain severity and pain-related interference measured by the Brief Pain Inventory. Inclusion criteria were diagnosis of Crohn’s disease (CD) or ulcerative colitis (UC) for more than 6 months and 16 years or older. Exclusion criteria included insufficient command of spoken English, diagnosis of indeterminate colitis and inability to provide informed consent. Participants were recruited via outpatient clinics and online; clinic participants were recruited consecutively from three National Health Service gastroenterology outpatient clinics in three London-based hospitals and online participants were recruited via the UK Crohn’s and Colitis charity website. Clinic-recruited participants had a clinician-confirmed diagnosis of CD or UC and once consented, completed a paper questionnaire in clinic or at home and then returned their questionnaire by post. Online participants provided consent and completed the questionnaire online (https://www.onlinesurveys.ac.uk/).

Sociodemographic and clinical data collection

The questionnaire included clinical and sociodemographic information, including IBD diagnosis, medication and smoking status, pain medication, pain-related comorbidities, strategies for pain management and classification for chronic pain. This was defined as “pain occurring every day for 3 months within the last 6 months”, which has been utilised in previous chronic IBD-pain research. Disease activity (Harvey Bradshaw Index (HBI) for CD and Simple Clinical Colitis Activity Index (SCCAI) for UC was completed by a clinician or the participant in the clinic and online groups, respectively. A score of < 5 was considered as inactive disease. A stool sample was requested from clinic participants to measure faecal calprotectin, with a score of > 250ug/g used to indicate active disease. Data on IBS and fatigue severity were collected using the IBS symptom severity score and IBD-fatigue questionnaire (Section I).

Study questionnaires

Pain severity and Pain interference
Brief Pain Inventory Short-Form (BPI) was used to assess pain severity and pain interference. Pain severity includes 4 items, including present pain, worst pain, least level of pain and average pain severity in the previous 24 hours, yielding a mean pain severity index score. Pain interference has 7 items, assessing general activity, mood, mobility, work, relationships, sleep and enjoyment of life. A mean severity scoring of 1-3 was classified as mild pain, 4-6 moderate and 7 or more severe pain, using pre-defined cut-offs.

**Depression**

Patient Health Questionnaire-9 (PHQ-9) is a self-report tool for case finding and assessing major depressive disorder. The tool assesses depressive symptoms within the last two weeks, and each item is rated on a 4-point scale reflecting the frequency of the depressive symptom (e.g. ‘never’ to ‘nearly every day’). Scores yield presentation of minimum (PHQ-9 score 0-4), mild (PHQ-9 score 5-9), moderate (PHQ-9 score 10-14), moderate to severe (PHQ-9 15-19) and severe depressive symptoms (PHQ-9 score ≥20).

**Anxiety**

Generalised Anxiety Disorder-7 (GAD-7) assesses probable cases of an anxiety disorder and symptom severity and shows good reliability and validity. Participants are asked how bothered they have been in the previous two weeks by 7 core symptoms, with response items rated 0-3 (‘not at all’ to ‘nearly every day’). The GAD-7 produces a total score of 21, with mild, moderate and severe levels of anxiety symptoms cut offs standing at ≥5, ≥10, and ≥15, respectively.

**Pain Catastrophising**

Pain Catastrophising Scale measures the extent to which patients ruminate, exaggerate or magnify the threat of pain sensations. It is comprised of 13-items measuring rumination, magnification and helplessness. Higher scores reflect a greater tendency to catastrophise about pain, with overall scores ranging from 0-52; 30 or more indicates clinical relevance.

**Cognitive and Behavioural Response to Symptoms**

The Cognitive and Behavioural Response to Symptoms Questionnaire (CBRQ) measures 5 cognitive and 2 behavioural subscales. Cognitive subscales include catastrophising, damaging beliefs, fear avoidance, embarrassment avoidance and symptom focusing. Behavioural subscales include all or
nothing behaviour and avoidance/resting behaviour. As catastrophising was measured elsewhere (see above), the catastrophising scale was removed. Items are rated on a 5-point Likert-scale ranging from ‘strongly disagree’ to ‘strongly agree’. The overall score is calculated from the total of items within subscales. The CBRQ has been used in different illness populations previously, including IBD.33

Stress

Perceived Stress Scale34 assesses participants’ appraisals of potential stressful situations within the previous month. Items require participants to indicate how often they have felt, for example, ‘unable to cope with all the things you had to do’. Ten items are scored on a 5-point scale, yielding an overall score of 0-40; higher scores indicate greater perceived stress, the extent to which the individual has felt overwhelmed by stressful situations within the last month.

Pain self-efficacy

Pain Self Efficacy Questionnaire35 assesses participants’ belief that they are able to accomplish a range of activities, despite their pain. Participants rate the 10 items on how confident they feel in their ability to carry out tasks (7-point scale; ‘not at all confident’ to ‘completely confident’). For example, ‘I can still do many of the things I enjoy doing, such as hobbies or leisure activity, despite the pain’. Total scores range from 0-60, greater scores demonstrating stronger self-efficacy beliefs.

Pain acceptance

Chronic Pain Acceptance Questionnaire (CPAQ-8)36,37 addresses both activity engagement and ‘pain willingness’. Eight items are scored on a 6-point Likert scale from ‘never true’ to ‘always true’, greater scores indicating greater acceptance of pain.

Mental well-being

Mental Health Continuum Short-Form (MHC-SF)38 is a 14-item measure assessing emotional (3 items), psychological (6 items) and social well-being (5 items). It demonstrates excellent internal consistency (Cronbach’s alpha >0.8). Items are rated 0-5 from ‘never’ to ‘every day’, total scores ranging from 0-70. Individuals who answer ‘every day’ or ‘almost every day’ for at least one of the three signs of hedonic well-being and at least six of the eleven signs of positive functioning are considered to have ‘flourishing well-being’. ‘Languishing mental health’ is considered if an individual has answered low levels (‘never’ or ‘once or twice’) to at least one measure of hedonic well-being and at least six measures of positive
functioning. Those who don’t fulfil either ‘flourishing’ or ‘languishing’ mental health are categorised as moderately mentally healthy. Higher scores represent higher levels of mental well-being.

**Dietary behaviour**

Dietary behaviour was assessed by 4 items: ‘I avoid certain food or drinks which I know makes my pain worse’; ‘I skip meals or eating to avoid worsening my pain’; ‘I tend not to eat out or eat socially because of the risk of making my pain worse’; ‘My eating patterns have changed because of my pain’. Cronbach’s alpha demonstrated that the four items have high internal consistency (α = 0.82). Items are rated from 0-4 (strongly disagree to strongly agree), and higher scores indicate greater impact of pain on dietary behaviour, with scores ranging from 0-16.

**Sample size**

According to Cohen[^39] to test a medium sized multiple correlation with 80% power and a significance level of 0.05, a minimum sample size of 107 participants for a regression model with eight independent variables (parameters) would be required. Adding another ten variables would increase the sample size required to about 160. A larger sample size of approximately 300 was proposed to allow for potential sub-group analyses.

**Statistical methods**

Missing data were replaced with imputed values using the Multiple Imputation Chained Equation Method (MICE) in Stata version 15. Overall, 15.6% of all values were missing, 92.9% of the variables had at least one missing value and 93.9% of 297 participants had at least one missing value. All variables in the regression model, except for clinical/demographic variables which had no missing data and some variables with high rates of missing data (faecal calprotectin, stoma/ileo-anal pouch, and BP item 7), were included in the imputation model. Twenty imputed datasets were generated which exceeds the minimum of 10 based on the fraction of missing information[^40]. These data were transferred into SPSS for further analysis.
Exploratory variables were described using frequencies, percentages, means and standard deviations. General psychological measures (depression, anxiety, stress, mental well-being) were compared between the Pain and No Pain groups using an independent two groups t-test.

Multivariable regression analyses examined whether psychosocial factors predicted pain outcomes, after controlling for sociodemographic and clinical factors. Significant factors associated with pain severity or pain interference from univariate analyses were entered into a 3-block multiple regression model (1: sociodemographic, 2: clinical and 3: psychological factors). Regression models were fitted to each of the 20 imputed datasets and then combined to produce averaged estimates, overall statistical tests and measures of fit ($R^2$).

To determine whether the recruitment group (clinic/online) moderated the effect of psychosocial measures on pain severity and interference, the change in fit of the regression model following the addition of the moderating effects to the overall model was tested. If the test of moderating effects was not statistically significant then the data would be analysed as single sample with recruitment group added to the block 1 explanatory variables (see above) in the regression.

The threshold for statistical significance was set at $p < .05$. Analyses were conducted using SPSS version 25.

**Ethical Considerations**

This cross-sectional study was approved by the London-Surrey Border Ethics Committee (17/LO/1527). All participants provided consent before taking part and were given a unique study ID to ensure anonymity.

**Results**

**Descriptives**

A total of 297 participants completed the questionnaire; 183 CCUK-recruited online participants and 114 participants from gastroenterology outpatient clinics. 28 indicated no pain (summed score of 0 on
the BPI Pain Severity) and 269 participants reported some degree of pain (90.6%). 26 participants were removed from the pain group due to incomplete data on pain-specific questionnaires, resulting in 243 participants in the pain cohort for univariate and multivariable analyses. Sociodemographic and clinical data is presented in Table 1. Of the 297 participants, 181 (60.9%) had a diagnosis of CD, 190 (64%) were female and 219 (73.7%) were White-British. Mean age was 36.3 years, with participants on average being diagnosed for 9 years. Mean disease activity score was 6.60 (SD = 5.42) and 4.91 (SD = 3.31) for the HBI and SCCAI, respectively. The most common IBD medication was thiopurines (30.5%).
Table 1. Socio-demographic and clinical profiles of overall cohort (n=297)

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IBD diagnosis (CD/UC)</strong></td>
<td>181/116 (60.9/39.1)</td>
</tr>
<tr>
<td>Gender (Female/Male)</td>
<td>190/107 (64.0/36.0)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White-British</td>
<td>219 (73.7)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>No formal qualifications</td>
<td>11 (3.7)</td>
</tr>
<tr>
<td>Vocational qualifications</td>
<td>17 (5.7)</td>
</tr>
<tr>
<td>School qualifications</td>
<td>37 (12.5)</td>
</tr>
<tr>
<td>Advanced school qualifications</td>
<td>45 (15.2)</td>
</tr>
<tr>
<td>University degree</td>
<td>111 (37.4)</td>
</tr>
<tr>
<td>Postgraduate degree</td>
<td>70 (23.6)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married/civil partnership/living with partner</td>
<td>132 (46.3)</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>35 (11.8)</td>
</tr>
<tr>
<td>Single</td>
<td>116 (39.1)</td>
</tr>
<tr>
<td><strong>Employment status</strong></td>
<td></td>
</tr>
<tr>
<td>Employed full-time</td>
<td>161 (54.2)</td>
</tr>
<tr>
<td>Employed part-time</td>
<td>44 (14.8)</td>
</tr>
<tr>
<td>Full or part-time education</td>
<td>37 (12.5)</td>
</tr>
<tr>
<td>Full-time domestic responsibilities</td>
<td>9 (3.0)</td>
</tr>
<tr>
<td>Retired</td>
<td>19 (6.4)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>20 (6.7)</td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>33 (11.1)</td>
</tr>
<tr>
<td>Previous smoker</td>
<td>64 (21.5)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>198 (66.7)</td>
</tr>
<tr>
<td><strong>Current anti-depressant use</strong></td>
<td></td>
</tr>
<tr>
<td>59 (19.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Previous surgery</strong></td>
<td></td>
</tr>
<tr>
<td>93 (31.3)</td>
<td></td>
</tr>
<tr>
<td><strong>IBD medication</strong></td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>6 (2.0)</td>
</tr>
<tr>
<td>5-ASA</td>
<td>96 (32.3)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>98 (33.0)</td>
</tr>
<tr>
<td>Mecaptapurine</td>
<td>16 (5.3)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>10 (3.4)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>25 (8.4)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>52 (17.5)</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>18 (6.1)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>32 (10.8)</td>
</tr>
<tr>
<td>Budesonide</td>
<td>13 (4.4)</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>11 (3.7)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>36.03 (12.71)</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
<td>9.62 (9.93)</td>
</tr>
<tr>
<td>No. of flares in prior 2 years</td>
<td>3.04 (2.21)</td>
</tr>
<tr>
<td>Disease activity score</td>
<td></td>
</tr>
<tr>
<td>HBI</td>
<td>6.60 (5.42)</td>
</tr>
<tr>
<td>SCCAI</td>
<td>4.91 (3.31)</td>
</tr>
</tbody>
</table>
Participants with pain

There was a significantly higher proportion of females in the group with pain (67.9% female) compared to the group with no pain (25% female). Participants with pain reported a greater number of flares in the previous 2 years and higher disease activity scores (HBI/SCCAI) compared to those reporting no pain. Mean scores and t-tests for psychological factors (non-pain specific) for the pain and no-pain groups are presented in Table 2.

Mean pain severity scores and other pain-related clinical data for the sample of participants with pain (n = 243) are presented in Table 3. One hundred a fifty-two (62.6%) reported mild pain, 77 (31.7%) reported moderate pain and 14 (5.8%) reported severe pain. The most common self-management strategy for pain was heat (49%), followed by exercise (32.5%). 40.3% of participants reporting pain met the criteria for a chronic pain diagnosis. Abdominal pain was the most common location of pain (88.5%). Half of participants reported low back pain and 39.5% reported headache/migraines. Pain medications are presented in Table 3 with paracetamol (35.4%) and opioids (18.5%) being the most commonly used.

Participants with active disease defined by the HBI or SCCAI reported significantly higher scores on pain severity in both CD and UC (p < .05). 75.2% and 75.6% of participants with CD and UC, respectively, scored at least moderate IBS symptom severity. Of the 43 participants with pain who provided a stool sample for faecal calprotectin, 27.9% with quiescent disease reported at least moderate pain.

Overall 27.6% showed 'languishing' mental well-being, 31.3% showed 'flourishing' mental-health and 41.2% were moderately mentally healthy.

Clinic vs Online participants

Differences were identified between participants recruited via the clinic or online. Disease duration was significantly longer in the clinic compared to the online group (12.5 vs. 8.3 years, p=.001). Number of self-reported flares in the prior 2 years (3.5 vs. 2.4, p<.001) and self-reported disease activity scores (HBI: 8.1 vs. 3.5, p<.001; SCCA: 5.8 vs. 3.7, p<.001) were significantly higher in the online participant
Participants recruited online reported significantly higher scores than clinic recruits for pain severity (3.7 vs. 2.7, p = <.001), pain interference (4.4 vs. 3.4, p = .012) and negative psychosocial variables (Supplementary Table 1). A significantly greater proportion of online than clinic participants were on anti-depressants (24.0% vs.13.2%, p=.030), met the classification for chronic pain (48.5% vs. 24.4%, p<.001) and listed co-codamol as their pain medication (17.4% vs. 3.7%, p=.002). Of the online participants with pain, 8.7% and 4.0% of the online cohort had a current stoma or ileo-anal pouch, respectively. There were insufficient data due to missingness to analyse clinic participants with stomas/ileo-anal pouch.

Table 2. Means and standard deviations of pain and general psychological factors in pain and non-pain cohort

<table>
<thead>
<tr>
<th></th>
<th>Pain Cohort (n = 243)</th>
<th>No Pain Cohort (n = 28)</th>
<th>Mean difference, 95% CI, p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General psychosocial measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>Mean (SD)</td>
<td>10.66 (6.97)</td>
<td>4.36 (5.86)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8.28 (5.91)</td>
<td>4.27 (5.26)</td>
<td>4.01, -6.30 to -1.71, p=.001*</td>
</tr>
<tr>
<td>Stress</td>
<td>22.88 (7.82)</td>
<td>15.93 (6.37)</td>
<td>6.95, -9.92 to -3.90, p&lt;.001*</td>
</tr>
<tr>
<td>Mental well-being</td>
<td>39.11 (15.97)</td>
<td>45.18 (16.14)</td>
<td>-6.07, -0.01 to 12.53, p=.050</td>
</tr>
<tr>
<td><strong>Pain-specific measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain self-efficacy</td>
<td>32.67 (15.65)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain catastrophizing</td>
<td>18.58 (13.06)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain fear avoidance</td>
<td>12.12 (5.41)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom focusing</td>
<td>12.79 (5.89)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embarrassment avoidance</td>
<td>10.44 (6.90)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All or nothing behaviour</td>
<td>9.78 (5.47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidance resting</td>
<td>13.32 (7.26)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain acceptance</td>
<td>27.16 (5.06)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant at p<.05
Insert Table 3. Pain-related characteristics of overall cohort (n=243)

<table>
<thead>
<tr>
<th>Pain-related factors</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Severity (mean, SD)</td>
<td>3.33 (1.96)</td>
</tr>
<tr>
<td>Pain Interference (mean, SD)</td>
<td>4.06 (2.92)</td>
</tr>
<tr>
<td>No. of Pain Locations</td>
<td>3.52</td>
</tr>
<tr>
<td>Pain severity rating:</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>152 (62.6)</td>
</tr>
<tr>
<td>Moderate</td>
<td>77 (31.7)</td>
</tr>
<tr>
<td>Severe</td>
<td>14 (5.8)</td>
</tr>
<tr>
<td>Chronic Pain Diagnosis</td>
<td>98 (40.3)</td>
</tr>
<tr>
<td>Pain Medications:</td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>86 (35.4)</td>
</tr>
<tr>
<td>Co-codamol</td>
<td>31 (12.8)</td>
</tr>
<tr>
<td>Opioid</td>
<td>45 (18.5)</td>
</tr>
<tr>
<td>Antispasmodic</td>
<td>12 (4.9)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>11 (4.5)</td>
</tr>
<tr>
<td>Pregabalin/Gabapentin</td>
<td>7 (2.9)</td>
</tr>
<tr>
<td>Pain-related conditions:</td>
<td></td>
</tr>
<tr>
<td>Low back pain</td>
<td>122 (50.0)</td>
</tr>
<tr>
<td>Migraine/Headache</td>
<td>96 (39.5)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>51 (21.4)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>20 (8.2)</td>
</tr>
</tbody>
</table>

Univariate analyses

Univariate analyses of sociodemographic and clinical factors associated with pain are presented in Supplementary Tables S2-4. Greater pain severity scores were associated with female gender and previous surgery. Anti-depressant use was significantly associated with pain interference. Steroid use (prednisolone) was significantly associated with greater pain severity and interference. Azathioprine and methotrexate were significantly associated with greater pain interference. No other IBD medication was significantly associated with pain outcomes. Current smoking, employment and education status were all significantly associated with pain outcomes (p < .05). Higher educational attainment and being employed was associated with less pain severity. Dummy variables were created for low educational attainment and unemployed or retired for multivariable analyses. Fatigue significantly correlated with pain severity (r = 0.49) and pain interference (r = 0.42).

Pearson correlations of psychosocial factors associated with pain are presented in Supplementary Table S4. Pain severity significantly correlated with all psychological factors. Pain interference
significantly correlated with all psychological factors, excluding pain acceptance. Greater pain severity and interference were associated with greater impact on dietary behaviour \( r = 0.32 \) and \( r = 0.39 \), respectively).

*Multivariable analyses*

Collinearity diagnostics revealed significant intercorrelations between some independent regression variables. The final set of independent variables selected for multivariate analyses did not violate multicollinearity assumptions (VIF < 2, condition index < 30).

The addition of the six moderators (effect of recruitment group on the relationship between psychosocial factors and pain) did not improve the fit of either model. In both cases the F-test was not statistically significant (Pain severity: \( F[6, 201] = 1.16, p = .39 \), pain interference: \( F[6, 201] = 1.23, p = .29 \)). Changes in the \( R^2 \) were small (Pain severity: 45.6% to 47.4% \( \Delta = 1.8\% \), Pain interference: 49.7% to 51.5% \( \Delta = 1.8\% \)). A decision was therefore taken to drop the moderating effects whilst retaining source of recruitment in the main effects model.

Multivariable analyses of pain severity and pain interference are presented in Tables 4 and 5 respectively.

For pain severity the addition of psychosocial factors to the regression model containing sociodemographic and clinical factors was statistically significant \( F(18, 225) = 9.429, p < .001 \). Sociodemographic factors explained 17.6% of the variance in pain severity in the overall model. Clinical factors explained an additional 17.9% and psychosocial factors explained a further 9.5% of the variance in pain severity. The overall model explained 45.6% of the variance in pain severity.

For pain interference, the addition of psychosocial factors to the model was statistically significant \( F(18, 225) = 11.110, p < .001 \). Socio-demographic factors explained 8.9% of the variance in pain interference, and clinical factors explained an additional 16.2% of the variance. Psychological factors explained a further 24% of the variance in pain interference. The overall model explained 49.7% of the variance in pain interference.
Table 4 Multivariable regression analyses of socio-demographic, clinical and psychological factors predicting pain severity in pain cohort (n=243)

<table>
<thead>
<tr>
<th>Pain Severity</th>
<th>Block 1</th>
<th></th>
<th>Block 2</th>
<th></th>
<th>Block 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B**</td>
<td>95% CI</td>
<td>ΔR²</td>
<td>B**</td>
<td>95% CI</td>
<td>ΔR²</td>
</tr>
<tr>
<td>Socio-demographic</td>
<td>-0.00</td>
<td>-0.021, 0.021</td>
<td>0.176</td>
<td>-0.021, 0.017</td>
<td>0.179</td>
<td>-0.010, 0.029</td>
</tr>
<tr>
<td>Age</td>
<td>-0.00</td>
<td>-0.021, 0.021</td>
<td>0.176</td>
<td>-0.021, 0.017</td>
<td>0.179</td>
<td>-0.010, 0.029</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>-0.50</td>
<td>-0.76, -0.24</td>
<td>-0.36</td>
<td>-0.83, 0.10</td>
<td>-0.40</td>
<td>-0.83, 0.042</td>
</tr>
<tr>
<td>Unemployed/retired</td>
<td>1.30</td>
<td>0.55, 2.03</td>
<td>0.79</td>
<td>0.11, 1.47</td>
<td>0.43</td>
<td>-0.22, 1.09</td>
</tr>
<tr>
<td>Low Educational Attainment*</td>
<td>0.49</td>
<td>0.20, 0.79</td>
<td>0.17</td>
<td>-0.35, 0.69</td>
<td>-0.14</td>
<td>-0.65, 0.36</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.89</td>
<td>0.50, 1.28</td>
<td>0.63</td>
<td>-0.073, 1.34</td>
<td>0.55</td>
<td>-0.12, 1.23</td>
</tr>
<tr>
<td>Recruitment Group</td>
<td>1.08</td>
<td>0.82, 1.34</td>
<td>0.36</td>
<td>-0.14, 0.85</td>
<td>0.30</td>
<td>-0.19, 0.79</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>-0.30</td>
<td>-0.79, 0.20</td>
<td>-0.25</td>
<td>-0.72, 0.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azathoprine</td>
<td>0.10</td>
<td>-0.60, 0.80</td>
<td>0.12</td>
<td>-0.55, 0.79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>-0.31</td>
<td>-0.78, 0.17</td>
<td>-0.34</td>
<td>-0.79, 0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous surgery</td>
<td>0.38</td>
<td>-0.78, 1.54</td>
<td>0.13</td>
<td>-0.96, 1.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAI score (HBI/SCCAI)</td>
<td>0.28</td>
<td>-0.24, 0.81</td>
<td>0.25</td>
<td>-0.26, 0.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain catastrophising</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Pain self-efficacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fear avoidance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Damage beliefs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All or nothing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative R²</td>
<td>0.176</td>
<td></td>
<td>0.355</td>
<td></td>
<td>0.451</td>
<td></td>
</tr>
</tbody>
</table>

*below GCSE educational attainment, ** unstandardised beta, ΔR² = R-squared change, significant coefficients highlighted in bold
Table 5. Multivariable regression analyses of socio-demographic, clinical and psychological factors predicting pain interference in pain cohort (n=243)

<table>
<thead>
<tr>
<th>Pain-related interference</th>
<th>Block 1</th>
<th>Block 2</th>
<th>Block 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B**</td>
<td>95% CI</td>
<td>ΔR²</td>
</tr>
<tr>
<td>Socio-demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.01</td>
<td>-0.044, 0.023</td>
<td>.089</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>-0.33</td>
<td>-1.14, 0.47</td>
<td>-0.20</td>
</tr>
<tr>
<td>Unemployed/retired</td>
<td>1.34</td>
<td>0.24, 2.56</td>
<td>-0.13</td>
</tr>
<tr>
<td>Low Educational Attainment*</td>
<td>0.41</td>
<td>-0.46, 1.30</td>
<td>1.49</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.14</td>
<td>0.34, 1.97</td>
<td>0.23</td>
</tr>
<tr>
<td>Recruitment Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>0.23</td>
<td>-0.89, 1.36</td>
<td>-0.31</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>-0.31</td>
<td>-1.071, 0.46</td>
<td>0.23</td>
</tr>
<tr>
<td>Azathoprine</td>
<td>1.89</td>
<td>-0.074, 3.86</td>
<td>-0.31</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>-0.007</td>
<td>-0.83, 0.82</td>
<td>1.89</td>
</tr>
<tr>
<td>Previous surgery</td>
<td>1.203</td>
<td>0.82, 1.59</td>
<td>0.23</td>
</tr>
<tr>
<td>DAI score (HBI/SCCAI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>0.120</td>
<td>0.063, 0.18</td>
<td>0.120</td>
</tr>
<tr>
<td>Pain catastrophising</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain self-efficacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fear avoidance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Damage beliefs</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>All or nothing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative R²</td>
<td>.089</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*below GCSE educational attainment, ** unstandardised beta, ΔR² = R-squared change, significant coefficients highlighted in bold
Discussion

This study aimed to develop a better biopsychosocial understanding of pain in adults with IBD. Results demonstrate that pain is a prevalent problem and that emotional, cognitive and behavioural processes are associated with pain in addition to demographic and disease processes (findings summarised in Figure 1). Psychosocial processes explained an additional 9.5% and 24% of pain severity and pain interference, respectively. Although complete elimination of pain may not be possible due to the relapsing remitting nature of IBD, targeting potentially modifiable psychological factors related to pain severity and interference may be of value to improve functioning and quality of life.

Over a third of participants with pain reported at least moderate pain severity, and a substantial number of participants had chronic pain and were on anti-depressants. Previous use of the BPI in an IBD population has shown similar distributions for mild, moderate and severe pain\textsuperscript{28}, however a lower proportion of individuals in this study reported no pain (9.4%). After paracetamol, opioids were the most frequently listed medication for pain, used by 18.5% of individuals with pain. This supports increasing trends of opioid prescription evident in non-cancer pain in the UK\textsuperscript{41}. Research demonstrates the adverse effects of prolonged opioid use in IBD, including dose-dependent effects on morbidity and mortality and greater healthcare utilisation\textsuperscript{42}. In a US study of Crohn’s disease (CD), 37% of patients diagnosed with concomitant functional symptoms were misusing opioid medication, measured by a prescription monitoring programme\textsuperscript{43}. Clearer defined prescribing criteria for clinicians and greater awareness and support for patients are vital to reduce use of opioids in IBD.

Emotional factors including depression and anxiety were associated with increased pain severity and interference. Pain is likely a distressing experience for people with IBD. In turn, a top-down affective dimension in pain processing may create a vicious cycle of pain and distress \textsuperscript{3}. Although acute stress has a role in buffering noxious input (facilitating a ‘fight or flight’ response), chronic stress, worrying and hypervigilance may disrupt descending inhibitory control mechanisms, enhancing the experience of pain\textsuperscript{3}. A bi-directional association between depression and visceral pain in IBD may be explained by dysregulated signaling along the gut-brain axis\textsuperscript{44}. Microbial exposure and regulation in response to psychosocial stressors is another recognised mechanism explaining the interaction between persistent inflammation and depression\textsuperscript{45}. 

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To our knowledge, this is the first study in IBD to show an association between pain and certain positive psychological constructs, namely pain self-efficacy and psychological well-being. Alongside identifying psychosocial risk factors that are anticipated to exacerbate pathology, understanding positive psychological processes may be of equal value in the aim of preventing or reducing pain-related distress and disability. Self-efficacy, defined as an individual’s perceived ability to carry out behaviours to meet a goal or outcome, is a widely empirically-supported mechanism in the context of adopting new health behaviours, adjusting beliefs or engaging in helpful coping strategies. It has been associated with less impairment and distress in chronic pain, and improved outcomes in adult and child IBD populations. Greater psychological well-being or optimism may be another important construct in increasing one’s likelihood of engaging in helpful coping strategies. In support, levels of gratitude in IBD have significantly predicted lower depression in a longitudinal study. These positive psychological factors may serve as ‘resilience mechanisms’ facilitating adjustment in chronic illness and buffer the impact of symptoms. Understanding both risk factors and resilience factors in IBD may help to identify patients who exhibit ‘low resilience’ and may be more likely to develop functional symptoms. Self-efficacy and psychological well-being, among other positive psychological constructs, can be targeted in interventions through building of self-confidence, control and self-management skills.

An association between greater pain and fear avoidance and catastrophising about pain echoes findings in previous IBD studies, with the latter shown to predict functional disability in adolescents with IBD. Other cognitive-behavioural responses to symptoms associated with pain identified in this study included symptom focusing, beliefs that symptoms are sign of damage, all or nothing and avoidance-resting behaviours in response to symptoms, which have not previously been investigated in IBD-pain populations. It is thought that avoidant thoughts and behaviours may lead to the development of chronic pain by an increasing fear of movements and inactivity, leading to disability, lethargy and low mood. All or nothing behaviours refer to cyclical periods of intense activity when feeling well, leading to burn-out, over-exhaustion and prolonged periods of rest. Setting realistic goals for daily activity rather than being governed by symptoms may be a helpful strategy, such as through graded activity and exposure techniques. Identification of pain-specific cognitive and behavioural processes in this study builds on a biopsychosocial understanding of IBD-pain and further identifies important treatment targets for future pain management interventions in IBD.
The lack of association between pain acceptance and outcomes is inconsistent with previous research. Pain acceptance has shown significant associations with resilience and less negative mood in chronic IBD-pain populations. Illness acceptance has been shown to predict personal growth, relationship satisfaction and life satisfaction. Mindfulness interventions, of which acceptance is a key tenant, have shown positive outcomes in IBD-patients with functional abdominal symptoms. A lack of an association in this study may be explained by the use of a chronic pain acceptance questionnaire with a sample who did not all meet chronic pain criteria. Alternatively, it may be that pain acceptance is more strongly associated with improvements in mood and quality of life rather than influencing pain outcomes directly. Both pain and illness acceptance warrant further investigation in IBD.

Female gender, current smoking status and steroid use were significantly associated with pain outcomes, consistent with previous research. Moreover, the study demonstrated significantly greater levels of pain, distress and disease activity in the online-recruited cohort. This suggests that the online community may be particularly vulnerable and a key target sub-population for an intervention. Recently, a meta-analysis examined the differences in CBT trial results in individuals recruited in clinical services compared to open community recruitment, where participants self-refer to take part in studies. In 53 comparisons of internet-based CBT versus waitlist control, open community recruited populations demonstrated greater reductions in anxiety symptoms, which were partly explained by greater treatment adherence and stricter exclusion of severe depression in open community groups. This, and our study findings, suggest that online self-referring individuals may be more likely to present higher pain and distress, and possibly engage and benefit more from psychological interventions. However, recruiting from an online source only may limit generalisability to a ‘clinical’ population.

Significant associations between disease activity and pain suggests that disease management should remain a key therapeutic target when pain is reported. However, the use of self-reported indices to measure disease activity in this study may be conflated by affective distress. A recent study showed that 29% of IBD patients with histological and colonoscopy-confirmed quiescent disease were erroneously classified as having active disease through the use of HBI/SCCAI, and fulfilled for Rome III criteria for IBS. Faecal calprotectin was not associated with pain in a sub-set of participants in this study, further highlighting the complex relationship between symptom reporting and pathophysiology in IBD. Inconsistencies between clinical and endoscopic biomarkers of both pain and disease activity in
IBD have been highlighted previously\(^3\) and support the use of objective and subjective markers, as well as validated patient report outcomes, to guide clinical decision-making.

An impact of pain on dietary behaviours identified in this study aligns with other work in IBD demonstrating the negative effects of abdominal pain on facets of eating or eating behaviour\(^{61}\). Future studies could explore whether regulating eating behaviours and assisting with smoking cessation helps to improve pain outcomes. Similarly, withdrawal from opioids could be considered. Pain was also associated with IBS severity scores and fatigue, reinforcing an overlap in symptomology\(^3\) and symptom clustering in IBD\(^{62}\).

The results of this study echo psychological processes identified in IBS and pain associated with other long-term conditions. Gastrointestinal-specific anxiety and illness cognitions have been identified as key mechanisms of treatment in IBS\(^{63}\); one study examining the effects of a brief cognitive behavioural therapy (CBT) intervention found a significant decrease in catastrophising, damaging beliefs and fear avoidance measured by the CBRQ\(^{64}\). Distress, catastrophising and fear avoidance were significantly associated with pain severity and interference in MS-pain\(^{20}\). Similar findings in this study suggest that addressing emotions and pain-specific cognitions and behaviours may be important in reducing pain severity and impact in IBD. These processes underpin techniques used in CBT. CBT has a good evidence base in IBS\(^{65,66}\) and chronic pain\(^{67}\) and growing evidence base in IBD, showing improvements in quality of life and other psychological outcomes\(^{68,69}\).

There are several limitations in this study. Firstly, self-reported disease activity was measured for the online cohort, and this group of individuals may have been self-selecting with pain, whereas participants in clinic were approached consecutively. This may explain the higher scores for disease activity, pain and psychological factors in the online group. Although this study aimed to provide an objective measure of disease activity in clinic-recruited participants, only a small sub-set of participants returned samples, therefore faecal calprotectin levels were not included in the multivariable analysis. This study did not measure sensory testing, mucosal signaling molecules relevant to pain (TRPV1) or other physiological markers. Finally, the cross-sectional nature of the study limits conclusions regarding the direction of causality between pain and psychological factors.
Future research on pain in IBD should assess pain severity, disability and pain-related beliefs using validated pain tools. Studies of longitudinal design should aim to examine the effects of psychological factors on pain severity and impact over time. Inclusion of objective markers of disease activity and other physiological markers of pain can strengthen further studies in understanding the interaction between psychological, central and peripheral processes.

Figure 1. What does this study add?

<table>
<thead>
<tr>
<th>What do we know already?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain is a common symptom of IBD</td>
</tr>
<tr>
<td>Over a third of people with IBD continue to report pain in remission, defined by clinical and endoscopic markers</td>
</tr>
<tr>
<td>Pain is understood as a biopsychosocial problem, involving neurobiological, peripheral factors and central factors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>What does this study add?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many patients experience pain which is chronic and report the use of opioids and anti-depressants</td>
</tr>
<tr>
<td>Emotions, cognitions and behaviours are significantly associated with pain severity and pain-related interference in IBD, including pain-specific cognitions and behaviours</td>
</tr>
<tr>
<td>Positive psychological factors, namely pain self-efficacy and positive psychological well-being, are associated with less pain</td>
</tr>
<tr>
<td>Results suggest that addressing emotions and pain-related cognitions and behaviours are important treatment targets for future pain management interventions in IBD</td>
</tr>
</tbody>
</table>
References


61. Coates MS, C; Navabi, S; Williams, E. Abdominal Pain in Inflammatory Bowel Disease Impacts Dietary Habits Independently of Inflammation. *Gastroenterology*. 2018;154(6):S-413.


5.3 **Rationale for cross-sectional design**

Cross-sectional studies provide an insight into a given population of individuals to explore certain outcomes and associations. Although this is measured at a single time point, they allow for multiple hypotheses to be tested, given the inclusion of multiple independent and dependent measures that can be explored (Mann, 2003). Moreover, they are relatively easy, quick and a cost-effective way of collecting data and negate any risk of loss of follow-up of participants (Sedgwick, 2014). To develop an understanding of psychosocial factors associated with pain in IBD, a cross-sectional study design was chosen to test the association of selected psychosocial factors with IBD-pain, based on the systematic review, theoretical model (BIS/BAS) and supporting research in IBD, IBS and chronic pain. This aimed to guide intervention development and build a theoretical model of IBD-pain by testing specific independent variables and their relationship with pain severity and interference in a sample of adults with IBD. This study design also provided an opportunity to understand the prevalence and sociodemographic and clinical characteristics associated with pain in IBD. Examining psychosocial factors and pain longitudinally would have allowed for robust exploration of the impact long-term, however this study design was not feasible within the thesis timeline.

5.4 **Rationale for recruitment methods and sources**

To optimise wide recruitment of individuals with IBD, two recruitment methods were selected. This included recruiting participants from three tertiary care London-based hospitals, where individuals were approached during an IBD outpatient clinic. However, it was argued that sole use of this recruitment method may risk inclusion of more acutely unwell or clinically complex patients and thus not necessarily generalisable to an overall IBD population. Therefore, it was also decided to recruit participants online through an IBD charity forum (Crohn’s and Colitis UK). This would consequently result in a wider outreach to individuals with IBD who are not attending central London and teaching hospitals, but also accessing those who may have functional difficulties attending hospitals during the recruitment period for this study. The advantages of reaching out to online communities in IBD has been explored and summarised previously (Long et al., 2012; Coulson, 2013; Coulson, 2015a; Coulson, 2015b). Therefore, the two recruitment methods were chosen to optimise the generalisability of the study sample to the wider IBD population.
However, limitations to this decision included that online participants may have been self-selecting compared to a consecutive approach carried out in outpatient clinics. Furthermore, online participants were required to provide their own confirmation of a diagnosis of IBD and complete a self-reported disease activity rating rather than completion by a clinician. However, this recruitment method has been used across a number of studies in IBD, which have similarly used items on patient-reported disease activity (Jones, 2007; Taft, 2009; Moradkhani et al., 2011).

5.5 Study questionnaires (presented in Appendix B)

5.5.1 Pain and psychosocial measures

5.5.1.1 Brief Pain Inventory

The Brief Pain Inventory (BPI) (Cleeland & Ryan, 1994) was selected as the primary outcome measure to assess pain in the cross-sectional study. It measures pain severity and pain-related interference. This is important, as assessment of the pain experience in patients requires consideration beyond pain severity, including perceived functional impact. Pain intensity is comprised of four items, assessing pain levels currently, on average, at its worst and at its least level, and is scored from a rating of 0-10 with higher scores indicating greater severity of pain. Pain-related interference is divided into 7-items, measuring aspects such as impact of pain on general activity, mood, relationships and sleep. These are also rated from 0-10 with greater scores indicating greater impact of pain. The BPI also includes a body diagram for completers to indicate where they experience pain, an item assessing the extent to which pain medication has provided symptom relief and an initial screening item (this latter optional item was removed as it is not included in the psychometric testing as stated by the BPI manual).

The BPI pain severity and interference items have demonstrated good construct and criterion validity and acceptable to excellent test-retest reliability (Keller et al., 2004; Mendoza et al., 2006; Erdemoglu & Koc, 2013). While the BPI was initially developed for cancer-related pain, it has been used for a wide range of pain studies; it has demonstrated good validity across several languages (Cleeland, 2009) and excellent internal consistency and test re-test values in a sample of people with IBD (Jelsness-Jørgensen et al., 2016). The BPI has demonstrated high correlations with quality of life bodily pain dimensions (eg, SF-36) as well as items on UC and CD disease activity indices such as the SCCAI and SCDAI (Jelsness-Jørgensen et al., 2016). The BPI is recognised as a comprehensive measure in the
field of acute pain conditions or pain related to a chronic disease condition (Turk et al., 2016) and is advocated as an established outcome measure by the British Pain Society (BPS, 2019). The BPI is also recommended by the Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT) for chronic pain clinical trials (Dworkin et al., 2005). Other valid pain questionnaires, such as the McGill or Pain Detect questionnaires were not selected as the primary outcome, as these take a greater focus on assessing the pain quality, location or pattern of pain, which was not the primary research question of interest. The BPI also provides a clear layout and succinct questionnaire length and structure, which is user-friendly and feasible to use in clinical and online settings.

5.5.1.2 Patient Health Questionnaire

The Patient Health Questionnaire (PHQ) 9-item (Kroenke et al., 2001) version was used to measure depressive symptoms. This measure is used extensively both in research and primary and secondary care settings for screening and assessment. The PHQ-9 version is a brief measure which can be completed in less 5 minutes and can be used as a diagnostic measure of major depression and other disorders, based on the *International Classification of Diseases* (10th Edition, ICD-10) and *Diagnostic and Statistical Manual of Mental Disorders* (4th Edition, DSM IV, American Psychiatric Association, 1994) (Lowe et al., 2004). The PHQ-9 can also measure worsening or improvement of depressive symptoms over time. The 9 items assess the number of days in the previous two weeks that the individual has been bothered by the items, such as ‘poor appetite or overeating’, ‘feeling down, depressed or hopeless’. The PHQ-9 also has a suicidal ideation item of ‘thoughts that you would be better off dead or hurting yourself in some way’. As a screening tool, using a cut-off point of 11, the PHQ-9 has demonstrated 95% sensitivity and 88.3% specificity in adults with MS and depression (Patrick & Connick, 2019). It is considered an effective and quick measure of assessing depression in adults (Spitzer et al., 2014). A scoring of 10 points or greater is considered a ‘yellow flag’ and possible clinical significance, and 15 points indicating individuals which actively require treatment or intervention. The PHQ-9 has been use in IBD populations (Byrne et al., 2017), including as a measure of suicidal ideation assessment (Lister et al., 2018), and is used as a core outcome measure for depression in Improving Access to Psychological Therapies (IAPT) services in the UK.
5.5.1.3 Generalised Anxiety Questionnaire

The General Anxiety Questionnaire 7-item version (GAD-7) was used to measure anxiety (Spitzer et al., 2006). This is an effective and quick measure to screen and measure anxiety, and has been used in primary care (Ruiz et al., 2011), the general population (Löwe et al., 2008) and a number of anxiety disorders, including anxiety disorder, social and panic phobia and post-traumatic stress disorder (Kroenke et al., 2007; Williams, 2014). Items include the extent to which, over the previous two weeks the individual has been feeling ‘bothered’, ‘anxious’, ‘worry too much’ and ‘having trouble relaxing’. Research has demonstrated sensitivity and specificity of the GAD-7 as 89% and 82%, respectively. The GAD-7 has also been used in IBD research (Byrne et al., 2017; Bernstein et al., 2018; Jordan et al., 2019) and other long term conditions such as MS (Cooper et al., 2011) and cardiovascular disease (Glozier et al., 2013) and is used as a core outcome measure for anxiety in IAPT services in the UK (Clark, 2011). A scoring of between 10-14 and 15 indicates moderate and severe levels of anxiety symptoms, respectively (Spitzer et al., 2006).

5.5.1.4 Pain Catastrophising Scale

The Pain Catastrophising Scale (PCS) (Sullivan et al., 1995) was used to measure catastrophising thoughts, which is thought to serve as a key mediator between pain and pain-related disability (Besen et al., 2017). The PCS is comprised of 13-items and three subscales, rated on a five-point scale (0 = not at all, 5 = all the time). Items refer to rumination, magnification and helplessness in appraising the threat value of a pain stimulus. Higher scores indicate greater pain catastrophising and total score of 30 or above represents clinically relevant levels of catastrophising (representing the 75th percentile of score distribution in chronic pain samples) (Sullivan et al., 1995). The measure has demonstrated validity, reliability and internal consistency (Osman et al., 1997) and has been translated into several non-English speaking languages (Leung, 2012). It is used widely in research and clinical practice as a quantitative measure of the pain experience and has demonstrated internal consistency to an adequate to excellent level (Sullivan et al., 1995; Osman et al., 1997). The measure has been applied to abdominal pain research in paediatric IBD research (Wojtowicz et al., 2014) as well as chronic MS-related pain (Harrison et al., 2015b).
5.5.1.5 Cognitive and Behavioural Responses to Symptoms Questionnaire (CBRQ)

The CBRQ is a 42-item questionnaire consisting of five cognitive and two behavioural subscales, measuring different responses to symptoms. The measure can be modified to refer to the symptom in question (pain), with the five cognitive sub-scales referring to symptom focusing, fear avoidance, beliefs that symptoms are a sign of damage to the body (damage beliefs), embarrassment avoidance and catastrophising thoughts. Two behavioural subscales are all or nothing behaviours and avoidance resting behaviours. Internal reliability of the measure has been demonstrated as acceptable in a prior study (Skerrett & Moss-Morris, 2006). Items are rated on a five-point scale ranging from never or strongly disagree (0) to all the time or strongly agree (4). The measure has been applied across a wide range of conditions and chronic symptoms, including fatigue in IBD (Artom et al., 2017a) and MS (Skerrett & Moss-Morris, 2006; Knoop et al., 2012; Casey et al., 2016; Carroll et al., 2019) and IBS (Chilcot & Moss-Morris, 2013). This measure was used as a measure to identify in more depth potential cognitive and behavioural processes associated with IBD-pain which may be targeted in an intervention. As the Pain Catastrophising Scale was utilised as a more comprehensive measure, this cognitive subscale was removed from the CBRQ for this study.

5.5.1.6 Perceived Stress Scale

The Cohen Perceived Stress Scale (Cohen et al., 1983) is a measure used to assess an individual’s cognitive and emotional appraisal of situations as stressful within the last month. The measure is comprised of 14-items, ranging from 0 (never) to 4 (very often), with total scores ranging from 0-56 and higher scores indicating greater perceived stress. This is summarised by reverse scoring negative items and adding positively stated items. It was designed for use in community samples and has shown good test-retest and internal validity (Langhorst et al., 2013). In IBD, this measure has been used extensively in measures of stress and symptom activity (Levenstein et al., 1994; Bernstein et al., 2016; Sexton, 2017), including studies on CD patients where a total scoring of more than 21 was used to signify high perceived stress (Bitton et al., 2008; Langhorst et al., 2013).

5.5.1.7 Pain Self-Efficacy

The pain self-efficacy (PSE) questionnaire (Nicholas, 1989) measures the extent to which an individual believes in their ability to carry out their goals and social activities, despite their pain. It was developed based on Bandura’s social cognitive theory of self-efficacy (1977) and has been used extensively in
chronic pain studies and in various countries and clinical settings (Nicholas, 2007). The measure consists of 10-items measured on a 7-point scale (0 = not at all confident, 6 = completely confident). A total score is computed by a sum of the 10 items yielding a maximum score of 60, indicating greater self-efficacy beliefs. Items concern general activities such as ability to carry out household chores, enjoying hobbies or leisure activities or living a normal lifestyle, despite the pain. Findings from numerous studies have demonstrated the psychometric properties of the pain self-efficacy questionnaire, including test-retest reliability, internal consistency and validity (Nicholas, 2007). Pain self-efficacy has been recognised as a resiliency factor associated with improved functional outcomes (Stewart & Yuen, 2011) and in several studies is associated with low intensity and unpleasantness rating of pain and less disability (Edwards et al., 2016). Moreover, pain self-efficacy has been identified as a mechanism of change in CBT-related improvements in pain and related disability, and therefore is deemed as an important process variable for intervention studies (Costal et al., 2011; Edwards et al., 2016). The PSE demonstrates strong correlations with corresponding pain measures such as coping and pain-related disability (Nicholas, 2007).

5.5.1.8 Chronic Pain Acceptance

The chronic pain acceptance 8-item questionnaire (CPAQ-8) (Fish et al., 2010) was used to measure pain acceptance. This is a shorter version of the original 20-item questionnaire (McCracken et al., 2004), which has two subscales of activity engagement - the extent in which an individual engages in activities despite having pain and pain willingness - the degree to which a person abstains from attempt to control or avoid the pain. The shortened 8-item measure demonstrates shows good psychometric properties and original two-factor structure as per the extended 20-item version through confirmatory factor analyses (Fish et al., 2010; Baranoff et al., 2014; Rovner et al., 2014), including evidence of test-retest reliability and validity (Fish et al., 2013). The 8-items are scored from 0-6 (never true to always true) and include items such as ‘I lead a full life even though I have chronic pain’ and ‘I avoid putting myself in situations where my pain might increase’. Scores range from 0 to 48 with higher scores indicating greater pain acceptance. The CPAQ-8 has been applied and validated in a number of chronic pain studies (Fish et al., 2010; Fish et al., 2013; Rovner et al., 2014; Baranoff et al., 2014). The CPAQ was included as pain acceptance has been proposed as a ‘resilience mechanism’ that can be mapped onto intervention techniques (Goutbert & Trompetter, 2017) particularly with reference to the ‘sustainability’ (rather than ‘recovery’) aspect of resilience. While it was noted that there is some overlap between
CPAQ and pain self-efficacy questionnaire, as they are both addressing engagement of activities and functioning despite the presence of pain, it is argued that they take different approaches. Pain self-efficacy addresses one’s confidence in the ability to these tasks, whereas the CPAQ is measuring one’s engagement in activities despite the presence of pain and the ability to disengage with their thoughts about their pain and parking those thoughts.

5.5.1.9 Mental Well-Being

Positive affect or mental well-being was measured using the mental health continuum short form (MHC-SF) (Keys, 2002). The MHC-SF consists of items assessing psychological, emotional and social well-being, which are thought to contribute to a positive mental health state (Keys, 2002). Emotional well-being refers to hedonic factors within happiness, while psychological well-being concerns eudaimonic aspects such as personal growth and self-actualisation (Ryff, 1989; Ryff, 2014). Social well-being contains items assessing social integration, contribution and coherence. The measure consists of 14-items with items asking respondents over the last month how often they have felt with regards to items, scored on 6-point Likert scale ranging from ‘every day’ to ‘never’. To meet the classification for ‘flourishing mental health’ Keys (2002) argues that respondents must answer positively to one out of three emotional well-being items and six out of 11 psychological and social well-being items (indicating a combination of functioning well and feeling good about life). The MHC-SF has been used within chronic pain studies (Gilmour, 2015) and has shown good internal and test-retest reliability and convergent and discriminant validity (Keyes, 2008; Lamers, 2011). The MHC-SF was selected over other measures, such as the Engaged Living Scale, because it was argued that the CPAQ and PSE assess an individual’s functioning and engagement in goals (e.g. despite the presence of pain) and therefore it seemed of more interest and adherent to the BIS/BAS model to explore other areas of protective BIS factors, such as positive affect.

5.5.2 Sociodemographic and clinical data collection

5.5.2.1 Disease activity

The Harvey Bradshaw Index (HBI) (Harvey & Bradshaw, 1980) and Simple Clinical Colitis Activity Index (SCCAI) (Walmsley et al., 1998) were chosen as measures of subjective disease activity for CD and UC, respectively. The HBI is a simple to use, 5-item questionnaire assessing aspects such as general well-being, severity of abdominal pain, liquid stools, abdominal mass and complications. Items are rated
based on the previous day and have shown to correlate well with other disease activity indices for CD including the CDAI (Vermeire et al., 2010). Limitations of this measure include less applicability for perianal disease (Walsh et al., 2016). The SCCAI is a valid and reliable measure of disease activity in UC and includes key aspects such as incontinence. It is one of the most widely used disease indices (de Jong et al., 2018), correlates well with objective disease activity measures (Higgins et al., 2005) and can be completed by clinician or patient.

For clinic and online-recruited participants, disease activity indices were completed by a clinician and self-report, respectively, as clinician completion for participants recruited remotely was not feasible. While this may have caused some discrepancy, it is argued that clinician reporting is guided by patient reports of symptoms. Addressing limitations in collection of a subjective disease activity marker only, a faecal calprotectin stool sample was requested from clinic-recruited participants. However, the study found that return rate of these samples was low across the three study sites, despite facilitating the return procedures via postal service direct to the laboratory for analysis rather than in-person delivery at the respective hospital sites. This may have been avoided by closer monitoring by the researcher or through voucher/monetary reimbursement to participants who had returned their samples.

5.5.2.2 Pain and other symptoms

The inclusion of other clinical data collection, namely IBS symptom severity and fatigue, allowed for the opportunity to investigate IBD-pain in the context of other symptoms. For example, the inclusion of the IBS symptom-severity score (IBS-SSS) (Francis, 1997) was argued to be informative to understand the overlap of pain and broader IBS symptoms. It was hypothesised that there would be a considerable overlap (Bielefeldt et al., 2009; Grover et al., 2009; Quigley, 2016), given that abdominal pain is a primary symptom of IBS, and this would reinforce the testing of psychosocial processes and guidance of interventions previously tested in IBS/IBS-IBD for IBD-pain. Similarly, the overlap between pain and fatigue is evident from previous research in IBD (Jelsness-Jørgensen et al., 2017; Chavarria et al., 2019), including the systematic review (Sweeney et al., 2018). This provided a rationale for inclusion of an IBD-fatigue assessment scale (Czuber-Dochan et al., 2014) to examine the strength of the relationship and inform prior research on symptom clustering (Conley et al., 2017; 2018) and an understanding of possible overlapping of psychosocial processes across chronic symptoms.
5.5.2.3 Pain and diet

Research has demonstrated the psychosocial impact of food and eating in IBD, and the role that pain plays within this (Coates et al., 2018; de Vries et al., 2019). Consequently, many patients may minimise food intake or food groups, and risk malnutrition or exacerbation of symptoms (Ilzarbe et al., 2017; Schink et al., 2017). While questionnaires exist on food-related quality of life in IBD (Hughes et al., 2016), they do not specifically address the relationship between pain and dietary behaviours, and therefore it was decided to include four items on this to explore in the cross-sectional study. This method of data collection has also been used in other studies on dietary impact of IBD-pain and were discussed in the updated systematic review (Chapter 4 Section 4.6). Diet-related experiences and behaviours is a growing area of IBD research, to better understand the impact of pain on this aspect of daily functioning compared to others (e.g. physical activity, work, relationships). This also aligns with a previous research priority setting in IBD from patients and clinicians, where a better understanding around the role of diet was included in the top 10 questions (Hart et al., 2017).

5.6 Implications of cross-sectional study for BIS/BAS model

The findings from this cross-sectional study contribute to the development a BIS/BAS model of IBD-pain. This dual factor model guided exploration of both negative risk factors and potential protective positive psychological factors associated with pain. The model proposes that processes within BIS and BAS cycles will positively correlate, and processes between BIS/BAS system will negatively correlate, which was confirmed in this study (see Appendix B.2.5 for full table of Pearson correlations). The hypothesis that BIS-related emotional, cognitive and behavioural processes are associated with greater pain was confirmed in this study. With regards to BAS-related process, the significant negative associations identified between pain and pain self-efficacy and psychological well-being reinforce cognitive and emotional factors, respectively, that may be buffering the impact of pain in individuals with IBD. However, pain acceptance was the only BAS-related measure tested in this study that did not show an association with pain. This may have been as a result of using a chronic pain acceptance questionnaire for a sample who did not all meet the classification for chronic pain. Secondly, it may be that individuals with IBD do not find acceptance a helpful approach towards less pain severity and better functioning. However, acceptance has a strong evidence base in the chronic pain literature and growing increasingly in IBS and IBD. Therefore, this was explored through alternative data collection means, in the qualitative study presented in the following chapter, as it may be that acceptance is a helpful
approach for individuals and therefore important to take forward in the BIS/BAS model of IBD-pain and thus intervention development and treatment targets.

5.7 Chapter 5 Summary

This chapter has presented a cross-sectional study investigating psychosocial factors associated with pain. The study provides evidence of the relationship between negative and psychosocial factors associated with pain and therefore builds on the BIS/BAS theoretical model. While a longitudinal design was not feasible within the thesis timeline, ethics obtained for the cross-sectional study also approved one and two-year follow up of participants with the same questionnaire. This data will be collected and analysed separate to this thesis and provide an understanding of the potential long-term impact of psychosocial factors on pain. The cross-sectional study confirms psychosocial factors that were identified in the systematic review, such as depression, anxiety, fear avoidance and pain catastrophising as well as other pain-specific psychological processes, including symptom focusing, pain self-efficacy and all or nothing behaviour. These findings guide intervention development by informing areas for treatment target. However, other types of data collection methods, such as qualitative exploration, can serve to unpick other key psychosocial processes operating in the context of IBD-pain that cannot be sufficiently captured by self-report questionnaires. This, combined with recommendations of mixed methods research in the MRC framework guidance (Craig et al., 2008; Bleijenberg et al., 2018), provides the rationale for a qualitative study which is presented in the following chapter.
Chapter 6 Qualitative study

6.1 Chapter overview

Chapter 5 used quantitative methods to explore psychosocial factors associated with pain in IBD and identified both risk negative factors and protective positive psychosocial factors, which informed the BIS/BAS model of chronic pain. The strengths and limitations of a cross-sectional design were discussed in Chapter 5 and earlier in Chapter 3 (Section 3.3.6). For example, use of data collection through questionnaires may be viewed as reductionist, restricting individuals’ views and experiences into pre-defined constructs and ratings. The use of qualitative methods can provide a rich and insightful account of an individual’s psychosocial processes that may not be captured through quantitative means. Moreover, the combined use of mixed methods can be a powerful tool in developing a conceptual understanding of a problem to guide intervention development (Craig et al., 2008; Tariq & Woodman, 2010). This chapter presents the publication of the qualitative study: “It’s about willpower in the end. You’ve got to keep going: a qualitative study exploring pain in inflammatory bowel disease” (Published article: British Journal of Pain). Given the restrictions in length of a published article, this chapter describes aspects of the study in more depth, including the rationale for using thematic analysis, recruitment procedures and further information around the process of generating codes and themes from interviews.

The study presented in this chapter is presented in the following article:


All study documents are included in Appendix C.
6.2 Published article

**Title:** “It’s about willpower in the end. You’ve got to keep going”: a qualitative study exploring pain in inflammatory bowel disease.

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**Key words:** inflammatory bowel disease; pain; qualitative study; thematic analysis

**Conflicts of interest:** None
Abstract

Background: Pain is a widely experienced symptom of inflammatory bowel disease (IBD), which has significant psychological and functional impacts on patients. Understanding the aetiology and management of chronic pain is a poorly understood area of IBD research. This qualitative study aimed to explore the experiences of individuals with IBD and pain, the pain management strategies they use and any needs for future pain management interventions.

Methods: Fourteen individuals with IBD were purposively recruited and interviewed (face-to-face or telephone) using a topic guide. Interviews were transcribed and analysed using inductive thematic analysis.

Results: Themes identified were ‘vicious cycles’, ‘findings solutions’ and ‘attitudes’. The experience and impact of pain were rarely viewed in isolation, but rather within the context of a cycle of IBD symptoms. Other ‘vicious cycles’ identified included anxiety, avoidance and inactivity and poor understanding and communication. Pain management included short and long-term strategies. Searching for a solution for pain had an emotional impact on individuals. There were contrasting attitudes from participants, including defeat, tolerance and acceptance.

Conclusions: This study provides an understanding of the experience of pain in IBD. The interaction of pain with accompanying IBD symptoms has an emotional and physical impact on individuals, and creates a barrier to adequate assessment, understanding and treatment of pain. Patients rely on their own experiences and a trial and error approach to apply helpful strategies. Adjuvant behavioural therapies may be beneficial for patients experiencing pain and psychological distress, and to facilitate self-management.

Key words: Inflammatory Bowel Disease, Pain, Qualitative Study, Thematic Analysis
Introduction

Inflammatory bowel disease (IBD) is a chronic gastrointestinal disease with a relapsing and unpredictable prognosis. It affects between one in 200 and one in 300 people in high-income countries and has rising incidence rates in low and middle-income countries (1-3). IBD is mostly comprised of Crohn’s disease (CD), where inflammation can occur anywhere from the mouth to the anus, and ulcerative colitis (UC), affecting the colon only. Symptoms of IBD include weight loss, diarrhoea, fatigue and abdominal pain, which result in a low quality of life and symptom burden for patients. Developing a thorough understanding and optimising management of IBD symptoms, predominantly pain and fatigue, were among the top 10 questions raised in a research priority setting by patients and clinicians (4). Pain is experienced by up to 70% of patients in active disease and 20-50% of patients in remission (5). In active disease, bowel dysmotility and disease-related complications such as strictures, adhesions and fistulas are among contributing factors (6, 7). However, joint pain has also widely been reported by patients (8). The aetiology of chronic pain is a poorly understood area of IBD, with research to date addressing visceral hypersensitivity, dysregulated central and peripheral pain signalling and psychological factors as important areas for investigation (5).

With a current limited understanding of pain in IBD, treatment approaches to pain management in IBD is a similarly under researched area. In periods of active disease, optimising IBD medical therapy, and if necessary, surgery, are used to alleviate pain symptoms and underlying exacerbating factors such as inflammation. However, use of these approaches in remission is invasive, distressing and can put patients at further risk of complications. Norton et al.’s (9) systematic review reinforced the heterogeneity in approaches for pain management in IBD, including a range of pharmacological (e.g. antibiotics, nicotine patches, cannabis), dietary (e.g. low FODMAP diet) and psychological approaches. Promising results were found for psychological approaches, such as disease-specific cognitive behavioural therapy (CBT) (10), stress management (11) and cognitive skills training (12). However methodological shortfalls and small samples sizes limited conclusions in this area.

It is recognised that pain in IBD is a biopsychosocial construct (5). A recent systematic review by Sweeney et al. (13) identified that a range of clinical factors and both negative and positive psychosocial factors were associated with pain in IBD. Depression, anxiety, stress and pain catastrophising were
among negative psychosocial factors associated with greater pain severity and pain-related interference. Conversely, active coping, perceived social support and an internal locus of control was associated with less pain. The majority of included studies were of cross-sectional design which limited causative inferences, however the review suggests that psychosocial factors may play an important role in pain in individuals with IBD.

To develop a better understanding of IBD pain and facilitate the development of effective interventions, further research is required. This includes gaining a better insight into patient’s experiences of pain, their understanding of pain in IBD and current strategies used to manage this burdensome symptom. Moreover, for the development of effective interventions, research is required to gain a better insight into the needs of patients. The informative role of qualitative research is evident in intervention development for HIV-related chronic pain (14) and cancer-related fatigue (15). In IBD, one qualitative study explored pain in hospitalised patients (16). This revealed the frustration and perceived stigma felt by patients with IBD experiencing pain. However, no qualitative studies have explored the experiences of pain in IBD outside a hospitalised context. Therefore, the aim of this qualitative study is to gain a better understanding of i) the experience of pain in IBD ii) individuals’ current management strategies for pain iii) the needs and preferences of individuals with IBD for future pain management interventions.

Methods

Design

A qualitative study using in-depth semi-structured interviews. A purposive sampling technique of maximum variation (17) was used to capture participants with a range of clinical and demographic backgrounds, who were all experiencing pain related to their IBD. Ethical approval for the study was obtained from London-Surrey Borders Ethics Committee (17/LO/1527).

Participants
Eligibility criteria included: i) a clinician-confirmed diagnosis of CD or UC ii) diagnosed for a minimum of six months iii) over 16 years of age iv) ability to read and write English v) experienced pain related to their IBD.

Procedure

Participants for this study were purposively selected from a database of patients recruited from three National Health Service outpatient gastroenterology clinics and took part in a cross-sectional survey on pain in IBD. Those who agreed to participate in further studies and met our eligibility criteria were contacted by email and invited to take part in this qualitative study. Seventeen patients were contacted by email, of which fourteen replied. Participants were given a choice of either face-to-face or telephone interview. Those who opted for the former provided written consent and those who opted for telephone interview provided verbal consent, as recorded within the interview. A semi-structured interview schedule was followed, of which questions and probes were developed and agreed by the research team and reviewed by patient public involvement members (Table 1).

Individual one-off interviews were conducted by a female PhD student (LS) with experience in conducting interviews and leading a research project in IBD-pain. Field notes were taken during interviews and no other non-participants were present. There was no previous relationship between the participants and the researcher and participation had no impact on individual’s clinical care. Interviews were audio-recorded and anonymised, and transcribed verbatim by a professional transcriber. Further participant invitations were stopped once no new themes were emerging from interviews, indicating that data saturation had been reached (18).
Table 1. Topic guide for IBD pain interviews

<table>
<thead>
<tr>
<th>Question</th>
<th>Probes</th>
</tr>
</thead>
</table>
| Can you tell me about the pain you experience, in relation to your IBD? | • Do you experience pain in active disease and in remission?  
• Do you experience different types of pain?  
• How would you describe the pain sensations? And location? Same location or different?  
• What is the pattern of the pain, continuous or intermittent?  
• How does your pain impact you, daily? E.g. sleep, mood, social relations, work, physical activity |
| What other symptoms do you experience in relation to your IBD?          | • How much does pain interfere in your daily functioning in comparison to these other symptoms?  
• Have you found that your pain is associated with any of your other symptoms?  
• What do you think is causing your pain, in active disease? And in remission?  
• What are your thoughts or concerns when you experience pain? |
| Can you tell me about some of the ways that you manage your pain?       | • What strategies have you found helpful in reducing your pain levels?  
• What strategies have you found not helpful in reducing your pain levels?  
• How do these techniques help you? Physically/mentally?  
• Do you react similarly to different types of pain? Do you use the same techniques for different types of pain (if you experience different types of pain)?  
• Tell me about a typical day of yours when you are in pain, and when you are not in pain. |
| How do others around you react to your pain?                            | • To what extent do you have supportive friends and family that help you manage your symptoms?  
• To what extent do you disclose your pain to loved ones?  
• To what extent do you think others understand what you are experiencing? |
| What do you think could be done to help you with your pain?             | • Are there particular areas in your life where you feel you need better support with regards to your pain? E.g. exercise, diet, medications, social activities, work  
• What would help you better manage your pain symptoms on a daily basis, or when you experience pain?  
• In an online treatment programme, what type of skills or information do you think would be most useful to have with regards to managing your pain?  
• Is there anything from healthcare professionals and treatment that you would like to help with your pain?  
• What could be addressed more in treatment for your pain? |

Analysis

Inductive Thematic Analysis using the Braun and Clarke method (19) was used to analyse interviews. Three authors (LS, LB & ZK) read through all transcripts and recordings were listened to repeatedly, to familiarise authors with the data and initiate generation of codes line by line. Transcripts were analysed using both paper and pen method and computer software NVivo Version 11, to allow codes to be grouped into sub-themes and overarching themes. The research team met regularly to discuss, refine and agree on codes and themes, using diagrams and supporting quotes to facilitate decision-making.
and repeatedly re-read transcripts to ensure that codes, sub-themes and themes accurately reflected the data set.

**Results**

Fourteen individuals with IBD were interviewed, with interviews lasting between 30-60 minutes. This consisted of 8 females and 6 males, with age of participants ranging from 17 to 55 years. The sample was predominantly (64%) of White-British origin. Demographic and clinical details of interviewees are provided in Table 2.

**Table 2. Details of interviewed participants**

<table>
<thead>
<tr>
<th>Participant</th>
<th>Gender F/M</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Ethnicity</th>
<th>Disease Duration (yrs.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>36</td>
<td>UC</td>
<td>White – other</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>22</td>
<td>CD</td>
<td>White British</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>47</td>
<td>UC</td>
<td>White British</td>
<td>19</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>46</td>
<td>UC</td>
<td>White British</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>41</td>
<td>CD</td>
<td>White British</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>17</td>
<td>UC</td>
<td>Black or Black British African</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>55</td>
<td>UC</td>
<td>Mixed – White and Black African</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>31</td>
<td>CD</td>
<td>White British</td>
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<td>9</td>
<td>M</td>
<td>20</td>
<td>UC</td>
<td>Asian or Asian British – Pakistani</td>
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<tr>
<td>10</td>
<td>F</td>
<td>34</td>
<td>CD</td>
<td>White British</td>
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<tr>
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<td>M</td>
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<td>UC</td>
<td>White British</td>
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<tr>
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<td>F</td>
<td>23</td>
<td>UC</td>
<td>White Irish</td>
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<tr>
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<td>F</td>
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<td>UC</td>
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<td>5</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>36</td>
<td>CD</td>
<td>White British</td>
<td>7</td>
</tr>
</tbody>
</table>

Key: M – male, F = female, UC – ulcerative colitis, CD – Crohn’s disease

Three key themes were identified from the data, ‘vicious cycles’, ‘findings solutions and ‘attitudes’, which were each split into further sub-themes (Figure 1). These are described in turn below with supporting quotes and participant number in brackets.
Theme 1. Vicious Cycles

Both the experience and impact of pain were described by participants amongst other IBD symptoms. There were a number of ‘vicious cycles’ identified within this context. Consequently, this theme is broken down into i) ‘cycle of IBD symptoms’ ii) ‘cycles of anxiety’ iii) ‘avoidance and inactivity’ iv) ‘poor understanding and communication’ and v) ‘breaking the cycle’.

i) Cycle of IBD symptoms

Pain was often embedded within a cycle of accompanying IBD symptoms, most notably pain was frequently experienced with fatigue and feelings of urgency. For example, pain not only “creates exhaustion” (7) but also the feeling of being “run down” was also associated with “a bit of a bad belly, a bit of discomfort” (8).

Similarly, pain was frequently viewed as a warning signal of urgency:

“There’s a sense that the pain could be so much that you wouldn’t have control of your own bowel” (6)
…as well as pain surrounding the passing of stools:

“[There is] pain associated with, after going to go the toilet. And in the lead-up as well, the lower bowel sort of cramp pain sort of tightness” (3).

Stemming from this recurrent cycle of symptoms, it was felt by participants that it was difficult to identify when they were experiencing a flare, and some would continue to experience symptoms in remission:

“I find it very difficult to identify a flare, because of my normal sort of low grade, bad bowels and pain and fatigue and bloating” (1).

The impact of pain was often linked with fatigue and/or urgency, particularly in relation to individual’s social and physical functioning. A fear of not being in control was a key barrier to enjoying social activities:

“My social life has really taken a blow because I’m a bit scared to do things in case the pain comes back and I’m not in my own safe environment” (14).

It was also felt that the combination of pain and recurrent urgency impacted participant’s energy levels and functioning:

“You wake up with energy and you’re like yes I’m ready to go, then you’re in the bathroom or you’re experiencing discomfort and you’re exhausted. It’s incredibly exhausting” (7).

Alongside the social and physical impact, pain and associated IBD symptoms affected individual’s ability to work. Participants were worried about missing days off work due to sickness, poor performance whilst at work or perceived stigma from colleagues:

“At work you get the feeling that some colleagues might think that you are just malingering. You get a bit of paranoia” (3).
This in turn had an impact on participant's health:

“There seems to be this vicious cycle where the stress created from poor performance affecting my health and my health is affecting poor performance. And there seems to be no way out” (3).

Several participants had to stop working altogether or become self-employed to regain some control:

“I tend to shy away from work when [the pain is] particularly bad and just go back when I think I can cope with it” (10).

To help alleviate the stress caused by work and pain, one participant expressed their needs of wanting more information to be available about pain in the workplace:

“I think education for employers would be really helpful, about the impact of chronic pain has on people’s physical and mental health and their ability to work” (1).

A consequence of pain being entangled with other IBD symptoms resulted in participant's feeling that pain was not addressed exclusively and did not take priority for healthcare professionals:

“it’s all about the bowel movements. It’s all about how often you go to the loo. And what you’re eating…I don’t think they focus on the pain so much.” (14).

ii) Cycles of Anxiety

Pain had an emotional impact on participants, who often expressed their distress and concern. Experiencing pain was often perceived as a warning signal for either urgency or something serious related to their disease such as being “worried my bowel was going to perforate” (12), which in turn created stress and anxiety, making participants feel more unwell or unable to cope. For one participant, “…it’s the uncontrolled, uncertainty thing” (12) that appears to be a key contributor in this anxiety:
“With the more acute pains, it makes me feel tense, it makes me tense up and then, and then my stomach tenses up and then it can get worse” (14).

Pain location, sensation and intensity varied considerably between participants, however it was noted that when pain was experienced in the abdominal region compared to other types of pain, this created the most anxiety for participants:

“…whenever [the stomach pain] happens, it’s a reminder of what could happen. I don’t get that with the joint pain so much, because it doesn’t feel like it’s related to the disease, even though it is, because it’s in my knee. And obviously, Crohn’s is in the bowels. So even though it is related, it doesn’t feel like it’s related as such. It doesn’t really kind of trigger those thoughts” (2).

iii) Inactivity and Avoidance

When experiencing symptoms, notably pain and fatigue, participants felt that this resulted in low motivation and energy to engage in activity:

*When you’ve got low energy levels and your pain is worse…. you just want to sit there and not move and not do anything. And then things get worse and worse and worse*” (5).

Participants recognised, however, that inactivity had a negative impact on mobility and overall health, which in turn made them feel less confident or able to engage in exercise. This negative feedback loop seemed to be a repeated occurrence:

“It does feedback – no exercise, poor health and poor health to do exercise. And back again” (3).

…and consequently impacted participant’s perceptions of feeling enfeebled or “aged”, “…like an eighty-year old” (13) and “it’s almost as if I’m living in an older man’s body” (3).
Despite this, participants recognised that exercise could be an effective strategy to help with pain and other symptoms, but the fatigue was a key barrier to achieving this:

“I’ve never really tried exercise. And yes, I don’t know whether that would help or not. But I’d be willing to try. But with the fatigue, I find it really, really difficult to motivate myself to do any sort of regular exercise” (14).

iv) Communication and understanding

Participant’s embarrassment and concealment of their symptoms appeared to clash with their frustration at a lack of understanding and awareness around IBD. This revealed a vicious cycle with regards to poor communication (to colleagues, peers, family) and a poor understanding of what participants were going through. Being aware of this lack of understanding made participants feel less likely to disclose what their pain was caused by, as they felt that they would need to explain their disease, which is “something very intimate and personal and kind of embarrassing” (6).

“I wouldn’t really share the pain side of things, because I’d have to explain that was like the bigger picture” (2).

One participant shared that she had sought support through psychotherapy to help her communicate with her loved ones more effectively about her disease. A lack of understanding also transcended to participant’s frustration at their own lack of understanding, and thus inability to effectively communicate what their pain felt like:

“…it’s not like a stabbing pain, it’s not like acid, I don’t understand it. It’s a new pain. Because I don’t fully understand, I don’t know how to explain it to anyone else” (6).

v) Breaking the Cycle
Participants were aware that they needed to break out of these vicious cycles to manage their pain in the long term, such as recognising the negative impact of prolonged periods of rest or inactivity. Although having a “safe environment” (12) such as “being at home” felt “more comfortable” (14), it was also viewed as a “trap” (7).

In line with this, one participant said:

“It’s counterintuitive because when you’re sick, usually you’re supposed to relax and get better… You have to break that cycle. And you just have to go for a walk, you have to muster the energy to get up and do something” (5).

As well as motivating oneself to be active, another participant discussed breaking their cycles of angst that comes with pain… “I think the moment the pain comes back, it makes me worry and I have to break that cycle” (12).

Theme 2. Finding Solutions

The findings revealed the lack of a standardised approach to pain management in IBD. Participants relied on their own set of strategies, which they had adopted predominantly through learning from their own previous experiences through a ‘trial and error’ approach. These included a combination of both short-term strategies to relieve pain and long-term strategies to prevent pain onset and flaring of IBD symptoms. Many participants were still searching for solutions and looked for support or advice from their healthcare professionals, family or the IBD community. However, the act of searching itself had an emotional impact. The theme of ‘Finding Solutions’ is broken down into four sub-themes i) Learning through Experience ii) Short versus Long Term Strategies iii) Medication Concerns iv) Searching.
i) Learning through Experience

In finding the right solutions for managing their pain and IBD symptoms, it appeared that participants used their own set of strategies from personal experiences. Participant’s agreed that learning what worked for them through monitoring their symptoms over time was a useful way of finding their solutions:

“I think, with time, you definitely get to know your body and your pain better” (10).

For example, one participant recommended a grading approach to help manage the impact of diet and symptoms, which they utilised and had learnt over time:

“This is the traffic light system – green you can eat all the time, red just don’t touch it, it’s not going to be a pleasant result, yellow, from time to time you can dabble on these food, but don’t have too many too often” (5).

Conversely, two participants felt that they wanted to be told what to do to manage their pain and overall IBD “that’s the one thing I would say would be helpful to manage it – actually have somebody to tell what do to” (8) “I need to know what I can take and can’t take” (12).

ii) Short versus Long Term Strategies

Arising from previous experiences, it was apparent that the strategies used by participants fell into two main categories. Firstly, participants spoke of using short-term, immediate relief-type strategies. These included application of heat, physical or dietary soothing techniques, breathing/relaxation exercises, distracting oneself or being near the vicinity of a toilet:

“…teas, herbal teas, yoga, sometimes a hot water bottle. Loose fitting clothing” (7).

The extent to which participants drew from social support in times of pain varied between individuals. Some expressed great support and empathy from their loved ones:

“My husband, he’s amazing. He almost absorbs the pain for me sometimes” (7)
However, others shared that they preferred to cope alone:

“When I’m in pain, I just want to be completely alone and use the restroom” (6).

Long-term or maintenance strategies were also used by participants. These included taking a holistic approach to maintaining a healthy lifestyle, which was indirectly perceived to help with managing pain. A frequently discussed topic was around diet as a key maintenance solution to managing pain and flares. When pain was experienced in periods of remission, many participants attributed this to eating something they shouldn’t. However, there was significant heterogeneity in the types of dietary approaches for IBD pain management:

“When I realised I had too much dairy milk, it would hurt more” (7).

However, some participants struggled to find any dietary solution that worked for them:

“I get a bit confused with it because I think to myself I’m trying to like eat healthy and it still comes on. So, I don’t know what route to take” (3).

This confusion appeared to be exacerbated by the lack of consistent advice given from healthcare professionals “the stoma nurses have a very different opinion to the dieticians” (13).

Several participants identified that exercise or being active helped ease their pain:

“Staying active definitely helps me. But even if it’s just psychologically it definitely feels like it helps with the overall management of the disease.” (2).

However, this was not a uniformly agreed among all participants:

“Exercise makes it worse, yes. Definitely” (1).

Meditation was discussed by several participants, but the degree to which is was effective or helpful varied between individuals:

“A couple of years ago I introduced myself to meditation, because I felt like that – and I still think it’s really important” (7).

“I’ve looked into things like meditation. But it doesn’t really work for me” (3).
iii) Medication Concerns

Generally, participants were apprehensive about the long-term use of pain medication. Although some commented on how it was the only effective solution to keep their pain at bay, there were unwanted complications and side effects that came with taking it:

“Sometimes I end up having to take codeine, even though you’re not really supposed to - to mask the symptoms, but it does bung you up” (11).

“You can feel quite nauseous after a while, especially in the mornings after Tramadol” (3).

Moreover, it was viewed by one participant as the ‘last resort’ once they had exhausted their list of coping strategies:

“The only way I’ve found to be able to cope with those kinds of situation is that I’ve had to resort to taking pain relief because then at least I can get through” (10).

It was agreed among several participants that pain medication was not a sustainable solution in the long term, with one participant sharing their apprehension of becoming dependent on medication.

“I don’t want to become an addict” (13).

Others found that medication did not reduce their pain symptoms at all:

“I generally don’t use paracetamol or ibuprofen for the pain, because I don’t feel that they work for me” (9).

One participant shared their frustration at pain medication being their only offered solution:

“I’d really like someone to offer me an alternative to taking paracetamol constantly” (14).

iv) Searching

For other participants, it was evident that, despite having tried many strategies previously, they were still searching for a solution to their pain. One participant discussed how they were working with their healthcare professional on this continued search:
“I’m sure [my gastroenterologist] doesn’t know, I think he is good on patient-centred care, and together we’re trying to find a solution to how to make my pain better or go away” (1).

However, others felt dissatisfied with the lack of accessibility to their clinical team or the solutions offered to them. As a result, they were forced to look elsewhere for helpful solutions, such as IBD forums and close relatives with a clinical background:

“I don’t think I’ve been offered anything. A lot of it is me trying to find out what other people have tried” (10).

For some, this search was focused on findings ways to eliminate the pain completely, as the psychological and functional impact of pain was less tolerable than other symptoms:

“Making the pain go away is honestly the best thing for me. I would rather have the symptoms than have the pain, because the pain is just so frustrating that you can’t do a lot” (6).

For others, their search was focused on the need for psychological support to manage the disease, or feeling more equipped to cope or control the pain:

““For me, it’s having a plan, having the pain under control, having routine appointments, always knowing that I have someone to talk to if it gets bad. And yes, addressing the anxiety issue that it brings as well” (7).

It was clear that there was an emotional impact and relentlessness to participant’s search for a solution. A key barrier to finding an adequate solution for some was rooted in participant’s and healthcare professionals lack of understanding of the causes of pain:

“Everyone keeps saying ‘oh it’s IBS [Irritable Bowel Syndrome], it’s just IBS. But I don’t think it’s just IBS because it’s pretty constant and IBS can be managed by the medications that I take” (14).

This resulted in many participants feeling frustrated with the process and convey feelings of hopelessness:
“I feel kind of disheartened with other solutions, unless that means for sure, that is an evidence-based intervention that worked to get rid of people’s pain completely” (1).

Several participants also expressed that surgery was their “big fear” (2) and that this would be a consequence of not being able to find a solution to their pain:

“I get a bit pessimistic about the pain never going away. And I worry a lot about the kind of the future ache in my colon. And recently I’ve started to worry a lot about having to get it taken out” (1).

**Theme 3. Attitudes**

The theme of ‘attitudes’ summarises the different approaches participants had towards their pain. As aforementioned, the act of searching for a solution led to individuals feeling hopeless and frustrated. Other attitudes taken by participants included tolerance, defeat and acceptance.

Participants had experienced pain so continually or frequently (“mentally draining” (4) “unrelenting” (13)) that they felt conditioned to a baseline level of some pain. This tolerance then became a barrier to effectively communicating pain in consultations:

“I just say it’s not that bad. And it’s become not that bad, because I deal with it on a daily basis” (6).

Participants reported that they frequently persisted with activities and daily demands, despite an awareness that their pain may be indicative of a flare. This ‘keep going’ attitude would be counterproductive at times, leading participants to feeling burnt out:

“The pain is telling me something’s not right and I need to rest, and then I push myself too far, I end up going more steps back than forward” (10).

Participants’ tolerance also reached a threshold for some, as they expressed getting to breaking point, when, for example pain became very severe or they were feeling stressed with daily demands:

“…if I get to the point where it’s a bit unbearable, I’ll go to the pub and just get to the point of I don’t care” (8).

Many participants expressed feeling defeated by their pain, particularly with regards to confidence and motivation to continuously cope with their pain. This stemmed from both the unrelenting nature of pain as well as participant’s feeling like they had exhausted all their possible solutions:
“Now I just feel like the pain has kind of beat me down” (1).

Part of this notion of feeling defeated included participants feeling like they had to succumb to ‘resorting to taking pain relief’ (10) as well as participant’s feeling like they had been defeated by the pain in both their social and work roles:

“It [pain] just slows you down massively and you’re trying to be the best mother you can be” (13).

Conversely, others spoke of ‘being a fighter’ and “not [having] the choice but to fight” (13) or being from a stoic family who took an “annoyingly hard” approach (5). Aligning with this notion of battling with pain included efforts to control pain or using strong pain killers as “weapons of choice” (3).

On the other hand, some participants demonstrated a positive attitude, which was partly driven by having some level of acceptance of their pain, or by taking a different perspective. This acceptance appeared to have a positive effect on individual’s ability to cope:

“Once you start making peace with the pain, it’s almost like you have more control of it” (7).

A positive attitude also provided participants with motivation and resilience to implement the strategies they had previously found helpful:

“[It’s] kind of motivating! If you sit there you’re just going to get more pain and it’s just going to get worse. I think the more you walk, it’s almost like your body starts working” (5)

Other examples of the contrasting nature of these different approaches (tolerance versus acceptance) are presented in Table 3.
Table 3. Example quotes of sub-themes of ‘Attitudes’ - Tolerance and Acceptance

<table>
<thead>
<tr>
<th>Tolerance</th>
<th>Acceptance</th>
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<tbody>
<tr>
<td>“With having the children, I’ve had to find a way to cope. So, if it’s passable, then I just grin and bear it” (10)</td>
<td>“You just have to embrace it is what it is. And try and find a way to make it fit into your life” (5)</td>
</tr>
<tr>
<td>“I’ve just got to like bite the bullet, you know, it’s quite uncomfortable” (3)</td>
<td>“I just tend to get on with it, at the moment. I try to, you know, to just accept it” (4)</td>
</tr>
<tr>
<td>“You have to get on with life. And you’re in agony” (10)</td>
<td>“Make friends with your pain, be aware of it, and almost have a communication with it” (7)</td>
</tr>
<tr>
<td>“It’s become part of me, which has been hard to get used to, but you’ve got used to have to deal with it” (7)</td>
<td>“It’s about building, you know, within, you kind of have to look into how your body is.” (5)</td>
</tr>
<tr>
<td>“I think, it’s just about willpower in the end. You’ve just got to keep going” (13)</td>
<td>I’m much better, oh my God, before, I would be like oh, a mess, a mess. I’d basically hide under the – but it isn’t, what good does that do you?” (7)</td>
</tr>
<tr>
<td>“Not being able to pull out of something, it just makes me have to cope” (1)</td>
<td>“I’m just like, “Oh stop feeling sorry for yourself, just get on with it. There are people around that don’t have legs. There are people around, you know, that have much worse stuff than you have, just stop it, deal with it” (7)</td>
</tr>
<tr>
<td>“Sometimes you don’t always want to pick yourself up. But you have to” (8)</td>
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Discussion

This is the first qualitative study to explore pain in IBD in a non-hospitalised context and has provided an insight into the experiences and impact of pain on individuals with IBD. The study highlights that the experience and impact of pain are rarely viewed in isolation but rather are embedded within the overall experience of IBD symptoms, mainly pain’s interaction with fatigue and urgency. Patients described this cycle as having a significant impact on emotional and physical functioning and acting as a key barrier to effective communication and management of pain. The breadth of strategies used among participants reinforces the lack of a clear consensus around optimal pain management in IBD, as supported by prior research finding a wide variety of interventions for abdominal pain in IBD (9). Moreover, the heterogeneity of pain profiles between individuals and balance with controlling the disease creates further challenges to pain management.

The sub-theme of cycles of IBD symptoms adds to the recent yet small body of literature in IBD on symptom clustering. In IBD fatigue research, patients with chronic fatigue have shown increased scores for pain intensity (20). This has parallels in other long-term conditions such as rheumatoid arthritis (RA) and multiple sclerosis (MS) (21, 22). In a qualitative study on MS-pain, Harrison and colleagues (22) identified unhelpful cycles of pain, fatigue and weight gain that came with avoidant techniques. These
cycles may be explained by the exhausting nature of pain, or the impact that fatigue has on implementing strategies to manage pain (21). Alternatively, these may occur in parallel, as has been shown in RA longitudinal research (23). A recent longitudinal study in IBD examined symptom clustering and found that a third of its sample reported high symptom burden, which remained stable over 1 year (24). Importantly, the study showed that only 19% of participants who transitioned into remission status over this period showed reduced symptom burden. This is supported by findings from the current study, which demonstrated the ongoing experience of symptoms in remission and their collective impact. It is apparent that despite reaching clinical and endoscopic remission, IBD medical therapy does not always achieve symptom relief for patients (25). It is important to recognise the persistent and collective nature of symptom burden in IBD and address how symptoms can be targeted in self-management interventions.

There was divided opinion and approaches used for managing pain. Diet was often discussed in relation to pain in remission. Some used food-specific strategies in acute pain episodes such as herbal teas, plain foods or exclusion of food groups. Diet in IBD is a complex and inconclusive area, with individual differences in gut microbiota seen to be a key influential factor (26). In this study, participants dietary approach was usually a result of learning from prior experience, however participants also recognised that food and symptoms were not always consistent. This added to a lack of understanding around the influence of diet on pain and frustration associated with an ongoing search for a solution. A recent study comparing dietary behaviour among IBD patients with and without pain showed that patients pain in quiescent disease or mild inflammation showed more negative views on their appetite and sense of taste, ate significantly fewer meals, lost weight more frequently and had a reduced time to satiety (27). Other research has demonstrated the discordant views among patients and clinicians regarding the role of diet in IBD, including differing opinions within different types of clinicians (28). Clearly a better understanding and unified approach to diet, pain and IBD is required.

A similarly divided opinion existed for the role of pain medication in IBD. Generally, use of pain medication was viewed negatively, be this due to apprehension over side effects or associated long-term risks with stronger pain medication. Opioid dependence is becoming an increasingly recognised issue in IBD, with prevalence rates rising in England (29) and the USA (30). Ample evidence now demonstrates the clinical characteristics and associated risks of long-term opioid use, including psychiatric diagnosis, hospitalisation and development of narcotic bowel syndrome (31, 32). Patient
awareness of the risks associated with these approaches, as well as identification of at-risk individuals of chronic opioid use (33, 34), should be of concern to clinicians during discussion of pain management.

Despite varying opinions and approaches used among participants, the majority took a holistic approach to managing their pain and IBD. However, the need for more psychological support was voiced, as participants expressed the emotional toll and relentlessness of coping with their pain and other IBD symptoms on a daily basis. This need is well-supported in both qualitative and quantitative IBD research (35-39). Alongside a lack of addressing mental health issues, patients also generally felt dissatisfied with the level to which pain specifically is addressed in consultations, with it frequently being buried underneath assessment of bowel patterns or aims towards remission targets. Assessment of pain in routine clinical practice is usually embedded within global rating measure of disease activity, such as the Harvey Bradshaw Index (40) or Simple Clinical Colitis Activity Index (41). This not only confines individual’s rating of pain to the abdominal region but hinders a more comprehensive assessment of pain. The study’s findings resonate with several studies demonstrating patient’s need of pain being more adequately addressed and the discrepancy between clinician’s and patients views on patient priorities (4, 42). Disentangling pain from other IBD symptoms appears a challenge both for patients and within clinical consultations.

This study demonstrated participant’s resilience and stoic approach to pain. Resilience, defined as “effective functioning despite exposure to stressful circumstances and/or internal distress” (43, 44) is an increasing area of research in chronic illness and pain, and highlights the need to recognise protective factors which allow some individuals to function in the face of pain (45). Participants who appeared accepting of their pain conveyed the positive impact this had, such as having greater perceptions of control and daily functioning. This contrasted with other participants who conveyed frustration and hopelessness in their search for a solution. Similarly juxtaposing approaches have been demonstrated in musculoskeletal pain qualitative research, which identified fighting versus acceptance of pain as one of several ‘adversarial struggles’ for chronic pain patients (46, 47). In IBD research, greater disease acceptance has been associated with better adjustment outcomes, including social and emotional functioning (48). A better understanding of positive psychological processes in the context of IBD pain may have important implications for pain management interventions and provide an explanation as to why some individuals may be at greater risk of psychological distress and chronic IBD pain.
Limitations of the study include the exclusion of non-English speakers and a predominant White-British cohort, limiting the transferability of findings to other cultures. However, the purposive sampling framework used aimed to include a balance of gender, IBD diagnosis, age and disease duration. Findings can also only be drawn from one time point, and it is important to recognise processes of change over time which could be captured in more longitudinal research. Participants current disease activity was not measured at time of interview, thus limiting the extent to which their pain could be explained by inflammatory of disease-related processes. Findings were not returned to participants for feedback or validation. This is a controversial issue in qualitative research, as it is argued that ‘member-checking’ invites its own limitations and incongruences (49). Lastly, prior knowledge and understanding of chronic pain and psychological processes by the authors and interviewer may have resulted in bias in interviewing and analytical processes. However, the use of group meetings to moderate and critique codes and themes before arriving at the results aimed to negate this degree of bias.

**Clinical implications of findings**

The findings highlight the lack of a defined treatment pathway for patients with IBD experiencing pain. Consequently, participants rely on their personal set of strategies to self-manage their pain and associated IBD symptoms. Given the heterogeneity in pain and disease profiles, the task of reaching a definitive approach for pain management in IBD may be challenging. However, it is important that clinicians can offer evidence-based self-management techniques to patients and facilitate patient autonomy and confidence to cope with pain. As a result, further research is needed in this area of IBD. Results also reinforce the need for more robust and holistic assessment of pain in IBD, separately from global disease activity rating.

Participants expressed the need for better psychological support and assessment of pain in clinical practice. Psychological intervention may be a helpful adjuvant approach for patients experiencing pain and psychological distress. For example, techniques used in cognitive behavioural therapy (CBT) may help alleviate stress, anxiety and avoidant behaviours caused by and contributing to pain. Acceptance appeared to facilitate participant’s ability to apply helpful strategies and has been a widely recognised mechanism in the chronic pain literature (50, 51). Acceptance and mindfulness are key tools used in both in CBT and acceptance and commitment therapy (ACT). Positive psychological techniques,
alongside reducing negative thoughts and behaviours, hold merit in pain management interventions and show increasingly promising evidence (52, 53).

Conclusions

Pain is a highly burdensome and poorly understood symptom of IBD. Both the experience and impact of pain interacts significantly with accompanying IBD symptoms. Consequently, it is difficult to effectively assess and treat pain, and have a clear understanding of its aetiology. Due to the heterogeneity in pain profiles and interaction with disease prognosis among patients, use of pain management strategies rely on patient learning from their own prior experiences, including use of short-term pragmatic strategies and long-term maintenance solutions. This group of individuals with IBD demonstrate a resilient approach, tolerating daily levels of pain despite searching for adequate solutions. It is important to support patients in their ability to self-manage and negate risk of emotional distress by facilitating understanding of their symptoms and good therapeutic communication.

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Ethical Approval: Ethical approval for the study was obtained by London-Surrey Borders Ethics Committee (17/LO/1527).

Informed Consent: All participating individuals provided informed consent prior to undertaking interviews

Contributorship: All listed authors made a significant contribution to this manuscript. LS, CN, RMM and WCD contributed to study design and set up. LS, LB and ZK coded and analysed the data. All authors were involved in generation of final themes and codes. All authors read and provided approval on the final version of this manuscript.
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6.3 Rationale for thematic analysis

Thematic analysis is a method for describing, organising and analysing a data set and generating themes within it (Braun & Clarke, 2006). It aims to identify patterns and implicit and explicit meaning within qualitative data to provide a rich account of large datasets (King, 2004). Through immersing and familiarising oneself with the data, codes are generated and summarised into themes, which are commonly displayed in a thematic map to provide an understanding of the relationship between codes and themes. Braun & Clarke (2006) posit that thematic analysis is divided into six phases (Table 4), which should be considered in a recursive rather than linear fashion, so that qualitative researchers are repeatedly revisiting raw data and critiquing codes and themes over a period of time (Ely et al., 1997). Thematic analysis provides a systematic and practical approach and can be used for a breadth of research questions and epistemologies (Nowell et al., 2017). Many researchers have used a thematic analytic approach to inform the development and design of health interventions (Corrigan et al., 2006; Rousseau et al, 2019) and in process evaluation, such as identifying factors related to implementation and informing the identification of active ingredients (Haynes, 2014; Murdoch, 2016). Moreover, thematic analysis has been used to explore experiences of chronic symptoms to better understand associated modifiable factors that may be targeted in an intervention, including in cancer-related fatigue (Corbett et al., 2016) and chronic pain (Merlin et al., 2017; Solem et al., 2019).

However, thematic analysis has also received criticism due to its potential subjectivity, as it is considered theoretically flexible and not fixed to an epistemological position or philosophical stance (Braun & Clarke, 2006; 2019; Nowell et al., 2017). Yet, clarity and communication throughout the process in qualitative research is vital, such as what researchers are doing, why they are doing it and which methods they are using, given the possible subjectivity and bias within interpretation. Recognising this limitation, Braun and Clarke (2019) have highlighted the importance of ‘reflexive’ thematic analysis, which allows the researcher to be at the heart of interpretation by immersing themselves in the meaning of the data, while being reflective and transparent of philosophical assumptions. Indeed, this can be achieved through reflexivity (discussed in Section 6.6), (Tobin & Begley, 2004), peer-review collaborative coding and use of audit trails (Koch, 1994; Braun & Clarke, 2019), allowing the data to be interpreted, analysed and reported in a rigorous and transparent way. How actions and evidence within this thesis were mapped onto the six stages of thematic analysis are presented in Table 4.
Table 4 Braun & Clarke (2006) stages of thematic analysis

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description of the process</th>
<th>Actions undertaken /evidence in thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>Familiarising yourself with the data</strong></td>
<td>Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.</td>
<td>Thesis author &amp; two researchers repeatedly read and reviewed transcripts with sticky notes (Appendix C.2.1).</td>
</tr>
<tr>
<td>2. <strong>Generating initial codes</strong></td>
<td>Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code.</td>
<td>Codes written on margins of transcripts and generated through summary notes made on top of each transcript (Appendix C.2.2).</td>
</tr>
<tr>
<td>3. <strong>Searching for themes</strong></td>
<td>Collating codes into potential themes, gathering all data relevant to each potential theme.</td>
<td>Tables generated with draft sub-themes and codes and supporting quotes (Appendix C.2.3)</td>
</tr>
<tr>
<td>4. <strong>Reviewing themes</strong></td>
<td>Checking if the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic ‘map’ of the analysis.</td>
<td>Draft sub-themes mapped against quotes (Appendix C.2.3). Draft thematic maps defined and refined (Appendix C1)</td>
</tr>
<tr>
<td>5. <strong>Defining and naming themes</strong></td>
<td>Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme.</td>
<td>Draft thematic maps defined and refined (Appendix C1).</td>
</tr>
<tr>
<td>6. <strong>Producing the report</strong></td>
<td>The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature, producing a scholarly report of the analysis.</td>
<td>Example quotes, final thematic map and overall report provided in publication (Section 6.2).</td>
</tr>
</tbody>
</table>

6.4 **Study methods**

6.4.1 **Recruitment and sample characteristics**

An explanatory design was used to guide sequencing of quantitative and qualitative studies (Creswell et al., 2003), to allow for an in-depth exploration of concepts emerging from the cross-sectional study, other psychosocial processes and the needs of people with IBD-pain from a pain management intervention. As such, participants from the cross-sectional study, who had consented to further research and experienced pain were approached to take part in the qualitative study. These participants had answered positively to items about experiencing pain in remission and/or scored moderate to high on the Brief Pain Inventory (≥4/10) in the cross-sectional study. This combination of screening methods was used to capture individuals experiencing pain and differing levels of impact and severity. Purposive
Sampling was also carried out to ensure that individuals to be interviewed spanned a range of sociodemographic and clinical backgrounds, such as different ages, genders, ethnicity and IBD diagnoses, referred to maximum variation sampling (Palinkas et al., 2015). This method was anticipated to facilitate a diverse and full understanding of the studied phenomenon and ensure that development of content for the intervention was accessible to different groups of individuals with IBD-pain. Selection of participants displaying different scores on pain-related interference and psychosocial measures using maximum variation allowed the qualitative interviews to draw from experiences from individuals who varied in their reports of pain impacting on their daily functioning and activity. For example, it was argued that through interviewing an individual with high pain severity but low pain-related interference and lower scores on negative psychosocial measures, data may have the potential to inform protective psychosocial aspects and guide treatment targets within intervention development. This is supported by Goutbert & Trompetter’s (2017) two factor model of risk and resilience in chronic pain, arguing that it is equally as important to learn from individuals with pain who do not report pain-related disability.

One limitation of the study was that interviewed participants were not screened for disease activity prior to their recruitment. Disease activity was measured through disease activity indices and/or faecal calprotectin in the cross-sectional study, which was collected several months earlier. Consequently, the current disease status of the interview sample was not collected. This may have influenced the context of the interviews, such that individuals in a flare may have reported more extreme opinions in response to topic guide items. However, as discussed in Chapter 1 Section 1.2.3, the distinction between active disease and remission is not always clear and is based on several subjective and objective markers. This was supported by some participant quotes, who shared that they personally found it challenging to identify a flare, due to their “normal low grade, bad bowels and pain, fatigue and bloating” (Participant 1). Furthermore, earlier questions in interviews asked about pain in remission and active disease, to allow for possible exploration about how this pain differed and whether coping or management strategies varied for different contexts.

6.5 Analysis

Inductive thematic analysis was used, where no pre-determined framework or top-down structure was applied to guide analysis of the data (Frith & Gleeson, 2004). Rather, findings were data-driven, which allowed for a pure interpretation of the data, conducted through line-by-line coding of transcripts to
generate codes and themes. This ensures that themes are sufficiently linked to the dataset (Patton, 1990).

The generation of codes, sub-themes and themes was carried out by the author of this thesis and two other researchers, who met on several occasions after reading and re-reading transcripts to discuss and deliberate. During this iterative process of collaboration and reflexivity (Braun & Clarke, 2019), draft thematic maps were created to conceptualise the relationship between sub-themes and themes based on early discussions, which resulted in an initial six themes. Sub-themes were also explored using draft visual diagrams to conceptualise codes within sub-themes and generation of sub-theme titles. Initially, a sub-theme around ‘Symptom’ was created, given that many quotes indicated the different sensations, timeline, intensity and patterns of pain experienced, and the interaction of pain with other IBD symptoms, such as fatigue and urgency. However, after discussion and revisiting quotes and codes within the research team, it was agreed that throughout the quotes, pain (of different sensations and intensity) was embedded within the overall IBD experience, and it was the collective impact and interaction of IBD symptoms which were associated with the sub-theme of ‘vicious cycles’ of anxiety, inactivity and lack of communication. Similarly, the term ‘resilience’ was removed, as sub-themes of ‘motivation’ and ‘optimism’ were not represented strongly enough by quotes. Rather, quotes were more appropriately represented within the sub-theme of ‘acceptance’, under the theme of ‘attitudes’. Thus, after re-reading the transcripts and revisiting codes, the number of themes was refined to generate the final thematic map, consisting of three overarching themes (see publication). See Appendix C1 for evidence of the evolving themes through generation of draft thematic maps.

6.6 Reflexivity

Reflexivity is a key process within qualitative analysis to ensure transparency throughout the interpretative, analytic and reporting process and provides an opportunity for researchers to be self-critical in their interpretation. It allows one to “reflect inward towards oneself as an inquirer; outward to the cultural, historical, linguistic, political, and other forces that shape everything about inquiry; and, in between researcher and participant to the social interaction they share” (Sandelowski & Barroso, 2002, pg. 222). Importantly, it is distinct from reflection, which describes the process of thinking about something after an event or situation, whereas reflexivity is an ongoing, dynamic and immediate sense of self-awareness and the influence of cognitive structures on meaning (Holmes, 2010). A reflexive
journal can be one tool to document one’s internal and external dialogue on decision-making throughout the study process (Lincoln & Guba, 1985; Tobin & Begley, 2004). Reflecting on decision-making spans consideration of questions within the topic guide, how questions are asked and what interactions occur with interviewees and any personal values or insights that may influence interpretation of data or theme generation or terminology. An example of the thesis author’s reflections on interactions during interviews is presented in Appendix C3. Attending a training course on qualitative methods and peer-debriefing with nursing students and supervisors also provided the space for the thesis author to reflect on personal assumptions and beliefs that may influence several stages of the study process. For example, the thesis author reflected on their academic background in Health Psychology and understanding of psychological theory in chronic pain, and how these may have influenced i) selection of a purposive sampling method ii) defining topic guide items, codes or themes iii) interpreting psychosocial processes within transcripts iv) overall reporting of the study. An extensive paper trail was provided when analysing transcripts, including generation of several thematic maps and tables of quotes (Appendices C1 & C2), demonstrated the evolving impressions, reflection and summarising of the data and how themes encapsulated supporting sub-themes and quotes (Cutcliffe & McKenna, 1999; Morse & Richards, 2002; Nowell et al., 2017). Therefore, use of an audit trail and reflections in peer debriefing and training contributed to the robustness and ‘trustworthiness’ of the study’s findings.

6.7 Implications of qualitative findings for BIS/BAS model

The findings from the qualitative study provided an insight into psychosocial processes in IBD-pain; it expanded concepts identified earlier in the cross-sectional study as well as introduced other psychosocial processes which inform the BIS/BAS model of IBD-pain. For example, the theme of ‘vicious cycles’ supported the identification of BIS-related processes in the cross-sectional study, such as cycles of pain and anxiety or pain and fear avoidance and the impact this has for exercise. ‘Vicious cycles’ and ‘breaking the cycle’ also supported the BIS/BAS hypothesis of how emotions, thoughts and behaviours operationalise, and how psychological interventions aim to break the cycle of BIS-related content and/or strengthen BAS-related processes (Jensen et al., 2016). Findings in the qualitative study support the association between pain and low mood, with approaches such as ‘defeat’ and ‘tolerance’ demonstrating the battling stance individuals took towards their pain. Other psychosocial processes presented in the qualitative study included the importance of communication and understanding, which relates to the possible protective role of perceived social support identified in the systematic review. In
contrast to the cross-sectional study, acceptance was identified as a potential helpful approach toward pain, and data suggested that acceptance facilitated a more active and positive approach to manage pain. This therefore supports the inclusion of acceptance into the BAS-related cycle and a guidance of treatment targets in intervention development.

6.8 Chapter 6 summary
This chapter has presented a qualitative study on pain in IBD. Findings further highlight that pain has a significant impact on the psychological and physical functioning of individuals, and that due to the heterogeneity in the nature and cause of pain between individuals, pain in IBD is challenging to understand and therefore manage. However, some participants demonstrated an active approach despite pain, sharing that through previous experiences they were able to implement their own personal short and long-term strategies. Additionally, findings demonstrated the contrasting attitudes taken by individuals, including acceptance versus feelings of defeat and tolerance in an unrelenting battle with pain. Results support findings in the previous chapter on the role of negative psychosocial processes associated with pain and have identified new psychosocial processes to build a BIS/BAS model of IBD-pain. Amalgamating quantitative and qualitative findings into the conceptual model is a critical step in intervention development and identifying how these can be addressed in an intervention, using theoretical and evidence-based techniques. This phase of intervention development is presented in the following chapter.
Chapter 7 Theoretical and intervention development

7.1 Chapter overview

In the aim of developing a self-management intervention for pain in IBD, the systematic review and mixed methods studies in preceding chapters have identified modifiable psychosocial factors associated with pain in IBD. These findings emphasise a biopsychosocial model of IBD-pain and inform the development of a BIS/BAS model (presented in Chapter 2) of IBD-pain. The MRC framework (Craig et al., 2008; Bleijenberg et al., 2018) recommends the use of theory to guide intervention development and mapping tools such as a logic model to conceptualise how identified mechanisms within a theory can be mapped onto intervention techniques and outcomes. As such, this chapter presents a BIS/BAS model of IBD-pain informed by findings in Chapters 4-6. It provides a rationale for the use of cognitive behavioural therapy (CBT) as the basis of the intervention, including its alignment with key tenets of the BIS/BAS model, its evidence-base in chronic pain and long-term conditions and its complementary approach to a self-management intervention. How CBT techniques were mapped onto processes within the BIS/BAS model of IBD-pain is discussed and summarised in a logic model. The aims, format and content of the intervention are discussed, including a detailed summary of the intervention development process, rationale for and description of each of the sessions and facilitator support. An example of an intervention session in full is presented in Appendix D3.

7.2 Theoretical development and rationale for CBT approach

7.2.1 Contributions from systematic review, cross-sectional study and qualitative study

Previously, a conceptual model of IBD-pain argued that pain in IBD is a biopsychosocial construct, influenced by central and peripheral factors (Bielefeldt et al., 2009). This model suggested that top-down processes such as hypervigilance, affect and worry were pertinent factors (presented in Chapter 1 Section 1.8.5). This was a significant step forward in developing our understanding of chronic pain in IBD. However, to effectively develop an intervention for this burdensome symptom, a greater depth of knowledge is required to unravel key psychological processes in the context of IBD-pain.

The systematic review in Chapter 4 highlighted the role of emotional and cognitive-behavioural factors and protective psychological factors associated with pain in IBD. This supported a two-factor processing
framework such as the BIS/BAS model of chronic pain, whereby risk and protective factors may be operating in the context of IBD-pain. Results from the cross-sectional study in Chapter 5 confirmed that emotional (depression, anxiety, stress) and cognitive-behavioural factors (fear avoidance, pain catastrophising) are associated with IBD-pain. It also revealed other symptom-specific cognitive-behavioural processes such as symptom focusing, beliefs that symptoms are a sign of damage and all-or-nothing behaviours. Pain self-efficacy and psychological well-being were associated with less pain, shedding light on positive psychosocial constructs not yet investigated in IBD-pain populations. Qualitative findings in Chapter 6 further demonstrated that anxiety and fear avoidance were key processes, as individuals felt that they were frequently caught in ‘vicious cycles’ of negative emotions and inactivity as a result of their pain. Communication and understanding were also important to individuals with IBD, emphasising the importance of social support. Furthermore, the qualitative study suggested different attitudinal approaches that individuals took in relation to their pain (acceptance, tolerance, defeat). Those reporting an accepting approach appeared to have a greater sense of control of their pain and motivation to engage in helpful coping strategies.

7.2.2 BIS/BAS model of IBD-pain

Synthesising findings from the systematic review and mixed methods studies has provided a greater in-depth understanding of psychosocial factors associated with pain in IBD. This has allowed for a BIS/BAS model of IBD-pain to be developed from these findings, presented in Figure 12 (page 193). Factors in bold indicate those identified in the mixed methods studies and non-bold factors indicate findings from the systematic review. The model incorporates not only psychosocial processes but IBD-specific processes that may be triggering or contributing to input of pain signals, and that are important to acknowledge in a disease-specific biopsychosocial model of chronic pain.

The BIS/BAS model of IBD-pain suggests a range of interacting neurobiological, luminal and psychosocial processes, alongside physiological processes in both central and peripheral nervous systems. First, initial disease-related physiological and neurobiological triggers of IBD result in sensory and central input of pain. This may include gut-related processes (permeability, motility), visceral hypersensitivity or occult inflammation (Bielefeldt et al., 2009; Srinath et al., 2012; Srinath et al., 2014; Gracie & Ford, 2015; Spiller & Major, 2016) (described in detail in Chapter 1 Section 1.8). This central input of pain can either lead to BIS or BAS activation (or both), depending on the individual’s physiological state, learning history, focus of attention or predispositions (Jensen et al., 2016). If the
individual doesn’t have the necessary resources to adapt or function through pain (BAS-content), then the perception of pain is likely to activate BIS-related content. These will operate in the aim of maximising the likelihood of avoiding or reducing pain or shifting attentional focus to threat-related cues.

BIS-related processes in response to IBD-pain may include fear avoidant or catastrophising thoughts, engagement in avoidant or prolonged resting behaviours or feelings of stress or anxiety. While some of these behavioural responses may be necessary in periods of acute pain (e.g. IBD flare), their prolonged and maintained use in response to chronic pain may have detrimental effects on an individual’s psychological and physical functioning. The presence of one BIS-related factor can then have an effect on other BIS-associated factors, such that the individual may experience depressive symptoms linked to negative thoughts and avoidance behaviours. These processes in turn can amplify the pain experience through CNS processes (Bielefeldt et al., 2009) or through exacerbating disease-related and inflammatory processes through cortisol production. Stress, for example, has been shown to have an exacerbating effect on symptom severity in both IBS and IBD populations. Not only can stress lower pain thresholds and coping resources but can lead to stress-induced inflammatory processes via activation of the hypothalamic-pituitary adrenal (HPA) and sympathomedullary (SAM) axes (Mawdsley & Rampton, 2005; Graff et al., 2006; Maunder & Levenstein, 2009).

Alternatively, through personal, social and environmental factors, an individual may have strengthened BAS-related content such as flourishing mental well-being, self-efficacy or perceptions of social support (Sweeney et al., 2018). In this regard, one may be more likely to adapt and reach personal goals in the presence of pain, leading to the reduction of psychological distress, (and therefore) pain and pain-related interference. Like the BIS cycle, BAS-related cognitions, emotions and behaviours have an influence on each other such that the effects of BAS-cognitions (e.g. self-efficacy) are likely to facilitate BAS-related behaviours and emotions. The strength of BAS-related processes may be undermined or challenged by temporary physiological states or attentional resources, such as particularly severe pain, active disease or disease-related complications. In summary, although pain is an inevitable symptom in patients with IBD, BAS-associated processes are suggested to attenuate the impact of pain and increase the likelihood that individuals carry out daily goals and functioning.

As well as psychosocial processes, clinical and environmental factors may exacerbate the pain experience (Figure 12). For example, fatigue can influence pain perception by sleep disturbance, lower
pain tolerance, interfere with coping skills (Jelsness-Jørgensen et al., 2017) and affect levels of melatonin which can modulate visceral sensitivity (Danilov & Kurganova, 2016). Fatigue may be caused by prolonged experiences of pain due to physical and psychological consequences of having pain. Fatigue may also result in more pain due to depleted resources and coping skills to deal with pain (Pollard et al., 2006). This is supported by evidence of the strong association between pain and fatigue in both qualitative and cross-sectional studies presented in this thesis. Other clinical and environmental factors affecting pain that were identified in the systematic review and cross-sectional study include smoking status, steroid use, previous surgery and gender.

Figure 12 BIS/BAS model of IBD-related pain. Highlighted bold with (a) denotes psychosocial factors associated with pain identified from the cross-sectional study and (b) denotes findings from the qualitative findings. Not in bold and with (c) are psychosocial/clinical factors identified in the systematic review. + sign between BIS and pain signifies exacerbating effect of BIS activation on perception of pain and – with BAS signifies the protective and reducing effect on pain perception.
7.2.3 Cognitive behavioural therapy and the BIS/BAS model of IBD-pain

The BIS/BAS model argues that pain will activate BIS-related emotions, thoughts and behaviours to maximise the likelihood of withdrawal or hypervigilance (to pain-related cues) to avoid further threat of pain. For example, in an individual with IBD, pain may activate feelings of anxiety, catastrophising thoughts (around a possible flare) and withdrawal behaviours, and attentional resources may be directed toward focusing on further pain. A key aim of psychological intervention in the context of BIS/BAS is to reduce the automaticity of BIS activation and form helpful associations to generate new ‘schema’ associated with pain that facilitate goal-directed behaviour. This resonates strongly with key principles and techniques of CBT. CBT, like the BIS/BAS framework, conceptualises that experiences are broken down into emotions, thoughts and behaviours. CBT can provide individuals with the necessary skills and techniques to reduce negative emotions and thoughts and unhelpful behaviours, which in the long-term are thought to exacerbate the pain experience. Through CBT techniques, individuals learn to develop more helpful ways of thinking in response to chronic pain that align with achieving personal goals (Turk et al., 1983). In the BIS/BAS model of chronic pain, these processes are argued to facilitate the weakening of BIS-related activation and strengthening of BAS-related content to improve mood and goal-directed behaviour (Jensen et al., 2016). Therefore, this provides a strong rationale for the use of a CBT approach as the basis of the intervention. Further rationale is discussed below, including CBT’s evidence-base in IBD and other long-term conditions, the strengths of online CBT and its complementary approach in enabling self-management.

7.2.4 CBT and self-management

Self-management is defined as an individual’s ability to cope with the multiple facets of having a chronic condition, including the symptoms, treatment and physical and psychosocial impact (Barlow et al., 2002). It encapsulates the complexity of living, coping and continued functioning with a chronic illness and the demands that come on a daily basis. This resonates strongly with IBD, where the patient has to cope with interacting and embarrassing nature of symptoms, the unpredictability of relapse, interaction and side effects of complex drugs, numerous appointments and surgical procedures and the overall physical and functional impact of having the disease (Plevinsky et al., 2016). CBT has been identified as one of the most effective approaches in facilitating self-management, across a myriad of long-term conditions and ages (Hofman et al., 2012). Enhancing self-management skills through a CBT intervention provides a powerful platform to provide education and support, empower patients to help
them to feel more in control of their disease and support adaptive behaviour change. Also intrinsic to self-management is developing an individual’s ability to appraise and take appropriate action in a given situation and with given resources (Lorig & Holman, 2003).

In a number of chronic conditions, self-management programmes have been shown to improve quality of life and clinical outcomes including pain, and reduce disability and healthcare utilisation (Barlow et al., 2002; Barlow et al., 2010). In the context of self-management for chronic pain, the Institute of Medicine of the National Academies (2011) report argued for the use of pain education at an early stage for patients (e.g. soon after pain onset or disease onset) through self-management interventions to bring about pain relief and reduce pain-related disability and chronicity (Steglitz et al., 2012). Numerous systematic reviews have shown that pain interventions through a self-management education programme can be efficacious for improvement in physical and psychological outcomes, including reviews in HIV (Millard et al., 2013) as well as other interventions developed in diabetes, arthritis and asthma (Barlow et al., 2010). To date, the majority of self-management interventions in IBD have been focused on disease rather than symptom management (Conley et al., 2017). Tu et al.’s (2015) systematic review demonstrated that self-management interventions in IBD have shown improvements in health-related quality of life, and that an educational component with additional behavioural change techniques, administered remotely, resulted in greater improvements.

7.2.5 Cognitive behavioural therapy in inflammatory bowel disease

While CBT is a complementary and synthesising approach with the notion of self-management and the BIS/BAS framework, it is important to consult the literature for evidence in IBD and other long-term conditions. Overall the collective evidence in IBD suggests that CBT is beneficial for quality of life and psychological outcomes in IBD (McCombie et al., 2013; Timmer et al., 2011; Gracie et al., 2017; Ballou & Keefer, 2017; Li et al., 2019). Less conclusive evidence has demonstrated the effects of CBT on improvements in physical outcomes such as disease activity or reduced risk of relapse. A systematic review of online CBT for IBS and IBD found that there was inconclusive evidence to support the efficacy for psychological outcomes but more promising evidence for reduction in outcomes of gastrointestinal-related anxiety and disability (Hanlon et al., 2018). In paediatric and adolescent populations, there is stronger evidence for CBT for depression and anxiety, quality of life and coping (Szigethy et al., 2007; Grootenhuis et al, 2009). An RCT in paediatric IBD has also shown efficacy on disease course, as well as depression and quality of life (Szigethy et al., 2014).
Inconclusive findings from reviews on CBT in IBD may be explained by conflicting results and methodological limitations in studies. Mikocka-Walus et al. (2017) compared the effects of an 8-week face to face versus online CBT intervention on disease activity and psychological outcomes in IBD. The study found no significant differences in remission rates at 6, 12 and 24 months and a high attrition rate by the end of the study at two-year follow up (67%), which was significantly higher in the online group. However, the study found equivocal efficacy in both modes of delivery and improvements in quality of life in a sub-population of participants presenting greater baseline psychological distress. This suggests that patients ‘in need’ of psychological support were more likely to benefit from a CBT intervention (Mikocka-Walus et al., 2015). Conversely, psychiatric comorbidity was associated with greater chance of drop-out in an online CBT study in IBD (McCombie et al., 2016). A benchmarking study of face to face transdiagnostic CBT recruited individuals with IBD who displayed significant levels of anxiety and depression, and found a large mean effect size on mood, anxiety and symptomatic disease activity (Jordan et al., 2019). Scores for quality of life significantly increased over the course of the study. These findings highlight that patients with greater psychological distress benefit from CBT but that use of an online platform requires some level of therapist input to optimise support and engagement.

The primary aims of these intervention studies have focused on key psychological outcomes (anxiety, depression, quality of life) or disease activity. However recently, CBT has been piloted for the management of fatigue in IBD (Artom et al., 2017b), and has an evidence base for chronic fatigue in other long-term conditions (Kangas et al., 2008; Thomas et al., 2010; Hewlett et al., 2011; Van Kessel et al., 2014; van de Akker et al., 2016). This more recent area of IBD research supports the use of psychological interventions for chronic and burdensome symptoms in IBD which are influenced by biopsychosocial factors.

To date, three intervention studies including a cognitive-behavioural component have been researched for IBD-pain, predominantly in younger populations of small sample size, and found no significant improvements on pain (Schwarz & Blanchard, 1993; McCormick et al., 2010) and some improvements on reports of anxiety (Reigada et al., 2013). Therefore, demonstrated efficacy of cognitive-behavioural approaches on pain outcomes in IBD is limited. However, none of these interventions included a comprehensive pain measure as their primary outcome measure nor were guided by a theoretical model of IBD-pain.
7.2.6 Evidence base for CBT in chronic pain, long-term conditions and IBS

CBT is an extensively researched and administered psychological therapy for chronic pain, aimed at improving functioning and quality of life (Edhe et al., 2014; Kerns et al., 2011; Knoerl et al., 2016). Systematic review and meta-analyses have demonstrated small to moderate effect sizes of CBT interventions on pain outcomes, mood, disability and catastrophising following treatment (Williams et al., 2012; Ehde et al., 2014; Eccleston & Crombez, 2017). It is a recommended psychological approach in the British Pain Society adult guidelines for pain management programmes (BPS, 2013). For example, the Pain Management Plan (PMP) is an NHS recommended CBT-based self-management programme for patients with persistent pain (Lewin, 2010). The PMP aims to provide patients with the techniques to adopt effective self-management strategies and a better understanding around the mechanisms of pain and how mood, thoughts and beliefs can influence the pain experience. Given the high occurrence of chronic pain with other co-morbidities such as poor sleep and anxiety, CBT also provides a psychoeducational element addressing the relation between these. Studies demonstrating the efficacy of the PMP to date have shown positive effects on pain-related disability, self-efficacy and patient satisfaction (Cole et al., 2012; Quinlan et al., 2016; Wilson, 2017). Previous research has demonstrated CBT efficacy in improving daily functioning and quality of life in fibromyalgia (Glombiewski et al., 2010), arthritis (Astin et al., 2002), facial pain (Aggarwal et al., 2011) and chronic headaches (Andrasik, 2007).

CBT has also been tested for chronic pain and fatigue in several long-term conditions. For example, CBT has demonstrated significant reductions in fatigue post-treatment and at long-term follow up in a number of studies in MS (van Kessel et al., 2014; Thomas et al., 2010; van de Akker et al., 2016), rheumatoid arthritis (Hewlett et al., 2011) and cancer-related fatigue (Kangas et al., 2008). CBT for chronic pain has been tested in MS (Ehde & Jensen, 2004; Jensen et al., 2011; Gromisch et al., 2019), rheumatoid arthritis (Sharpe, 2016) and HIV-related chronic pain (Uebelacker et al., 2016). Despite much heterogeneity in CBT treatment protocols and the extent to which they are tailored to the disease group, common aspects include psychoeducation on the relationship between stress and symptoms, understanding the role of unhelpful cognitive and behavioural responses to pain and the effect on mood and functioning.

CBT also shows a strong evidence base for treatment of functional symptoms in IBS (Ballou & Keefer, 2017) and is a recommended treatment in NICE guidelines for refractory IBS (NICE, 2015). Several
meta-analyses have demonstrated improvements in gastrointestinal symptoms, emotional well-being and quality of life compared to standard care as usual or placebo in IBS populations (Tang, 2013; Altayar et al., 2015; Laird et al., 2017). A systematic review of 18 RCTs showed that CBT led to significant reductions in IBS symptoms including pain, with a large pooled effect size (0.67) and a smaller effect size (0.21) on psychological outcomes (Hutton et al., 2005). More recently, a large RCT study comparing web-based and telephone-delivered CBT found large clinical and statistical improvements in quality of life, mood and symptom severity in a sample of 558 treatment refractory IBS patients, including at 24-month follow up (Everitt et al., 2019a; Everitt et al., 2019b). This not only reinforces the role of CBT in the context of functional gastrointestinal symptoms, but the equal efficacy of different modes of CBT delivery.

7.2.7 Role of e-health and online CBT

Notwithstanding the evidence-base for CBT in chronic pain and long-term conditions, one must acknowledge current barriers in access to and availability of psychological services for people with long-term conditions in the UK. Largely due to lack of funding and resources within the NHS, face to face psychotherapies such as CBT are not freely available to patients with IBD and poorly defined referral pathways can lead to delays in adequate assessment and psychological support for patients. Conventionally, CBT therapy requires input of 5-20 one-hour sessions delivered by a skilled clinical psychologist. The introduction of Improving Access to Psychological Therapies (IAPT) (Clark et al., 2009; Clark, 2011) has alleviated some of these barriers to psychological support for people with long-term conditions experiencing anxiety and depression. However, the need for more defined referral pathways to counselling or psychotherapy services is stated in several IBD guidelines (van Assche et al., 2010; van Assche et al., 2013; IBD Standards Group, 2013; NICE, 2015). Secondly, the impact of IBD and periods of severe acute flares on mobility can limited patient's ability to travel long distances to hospitals offering face to face psychological services (Hommel et al., 2011).

Acknowledging these barriers to conventional psychological services alongside a steep rise in e-health technology has led to the development of e-health interventions, such as online or internet-based CBT. E-health interventions utilise information and communication technology and range from health informatics, telemedicine to more sophisticated and interactive health apps. They allow patients to have immediate access to health information and education on the go, provide open communication between patients and their clinical team and measure multiple aspects of patient experience (Eccleston &
Crombez, 2017). Systematic reviews and qualitative research have endorsed the rising application of e-health in IBD and other gastrointestinal conditions (Knowles & Mikocka-Walus, 2014; Stiles-Shields & Keefer, 2015; Jackson et al., 2016; Walsh & Travis, 2018) and chronic pain management (Keogh et al., 2010; Solem et al. 2019). Use of e-health interventions in IBD can be highly effective in fostering patient engagement and self-management. In IBD for example, it can help patients feel more able to understand and manage acute flares and complex medication regimes and keep track of multiple healthcare visits for different procedures and clinic appointments. For a sub-set of less capable or older populations, access to health interventions through electronic devices may invite further barriers and may lead to greater feelings of isolation in coping with the disease. However, generally for IBD, which has a relatively young age of onset, patients are likely to be capable and welcoming of technology-based approaches within their healthcare.

Specifically, online CBT provides a dynamic, interactive and personalised platform through which patients can receive psychological support and develop CBT techniques remotely. A wide body of evidence has demonstrated the cost-effectiveness of online CBT (Hedman et al., 2012; Macea 2012; Kumar et al., 2017; Richards et al., 2018), and in 2006 it was advocated by NICE guidance for the treatment of anxiety and depression (NICE, 2006). In chronic pain, web-based CBT interventions have resulted in improved psychological and physical outcomes, including treatment satisfaction, functional changes and reductions in pain severity and medication use (Macea et al., 2010; Buhrman et al., 2016) and improvements maintained at 3 and 6-month follow-up (Williams et al., 2010; Dear et al., 2013). In a meta-analytic review of online CBT in chronic somatic conditions, greatest improvements were seen in disease-specific outcomes, including disease-related impact, highlighting the strength of tailored interventions (van Beugen et al., 2014). In IBS, online CBT has demonstrated positive effects on GI-specific anxiety and reduced disability (Hunt et al., 2009; Hanlon et al., 2018). Both web-based and high-intensity telephone CBT have demonstrated significant reductions in IBS symptoms and improvements in mood and quality of life (Everitt et al., 2019a). Similar demonstrations of comparable efficacy in mode of CBT delivery has been supported elsewhere. In meta-analyses and integrative reviews, internet-delivered CBT has shown similar efficacy compared to a face to face format, including in CBT for anxiety disorders (Romijn et al., 2019) and chronic pain (Kerns et al., 2011). A recent meta-analysis involving 155 trials demonstrated similar efficacy in individual, group, telephone and guided self-help CBT for the treatment of depression (Cuijpers et al., 2019).
Application of online CBT in IBD has received mixed findings. As discussed, issues around attrition rates has highlighted the need for some level of therapist involvement to facilitate participant engagement and adherence (Mikocka-Walus et al., 2017). Similar high drop-out rates of online CBT have been demonstrated in chronic pain including a systematic review of 11 RCT’s where there was an average drop-out rate of 26.6% (Macea et al., 2010). In a systematic review of online psychotherapy interventions in IBS and IBD, a combination of online interventions with face to face/therapist support was recommended to optimise cost-effectiveness as well as providing some component of human contact (Hanlon et al., 2018). This collectively supports the rationale for an online administered CBT-based self-management intervention for IBD-pain, with some therapist support.

7.2.8 Mapping BIS/BAS processes onto a CBT-based intervention: a logic model

Crucial to the development stage of MRC framework is clearly defining how intervention techniques map onto theoretical components. This is to facilitate replication of an intervention, transparency of causal assumptions and summarising key elements and hypotheses to test (Rogers, 2008; Baxter et al., 2014). There are a variety of methods recommended for this process. For example, the behaviour change taxonomy (BCT) was developed to address issues arising around lack of transparency on the ‘active ingredients’ of an intervention and poor description of protocols. Consequently, Michie and colleagues (2013) developed the Behaviour Change Wheel to guide researchers to select appropriate intervention techniques to facilitate behaviour change. However, the BCT was not utilised for mapping within this intervention development for three reasons. Firstly, as has been argued earlier in this chapter, both the IBD-pain BIS/BAS model and CBT suggest that cognitions and emotions are pertinent factors alongside behaviours, and therefore the aim is to target all these processes in an IBD-pain intervention. Secondly, behaviour changes described by the BCT do not encompass key aspects within CBT nor specify who should be making those behaviour changes. For example, the action of ‘goal setting’ is not specified, yet we know in CBT that patient (rather than therapist for the patient) goal setting is an integral part of the process in developing self-efficacy and skills of self-management. Finally, the therapeutic relationship within CBT is another crucial aspect where the patient can receive empathy, validation and support. These more in-depth therapeutic aspects such as guided discovery and Socratic questioning in CBT are thus not addressed in the BCT. It is known from other studies of CBT in IBD to date (Mikocka-
Walus et al., 2017) that therapeutic engagement is key to sustained motivation and engagement for patients with IBD.

Intervention mapping techniques can be carried out through other means. The MRC framework recommends the use of a logic model to visually display the pathways between key identified mechanisms, intervention components and desired outcomes, as guided by a theoretical model (Craig, 2008; Bleijenberg et al., 2018). However, recently it has been argued that guidance on developing logic models are sparse, despite the increasing emphasis of context in the new MRC framework guidelines (O’Cathain et al., 2019b). Others argue that logic models are insufficient to capture the complexity of interventions (Greenwood et al., 2016). Consequently, a typology of existing logic models has been proposed, specifying types 1-4 logic model (Figure 13). These refer to whether defining relationships between model factors is required and whether different contexts need to be accounted for, with Type 4 representing a ‘dynamic’ logic model that acknowledges both. Specifically, a Type 4 logic model displays how an intervention may interact with different contexts and therefore accommodates multiple intervention forms and stakeholder opinion (Mills et al., 2019). For this thesis, conceptualising key intervention components and mechanisms of change from the BIS/BAS model of IBD-pain was essential for the logic model. While contextual factors were considered for the intervention, such as PPI feedback from IBD nurses and online versus paper delivery, determining factors influencing the intervention in different contexts was outside the scope of the PhD. Therefore, a Type 3 logic model was developed for this thesis and is presented in Figure 14 on page 207. First, an overview of how content was developed is described.
7.3 Intervention development for IBD-pain

7.3.1 Intervention development: content

Intervention content was guided by the BIS/BAS model of IBD-pain presented earlier in this chapter (Figure 12). The thesis author drew from CBT-based intervention techniques to address the BIS/BAS processes and accordingly developed a draft treatment protocol of intervention sessions presented in Table 5. As discussed in Chapter 3 Section 3.5, this thesis was developed in parallel with a larger RCT on the management of pain, fatigue and urgency in IBD (BOOST). As such, a draft treatment protocol was similarly developed by the BOOST team, which incorporated findings from this thesis on IBD-pain, as well as neighbouring research in fatigue and urgency in IBD (Table 6) (Dibley & Norton, 2013; Norton et al., 2013; Artom et al., 2017a; Proudfoot et al., 2018). After comparing these two preliminary session plans, it was evident that there was significant overlap and a decision was made by the thesis author and BOOST team to collaborate and incorporate sessions. This resulted in the IBD-pain intervention
being comprised of seven core sessions (relevant across symptoms), and two pain-specific sessions (Table 7). Alongside observing the considerable overlap in session content between this thesis and BOOST, the thesis author acknowledged the advantages of administering an intervention online (discussed earlier in Section 7.2.7) compared to paper format. For example, this would allow content to be interactive and tailored, allowing patients to self-assess and have access to a more personalised self-management programme.

Session content was written by the author of this thesis and two post-doctoral researchers within IBD-BOOST. This process included consulting the literature on previous evidence-based CBT-based interventions such as fatigue in IBD (Artom et al., 2017b), irritable bowel syndrome (Regul8) (Moss-Morris et al., 2014), fatigue in MS (van Kessel et al., 2008) and primary chronic pain (Lewin, 2010; Cole et al., 2012). Permission was granted from all the listed authors. Aligning with CBT principles, each session included tasks to ensure that individuals practised the skills and techniques and worked towards their goals set within the sessions. Specific tasks associated with sessions are presented in Table 7. A more detailed description of the exercises and content within each intervention session is described in Section 7.3.5 on page 211.
<table>
<thead>
<tr>
<th>Session</th>
<th>Content</th>
<th>Details</th>
<th>Context within IBD-Pain BIS/BAS model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Psychoeducation on Pain and IBD</td>
<td>Development of acute to chronic pain Understanding mechanisms of pain in IBD – why/how it can persist</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Relationship between mood, thoughts, behaviours and pain</td>
<td>The Pain Cycle</td>
<td>Reducing automaticity of BIS-related processes</td>
</tr>
<tr>
<td>3</td>
<td>Identifying thoughts and mood in relation to pain &amp; Setting value-based goals</td>
<td>Thought and mood monitoring Managing unhelpful thinking</td>
<td>Reducing automaticity of BIS-related processes Identifying BIS-thoughts and emotions</td>
</tr>
<tr>
<td>4</td>
<td>Managing stress</td>
<td>Relaxation and breathing techniques</td>
<td>Reducing BIS-activation – anxiety, depression, stress, hypervigilance, catastrophising</td>
</tr>
<tr>
<td>5</td>
<td>Skills training and activity management</td>
<td>Graded activity and pacing</td>
<td>Reducing BIS-activation – fear avoidance, avoidant behaviours. Facilitating BAS activation – confidence, self-efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Graded exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stretching exercises</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Acceptance of pain</td>
<td>Mindfulness exercises Self-compassion</td>
<td>Facilitating BAS activation – improved mood, goal-directed behaviour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintaining value-based goals and setting self-rewards</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Coping with pain symptoms</td>
<td>Importance of regulating sleep Improving communication and social support</td>
<td>Facilitating BAS activation – sense of control, self-confidence and self-efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Managing medication and diet in relation to pain</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Managing setbacks and maintaining goal-directed behaviours</td>
<td>Develop set back plan to improve self-confidence</td>
<td>Building resilience (BAS)</td>
</tr>
</tbody>
</table>
Table 6 Draft intervention manual developed by the BOOST team

<table>
<thead>
<tr>
<th>Pain</th>
<th>Fatigue</th>
<th>Urgency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Understanding your IBD symptoms</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Activity scheduling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Improving your sleep</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Changing your thinking</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Managing stress and coping with emotions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social support, managing flare-ups and maintaining improvement</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>Fatigue</td>
<td>Urgency</td>
</tr>
<tr>
<td>Psychoeducation</td>
<td>Psychoeducation</td>
<td>Psychoeducation</td>
</tr>
<tr>
<td>Acceptance of pain and building resilience</td>
<td></td>
<td>Bowel re-training and pelvic floor re-training</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Practical &amp; social support</td>
</tr>
</tbody>
</table>

The logic model presented in Figure 14 summaries the BIS/BAS mechanisms to be targeted, the mapping of CBT-based intervention techniques and the relevant intervention sessions included in the final intervention (Table 7). Overall, the intervention aimed to reduce BIS activation and facilitate BAS activation and thereby reduce the severity and impact of pain, improve quality of life for people with IBD and chronic pain and foster attainment of goals which is central to CBT. Other important aspects related to IBD-pain are presented, such as fatigue, social support and communication, which were identified from the systematic review and mixed-methods studies in this thesis.
<table>
<thead>
<tr>
<th>Session Title</th>
<th>Session content</th>
<th>Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Understanding your IBD symptoms</td>
<td>Introduction to cognitive behavioural model. Introducing concepts of self-</td>
<td>Rating severity of symptom and how stressed you feel on a scale from 0-10 each day for one week. Record change in behaviours because of symptoms.</td>
</tr>
<tr>
<td></td>
<td>monitoring, symptom focusing and setting goals.</td>
<td></td>
</tr>
<tr>
<td>2) Balancing Your Activity, Eating and Exercise</td>
<td>Assessing activity levels and developing skills of graded activity. Benefits of</td>
<td>Reviewing activity goals and completing sleep diary for next session.</td>
</tr>
<tr>
<td></td>
<td>regular exercise. Exploring beliefs and fear avoidance. Setting goals for activity.</td>
<td></td>
</tr>
<tr>
<td>3) Improving Your Sleep</td>
<td>Assessing sleeping habits and patterns. Importance of sleep. Setting goals to</td>
<td>Reviewing sleep pattern and habit goals.</td>
</tr>
<tr>
<td></td>
<td>improve sleep patterns and habits.</td>
<td></td>
</tr>
<tr>
<td>4a) Changing Your Thoughts Part 1</td>
<td>Role of thoughts in cognitive behavioural model and vicious cycles. Identifying</td>
<td>Recording thoughts using thought record.</td>
</tr>
<tr>
<td></td>
<td>common types of unhelpful thinking.</td>
<td></td>
</tr>
<tr>
<td>4b) Changing Your Thoughts Part 2</td>
<td>Using examples of common unhelpful thoughts and own thinking to develop</td>
<td>Continue to record unhelpful thoughts and come up with alternative thoughts using thought records.</td>
</tr>
<tr>
<td></td>
<td>alternative ways of thinking about pain.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>controllable stressors. Mindfulness and relaxation exercises, including video and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>audio links.</td>
<td></td>
</tr>
<tr>
<td>6) Making the Most Out of Your Social Support</td>
<td>Types of social support, communication and disclosure and setting goals for</td>
<td>Working towards and reviewing goals to facilitate better social support and communication in areas where it could be improved.</td>
</tr>
<tr>
<td></td>
<td>social support.</td>
<td></td>
</tr>
<tr>
<td>7) Managing and Understanding Pain in IBD</td>
<td>Understanding the different causes of pain in active disease and remission.</td>
<td>Identifying one area of the vicious cycle and setting goals. Reviewing tasks and goals in prior sessions relevant to these.</td>
</tr>
<tr>
<td></td>
<td>Difference between acute and chronic pain. Cognitive behavioural model and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>vicious cycles in the context of pain.</td>
<td></td>
</tr>
<tr>
<td>8) The Role of Acceptance and Self-Compassion in</td>
<td>Acceptance and mindfulness strategies in the context of pain. Role of resilience</td>
<td>Completing “three good things” and self-compassion exercises.</td>
</tr>
<tr>
<td>Pain</td>
<td>and positive psychology.</td>
<td></td>
</tr>
<tr>
<td>9) Summary and Maintaining Improvement</td>
<td>Reviewing tasks and revisiting programme aims. Preparing for the future,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>sustaining and building upon improvement.</td>
<td></td>
</tr>
</tbody>
</table>
### Problem
Chronic pain in IBD in remission or mild disease

### Design
Guided by CBT principles and BIS/BAS model of chronic pain

### Processes to be targeted:
- Reduce BIS-associated emotions, thoughts and behaviours
- Increase BAS-associated emotions, thoughts and behaviours

### Treatment manuals in long-term conditions and pain mgmt plan
Findings from qualitative and cross-sectional data
Stakeholder involvement
Online platform

### Mechanisms
#### BIS-related processes (reduce):
- **Emotions**
  - Anxiety
  - Stress
  - Depression
- **Cognitions**
  - Catastrophising
  - Fear Avoidance
  - Symptom Focus
  - Damage beliefs
- **Behaviours**
  - All/Nothing
  - Avoidance
  - Resting

### Intervention Techniques
#### BIS-related techniques:
- Stress management
- Pain psychoeducation
- Psychoeducation
- Identifying negative thoughts
- Alternative thoughts
- Graded Activity
- Goal setting
- Psychoeducation on sleep/wake cycle

### Sessions (Table 7)
#### BIS-related sessions:

<table>
<thead>
<tr>
<th>Session 1</th>
<th>Session 2</th>
<th>Session 3</th>
<th>Session 4</th>
<th>Session 5</th>
<th>Session 6</th>
<th>Session 7</th>
<th>Session 8</th>
</tr>
</thead>
</table>

### Outcomes
- **Reduction in avoidant thoughts and behaviours and negative mood to worsen pain (BIS content)**
- **Increase in approach behaviours and positive mood and thoughts (BAS content)**

### Impact
- Reduced pain-related interference and pain severity
- Increased quality of life
- Facilitate goal attainment

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**Figure 14 Logic model of the processes to be targeted in the CBT self-management intervention for IBD-pain, based on the BIS/BAS model.**

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7.3.2 **Intervention development: service user involvement**

An invaluable aspect of intervention development was extensive patient public involvement (PPI). This ensured that content was tailored and relevant to an IBD population. The BOOST research team, including involvement from the thesis author, held meetings and events with stakeholders, including 87 people with IBD and 68 IBD nurses to provide feedback on the content, feasibility and usability of the intervention. This spanned gaining feedback on session content and layout using a think-aloud technique with 10 individuals with IBD, to more comprehensively testing the website for its user friendliness, readability, tone and relevance to IBD (n = 31). Thus, feedback was collected both quantitatively and qualitatively, and iterations were made to the content and website design by frequent research team meeting and communications with the web developing agency. PPI input revealed particular preferences held by patients and healthcare professionals, such as the use of online messaging, email reminders and links to external resources. Tailored content included psychoeducation on the relationship between stress and IBD symptoms and IBD-specific worries, such as stigma, IBD symptom and exercise and communication. Throughout the intervention, resources were provided via external links which participants could click on, including patient leaflets provided by Crohn’s and Colitis UK on ‘Food and IBD’ and ‘Employment and IBD’.

7.3.3 **Intervention development: facilitator support**

As discussed, previous studies of online CBT in IBD recommend some level of therapist support to facilitate adherence and improve attrition rates (Mikocka-Walus et al., 2017). However, given the current constraints and limited access to psychological support in the NHS (discussed earlier in 7.2.3), the level of therapist contact needed to be feasible. Therefore, an intervention ‘facilitator’ was included within the intervention, to support participants to develop their self-management skills and understanding of the intervention, rather than being a central figure to it. Initially, it was decided that this would be provided through phone calls between participant and facilitator every 3 weeks (at Week 1, Week 4, Week 7 and Week 9). However, from PPI feedback from IBD nurses, stakeholders questioned the feasibility of facilitators being able to provide this level of input. Meanwhile, individuals with IBD also expressed that they felt, in the context of an online self-management intervention, that this number of telephone sessions was not needed. Consequently, this was modified to an initial telephone session following Week 1 (lasting approximately 30 minutes), and subsequent in-site messaging between participant and facilitator driven by the participant (Figure 15). It was agreed between stakeholders and the intervention
development team that this combination was sufficient to provide participants with guided support throughout the intervention.

In the telephone session after Session 1, the facilitator would ask for a brief history to the participant’s IBD and pain symptoms (e.g. when they started, identified triggers) and review their vicious cycle using CBT techniques such as validation, Socratic Questioning and guided discovery (Padesky, 1993). These techniques refer to asking probing and open questions to facilitate patient awareness of their unhelpful thoughts and how to modify these in the context of their goals (Carrey & Mullan, 2004). The facilitator would also discuss participant’s programme aims and highlight specific sessions that may be particularly relevant (further contributing to a tailored treatment programme). The facilitator had access to their own BOOST facilitator dashboard on the website, which included a list of their assigned patients and a personal calendar to input dates of upcoming phone calls. Additionally, the facilitator was able to access information on the number of sessions/completed by their patients and view their patient’s vicious cycle and programme aims, to facilitate the telephone call and personalised messaging.

In the context of BIS/BAS, the intervention facilitator had a crucial role in establishing a good therapeutic relationship with participants. For example, this included provision of validation, positive feedback and empathy through phone calls and fostering pain self-efficacy. Pain self-efficacy, or one’s belief in their ability to carry out actions despite their pain (Bandura, 1977), can be targeted through a number of CBT techniques, including highlighting and generalising examples of success in therapeutic feedback and setting and achieving goals.

For the feasibility study in this thesis, the facilitator was a mental-health nurse with 9 years of experience working in the mental health sector. They received training in CBT from a Professor of Psychological Medicine with expertise in the area of CBT and online interventions. Frequent meetings were held between the facilitator and the author of this thesis to review any issues arising from participants and to review in-site messages throughout the programme.
7.3.4 Intervention development: website functionality and design

A key tenet of the online format was that the programme could be tailored to the individual. This included a patient dashboard page after logging in (Figure 16) where they could view their personal goals, calendar and messages to the facilitator. It also included a personalised model of their ‘vicious cycle’, where individuals were asked to fill in their own thoughts, emotions and behaviours in response to pain when in pain in Session 1. Different modes of content were presented throughout the treatment programme to ensure that content was varied. This included case examples provided in vignettes, patient quotes and audio or video links. Audio clips included mindfulness or breathing exercises and videos included a user tutorial to help navigate the website, patient stories from people who provided central PPI input and welcoming videos from the research team. To ensure that the online intervention provided aspects of support and encouragement which would otherwise be given in a face-to-face mode of delivery, the tone of content was written to provide individuals with validation of the impact and difficulties of their symptoms.
7.3.5 Intervention development: sessions and tasks

A summary of the intervention sessions is provided in Table 7 earlier in this chapter. Here, the chapter provides a brief overview of the content and tasks within each session.

7.3.5.1 Core sessions

Session 1 Understanding your IBD symptoms

The aim of the first session was to help individuals develop a better understanding of the factors contributing to their symptoms, in the context of a cognitive behavioural model. The session looked at an individual’s ‘vicious cycle’ and how thoughts, emotions and behaviours in response to symptoms inter-relate in the context of pain. This included psychoeducation around the ‘Fight or Flight’ model and role of stress hormones, which has been used previously in CBT intervention manuals (van Kessel et al., 2004; Lewin, 2010; Cole et al., 2012; Moss-Morris et al., 2014; Artom et al., 2017b). The session finalised with teaching individuals how to go about making a change to processes within a vicious cycle through the tool of self-monitoring. This included monitoring their pain in relation to daily activities and routine, how their pain varies from day to day, possible identified triggers of pain, how they respond to their pain (thoughts, emotions, behaviours) and what their patterns of activity are like. Individuals were asked to complete their aims for the programme. The task for this session was for participants to keep
a daily log of their stress levels (on a rating from 0-10) and any behaviour changes that occurred as a result of their pain (e.g. ‘I went to bed early and didn’t go to my gym class because I was in so much pain’). In the context of BIS/BAS, the use of psychoeducation in this session aims to negate emotions of worry and negative pain-related thoughts, thereby reducing the activation of the BIS. Additionally, the use of self-monitoring can foster a more detached, observer stance to one’s responses to pain.

Session 2 Balancing your activity, eating and exercise

Session 2 looked in more depth at activity and exercise and the Fear Avoidance model (Vlaeyen & Linton; 2000; Vlaeyen et al., 2016). This is widely used and recommended in pain management programmes to teach individuals an understanding of how fear avoidant thoughts and inactivity can exacerbate pain (Watson et al., 2010; Nicholas et al., 2011; BPS, 2013). In particular, the session aimed to help individuals identify what kind of activity pattern they have (underactive, overactive, ‘boom and bust’) and develop a more consistent pattern of activity, so that they are not governed by their symptoms. Many individuals with IBD-pain may adopt unhelpful behaviours over time as they are implemented and deemed helpful during periods of acute pain or flare. Alternatively, these behaviours may arise from a lack of energy, not wanting to further exacerbate the pain or to use the opportunity when their symptoms are at bay to get through as many daily activities as possible.

In addition, many people with IBD find it difficult to know what and how much exercise to do, given their symptoms. The session encouraged individuals to reflect what exercise they engage in, what beliefs they hold associated with exercises and explores types of exercise that may be helpful or of interest. Throughout the session, patient quotes were used to give individuals a sense of how being more active has been beneficial to others with IBD. Graded activity and goal setting are widely used CBT techniques and central to pain management interventions (Lewin, 2010; Cole et al., 2012; Williams et al., 2012; BPS, 2013). Such behavioural strategies in CBT can also help an individual identify and manage ‘safety behaviours’ (e.g. symptom focusing, toilet checking) (Salkovskis, 1996).

Session 2 also included education around consistent patterns of eating and aiming to not ‘overthink’ diet as it may contribute to a negative vicious cycle of thoughts, emotions and behaviours. Diet is a complex and widely researched area in IBD, and it was not within the remit of this self-management intervention to have a whole section devoted to dietary management in IBD. Moreover, dietary techniques that work for individuals and their symptoms are very heterogeneous, and therefore
overarching key messages in relation to diet and more specifically, eating, were presented in the later part of this session. The task for this session was to set activity and exercise goals. In preparation for Session 3, participants were also asked to complete a 7-day sleep diary. This session aimed to therefore target BIS-related cognitions and behaviours of avoidance, as well as eliciting approach behaviours through goal setting of activity/exercise (BAS).

Session 3 Improving your sleep

Session 3 took a focus on the importance of sleep, sleeping patterns and how to improve one’s sleep. A brief summary of the importance of sleep for health, recovery and energy was provided and how sleep problems in IBD is a common issue for many people. Participants were asked to review their sleep diary (completed as part of the My Tasks from Session 2) and review whether they fall into a particular sleep hygiene category; ‘erratic sleep’, ‘sleeping too little’, ‘sleeping too much’, ‘my sleep does not cause me any problems’. If sleep is not an issue for the individual, the session recommended that they may want to skip through certain sections of the session which may not be relevant to them. The session then looked in turn at each of the sleep hygiene categories, provides patient vignettes, common poor sleep hygiene vicious cycles/behavioural patterns and provides practical tips. Participants were then invited to set goals based on what they have learnt in the session.

Session 4a Changing your thoughts: Part 1

The main aim of Session 4 (split into two parts but aimed to be completed within the same week) was to help individuals identifying unhelpful thinking patterns they have in relation to their pain and come up with alternative, adaptive ways of thinking. Common unhelpful thoughts were explored, such as catastrophising, over-generalising, predicting the future, mind-reading, unhelpful thinking in the context of perfectionism, with patient vignettes, illustrations and examples provided throughout to give context (Figure 17). Individuals were then invited, as their My Tasks for Session 4a, to record a thought diary for at least 3 days in a row. Specifically, individuals were asked to record thoughts, which may be related to their IBD, pain or other events in their daily life. In addition to the unhelpful thoughts, they were asked to note what they were doing when the thought arose. Changes in cognitions have been shown as key mechanisms in mediation studies of CBT for chronic pain (Turner et al., 2007) and IBS (Windgassen et al., 2019), reinforcing the importance of session content around identifying and changing thoughts. Indeed, identifying negative automatic thoughts such as ‘I will never be well again’ is important
regardless of whether the pain is acute or chronic, as it allows the individual to cope with and respond in a more helpful way to their pain.

Session 4b Changing your thoughts: Part 2

While Session 4a was about identifying unhelpful thinking patterns, Session 4b served to help individuals come up with alternative ways of thinking. These may not necessarily be ‘positive thoughts’ but more realistic or helpful ways of understanding or interpreting a given situation. Participants were first asked to reflect on their thoughts, and whether they observed any common patterns between their thoughts and whether this mapped to any of the common unhelpful thinking patterns explored in Session 4a. As changing thoughts is not an easy task, the session explained that one of the techniques to helping individuals come up with alternative ways of thinking includes ‘weighing up the evidence’ which can break the habit of focusing on the more negative aspects (and therefore automatic BIS activation). Like the previous session, the task was to carry out completing their thought record in the next upcoming week but this time coming up with alternatives.

Figure 17 Illustrations displaying worry (left) and catastrophising (right) thoughts presented in Session 4a and 4b on changing thoughts

Session 5 Managing stress and coping with emotions

The ways in which stress builds up and impacts our symptoms were explored in more depth in Session 5. Participants were asked to identify their sources of stress, i.e. work or study, social occasions, relationships, medical procedures, thinking about the future, embarrassment of symptoms, finances etc. Relating back to the vicious cycle and cognitive behavioural model, ‘the stress effect’ was then explored in relation to emotions, behaviours and thoughts. Participants were invited to review their vicious cycle completed in Session 1 in more depth. The session provides stress management techniques including
setting priorities, self-care or rewarding yourself. Controllable and uncontrollable stressors are explored, and ways to identifying and manage these separate sources of stress. Session 5 also looked in more depth at emotions and invites participants to look back at this section of their populated vicious cycle. Certain emotions that come with having IBD were explored, such as embarrassment, anger, frustration, worry, sadness and depression. Ways of coping with emotions were suggested, including identifying unhelpful thinking (Session 4a & 4b), regulating everyday activities and taking up exercise to reduce negative emotions and stress (Session 2), and seeking social support (Session 6). Relaxation techniques and mindfulness exercises were also presented in this session, with supporting auditory links to carry out these exercises. Participants were invited to set session goals, either practising relaxation exercises or mindfulness as a way overcoming stress and negative emotions. The task for this session included completing a stress diary and working towards completing their stress management exercise.

Session 6 Making the most of your social support and communication

Session 6 looked at different types of social support (emotional, practical, informational) and the role of communication and disclosure. For participants who feel they have adequate social support, they were able to skip the appropriate sections less relevant to them. Otherwise, participants were asked to select what social support network they feel less satisfied with, including family, friends, sexual or love relationships, work colleagues, general public or the IBD community. Within the session, links to external resources were provided, such as a general information sheet on what IBD is (to provide to family or friend where communication may be sub-optimal) or a link to how to improve your employment life and what benefits people with IBD may be entitled to. Participants were invited to set goals where they feel they would like to improve their level of support and communication. The task for Session 6 included working towards and reviewing goals. This session is anticipated to facilitate BAS activation through cognitions of perceived social support (Sweeney et al., 2018) and approach behaviours in social support seeking.

7.3.5.2 Pain-specific sessions

Session 7 Managing and understanding pain in IBD

Session 7 looked more closely at pain in IBD, exploring the differences between acute and chronic pain, factors associated with IBD-pain, including biomedical factors, maintaining factors – the way we think,
feel and what we do and the environment. The session provided a psychoeducation of the psychobiological mechanisms in chronic pain in IBD, including chronic abdominal pain and joint pain, and explores different pain medications. Input from IBD healthcare professionals in intervention development ensured that education was provided on the different types and locations of pain in IBD that may indicate an IBD-related cause and the different mechanisms involved in acute and chronic pain. Throughout the session, links were made with previous sessions, such as the role of stress and emotions in relation to heightening the pain experience and ways to manage this (Session 5) or understanding the vicious cycle in relation to pain (Session 1), in more depth. Similar exercises in Session 4a and Session 4b were repeated; providing a patient example of how someone responded (emotions, cognitions, behaviours) when in pain, and what alternative thoughts this person could have had to help them better manage their situation. Finally, ‘Common Questions Around Pain in IBD’ were presented, which included some of the commonly felt frustration around pain ‘why don’t people take my pain seriously?’ and ‘how should I know when I should seek help when I’m in pain and when I should apply pain management strategies?’. The session finalised with inviting the participant to set goals for the pain-specific session, including the content/techniques learnt in earlier sessions in the programme. For example, goals set may be related to activity, stress management or developing alternative thoughts.

Session 8 The role of acceptance and self-compassion in pain

Session 8 looked at the concept of acceptance and self-compassion, and how these might facilitate coping and managing pain. Acceptance is a key aspect of CBT manuals for pain management programmes (Cole et al., 2012) and has a supporting evidence base in chronic pain interventions (Vowles et al., 2014; Feliu-Soler et al., 2018). In Session 8, acceptance was described as a different approach to pain, which some individuals with chronic pain find helpful, and patient quotes from the qualitative study are presented, which supports the use of acceptance as a helpful approach to overcoming the battle associated with pain. This session therefore provided a psychoeducation around acceptance and techniques to facilitate acceptance, such as mindfulness exercises.

The latter part of the session then explored the concept of resilience and how positive psychology techniques can help to improve positive mood and well-being, despite having IBD and pain. Alongside targeting negative affect, the BIS/BAS model proposes that improving positive emotions can have an
influence on BAS-associated processes (e.g. self-efficacy, approach behaviours) in the aim of reducing the impact of pain. For example, this may be through broadening awareness, attention and thoughts and behaviours (Waugh & Fredrickson, 2006; Rowe et al., 2007). Positive psychological interventions in chronic pain have previously used exercises aimed to improve self-esteem and self-worth (Goubert & Trompetter, 2017), such as the ‘Three Good Things’ task (Lee Duckworth et al., 2005; Seligman et al., 2005). Therefore, the session included exercises on ‘Three Good Things’ and ‘Self-Compassion’ as ways of thinking and reflecting more positively. Goals therefore related to acceptance-based exercises or positive psychology exercises, such as keeping a self-compassion diary, a self-compassion mantra, writing a self-compassion letter to oneself or being more aware of self-criticism and one’s suffering.

Session 9 Summary and maintaining improvement

The final session allowed participants to review their tasks and revisit their programme aims and set long-term goals for the future. Participants were invited to complete an exercise where they reviewed the strategies and key points they have learnt from each session and which of the sessions they think they have made the most gains, given their tasks and goals they have completed throughout the programme. Finally, the session included strategies for flare-ups and setbacks, including ‘don’t be too hard on yourself’ ‘think how you would speak to a family member or friend in a similar situation’ ‘think back to how you coped last time’ ‘plan for stressful times’.

7.4 Chapter 7 Summary

This chapter has presented an updated theoretical model of pain in IBD, using the BIS/BAS model framework and incorporating psychosocial factors identified from the cross-sectional and qualitative studies. The chapter has provided a rationale for the use of an online CBT self-management approach for an IBD-pain intervention and used a logic model to display the mapping of CBT intervention techniques to processes within the BIS/BAS model of IBD-pain. CBT has a wide evidence base in chronic pain and long-term conditions, including IBS, and aligns with the BIS/BAS framework of reducing automaticity and forming positive associations to improve functioning and goal-seeking behaviours. The chapter has described different aspects of intervention development, including the merging of pain and BOOST manuals, service user involvement, online functionality and description of content within sessions and tasks.
Administering the feasibility study through the BOOST website came with a number of advantages and disadvantages which should be addressed. As discussed, use of an online rather than paper delivery method allowed for the intervention to be dynamic and interactive, as well taking advantage of the many other benefits of e-health (discussed in Section 7.2.7). Secondly, the author of this thesis was given the opportunity to draw on and learn from a range of resources, such as web design, stakeholder involvement and professional expertise in developing interventions, therefore expanding their skillset and professional development.

However, for the core sessions, content was developed so that it related across multiple symptoms of IBD (pain, fatigue and urgency). This may have resulted in some sections of the sessions being less relevant to participants with chronic pain and not any problems with fatigue or urgency. However, consulting previous evidence in IBD of symptom clustering as well as sub-themes in the qualitative study, the presence of pain is commonly believed to be accompanied by symptoms of fatigue, or urgency, or both. Moreover, during the intervention development stage it was apparent that psychosocial processes identified in IBD-pain were shared across processes previously identified in IBD-fatigue research (Artom et al., 2017a; Artom et al., 2017b) as well as urgency (Dibley et al., 2013; Proudfoot et al., 2019). Nonetheless, key content (e.g. vicious cycles) was tailored to the symptom of pain, and the pain management intervention to be tested (in the following chapter) included only core sessions and pain-specific sessions, culminating in 9 sessions.
Chapter 8 Feasibility study

8.1 Chapter overview

The preceding chapter provided a comprehensive overview of the intervention development process, presenting a tailored theoretical model of IBD-pain based on previous thesis findings and using a logic model to summarise the mapping of CBT techniques onto IBD-pain BIS and BAS processes. Chapter 7 provided a rationale for the use of a CBT-based approach and a summary of the intervention sessions to be included in the self-management intervention for IBD-pain. This included content and tasks associated with sessions and the development of the ‘BOOST’ website platform, incorporating extensive stakeholder involvement. This chapter presents a feasibility study of the online-CBT based self-management intervention for people with IBD and chronic pain. This was supported by a ‘intervention facilitator’ and delivered over 9-weeks, with outcome measures assessing feasibility and acceptability of the intervention, and preliminary estimates of efficacy on pain, psychosocial and quality of life outcomes. The chapter presents the manuscript of the article for this study which is to be submitted for publication. All feasibility study documents are presented in Appendix D.
8.2 Submitted article manuscript

Title: Pain management in inflammatory bowel disease: feasibility of an online therapist-supported CBT-self-management intervention

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Key words: inflammatory bowel disease; pain; cognitive behavioural therapy; self-management

Conflicts of interest: None

All study documents are presented in Appendix D.
Abstract

**Background:** Chronic pain is a poorly managed symptom of inflammatory bowel disease (IBD). Cognitive behavioural therapy (CBT) has an evidence-base in functional gastrointestinal conditions and chronic pain. This study aimed to test the feasibility and acceptability of a 9-week online facilitator-supported CBT intervention, tailored for people with chronic IBD-related pain.

**Design:** A single arm pre-post design with nested qualitative interviews was used with 20 individuals with IBD and chronic pain, who were recruited through an online IBD charity and had consented to research in a previous survey or responded to an online charity advert. Individuals who indicated a pain-interference score of ≥4/10 (Brief Pain Inventory) and met inclusion criteria were invited to take part. Outcomes included recruitment and retention rates, pain interference and severity, quality of life and psychosocial measures.

**Results:** Of 145 individuals contacted, 55 (37.9%) responded. Two individuals were recruited from study advertisement. 20/57 (35.1%) met screening and eligibility criteria. 85% of the sample engaged with intervention sessions and 55% completed at least 5/9 sessions. 80% of recruited participants completed the post-intervention questionnaire at Week 9. Mean score for overall acceptability was 43.4 (0-70). Qualitative feedback demonstrated the value of thought monitoring and facilitator support. Scores improved for quality of life and pain self-efficacy, and reduced for depression, anxiety, pain catastrophising and avoidance resting behaviour.

**Conclusions:** Online CBT for chronic IBD-related pain appears feasible and acceptable. The study suggests positive effects for improving quality of life and reducing psychological distress, however online and face to face recruitment methods are recommended and establishing efficacy through larger randomised controlled trials is required.
Introduction

Abdominal pain is a key symptom of inflammatory bowel disease (IBD). Pain is a hallmark symptom for assessing disease activity, guiding treatment decision-making and serving as a key outcome in IBD clinical trials (1). Yet chronic pain is a poorly understood and managed symptom of IBD. While 70-80% experience abdominal pain during active disease, up to half of patients continue to experience pain when disease is seemingly controlled as indicated by endoscopic and clinical disease markers (2). Many patients also experience extra-intestinal joint or musculoskeletal pain (3). Contributing factors to the aetiology of chronic pain include visceral hypersensitivity and dysregulation of the central nervous system (CNS) (2). Recent research has shown that a range of psychosocial factors, including depression, anxiety and fear avoidance, are associated with pain (4). Depressive symptoms and pain catastrophising have been shown to mediate the relationship between pain and pain-related disability in IBD (5). This suggests that altering cognitive and behavioural responses and negative mood in relation to pain may have beneficial effects on reducing its severity and impact.

Treatment approaches to modifying pain in IBD have included pharmacological, psychological and dietary techniques, summarised in a review by Norton et al. (6). There is a lack of consensus or guidelines on how to optimally manage long-term pain in patients with IBD. In many cases, the first line treatment of chronic pain in IBD is pharmacological, but many of these approaches either risk gastrointestinal complications or have not been tested specifically in IBD-pain populations in large randomised controlled trials (RCTs) (7). Treatment strategies used for chronic pain do not always relieve symptoms for patients with IBD (8). Developing an individual's coping, self-efficacy and ability to self-manage can lead to improvements in both mental and physical outcomes (9). A growing consensus advocates the use of psychological therapies in IBD (10) with the aim of attenuating both psychological distress and associated symptoms.

Cognitive behavioural therapy (CBT) is one of the most widely used psychotherapies for chronic pain (11), and is a recommend treatment approach for psychological co-morbidity associated with long-term conditions (12). It is based on the principles that low mood, unhelpful thoughts and behaviours are interrelated and can perpetuate physical symptoms (13). Meta-analyses have demonstrated equal efficacy between different modes of CBT including comparable effects from face to face and guided internet-delivered CBT for psychiatric and somatic disorders (14) and adults with depression (15). In a
recent large RCT, both online and telephone therapist-supported CBT led to significant improvements in quality of life and reductions in irritable bowel syndrome (IBS) symptom severity and impact (16).

In IBD, evidence supporting CBT is less conclusive. Mikocka-Walus et al.'s (17) RCT compared online or face to face CBT with standard care and found no changes in disease activity, quality of life or psychological distress. However, sub-analyses demonstrated improvements in quality of life at 6-month in individuals with greater baseline distress. Jordan and colleagues (18) screened for low mood and moderate anxiety and found that face to face CBT led to improvements in quality of life and reductions in psychological distress and symptomatic disease activity. Therefore, despite equivocal evidence of CBT in IBD to date, further work is needed to explore its efficacy in appropriate key sub-populations of IBD. This includes individuals with psychological comorbidity but also chronic IBD symptoms which have a psychological component, such as fatigue (19) and pain.

For chronic pain associated with a range of conditions, CBT has shown to have a positive effect on mood and pain-related impact (20). These include tailored CBT interventions which are formulated specifically for pain but may have downstream effects on secondary outcomes. For example, disease-tailored CBT interventions have been shown to reduce depressive symptoms, pain severity and interference, in human immunodeficiency virus (HIV)-pain (21) and multiple sclerosis (MS)-pain (22). Given the high comorbidity between chronic pain and depressive symptoms in IBD (4), CBT is a promising and appropriate psychotherapeutic approach to reduce pain-related distress and disability and to facilitate self-management.

To our knowledge, no online CBT intervention has been tested and evaluated in the context of chronic IBD pain. The Medical Research Council (MRC) framework for developing complex health interventions (23) was used to guide the development of an online self-management intervention for IBD-pain. Intervention components were mapped onto key psychosocial processes associated with pain (4, 24) and incorporated input from patients and healthcare professionals to ensure that the intervention was relevant and tailored to people with IBD. The aim of this study was to assess the feasibility and acceptability of an online facilitator-supported CBT-based self-management intervention, tailored for IBD-pain and delivered over 9 weeks. Specifically, our objectives were:

i) Explore response, recruitment and retention rates.

ii) Explore adherence through completion and time spent on intervention sessions.
iii) Explore feasibility for the intervention facilitator through website usage and conducting a follow-up interview.

iv) Collect quantitative and qualitative measures of acceptability.

v) Examine preliminary estimates of efficacy on pain-related interference and severity, quality of life and psychosocial measures including emotions, cognitions and behaviours.

Methods

Design

A single arm pre-post feasibility study with a nested qualitative component. Full ethics approval was received from King’s College London KCL REC Committee, KCL ethics ID: RESCM-18/19-8806.

Participants

Participants were recruited online via an IBD charity website (Crohn’s and Colitis UK - CCUK) and had previously completed an online survey about IBD-pain and consented to future research contact, or responded to an online advertisement. Eligibility and pre-screening criteria were as follows:

Inclusion criteria:

• Definitive diagnosis of Crohn’s disease (CD) or ulcerative colitis (UC) received by a gastroenterologist

• Diagnosed with IBD for at least six months

• Aged 16 years of age or over

• Sufficient command of written and spoken English

• Chronic or intermittent pain experienced for at least 3 months or more

Exclusion criteria:

• An inability to provide informed consent

• Currently recruited into a pharmacological intervention/clinical trial

• Have recently undergone a course of CBT within the last six months

• Currently actively receiving psychotherapy or active psychological treatment.

Pre-screening criteria:
• Scoring of 4 or more out of 10 on the Brief Pain Inventory (BPI) pain-interference scale, representing at least moderate pain-interference.

• No identified ‘red flags’ indicating acute severe disease or pain likely to be attributed to other disease-related causes (see Supplementary Table 1).

Recruitment

Participants who had taken part in a previous IBD-pain questionnaire study and consented to future research were contacted by email and sent a Participant Information Sheet. Potentially interested participants were sent pre-screening and eligibility questions. If participants fulfilled these criteria, they were emailed with a consent form and were given the opportunity to ask any further questions. Recruitment took place over a 4-month period (February to May 2019). 145 individuals were contacted by email. Once all participants had been contacted from the cross-sectional study, recruitment was also advertised via a CCUK website page advertisement, to which two individuals responded expressing interest and were recruited into the study. All participants recruited into the study provided written informed consent.

Procedure

Once participants provided informed consent to participate, they were emailed a link to the baseline questionnaire to complete online and provided with a unique study ID. Questionnaire items included sociodemographic and clinical data (IBD diagnosis, disease duration, IBD medication, pain medication), pain and psychological measures. Participants were sent a stool sample kit for faecal calprotectin via post and asked to return their stool sample to the laboratory. Remission status was defined by a faecal calprotectin score of < 250 ug/g. Once the baseline questionnaire was completed, participants were provided with a link to access the intervention. LS provided the participants with the opportunity to ask any questions before enrolling them onto the website. At Week 9, participants were emailed a link to complete the post-intervention questionnaire and were asked if they were interested in participating in an interview to provide feedback over telephone/Skype or face to face. Follow-up feedback interviews lasted approximately 30 minutes per participant and were semi-structured using a topic guide (Supplementary Table 2) and probing questions and were carried out by a researcher (LS). An in-depth interview was also conducted with the intervention facilitator to further assess feasibility.
**Intervention**

The intervention was developed by a team at King’s College London and guided by extensive stakeholder input, including people with IBD and IBD clinicians and other CBT-based protocols in long-term conditions (16, 19, 26). It comprised of 9 sessions (Table 1) to be completed one session per week, with Session 4a and 4b to be completed in Week 4. Sessions were based on a CBT framework and included tasks for participants to complete in their own time, such reviewing set goals or practising skills learnt within the sessions. Sessions and tasks were interactive, allowing for participants to select items or write text relevant to them and included audio and video clips. Participants were invited to complete their own ‘vicious cycle’; a visual diagram of the individual’s personal model of their thoughts, emotions and behaviours associated with their IBD-pain. Character illustrations and patient vignettes were also provided throughout sessions to contextualise examples and provide stories of people with IBD. The intervention was delivered through an online platform called ‘BOOST’, developed for a larger RCT study on the management of pain, fatigue and urgency in IBD. Participants were instructed to complete core sessions (1-6 & 9) and pain-specific sessions (7-8) for the 9-week programme and not select symptom-specific sessions on fatigue and urgency (but had access).
Table 1. Intervention sessions, brief summary of content and tasks to complete

<table>
<thead>
<tr>
<th>Session Title</th>
<th>Session Content</th>
<th>Session Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1: Understanding your IBD symptoms</td>
<td>Factors contributing to pain, fatigue and urgency, looking at the vicious cycle, use of self-monitoring and setting programme aims. <strong>Intervention facilitator phone call</strong></td>
<td>Symptom diary</td>
</tr>
<tr>
<td>Session 2: Balancing your activity, eating and exercise</td>
<td>The importance of activity and exercise and looking at the fear avoidance model, eating patterns and setting goals.</td>
<td>Working towards and reviewing goals for activity. Sleep diary</td>
</tr>
<tr>
<td>Session 3: Improving your sleep</td>
<td>The importance of sleep and looking at different sleeping patterns and habits. Techniques to improve your sleep. Setting goals.</td>
<td>Working towards and reviewing goals for sleep</td>
</tr>
<tr>
<td>Session 4a: Changing your thoughts: Part 1</td>
<td>The contribution of thoughts and the impact of these on pain. Identifying unhelpful thinking.</td>
<td>Keeping a thought record in the context of pain</td>
</tr>
<tr>
<td>Session 4b: Changing your thoughts: Part 2</td>
<td>Developing alternating thoughts in the context of pain.</td>
<td>Keeping a thought record and coming up with alternatives</td>
</tr>
<tr>
<td>Session 5: Managing stress and coping with emotions</td>
<td>The effects of stress and how to manage it, including mindfulness exercises. Looking at different emotions. Setting goals</td>
<td>Working towards and reviewing goals for managing stress and keeping a stress diary</td>
</tr>
<tr>
<td>Session 6: Making the most out of your social support and communication</td>
<td>Looking at different types of social support. Improving communication and disclosure. Setting goals</td>
<td>Working towards and reviewing goals for social support and communication</td>
</tr>
<tr>
<td>Session 7: Managing and understanding pain in IBD</td>
<td>Difference between acute and chronic pain, cause of IBD-pain, looking at the vicious cycle in the context of IBD-pain.</td>
<td></td>
</tr>
<tr>
<td>Session 8: The role of acceptance and self-compassion in pain</td>
<td>How can acceptance help me? Looking at resilience, self-compassion exercises.</td>
<td></td>
</tr>
<tr>
<td>Session 9: Summary and maintaining improvement</td>
<td>Revisiting programme aims, preparing for the future, sustaining improvements and building on them.</td>
<td></td>
</tr>
</tbody>
</table>

Facilitator support

After completing Session 1 in the programme, participants were invited to speak with the intervention facilitator over the telephone (for approximately 30 minutes) to review Session 1, the participant’s personal cognitive behavioural model and their programme aims. Participants were also able to contact the intervention facilitator through in-site messaging on the website. The facilitator for this study was a mental health nurse, who received training in CBT from RMM prior to carrying out phone calls. To ensure treatment fidelity, the facilitator had regular supervision from the BOOST intervention team and used a checklist and prompt sheet to structure telephone sessions.
Feasibility outcomes

Data collection for feasibility included measuring the proportion (percentage) of individuals eligible from the online cohort, participants consenting and agreeing to take part in the study and participants completing the post-intervention questionnaire (retention). Withdrawal and drop-out rates and compliance to and completion of treatment sessions and session tasks were also assessed.

Acceptability

Acceptability was measured quantitatively and qualitatively through seven key areas (27). This included affective attitude towards the intervention (positivity), how much effort was perceived by individuals, to what extent the intervention was effective, how helpful the intervention was perceived to be, to what extent participants understood the workings of the intervention, how confident participants felt to complete the session and tasks within the interventions and how costly partaking in the intervention was for participants (effort, time spent, resources etc). These were measured through a visual analogue scale (0-10) in the post-intervention questionnaire, and overall acceptability was indicated through the total score (0-70). The seven constructs were also embedded within the topic guide (Supplementary Table 2) utilised in semi-structured interviews for qualitative feedback on participant experiences of the intervention.

Secondary outcome measures

Pain-Related Interference and Pain Severity

Pain-related interference and pain severity were measured using the Brief Pain Inventory (BPI) (25). Pain-related interference is measured in seven domains including impact of pain on relationships, work, sleep and exercise ranging between 0 (does not interfere) to 10 (completely interferes). Pain severity is assessed by 4-items, including pain at the worst and least in the previous 24 hours, pain severity on average and pain ‘right now’ ranging from 0 (no pain) to 10 (pain as bad as you can imagine). BPI also asks for ratings on the extent of relief pain medications have provided in the prior 24 hours.

Quality of Life

The United Kingdom (UK) version of the Inflammatory Bowel Disease Questionnaire (UKIBDQ) (28) was used to measure health-related quality of life. This is a UK version of the McMaster IBDQ (29) and
is a 32-item questionnaire assessing various aspects of health-related quality of life. Questions assess aspects of quality of life including bowel, emotional, physical and social functioning. Summary scores range from 30-120, with lower scores indicating poorer health-related quality of life.

*Disease activity*

Disease activity was measured through the IBD-control questionnaire (30). This is a 13-item measure that assesses disease control from a patient perspective, including items on change in bowel systems or IBD treatment, impact and overall rating of control in the past two weeks.

*Depression*

Patient Health Questionnaire-9 (PHQ-9) was used to measure depression (31). The PHQ-9 assess symptoms within the prior two weeks using a 4-point Likert scale ranging from ‘never’ to ‘nearly every day’. Greater scores represent greater number of depressive symptoms, with a scoring of 0-4 representing minimum, 5-9 mild, 10-14 moderate, 15-19 moderate to severe and >20 representative of severe depressive symptoms.

*Anxiety*

The Visceral Sensitivity Index (VSI) (32) was used to measure gastrointestinal-specific anxiety. This is a 15-item scale with items assessing affective, cognitive and behavioural aspects of anticipatory occurrence of symptoms, rated on a 1-6 scale (strongly disagree to strongly agree). Items include “I constantly think about what is happening inside my belly”, with greater scores indicating greater gastrointestinal-specific anxiety.

*Pain Catastrophising*

Pain Catastrophising Scale (33) was used to assess thoughts that involve rumination, helplessness or magnification which exaggerate the threat of pain sensations. The scale is comprised of 13-items with a Likert range of 0-4 (Not at all to All the time) with greater scores indicating greater extent of catastrophising thoughts.

*Cognitive and Behavioural Responses to Pain; Fear Avoidance, Avoidance Resting Behaviour and All or Nothing Behaviour*
One cognitive and two behavioural sub-scales from the Cognitive Behavioural Responses to Symptoms Questionnaire (CBRQ)(34) were used to measure Fear Avoidance, Avoidance Resting Behaviour and All or Nothing Behaviour. Fear Avoidance sub-scale responses range from ‘strongly disagree’ to ‘strongly agree’ and behavioural sub-scales rated from ‘never’ to ‘all the time’.

**Pain Self-Efficacy**

Pain Self-Efficacy questionnaire (35) assesses the extent to which individual’s believe they can carry out actions and tasks, despite their pain. Scores are rated from 0-60 with higher scores indicating greater self-efficacy.

**Resilience**

Connor-Davidson Resilience Scale (CD-RISC)-10 was used to measure self-perceived resilience(36). The overall CD-RISC 10 score ranges from 0-40, where higher scores represent greater resilience.

**Statistical analysis**

A sample size calculation was not required a priori for this single-arm feasibility study. Consulting guidelines on sample size for pilot studies (37) and a similar intervention in IBD (19), a sample size aim of 20 participant per arm was deemed an adequate to assess for feasibility and acceptability, and allow for 70% retention rate. Descriptive data were presented as means and standard deviations (continuous variables) and percentages (categorical variables) at baseline and post-intervention (Week 9). Independent sample t-tests were used to compare participants at baseline who completed the post-intervention questionnaire or were lost at post-intervention data collection. Statistical analyses were carried out using SPSS (Version 25).

**Results**

**Sample characteristics**

Twenty participants were recruited and consented into the study. Sociodemographic and clinical characteristics of the study sample are presented in Table 2. Mean age of participants was 38.4 years (range 22-58 years) and the majority were female (80%), of White British origin (95%) and had a diagnosis of CD (80%). Mean scores for pain, quality of life, self-reported disease activity and psychological outcomes for the overall sample at baseline are presented in Supplementary Table 3.
Characteristics of the baseline and post-intervention (analysis) group were similar. Of the 20 participants, 15 (75%) returned a stool sample, of which 12 (60%) were in clinical remission. In the 16 participants who completed the post-intervention questionnaire, 13 participants returned a stool sample for faecal calprotectin, of whom 10 (76.92%) were in clinical remission.

**Feasibility: response and recruitment rates**

Figure 1 presents the participant flow in identification, screening, enrolment, data collection and analysis stages. Of the 145 individuals approached about the study, 55 individuals responded (37.9% response rate). 20 individuals (inclusive of two individuals expressing interest from CCUK advert) with IBD met pre-screening and eligibility criteria and provided informed consent (36.4% recruitment rate from those who responded to the email).

**Feasibility: retention rates**

Of the 20 participants who consented to the study, 20 (100%) completed the baseline questionnaire and were enrolled onto the website. One participant withdrew from the intervention (but not the overall study, agreeing to complete the post-intervention questionnaire at Week 9). From the 19 remaining individuals, 17 completed intervention sessions (85%) of the recruited sample. Of the 9 possible sessions, 2 (10.5%) completed 0 sessions, 2 (10.5%) completed 1-2 sessions, 4 (21.1%) completed 3-5 sessions, 9 (47.4%) completed 5-7 sessions and 2 (10.5%) completed all 9 sessions. 16 participants from the 20 recruited and consented into the study completed the post-intervention questionnaire at Week 9 (80%). Analyses found that participants who did not complete follow-up questionnaire data (n = 4) did not significantly differ to completers (n = 16) in baseline pain severity (p = .511) or pain-related interference (p = .164), age (p = .259), employment (p = .113) or educational status (p = .876). Mean disease duration was significantly lower in post-intervention questionnaire completers (mean = 10.9 years) compared to non-completers (mean = 22.5 years, p = .043). Quality of life was higher and self-reported disease activity and avoidance resting behaviour was lower in post-intervention questionnaire completers (p < .05). All remaining psychological factors did not significantly differ between post-intervention questionnaire completers and non-completers at baseline.
Feasibility: participant usage and facilitator usage

On average, a mean number of 3 messages were sent from participants (n=19) to the facilitator (min 0, max 8) and mean average of 3 messages were sent from the facilitator to patient. Participants spent a mean time of 19.84 minutes on each session (median 14 minutes, range 1-100 minutes). Out of a scoring of 5, mean scores across sessions on helpfulness = 4.1, relevance = 4, easy to navigate = 4.4 and motivation to use strategies covered = 3.6. 18 out of 20 participants responded to the facilitator in-site message and carried out a facilitator phone call at Week 1, while 2 participants did not respond to any facilitator messages nor complete any intervention sessions after consenting to the study.
Table 2. Baseline sociodemographic and clinical characteristics of 20 consenting participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants completing baseline questionnaire (n = 20)</th>
<th>Participants completing post-Intervention Questionnaire (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), yr</td>
<td>38.40 (9.87)</td>
<td>37.12 (10.53)</td>
</tr>
<tr>
<td>Female</td>
<td>16 (80)</td>
<td>13 (81.3)</td>
</tr>
<tr>
<td>English/Welsh/Scottish/N Irish/British</td>
<td>19 (95)</td>
<td>15 (93.8)</td>
</tr>
<tr>
<td>University degree or higher</td>
<td>13 (65)</td>
<td>12 (75)</td>
</tr>
<tr>
<td><strong>Employment status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed full time</td>
<td>10 (50)</td>
<td>8 (38.1)</td>
</tr>
<tr>
<td>Employed part time</td>
<td>2</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Full or part time education</td>
<td>2</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Full time domestic</td>
<td>1 (5)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Retired</td>
<td>1 (5)</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>4 (20)</td>
<td>3 (20)</td>
</tr>
<tr>
<td><strong>Relationship status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/civil partnership</td>
<td>9 (45)</td>
<td>7 (43.8)</td>
</tr>
<tr>
<td>Living with partner</td>
<td>5 (25)</td>
<td>5 (31.3)</td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (5)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Single</td>
<td>5 (25)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis (CD/UC)</td>
<td>16 (80)/4 (20)</td>
<td>12 (75.0)/4 (25.0)</td>
</tr>
<tr>
<td>Disease duration mean (SD) (yrs)</td>
<td>13.20 (10.46)</td>
<td>11.20 (8.53)</td>
</tr>
<tr>
<td>Faecal calprotectin mean (SD) ug/g</td>
<td>175.69 (205.69)</td>
<td>178 (218.98)</td>
</tr>
<tr>
<td><strong>IBD medication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-ASA</td>
<td>6 (30)</td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>Thiopurines</td>
<td>4 (20)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Anti-TNF (infliximab/adalimumab)</td>
<td>3 (15)/4 (20)</td>
<td>5 (31.3)</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>1 (5)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Steroids (methotrexate/budesonide/prednisolone)</td>
<td>3 (15) /3 (15) /2 (10)</td>
<td>2 (12.5)/2 (12.5)/ 2 (12.5)</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>5 (25)</td>
<td>5 (31.3)</td>
</tr>
<tr>
<td>None</td>
<td>2 (10)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Previous surgery</td>
<td>12 (60)</td>
<td>10 (62.5)</td>
</tr>
<tr>
<td><strong>Surgeries</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resection</td>
<td>5 (25)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Colectomy</td>
<td>3 (15)</td>
<td>5 (31.3)</td>
</tr>
<tr>
<td>Stoma</td>
<td>2 (10)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>3 (15)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Previous smoker</td>
<td>5 (25)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>12 (60)</td>
<td>11 (68.8)</td>
</tr>
<tr>
<td><strong>Pain Locations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen</td>
<td>18 (85)</td>
<td>14 (87.5)</td>
</tr>
<tr>
<td>Joints</td>
<td>14 (70)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td>Back</td>
<td>13 (65)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td>Head</td>
<td>8 (40)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td><strong>Pain Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>10 (50)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Co-codamol</td>
<td>4 (20)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Opioids</td>
<td>10 (50)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>1 (5)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>NSAI/Ds</td>
<td>3 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>3 (15)</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Antispasmodics</td>
<td>1 (5)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>1 (5)</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>1 (5)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Other (anti-diarrhoeal, anti-bile acid)</td>
<td>0 (0)</td>
<td>3 (18.8)</td>
</tr>
</tbody>
</table>
Figure 1. Study Flow Diagram of participants approached, consented and recruited into study.
Feasibility: qualitative feedback from intervention facilitator

A follow-up interview with the intervention facilitator further supported that the intervention was feasible. Feedback was divided into themes around i) phone call and website usage ii) preparations and training and iii) provision of support.

i) Telephone and website usage

The facilitator said that telephone sessions generally kept to time and were easy to schedule with the patients using the in-site messaging and personalised calendar.

However, the facilitator shared that they felt another phone call halfway through, or at the end of the intervention, would have been beneficial, “to say “well done for completing it or let’s review some of your reflections””.

ii) Preparations and training

Despite little knowledge of CBT or IBD before the study, the facilitator said that adequate training and education in both helped them feel prepared. Receiving supervision on case studies and examples of patient vicious cycles were perceived as the most valuable training preparations.

“It’s about being prepared, proactive and going away and learning what you need to learn”.

Resources provided to the facilitator such as prompt sheets and the patient’s online populated vicious cycle were useful to assess and have throughout the telephone sessions with patients:

“The script kept me on a structure and a focus to make sure I was covering what I needed to”.

“I would print out [the patient’s] vicious cycle and key reflections [before the phone call] and start to put linking arrows next to things which I could support the patient in linking up”.

iii) Provision of support

While the majority of participants messaged infrequently after they had had their telephone session, a small number messaged throughout, to which the facilitator felt they had provided adequate support and feedback:
"I had one patient who messaged me frequently as they felt at times unwell and anxious that they wouldn’t meet the timescale to complete the intervention. I offered them reassurance and understanding”.

The facilitator experienced some challenges with supporting patients in their understanding of their vicious cycle during phone calls but used techniques to aid this process, such as giving praise and validation.

**Acceptability: quantitative findings**

The mean acceptability scores for the seven constructs, and the total overall score rating for acceptability (0-100) are presented in Table 3.

**Table 3.** Mean scores for seven acceptability constructs measured in post-intervention questionnaire

<table>
<thead>
<tr>
<th>Acceptability construct (0-10) (n = 16)</th>
<th>Mean (SD)</th>
<th>Min-Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positivity</td>
<td>6.25 (3.19)</td>
<td>0-10</td>
</tr>
<tr>
<td>Effortful</td>
<td>6.31 (1.82)</td>
<td>2-9</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>5.38 (3.30)</td>
<td>0-10</td>
</tr>
<tr>
<td>Helpful</td>
<td>5.12 (3.24)</td>
<td>0-10</td>
</tr>
<tr>
<td>Understand workings of intervention</td>
<td>8.56 (1.97)</td>
<td>5-10</td>
</tr>
<tr>
<td>Confidence to complete</td>
<td>8.19 (2.01)</td>
<td>4-10</td>
</tr>
<tr>
<td>Costly (time, resources)</td>
<td>3.50 (2.99)</td>
<td>0-8</td>
</tr>
<tr>
<td>Overall acceptability</td>
<td>43.31 (11.31)</td>
<td>20-62</td>
</tr>
</tbody>
</table>

**Qualitative feedback: participants**

Acceptability of the intervention was also assessed through semi-structured interviews. Three themes were identified. These were ‘Facilitator and individual input’, ‘Thoughts and reflection’ and ‘Content and format’. These were broken down into sub-themes and are described below, illustrated by verbatim quotes and study ID in brackets.

1. **Facilitator and individual input**
   
i) Knowing someone was there

Participants were positive about the facilitator role, agreeing that even though they did not feel the need to be in frequent contact, having a facilitator gave them a source of support and a personal element to the programme:
“I felt I knew she was there if I needed her but at the same time, I was able to take things on board and didn’t feel the need to go back [to her]” (18).

“It was nice to touch base and know there is a human being behind what’s happening” (04).

However, one participant felt that more contact would have been beneficial:

“I feel I would have liked more contact with her on maybe a fortnightly basis, in the form of her dropping a message to see how I was getting on” (05).

ii) Self-management and control

While there was appreciation for facilitator support, there was a sense of empowerment that came out of individual work and input into the programme. This included developing a greater sense of control and autonomy:

“That’s how I viewed the study, not that it was going to take my pain away but that it is the mechanism as to how you manage it and put you back in control” (18).

“Going through these sessions its actually making me realise, as people we are really powerful and we can take a lot on for ourselves” (05).

…and the ability to change things for oneself by practising the techniques from the sessions:

“For me it was the thoughts session which I thought “I can change myself” quite quickly” (10).

2. Thoughts and reflection

i) Usefulness of thoughts session

The sessions on thoughts appeared to be the most helpful for participants and the skills that they would most likely take forward and continue to practise in their daily lives:

“For me it was being able to identify the thoughts and rationalise them in a much better way” (18).

“[I’m] definitely keeping up with the exercises and thought processes, the coming up with alternatives, I sort of do that in my head now” (10).

For one participant, this skill helped “set them on the right path” and as previously they had been “stuck in a rut” (04).
ii) Understanding and responding to pain

The exercises and content within the intervention enabled participants to have a better understanding of their pain, which had a positive impact on the way they responded to their pain. In particular, the use of the vicious cycle exercise was helpful in allowing individuals to “break things down” (MPIBD18) and rationalise their experience.

“The aspects on identifying my stressors and my vicious cycle was interesting as it helps me understand the thought processes going on when I am in pain” (05).

“It’s helping with my confidence in that way to think okay that’s just normalised pain as opposed to specific pain that’s sharper” (04).

3. Content and Format

i) Content and tone

Participants provided feedback on the content and tone of the intervention; with some of it being a “little repetitive” (04) and more than one feeling that the tone was overly patronising. One participant commented that some of the content was over-simplified such as consistent pattern of eating and regular exercise, as they highlighted the complexity of diet in IBD and that exercise was not easy to achieve, given their symptoms and health. This was shared by others who commented on the brief content covered on diet, within the exercise and activity session.

One participant noted that there were not enough practical tips offered in the intervention to help people with their pain:

“There are other natural things like hot water bottles and certain stretches and exercises that are good for pain, actual practical self-management tips for pain which are non-medicinal. It would be nice to have something similar to this, for times of acute pain”(04).

However, other participants found the varied layout and format of content was a good way of presenting lots of information, and the use of vignettes helped with putting session content into context of IBD.

ii) Length and workload
Some sessions, such as the ‘Managing Stress and Coping with Emotions’ session was felt too long by participants and that the weekly completion of sessions and tasks was too demanding for some who were impacted by multiple symptoms of their IBD.

“I found the [tasks] difficult to complete on a weekly basis simply due to life getting in the way and extreme fatigue and pain that my current flare has been causing” (05).

One participant also commented that the repetitive goal setting was overloading for them, while others liked this repetitive structure of goal setting associated with tasks.

iii) Online platform

The advantages of using an online platform was commented on, as this facilitated self-management and overcame barriers of face to face therapy.

“It was nice to be able to do [it] in my own environment and as and when I had the time”. (04).

“Seeing the questions and having the scenarios, I could take it on board more” (18).

However, one participant commented on the limitations of the use of an interactive website as the options “narrow[ed] down’ individuals” issues into “fixed categories” (02) and that the structure of the programme prevented them from accessing later more relevant sessions at an earlier stage.

Several of the participants shared that the online intervention was timely and well received. For some this was because they felt that although their medications were controlled, they did not feel in control of their IBD symptoms, while for others, they had been on a waitlist to see a psychologist and this platform allowed them to overcome this inaccessibility and regain a sense of self-management.

Secondary Outcomes – changes to pain, QoL and disease activity

Table 4 presents mean scores and standard deviations for secondary outcomes at baseline and post-intervention for the 16 participants with both measures. Small decreasing effects were seen in pain-related interference and pain severity, whereas a greater difference was evident in improvement of quality of life at post-intervention (Cohen’s d = 0.72). Disease activity measured through the IBD-control also showed improvement at post-intervention.

Secondary outcomes – changes psychological outcomes
Depression and anxiety decreased, and pain self-efficacy increased with small to medium effect sizes. Pain catastrophising scores decreased on average by 6.45 at post-intervention. Resilience or fear avoidance demonstrated minimal changes between the two time points, however avoidance resting behaviour showed reductions with a medium effect size at post-intervention (Cohen’s $d = 0.64$).

**Table 4.** Mean scores at baseline and post-intervention for pain outcomes, quality of life, psychological factors and disease activity

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Baseline n = 16</th>
<th>Post-Intervention n = 16</th>
<th>Cohen’s $d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain interference (0-10)</td>
<td>5.90 (1.69)</td>
<td>5.03 (1.81)</td>
<td>0.49</td>
</tr>
<tr>
<td>Pain severity (0-10)</td>
<td>4.92 (0.92)</td>
<td>4.45 (1.83)</td>
<td>0.32</td>
</tr>
<tr>
<td>Quality of life (30-120)</td>
<td>74.94 (10.38)</td>
<td>82.94 (11.94)</td>
<td>0.72</td>
</tr>
<tr>
<td>Depression (0-27)</td>
<td>14.19 (4.90)</td>
<td>10.69 (6.86)</td>
<td>0.59</td>
</tr>
<tr>
<td>Anxiety (0-75)</td>
<td>58.56 (15.31)</td>
<td>52.75 (16.99)</td>
<td>0.36</td>
</tr>
<tr>
<td>Pain catastrophising (0-52)</td>
<td>22.73 (9.18)</td>
<td>16.27 (10.42)</td>
<td>0.66</td>
</tr>
<tr>
<td>Fear avoidance (0-24)</td>
<td>13.13 (4.21)</td>
<td>12.06 (5.79)</td>
<td>0.21</td>
</tr>
<tr>
<td>Pain self-efficacy (0-60)</td>
<td>27.25 (6.27)</td>
<td>30.88 (9.62)</td>
<td>0.45</td>
</tr>
<tr>
<td>Resilience (0-40)</td>
<td>25.38 (5.06)</td>
<td>25.00 (5.59)</td>
<td>0.07</td>
</tr>
<tr>
<td>Avoidance resting (0-32)</td>
<td>14.20 (4.80)</td>
<td>11.13 (4.79)</td>
<td>0.64</td>
</tr>
<tr>
<td>All or nothing (0-16)</td>
<td>12.93 (4.03)</td>
<td>12.67 (5.27)</td>
<td>0.06</td>
</tr>
<tr>
<td>IBD control (0-100)</td>
<td>67.31 (15.50)</td>
<td>75.94 (17.99)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

**Discussion**

The aim of this study was to test the feasibility and acceptability of a therapist-supported online CBT based self-management intervention for chronic pain in IBD. Results reveal that the intervention is feasible and acceptable to participants and support testing of the intervention in a larger multi-centre RCT study. Results suggest the beneficial effects of the intervention on quality of life and psychological outcomes, with significant reductions observed in this sample for depression, anxiety, pain catastrophising and avoidance resting behaviour.

Regarding recruitment and retention, response rates were not as high as anticipated (37.9%), which may have been a result of email contact only rather than face to face recruitment. In some cases, participants would express initial interest to partake in the study and then not make further contact with the research team. Whether this was due to intentional or unintentional forgetting is unknown. Alternatively, the recruitment rate may be explained by complications within email methods, as emails may have not reached potentially interested participants (e.g. getting lost to junk/spam folders as was initially reported by some participants). Once expressing interest and reaching the pre-screening stage, a large proportion of individuals either presented “red flags” (clinical symptoms indicating active disease...
or complication) or scored less than 4 on the pain-related interference questionnaire, resulting in a recruitment rate of 36.4%. It may have been that the screening criteria threshold for pain-related interference was too high, however a moderate pain intensity score of 4 or more has been used as a threshold for chronic pain interventions studies in other long term conditions (22) and ensured that those with capacity to benefit were included.

At least 70% of participants completed three or more treatment sessions and over half of participants completed at least 5 out of 9 sessions. These findings are similar to previous CBT intervention studies in IBD (17) (where 48.8% of participants completed more than 4 sessions) and in HIV-chronic pain (21), and therefore was deemed feasible. Two participants did not complete any sessions and one dropped out of the intervention after Session 1, as they felt the content was not helpful for them. Unfortunately, those who completed no sessions did not reply to the research team after multiple contact, including invitation to be interviewed. Reasons for noncompletion may have been general disengagement with the programme, business of daily life or, due to the relapsing-remitting nature of IBD, coping with a flare or general challenges of living with IBD. Indeed, one participant in qualitative feedback shared that weekly completion of sessions and tasks was too demanding given their illness and current levels of pain and fatigue while undertaking the intervention.

Those completing the post-intervention questionnaire had greater baseline quality of life and lower self-reported disease activity, suggesting that individuals with poorer health and quality of life either require greater support throughout the programme or medical management to be optimised more thoroughly before entering the programme. Unlike previous RCTs, this study did not find effects of baseline psychological distress on retention rates (38). Participants who did not complete the post-intervention questionnaire had been diagnosed with IBD for a significantly greater time period. It may be that individuals who have had a longer diagnosis may less likely to engage in such interventions, possibly because they have tried psychotherapy previously, have had greater length of time to adjust to their IBD or have greater understanding of their symptoms and aetiology compared to those more recently diagnosed. Participants who did not complete the intervention did not significantly differ from completers on pain, sociodemographic or any other clinic outcomes.

Generally, content of the programme was well received by individuals; participants were positive about the online format, the thoughts session, ‘breaking things down’ and empowering individuals to feel more
in control of their pain. Several participants felt that some of the content was patronising and oversimplified, particularly given the complexity of certain aspects of IBD, such as diet and difficulties of engaging in exercise. It was concluded by the research team that given the heterogeneity in IBD diet research, covering diet in depth was not within the remit and aims of this intervention. However, further work should aim to understand how information and development of skills regarding diet can be implemented into a self-management intervention for pain in IBD.

The effect of having a facilitator included in the programme for support and reflection was positive, despite participants not feeling the need to regularly message the facilitator on a daily or weekly basis. This is important given the findings in previous online CBT interventions in IBD, which found high dropout rates in the absence of any therapist support (17). Evidently, some level of therapeutic engagement is important for sustained motivation and support when individuals take part in a psychological intervention in this population. An average of 3 messages were received by the facilitator, exemplifying the feasibility of the use of an online messaging platform to converse with patients in future online interventions in IBD.

The study did not find a clinically meaningful reduction in pain severity or pain-related interference, which was likely because the study was not powered to detect a difference. It may also be that effects on pain-related impact are more likely to be observed at a long-term follow up, and only once techniques learnt in the programme are implemented in daily use by individuals will effects on pain outcomes be observed. In Gromisch et al.’s (22) recent study on an CBT intervention for MS-related chronic pain, there was a significant effect of time observed for pain severity and pain-related interference, indicating a greater improvement with duration of treatment. Over 70% of the sample recruited at baseline were in clinical remission, defined by faecal calprotectin. However, participants may have had a flare or disease-related complications thereafter, which could have confounded the intervention effects on pain scores.

Although the study was not adequately powered, results suggest that the intervention may have positive effects in reducing emotional distress and pain-related thoughts and behaviours. Previously, a reduction of four points in depressive symptoms with a final score of 10 or less has been considered a clinically meaningful reduction (39), which was observed in this study. Given the reduction in scores of avoidance resting behaviour, it was surprising that this was not accompanied by significant reductions in fear.
avoidant thoughts. Reduction in negative psychosocial processes may have been explained by a reduction in disease activity, as IBD-control scores improved over the course of the programme.

Scores in resilience showed no change during the programme. While one could argue that resilience may be more a trait than state factor, a systematic review of ‘resilience training programmes’ in individuals with chronic conditions found a modest but consistent benefit on several mental health outcomes, suggesting that resilience can be modified by an intervention (40). Leppin and colleagues contend that resilience is a “modifiable construct and not an inherent, immovable trait of individuals” (40)(pg. 2). Furthermore, a large proportion of these reviewed studies used the CD-RISC measure, as was used in the current study. While pain self-efficacy showed small to moderate improvements, an overall smaller effect on positive psychosocial outcomes may have been explained by a lesser focus on positive psychological techniques, which was included in one out of the nine sessions, compared to the majority of sessions aiming to modifying negative or unhelpful psychosocial processes. Alternatively, it may be that negative psychological processes are more amenable to change through intervention compared to positive, or that ‘resilience states’ are context dependent. Future research should endeavour to examine whether an intervention with greater emphasis on positive psychological intervention techniques results in improvement in resilience, self-efficacy and other positive psychological factors in IBD (e.g. optimism, self-regulation, perception of social support).

**Strengths and limitations**

A key strength of this study was the use of the MRC framework for complex health interventions (23) to guide development of this intervention, which facilitated the acceptability and feasibility of this intervention. This included extensive stakeholder involvement to ensure that content was relevant and tailored to individuals with IBD and chronic pain, and that session and task length was feasible given the demands of living with a chronic condition. Key limitations include the lack of both online and face to face recruitment methods to optimise recruitment rates, and a control group to determine initial estimates of efficacy in comparison with an active treatment arm, treatment as usual or waitlist control. A lack of long-term follow up limited our understanding of whether pain or other psychological outcomes showed improvements at a longer follow up, as pain or psychosocial outcomes may have demonstrated a delayed treatment effect. Finally, nested qualitative interviews were carried out by LS who was involved in the intervention development, and therefore social desirability bias may have been pertinent
during interviews and limited the information and views shared by participants. Related to this, participants who completed few or no treatment sessions were not interviewed, therefore issues regarding feasibility and acceptability for these participants were not collected.

**Conclusion**

This study has demonstrated the feasibility and acceptability of an online CBT-based self-management intervention for IBD-related chronic pain. The content, online format and facilitator support were well received by participants and preliminary estimates of efficacy demonstrated improvements in quality of life and reductions in negative affect and pain-related thoughts and behaviours. Further research is recommended in a large scale RCT to confirm efficacy of the intervention, using a combination of face-to-face and online recruitment methods to optimise uptake.

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Chapter 9 Discussion

9.1 Chapter Overview
This final chapter provides a summary of all the studies’ findings and their contribution to the wider literature, including developing a biopsychosocial understanding of IBD-pain and informing psychological interventions in IBD. Overarching strengths and limitations of thesis methodology and studies is presented, including critical evaluation of the application of the BIS/BAS theory of chronic pain and the MRC framework to guide complex intervention development. Implications for clinical and research settings are discussed, including future recommendations for IBD-pain research, management and assessment, and overarching thesis conclusions.

9.2 Summary of key findings
The aim of this thesis was to develop and feasibility test a self-management intervention for pain in IBD. Findings provide a unique contribution to an understanding around emotional, cognitive and behavioural responses to pain in IBD and provide important implications for future research into treatment approaches for IBD pain management. Guided by the MRC framework (Craig et al., 2008), a systematic review and quantitative and qualitative studies were undertaken to gain a better understanding of psychosocial factors associated with pain in IBD. The BIS/BAS model of chronic pain (Jensen et al., 2016) was selected as an appropriate and comprehensive theoretical framework to guide intervention development. This two-factor theory suggests the role of inhibitory-related ‘risk’ psychosocial factors associated with greater pain and approach-related ‘protective’ factors that buffer the impact and severity of pain. Identified psychosocial factors in the context of IBD-pain were mapped onto evidence-based intervention techniques, and a tailored CBT-based intervention for IBD-pain was tested for feasibility, acceptability and preliminary estimates of efficacy.

Results from 15 studies included in the systematic review (Sweeney et al., 2018; PhD paper 1) demonstrated negative and positive psychosocial factors associated with IBD-pain, including emotional, cognitive and behavioural processes. Depression and anxiety were the most commonly investigated psychosocial factors associated with pain, and cognitive-behavioural factors included pain catastrophising and fear avoidance associated with greater pain and perceived social support which was negatively associated with pain. The review provided preliminary support for a two-factor model and most studies were of medium to high quality. However, the majority of studies were limited in their
assessment of pain, using pain sub-scales from quality of life or disease activity measures. Therefore, this reinforced the need for future studies to utilise validated and comprehensive pain measures, assessing pain severity and impact or disability. Six reviewed studies assessed disease activity and found a relationship between active disease and pain, however four studies found that psychosocial factors remained significant when controlling for disease activity, further supporting a biopsychosocial model of IBD-pain. Given the literature discussed on psychosocial processes (Chapters 1-2) identified in primary chronic pain and IBS, further research was required to explore other psychosocial processes and their potential relationship with IBD-related pain.

The cross-sectional study (Sweeney et al., in press; PhD paper 2), inclusive of 183 NHS-recruited and 114 online participants from an IBD charity website, used the Brief Pain Inventory (Cleeland & Ryan, 1994) to investigate potentially modifiable psychosocial factors associated with pain severity and pain-related interference. This confirmed psychosocial factors associated with IBD-pain presented in the systematic review, such as depression, anxiety, pain catastrophising and fear avoidance. However, it also demonstrated that other specific cognitive-behavioural responses to pain, such as symptom focusing, damaging beliefs and all or nothing behaviour, were associated with IBD-pain. This revealed more specific unhelpful cognitive and behavioural strategies related to IBD-pain that could be targeted and potentially modified through an intervention. Moreover, supporting the BIS/BAS theoretical framework, the cross-sectional study showed ‘protective’ psychosocial factors - pain self-efficacy and flourishing mental well-being – were associated with less pain severity and related-interference. However, contrary to study hypotheses, pain acceptance was not significantly associated with pain outcomes, which may have been explained by the use of a chronic pain acceptance questionnaire in a sample who were not all experiencing chronic IBD-pain. Given the cross-sectional design, causality could not be determined, and it is indeed plausible that having less pain may foster flourishing mental well-being and self-efficacy. Nonetheless, findings suggest that targeting positive psychosocial factors may be of value in the context of intervention development for IBD-pain. Pain outcomes significantly correlated with disease activity scores measured by the HBI and SCCAI, which remained significant in the regression model. This reinforced that disease activity has a significant impact on pain outcomes and thus medical management should be optimised to reduce pain severity and disability. However, it was also considered that disease activity indices in IBD are completed largely through patient symptom reporting and therefore could be influenced by psychological distress, highlighting the possible bi-
directional relationship between negative affect and disease activity. Overall, the identification of pain-related emotional, cognitive and behavioural processes in the cross-sectional study informed the BIS/BAS model of IBD-pain and treatment targets for intervention development.

Accounting for limitations in a cross-sectional survey and adhering to recommendations from the MRC framework guidance (Craig et al., 2008), a qualitative study was conducted to gain a further understanding of psychosocial processes in IBD-pain. Fourteen interviewed participants were asked about their experiences of pain, current pain management strategies and needs for a pain management intervention. Thematic analysis of transcribed interviews revealed three key themes; i) vicious cycles ii) finding solutions and iii) attitudes. The theme of vicious cycles was described in the context of pain and other IBD symptoms, namely fatigue and urgency, and the overall impact these had on inactivity, anxiety and lack of communication or understanding about IBD. The heterogeneity in the nature and triggers of pain and lack of guidance from healthcare professionals resulted in individuals implementing their own personal coping strategies, which were largely based on previous experience. This included short and long-term strategies, such as modifying diet, and concerns were raised about long-term use of and reliance on pain medication. Yet, overall, many participants demonstrated their ongoing search for a solution for their pain. Different attitudes were taken in response to pain; some took an accepting approach which seemed to enable them to adapt and function more effectively. Contrastingly, others felt defeated by their pain, as they were in a constant battle of fighting or tolerating their pain, taking a ‘grin and bear it’ approach. Thus, qualitative findings highlighted the significant emotional and physical impact on individuals with IBD. The identification of sub-themes in vicious cycles supported the identification of anxiety and fear avoidance in the cross-sectional study. Moreover, contrasting attitudes and their emotional impact reinforced the influence of cognitive and emotional factors associated with IBD-pain.

Incorporating findings from the systematic review and mixed methods studies, a theoretical model of IBD-pain was developed and CBT techniques were mapped onto psychosocial processes in a BIS/BAS model to formulate the treatment protocol (Chapter 7). The intervention development process included extensive stakeholder involvement and integration with the IBD-BOOST study and culminated in the final intervention to be tested in the feasibility study. The feasibility study included 20 individuals with IBD and chronic pain and pain-related interference (scoring ≥4/10 on the Brief Pain Inventory). Although
response to study invitation and recruitment rates were low (possibly due to recruitment methods),
retention and completion of the intervention was generally positive; 85% of the consented sample
engaged in intervention sessions (58.8% completing at least five out of nine sessions) and 80% (n=16)
completed the post-intervention questionnaire. Quantitative and qualitative assessment demonstrated
the intervention was acceptable to participants. Feedback demonstrated the usefulness of the content
around monitoring and changing thoughts, that the intervention enabled participants to feel more in
control of their pain and that the support of the facilitator was valued. Facilitator feedback demonstrated
the importance of adequate CBT training prior to supporting patients and the feasibility of in-site
messaging with regards to volume and content. Small reductions were noted for scores in pain-related
interference and severity, and quality of life and pain self-efficacy appeared to improve following the
intervention. Reductions were seen in depression, anxiety, pain catastrophising, avoidance resting
behaviours and disease activity. Minimal changes were seen for scores of resilience, fear avoidance or
all or nothing behaviour. Overall, the study demonstrated that the intervention was feasible and
acceptable, and a full-scale RCT (with a greater sample size to provide adequate power to the study)
is required to demonstrate potential effectiveness and cost-effectiveness for IBD-chronic pain.

9.3 Contributions to the literature

9.3.1 Developing a biopsychosocial model of IBD-pain

Previously, research recognised that pain in IBD is a multifactorial construct, influenced by peripheral,
central, neurophysiological and psychological factors (Bielefeldt et al., 2009). This includes the role of
visceral hypersensitivity and dysregulated pain signalling, as well as central processes of negative affect
and hypervigilance, which can have a top-down disinhibiting effect on pain processing. While this
represented an important step forward in IBD-pain research and avenues for potential treatment
options, there still lacked a deeper understanding of psychosocial processes related to IBD-pain. The
systematic review presented in Chapter 4 was the first to synthesise findings on psychosocial factors
investigated in the context of IBD-pain, providing an insight into emotional, cognitive and behavioural
processes. This laid the foundations for intervention development, ensuring that techniques were
tailored to psychosocial processes identified in IBD-pain populations specifically. Indeed, Norton et al.
(2017) demonstrated the lack of theoretical guidance or justification in previous intervention studies for
abdominal IBD-pain management. For example, previous stress management or coping skills training
interventions were largely based on associations between stress and physical functioning in IBD (Garvia-Vega & Fernandez-Rodriguez, 2004; McCormick et al., 2010), rather than key explanatory processes related to pain severity and pain-related disability. The heterogeneity in pain management interventions further emphasised a lack of coherence regarding psychosocial processes in IBD-pain.

Psychosocial factors identified in the systematic review overlap with similar reviews, such as psychosocial factors and adjustment to chronic pain (Jensen et al., 2011) and a narrative review of psychological mechanisms in IBS-abdominal pain (Elsenbruch et al., 2011). For example, Jensen et al. (2011) included chronic pain populations from several long-term conditions, such as MS, spinal cord injury and muscular dystrophy, and found that catastrophising, resting coping responses and task persistence (related to all or nothing behaviour) were associated with pain and dysfunction. Stress, anxiety and depression have been identified as key psychological factors affecting central processing of pain stimuli and inhibitory pathways in abdominal pain in IBS (Elsenbruch et al., 2011). The overlap in psychosocial factors between IBS and IBD identified in this review supports the IBS-IBD continuum hypothesis of shared mechanisms contributing to functional symptoms, and the application of IBS interventions in the context of functional symptoms in IBD (described more in detail in Section 9.3.4).

Since the publication of the systematic review presented in Chapter 4, a further systematic review has explored psychosocial factors with IBD-pain, including impact on quality of life (Robertson et al. 2019). This included 23 articles, 10 and 13 studies with adult and paediatric populations respectively, and confirmed the relationship between depression, anxiety and low quality of life and pain, albeit with an inconsistent association with anxiety in paediatric samples.

The investigation of other pain-specific cognitive and behavioural responses in the cross-sectional study broadened a biopsychosocial understanding of IBD-pain. Embarrassment avoidance, all or nothing behaviour and avoidance resting behaviour suggest cognitive-behavioural strategies which, if become default or habitual responses in the long-term, could perpetuate psychological and physical function. For example, disruption of sleep-wake cycles through over-exertion of oneself (to meet demands when feeling 'well') or excessive rest can negatively impact symptoms, such as fatigue and pain (Strober & Arnett, 2005; Skerret & Moss-Morris, 2006). Symptom-focusing and damaging beliefs in the context of IBD-pain are particularly important and challenging to target therapeutically; individuals with IBD are likely to have experienced pain in response or prior to a disease flare or complication, and indeed will
naturally monitor their symptoms in managing their disease. However, greater levels of bodily scanning and rigid thoughts that pain is a sign of damage are also likely to have a significant impact on negative thoughts, low mood and impaired functioning (Lackner & Quigley, 2005; Bielefeldt et al., 2009). Therefore, the cross-sectional study moved beyond negative affect and hypervigilance toward pain-related cognitive and behavioural responses that may be contributing to pain and pain-related disability. This is informative for the development of an intervention as well as having clinical implications for practitioners (described in more detail in Section 9.8).

Investigating positive psychosocial factors in this thesis has broadened the lens on types of psychosocial processes that may be operating in the context of IBD-pain. The association between pain self-efficacy and mental well-being with less pain in the cross-sectional study supports the potential role of buffering psychosocial processes on developing pain, impact and psychological comorbidity. Furthermore, the sub-theme of ‘acceptance’ in the qualitative study suggested the positive impact that accepting approaches to pain may have on functioning and mood. Keefer et al. (2018) argue that screening for vulnerability and protective factors in patients, and early intervention on these processes, can reduce the risk of development of chronic functional symptoms or psychological comorbidity. How interventions targeting vulnerability and protective factors may be incorporated and implemented in gastroenterology practice is presented in Figure 18 (Keefer, 2018). This proposal aligns with the two-factor model in BIS/BAS and the potential role of screening chronic pain patients on BIS/BAS tendencies to guide ‘treatment matching’ (Day et al., 2015) (discussed in Section 9.4.4). The findings in this thesis provide a novel contribution to this notion of ‘positive psychogastroenterology’ by isolating protective psychological processes in the context of IBD-pain specifically. The tailored BIS/BAS model presented in Chapter 7 provided a comprehensive and evidence-based theoretical model to aid a biopsychosocial understanding of pain in IBD. The identification of positive psychological factors and implications for the BIS/BAS model of pain in IBD is described in more detail in Section 9.4 in this chapter.
9.3.2 Understanding the impact of pain in IBD

The cross-sectional and qualitative studies provided a greater understanding of the impact of pain on psychological and physical functioning. This is important not only for intervention development but to indicate other research areas of investigation required in the context of IBD-pain (described in Section 9.7). Research has shown the impact of pain on health-related quality of life (Schirbel et al., 2010; Zeitz et al., 2016), with fewer studies on specific areas of impact, such as work absenteeism (van der Have et al., 2015). This thesis has uniquely contributed to an understanding of IBD-pain using qualitative research and uncovered other areas where pain interferes with individuals emotional and physical well-being. The qualitative study provided an insight into pain in the greater context of individuals’ lives; worries around work performance, lack of understanding from peers, fear and low mood associated with inactivity and the positive impact that an accepting approach had with living with pain long-term.

To the knowledge of the thesis author, the qualitative study was the first to qualitatively explore IBD-pain outside a hospital context. One previous qualitative study revealed the stigma, lack of understanding and the role of the nurse with regards to pain control for people with IBD in the acute setting (Bernhofer et al., 2017). Parallels with the qualitative study in this thesis included the importance of caregivers or social support and the frustration shared about the unrelenting nature of pain.
The association between pain and impact on dietary behaviours in the cross-sectional study contributes to the growing literature on pain and food-related quality of life. Recent studies have shown the association between pain and skipping meals and overall less satisfaction with food (Coates et al., 2018; Czuber-Dochan et al., 2019a). Furthermore, the qualitative study showed that pain in remission was frequently attributed to diet, and participants had implemented a wide range of dietary strategies in an attempt to control pain. In the context of intervention development, these findings supported the inclusion of content on diet and the importance of regular eating for digestive function. While some dietary approaches tested in IBD have recently shown positive effects for functional symptoms such as bloating and flatulence (Cox et al., 2019), very restrictive diets can be challenging for patients and impact on food-related quality of life, and affect nutritional deficiencies leading to malnutrition (Czuber-Dochan et al., 2019a; Czuber-Dochan et al., 2019b). Thus, in the wider context, these findings suggest a need for further research to understand the role of diet and pain in IBD and intervention strategies for patients.

### 9.3.3 Psychological interventions in IBD

The evidence base for CBT interventions in IBD was reviewed in Chapter 7 Section 7.2.5 and demonstrated inconclusive findings, largely attributable to limitations in study methodology and heterogeneity in study aims. Several systematic reviews conclude that the effects of CBT on modifying disease status in IBD is weak, with outcomes of health-related quality of life and mood showing more promising effects (McCombie et al., 2016; Ballou & Keefer, 2017; Gracie & Ford, 2017; Li et al., 2019). For online psychological interventions, the evidence is similarly equivocal, with more promising evidence in IBS populations (Hanlon et al. 2018). However, this thesis differed by developing a psychological intervention for IBD-pain specifically, thus contributing to the novel and emerging area of psychological interventions for IBD-symptom management, rather than disease control. This reinforces the importance of tailoring interventions not only to a disease population, but to disease-related symptoms and understanding the impact, needs and psychosocial factors associated with symptoms to develop effective interventions. Thesis findings mirror research on psychosocial factors associated with fatigue in IBD, such as similarities in emotional (depression, anxiety) and cognitive-behavioural responses (avoidance) (Artom et al., 2016; Artom et al., 2017a), thus informing research on symptom clustering in IBD (Conley et al., 2017) and possibly shared psychosocial mechanisms underlying comorbidity of pain and fatigue in IBD (Jelsness-Jørgensen et al., 2017). In addition, the biopsychosocial
model of pain developed in this thesis contributes to the body of literature demonstrating the value of the disease-specific models of chronic pain, such as in research in MS and HIV-related pain, which have similarly led to tailored self-management interventions and shown positive outcomes in quality of life and reducing distress (Uebelacker et al., 2016; Gromsich et al., 2019).

Despite differences in primary outcomes between this thesis and prior CBT interventions for IBD, the thesis author considered several limitations in prior studies’ methodology. This referred predominantly to a lack of therapist support in an online intervention study (Mikocka-Walus et al., 2017) and appropriate screening criteria to identify individuals ‘in need’ and thus more likely to benefit from the intervention. This provided a strong rationale for guided therapist support of one telephone call following Session 1 and subsequent patient driven in-site messaging. Similarly, participants in the feasibility study were screened for pain-interference scores of ≥4/10 on the Brief Pain Inventory to identify individuals with at least moderate scoring of pain-related interference, as well as meeting the classification for chronic pain. While the intervention effects did not show changes in pain outcomes, changes were seen for quality of life, depression, pain catastrophising and self-reported disease activity, thus demonstrating beneficial effects on individuals experiencing IBD-chronic pain. Therefore, the results from the feasibility study informed the wider body of literature on psychological interventions in IBD for two reasons: i) having some level of therapist-support for online psychological interventions for individuals with IBD is beneficial for optimising retention and completion rates (as supported by qualitative feedback) and ii) appropriate baseline screening is recommended to optimise recruitment of individuals who are more likely to benefit from an intervention (e.g. higher scores on psychological distress, symptom severity or disability). However, the feasibility study highlighted other aspects to consider for future psychological interventions in IBD, such as the use of face to face and online recruitment methods to improve recruitment rates, and areas for improvement of content. This includes avoiding patronising or oversimplified language and providing more information on practical strategies to manage pain such as diet (discussed in research/clinical implications Sections 9.7 and 9.8).

9.3.4 Informing the IBS-IBD continuum

As discussed in Chapter 1 Section 1.8.4, psychological intervention for patients with IBS is a rapidly growing field and may be beneficial for patients with functional symptoms in IBD (Grover et al., 2009; van Tilburg et al., 2013, Hungin et al., 2015, Mayer et al., 2015; Quigley, 2016; Colombel et al., 2019).
However, before these approaches are tested and recommended in the context of IBD-pain, a better understanding of psychosocial processes is required. Thus, this thesis provided the opportunity for psychosocial factors within a suggested ‘IBS-IBD continuum’ to be explored. Conceptualising symptoms in IBD-remission as IBS, however, is a challenging and disputed area in the IBD literature. On the one hand, it has been argued that chronic symptoms, such as pain in quiescent IBD, indicate IBS-like pathophysiology. Indeed, parallels in central and peripheral processes, such as visceral hypersensitivity, gut permeability and top-down disinhibition disrupting pain pathways are shared hypothesised mechanisms between IBD chronic pain and IBS. On the other hand, cortical processing of visceral stimuli in UC patients has shown greater similarity with healthy controls than IBS patients in a rectal balloon distension study (Mayer et al., 2005), challenging this suggested overlap in peripheral central processing of pain.

Findings from this thesis have demonstrated the significant overlap in psychosocial processes in IBD-pain and IBS. For example, catastrophising and anxiety were identified as significant factors associated with symptoms severity in a cross-sectional study of IBS patients (van Tilburg et al., 2013). Similarly, a systematic review of mediators of CBT interventions for IBS demonstrated the mediating effects of gastrointestinal-related anxiety and cognitive and behavioural responses in explaining the mechanisms of CBT improvements on symptom severity and related functional impairment (Windgassen et al., 2019). Indeed, the IBS literature partly informed the selection of psychosocial factors to be investigated in the cross-sectional study, such as cognitive and behavioural responses to symptoms measured through the Cognitive and Behavioural Responses to Symptoms Questionnaire (CBRQ) (Skerrett & Moss-Morris, 2006), and gastrointestinal-related anxiety using the Visceral Sensitivity Index (VSI) (Labus et al., 2004) in the feasibility study. Similar significant associations identified with IBD-pain in the cross-sectional study support the overlap in modifiable psychosocial processes in IBD-pain and IBS populations, and the application of psychological interventions for IBD-pain previously tested for IBS. This not only includes CBT-based interventions but the investigation of other psychological interventions that are emerging, such as gut-directed hypnotherapy and acceptance and commitment therapy-based approaches (Ballou & Keefer, 2017; Sebastián Sánchez et al., 2017).

However, it is also important to consider aspects within the thesis that challenge this suggested overlap. In the qualitative study, one participant shared that treatment approaches used in IBS and the diagnostic
label of IBS-IBD had not been helpful for them. Although this summarises one individual’s experience, it flags that clinicians must be cautious not to rely on a diagnosis of IBS-IBD, as patients’ symptoms of pain may not be alleviated by IBS approaches and a holistic biopsychosocial assessment of patients’ needs is essential (described more in clinical implications Section 9.8). This is supported by other qualitative work in IBD which shows individual’s frustrations at misconceptions over IBD through labelling symptoms as IBS (Matini & Ogden, 2016). In the cross-sectional study, use of diagnostic criteria such as the Rome IV classification (Drossman & Hasler, 2016) to classify IBS in IBD, rather than the IBS-symptom severity score (Francis, 1997), may have revealed distinct psychosocial factors in individuals with IBD and pain only, compared to pain with accompanying gastrointestinal symptoms (e.g. change in stool frequency/appearance), and yielded greater clarity on disentangling mechanisms underlying this complex gut-brain continuum.

9.4 Critique of theory: implications for the BIS/BAS model

9.4.1 BIS/BAS hypotheses

To aid an understanding of how psychosocial processes may be operating in IBD-pain in this gut-brain continuum, the Behavioural Inhibition System and Behavioural Activation System (BIS/BAS) model of chronic pain was selected (Chapter 2). This framework suggests that two independent neurophysiological systems underlie behavioural responses to environmental cues and sensory information (Jensen et al., 2016). Within these independent but interacting systems are emotional, cognitive and behavioural processes, which in the context of anticipated threat or reward, are expected to activate the BIS or BAS system, respectively. The model posits that pain is expected to activate the BIS-system and thereby emotional (anxiety, fear), cognitive (hypervigilance) and behavioural (withdrawal) processes that serve to help the individual ‘stop, look and listen’ and focus their awareness to threatening cues or stimuli that may lead to harm or danger. While this is an inherently adaptive system, activating automatically outside our conscious awareness, these inhibitory processes are suggested to exacerbate the pain experience in chronic pain and lead to further pain and pain-related disability. A detailed summary and key strengths of the BIS-BAS model in relation to other psychological approaches to chronic pain are discussed in Chapter 2 Section 2.2.3-2.2.4. Key hypotheses from the model include the mutually interacting characteristics of BIS or BAS-related cognitive, emotional and behavioural factors and therefore can either be causal mechanisms or outcomes within BIS/BAS cycles. The model argues that psychosocial interventions operate by teaching individuals to ‘respond less
automatically’ and develop new associations which facilitate approach-behaviours, positive mood and goal attainment. Moreover, the model emphasises the evidence-base demonstrating the independent and distinct nature of these two systems, such that a decrease in negative affect does not necessarily indicate an increase in positive affect (Watson & Tellegen, 1985; Russell & Carroll, 1999). However, the two systems may have a mutually inhibitory effect on each other.

Aligning with the MRC framework, the selection of the BIS/BAS theory was used within intervention development, conceptualising psychosocial processes and intervention techniques. For example, results from the systematic review provided preliminary support for the BIS/BAS model, as negative risk factors and positive protective factors were identified. This supported further investigation into negative and positive psychosocial factors in the cross-sectional study, acknowledging the potential role of emotional, cognitive and behavioural factors associated with IBD-pain. Based on cumulative findings from the systematic review and mixed methods studies, the BIS-BAS model was then used to guide intervention techniques. This included informing the logic model in intervention mapping (Chapter 7 Section 7.2.8), and treatment targets to reduce BIS-related negative thoughts and unhelpful behaviours and increase BAS-related processes through techniques of behavioural activation and positive psychology.

### 9.4.2 Findings in support of the BIS/BAS model

Although the aim of the thesis was not to directly test the BIS/BAS model (Jensen et al., 2016), findings throughout thesis studies were supportive of the BIS/BAS model of chronic pain. Firstly, the BIS-BAS model suggests that BIS factors are positively related to other BIS-related processes and vice versa for the BAS. Indeed, the cross-sectional study demonstrated positive correlations between psychosocial factors within BIS and BAS-related cycles, and negative correlations between BIS and BAS (see Appendix B.2.5 for full correlations table). For example, pain self-efficacy negatively correlated with anxiety and fear avoidance, and positively correlated with psychological well-being. This supports prior research and central tenants to the framework, of the distinct and interacting psychosocial processes within BIS and BAS cycles (Jensen et al., 2016; Day et al., 2019). Furthermore, the BIS/BAS hypotheses that pain is positively associated with BIS-related processes and negatively associated with BAS-factors, which was also supported in the cross-sectional study findings for pain severity and related-interference (see Chapter 5). This contributes to a previous, albeit small, body of research on
the BIS/BAS model of chronic pain, which demonstrates the association between BIS/BAS systems and pain-related impairment and psychological functioning (Day et al., 2019; Serrano-Ibáñez et al., 2019).

Qualitative findings also aligned with principles of the BIS/BAS model. Findings echoed the role of cyclical processes that contribute to the negative experience around pain, particularly cycles of anxiety and inactivity (Chapter 6). The attitude of acceptance shared by some interviewees supports the protective role of BAS activation on pain perception and related impact, as it appeared to allow them to feel more in control of their pain and engage in meaningful activities. Interestingly, the qualitative study also revealed findings in relation to the dual processing of BIS/BAS cycles. Jensen et al. (2016) state that both cycles can be active at the same time; whichever cycle is activated and guides the behavioural response depends on the goal in question. The sub-theme of avoidance and inactivity under vicious cycles represented individual’s frustration at not being able to exercise because of their symptoms, despite willingness to try (and find solutions). This suggests evidence of some individual’s cognitive dissonance at wanting to try and find solutions for their pain yet having functional (fatigue) or psychological (fear) barriers that hinder them.

While the BIS/BAS model of chronic pain does not prescribe a single interventional approach, it suggests that psychosocial interventions operate by targeting BIS or BAS cycles, or both. Consequently, the model hypotheses that interventions targeting BIS or BAS processes should see changes in emotional, cognitive and behavioural outcomes within the targeted cycle. CBT uses a wide range of intervention techniques, including cognitive restructuring and behavioural activation, and thus has the potential to target BIS and BAS processes. The logic model presented in Chapter 7, summarised how CBT techniques were mapped onto processes identified in the BIS/BAS model of IBD-pain. Expected outcomes from the intervention included a reduction in BIS-related processes and an increase in BAS-related processes. In support of the model, albeit in an underpowered sample, the feasibility study showed reductions in depression, anxiety, pain catastrophising and avoidance resting behaviour, and improvements in pain self-efficacy. In the aim of reducing BIS activation, intervention sessions focused on reducing negative psychosocial processes; the vicious cycle exercise encouraged individuals to identify negative thinking patterns and emotions and unhelpful behaviours in response to their pain. Psychoeducation, such as of the fear avoidance model (Session 2) and exploring
mechanisms in acute and chronic pain (Session 7), aimed to reduce BIS-related processes of pain catastrophising, fear avoidance and avoidance resting behaviours. The effects of psychoeducation are suggested to change the meaning individuals’ give to their pain, shifting their response of ‘I need to act to stop this pain’ to an understanding that, the pain they frequently experience, does not necessarily imply physical damage or threat, and may be due to other factors (e.g. hypersensitivity, dysregulated pain signalling). This is anticipated to lessen emotional arousal and widen the possibility of engaging in potentially more helpful strategies, such as engaging in valued and goal-directed behaviour. Accompanying findings included reductions in pain catastrophising and avoidance resting behaviour. In this regard, psychoeducation is a form of guided discovery, as individuals can contextualise the information provided where it is relevant to them. Surprisingly, no changes were seen for fear avoidance. This may reflect ongoing challenges in thoughts around engagement in physical activity when experiencing IBD symptoms. Indeed, recent research has shown that one third of patients with IBD significantly reduce activity levels following diagnosis (Gatt et al., 2018).

Regarding BAS-related factors, treatment techniques aimed at improving self-efficacy included positive feedback and validation provided by website content and the facilitator (to highlight examples of success) and setting and reviewing completion of goals in tasks. Behavioural activation was similarly targeted through goal setting techniques, particularly in Session 2, when participants were invited to set goals in relation to exercise and maintaining a consistent pattern of activity. Improvements in pain self-efficacy therefore support the model, exemplifying the effects of intervention techniques on the BAS cycle. No change was evident for self-reported resilience, and the feasibility study lacked a measure of BAS-behaviour, thus not enabling a better understanding of intervention effects on BAS processes. However, it is important to acknowledge that the feasibility study was conducted with a small sample of people with IBD, data was only collected at pre and post treatment with no longer-term follow-up findings. Therefore, these data only provide tentative preliminary support of the short-term effects of a psychosocial intervention on BIS/BAS processes.

9.4.3 Findings challenging the BIS/BAS model
Albeit in a small, underpowered feasibility study with no longer-term follow-up, a key finding challenging the BIS/BAS model was the limited change in pain outcomes following the intervention. The model predicts that deactivation of BIS-related processes and/or activation of BAS are anticipated to reduce
pain perception. At post-intervention, pain severity and pain-related interference showed no change. This may have been due to several reasons. As the IBD-pain intervention was amalgamated with the treatment protocol for IBD-BOOST, sessions included core general symptom management sessions and 2 symptom-specific sessions on pain. Therefore, an intervention more clearly focused on IBD-pain, rather than multiple IBD symptoms, may have yielded a stronger effect on pain outcomes. Alternatively, the effects of BIS and BAS processes on pain perception may have a weaker influence in the context of disease-related pain, when biological factors are pertinent. The BIS/BAS model of IBD-pain (presented in Chapter 7) acknowledges the role of neurobiological and other clinical/environmental factors contributing to IBD-pain. Participants recruited into the feasibility study were screened for ‘red flags’ of clinical symptoms indicating severe disease or complications and a faecal calprotectin sample was collected, which indicated that over 75% of the sample were in clinical remission at baseline. These data were collected at one time point rather than throughout the intervention or at post-intervention. Despite small changes in pain outcomes, quality of life and self-reported disease activity improved at post-intervention, suggesting positive effects of the intervention on overall self-management and functioning. Alternatively, reduced disease activity or placebo effects may have explained the improvement in quality of life.

The effects of BIS/BAS changes on pain perception may have had a delayed effect once cognitive and behavioural strategies had been implemented, therefore yielding possibly larger changes at a longer follow-up. Online access to the intervention was disabled for participants at week 9, however in nested interviews, participants expressed that they would continue to use strategies learnt in the intervention. Follow-up data collection was not possible due to the confinement within the PhD timeline, however future research testing the BIS/BAS model should endeavour to include longer follow-up assessment when investigating treatment effects on pain outcomes. Another suggested explanation for the null finding on pain outcomes may be due to the use of self-reported indices to measure pain. Inclusion of physiological processing of pain, such as quantitative sensory testing (Rolke et al., 2006), may have yielded a different result (discussed further in Section 9.4.4). To our knowledge, this is the first test of the BIS/BAS model of chronic pain in the context of disease-related pain. Further research is warranted to understand the strength of the BIS/BAS on pain perception in both disease-specific chronic pain and primary chronic pain groups and testing the effects of a psychological intervention in primary chronic pain conditions where disease-related (e.g. inflammatory) causes are less pertinent.
Findings from the thesis also challenged the role of some BAS-related processes. The lack of association between pain and acceptance in the cross-sectional study contrasted with previous chronic pain research, where higher acceptance has been associated with improved functioning (Vowels et al., 2008) and adjustment (Esteve et al., 2007). However, as previously discussed in Chapter 5 Section 5.6, the lack of findings may have been explained using the chronic pain acceptance questionnaire in a sample who all were not experiencing chronic pain. In contrast, qualitative findings seemingly supported the role of acceptance as a BAS-related cognition in facilitating goal attainment and suggested its relationship with positive mood and approach behaviours. Further qualitative and quantitative research into the construct and impact of acceptance in IBD-pain is warranted. Resilience as a BAS-related construct was also questioned in thesis findings, as resilience scores showed no changes post-intervention in the feasibility study. One could argue that resilience is a BAS-related trait factor and therefore less amenable to change through relatively ‘brief’ positive psychological intervention techniques. It may be unsurprising that no changes were seen in self-reported resilience, as positive psychology was not the primary focus of the intervention. A review of ‘resilience training programmes’ has found that they have led to improvements in resilience scores using the CD-RISC questionnaire, challenging the conception that resilience is an unmodifiable construct (Leppin et al. 2014).

### 9.4.4 Implications for future research of the BIS/BAS model

The online CBT-based intervention for IBD-pain tested in this thesis contributes to the small body of evidence testing the BIS/BAS model of chronic pain. However further research is required to comprehensively critique and test this model, and many questions remain unanswered that require further investigation.

The CBT intervention was predominantly rooted in techniques targeting BIS-related factors. Despite some techniques aimed at behavioural activation and improving self-efficacy and use of a logic model to target both BIS and BAS cycles, the sessions mostly focused on modifying unhelpful thinking patterns and behaviour. Therefore, future research should aim to unpick what effects positive psychological interventions have on targeting BAS-related processes, including self-efficacy, optimism, resilience and goal-seeking behaviour. BAS-related behaviours were not explicitly measured in this thesis. Including a subjective or objective measure of reward seeking behaviour, such as Carver & White’s BIS/BAS scale (1994; 2013), may have found positive effects of the
intervention on BAS behaviours, rather than relying on BAS-related cognitions. Intervention techniques more directly targeting the BAS system may include greater emphasis on validating and practising self-efficacy beliefs or motivational interviewing techniques. Alternatively, mindfulness or ACT-based approaches are suggested to have a greater emphasis on developing a more detached, observer stance to thoughts and therefore allow individuals to move more flexibly between BIS and BAS systems (Jensen et al., 2016). In an attempt to develop an understanding of the effects of ACT in IBD-pain, a grant has been awarded to a team of applicants, including the thesis author, to feasibility test a group-based ACT intervention for chronic pain in IBD, funded by the CCUK Pain Collaborative Award (https://www.crohnsandcolitis.org.uk/research/pain-collaborative-research). Results from this latter study will inform the literature on an acceptance-based approach in IBD-pain and possible subsequent work investigating the effects of ACT on BIS/BAS systems.

The cross-sectional study found a negative association between pain self-efficacy and mental well-being with pain. While direction of causality could not be determined through cross-sectional design, a question that remains to be clarified in the model is how the BAS system can be activated when an individual is experiencing chronic pain (and thus anticipated to lead to reduced pain-related disability). The BIS/BAS model contends that if both systems are active in the presence of environmental or sensory cues, then the system that governs behaviour ultimately depends on the goal in question. Through intervention techniques, an individuals’ goal may be modified from focusing on pain or withdrawing to avoid pain (BIS), towards meaningful and value-based goals (BAS). Yet it is unclear what mechanisms underlie the activation of BAS prevailing over BIS in the context of pain. One could speculate that in the presence of pain, the BIS system is activated (automatically in response to detecting threat) but through self-soothing emotional (e.g. stress management), cognitive (e.g. psychoeducation, schematic activation) and behavioural (e.g. activity engagement) techniques, this deactivates a ‘threat response’ and activates a ‘drive response’.

This process aligns with principles in compassion-focused therapy (Gilbert; 2005; 2009; 2014), which proposes that three affective regulation systems - threat, soothe and drive - guide our response to internal and external cues. How this process might be incorporated into the BIS/BAS model of IBD-pain is presented in Figure 19. On the other hand, when experiencing pain, individuals may also anticipate predicted reward from particular actions through learned experience, such as engaging in physical or
social activity, that have previously led to improved mood, positive thoughts and distraction, thus anticipating ameliorating effects on pain. In an attempt to understand mediating factors in BIS/BAS activation, Serrano Ibáñez and colleagues (2018) investigated the role of emotional regulation, namely emotional suppression and cognitive reappraisal, on BIS and BAS activation in a sample of patients with chronic musculoskeletal pain. Trait BIS and BAS activation were measured using the Sensitivity to Punishment and Reward Questionnaire (Aluja & Blanch, 2011), which includes 10-items each for BIS and BAS, such as ‘are you often afraid of new or unexpected situations?’ (BIS). Interestingly, BIS activation showed associations with (less) cognitive reappraisal and (greater) emotional suppression and negative affect, however the relationship between BAS and emotional regulation was inconsistent, and BAS was associated with positive and negative affect. Further research is therefore needed to explore mechanisms behind BAS activation in chronic pain. This includes exploration of suggested hypotheses around direct BAS activation through perceived reward from goals (and their potential reducing effects on pain) or indirect through a ‘soothing’ system which may be implemented in response to threat detection (BIS).
Figure 19 Suggested additions to BIS/BAS model of IBD-pain (presented in Chapter 7) incorporating the three affective regulation systems posited in compassion-focused therapy (Gilbert, 2005; 2009; 2014). Pain perception anticipated to activate the ‘threat detection system’ and inhibitory processes. Self-soothing techniques developed through psychological techniques deactivate the threat system and activate the reward system, signalling BAS activation and related BAS-processes.

As described in Section 7.2.2 (a) denotes psychosocial factors associated with pain identified from the cross-sectional study and (b) denotes findings from the qualitative findings. Not in bold and (c) are psychosocial/clinical factors identified in the systematic review. + sign between BIS and pain signifies exacerbating effect of BIS activation on perception of pain and – with BAS signifies the protective and reducing effect on pain perception.
One limitation of the thesis was the lack of measures to investigate implicit processing of pain information, given that elements of the BIS/BAS cycles are proposed to operate outside of conscious awareness and executive control. For example, this may include tasks to measure cognitive biases, such as the dot-probe task (Fashler & Katz, 2016), memory recall (Schoth et al., 2019) or homophone tasks (Pincus et al., 1996). Overall, evidence of cognitive biases to pain-related information in chronic pain patients shows small to moderate effect sizes and is heterogeneous (Crombez et al., 2013; Todd et al., 2018). However, it is argued that cognitive biases are highly influenced by functional and contextual factors (Van Ryckeghem et al., 2019), such as the salience of a goal, which is supportive of the BIS/BAS framework. The cross-sectional and feasibility studies in this thesis did not include a measure of reward/punishment responsiveness, such as the BIS/BAS questionnaire by Carvery & White (1994; 2013) or Sensitivity to Punishment and Sensitivity to Reward Questionnaire (Aluja & Blanch, 2011). While these measures may have provided a more in-depth investigation of how the BIS/BAS model operates, this was not the core aim of the thesis. Selection of psychosocial measures throughout thesis studies was informed by previous research in IBD-pain, primary chronic pain and IBS, and importantly ensured that psychosocial measures could be mapped onto evidence-based psychological techniques during the intervention mapping phase.

Laboratory-based measures of pain perception, such as Quantitative Sensory Testing (Rolke et al., 2006) or Conditioned Pain Modulation assessments, may have indicated interesting findings on the effect of psychosocial intervention targeting BIS/BAS systems on sensory pain perception or pain inhibitory pathways. Research groups at the University of Cambridge (funded by CCUK) and King’s College London (funded by Biomedical Research Centre) are currently researching IBD-pain in the context of pain sensory testing and frontal lobe functioning, for both of which the thesis author is a collaborator.

Jensen et al. (2016) emphasise that individual differences are an important facet of the BIS/BAS model, and that individuals can express greater tendencies in BIS or BAS trait factors. Stratifying individuals based on trait tendencies prior to intervention and tailoring intervention techniques may lead to better psychological and pain outcomes (Day et al., 2015). For example, an individual may demonstrate a low level of BAS-related factors (e.g. positive affect), but not necessarily display catastrophising thoughts or avoidant responses (BIS), and therefore may benefit more from BAS-orientated techniques.
Therefore, ‘treatment matching’ based on BIS/BAS assessment is an important area of investigation in the aim of optimising treatment efficacy (Day et al., 2015). The intervention in this thesis did not include separate BIS and BAS interventions or baseline screening of BIS or BAS using a BIS/BAS measure (Carver & White, 1994; 2013) to stratify patients. However, the programme was personally tailored throughout. For instance, Session 2 invited individuals to reflect on their behavioural responses to pain and reflect on their activity patterns, such as ‘over activity’, ‘underactivity’ or ‘boom and bust’ activity types. Subsequently, suggested examples were given to the participant when setting activity goals, depending on their type of activity pattern. Future work should aim to look further into the realm of patient stratification and treatment-matching in the context of BIS/BAS.

9.5 Critique of methodology: application of MRC framework

The rationale for using the MRC framework and its strengths were discussed in Chapter 3. Selection of this guidance included considering a recently developed taxonomy of intervention development approaches and key guidance questions by O’Cathain et al. (2019a). The MRC framework developed by Craig et al. (2008) was used for this thesis, as well as further specific recommendations published on the development phase (Bleijenberg et al., 2018) and process evaluation (Moore et al., 2015). However, an updated version of the MRC framework was published by O’Cathain and colleagues (2019b). While this incorporated many of the subsequent recommendations by Bleijenberg et al. (2018) and Moore et al. (2015), a key recommendation was consideration of context to aid optimising long-term implementation of a complex health intervention. ‘Context’ can refer to the population or individual level or relevant political, social, cultural or economic factors that may affect funding, engagement or delivery (Moore et al., 2019). In this thesis, greater consideration of context may refer to understanding challenges from intervention facilitators to support the intervention or factors influencing individual referral and engagement with the intervention, if it were to be implemented in clinical practice. In the IBD-BOOST study, much of the intervention development process involved conducting extensive PPI interviews and focus groups with IBD nurses (who will be the intervention facilitators) to understand potential barriers to supporting the intervention. For example, when developing intervention content, it was important to consider different ethnicities, genders and reading abilities to ensure that content was accessible to a diverse population. Expert clinician input for the ‘red flags’ screening of disease-related processes to consider for IBD-pain (and fatigue and urgency) allowed for important disease-related contextual factors to be considered prior to recruitment, and to target participants with pain without

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identifiable medical cause. However, one could argue that a self-management intervention would be of great value and potential efficacy in reducing psychological distress for individuals with pain even with an identifiable medical cause, and that pharmacological treatment does not always alleviate pain in these patients. Indeed, four participants in the feasibility study expressed interest in taking part but presented ‘red flags’ and therefore were not eligible for the study. In this regard, a psychological self-management intervention should be recommended in parallel with pharmacological approaches for patients with IBD-pain (discussed more in clinical implications of findings Section 9.8).

How thesis studies were mapped onto MRC phases was presented in Chapter 3, however some phases could have been more thoroughly investigated to inform intervention development. For example, Bleijenberg et al.’s (2018) phase of ‘determine the needs’ partly provided a rationale for the qualitative study. Despite the exploration of intervention needs being included in the topic guide for the qualitative study, this was not a major theme identified in qualitative interviews. Therefore, further interviews could have been conducted to specifically explore intervention needs in people with IBD pain. Indeed, this may have led to a greater emphasis on content around practical management strategies for pain, more content on diet, more careful consideration around engaging in exercise with IBD or an overall less patronising tone. However, as aforementioned, due to time and resources, comprehensive exploration of each stage within the MRC thesis was not possible in this thesis.

9.6 Strengths and limitations of thesis studies
While thesis findings contribute to the wider literature on IBD-pain and are informative for the BIS/BAS model of chronic pain, the thesis studies have limitations which must be considered. Limitations were considered in the study articles and chapter sections following these, however, will be briefly summarised again here with some further considerations and overarching thesis limitations.

9.6.1 Systematic review
The systematic review provided a comprehensive synthesis of the literature on psychosocial factors associated with pain in IBD. Strengths included the overall medium to high quality of studies, the large number of participants included, thorough investigation of whether authors measured disease activity, strict eligibility and search term criteria and breadth and relevance of databases. However, as the majority of included studies were of cross-sectional design, this hindered conclusions that could be made around causality. Indeed, it is plausible to expect that pain has a significant impact on negative
psychological and physical functioning, as well as the hypothesised impact that psychosocial factors may have on pain and related disability. Furthermore, as discussed in Chapter 4, search terms did not include IBS-IBD, which may have yielded a greater number of relevant studies or been informative of other pertinent psychosocial processes in the context of IBD-pain. Greater expansion of psychosocial terms may also have retrieved additional relevant studies. For example, in the systematic review published by Robertson et al. (2019), a study by Eluri et al. (2018) was identified, which demonstrated the association between pain interference and sexual function and sexual disinterest. Robertson et al.’s (2019) search criteria included social factors, including relat* and fam* which may have retrieved this study. Terms related to social factors were not included in the systematic review presented in this thesis, as the intervention was intended to be directed towards self-management and not necessarily involve social support networks. Additionally, Robertson and colleagues identified studies on IBD-pain and quality of life (Schirbel et al., 2010; van der Have et al., 2015; Katz et al., 2016), which was not the aim of the thesis systematic review, as it was not a modifiable psychosocial factor that could be targeted in an intervention. Nonetheless, as a result of PPI work undertaken in IBD-BOOST as well as guidance from other pain management interventions (Lewin, 2010; Cole et al., 2012), the intervention tested in the feasibility study included a session on making the most of social support and communication and impact of IBD symptoms on intimate relationships. The influence of social reinforcement and support is an important and worthy area of investigation in chronic pain, and further work should aim to unpick this further in the context of IBD-pain.

9.6.2 Cross-sectional study

Strengths of the cross-sectional study presented in Chapter 5, included a range of theoretically defined psychosocial measures to investigate the potential association with pain and generalisability of findings by recruiting individuals with IBD-pain in outpatient NHS clinics as well as online through IBD charity recruitment. Disease activity was collected through self-report and objective clinical markers. However, a limitation included a low return rate of stool samples to the laboratory for faecal calprotectin testing, despite providing participants with a postal service to avoid barriers of not being able to return to outpatient clinics. Another limitation, and a possible contributing factor to the high rates of missing data (and thus rationale for multiple imputation), was the inclusion of generic and pain-specific psychosocial measures which was given to a sample of people with IBD who were not screened for pain. The rationale for collecting data on all individuals with IBD (with or without pain) was to contribute to the
literature on the prevalence of IBD-pain and to explore differences in sociodemographic, clinical and psychosocial factors associated with pain and no pain. However, given the mixture of questionnaires (including a chronic pain acceptance questionnaire), findings may have been clearer if a screening questionnaire (as was used in the feasibility study) was included to recruit only individuals with IBD who were experiencing pain.

Other possible limitations to the cross-sectional study was the lack of the Brief Illness Perceptions Questionnaire (Broadbent et al., 2006), which may have been informative to develop a better understanding of negative perceptions around pain and comparability with other research on psychosocial factors associated with fatigue in IBD (Artom et al., 2017a). Human error by incorrectly presenting the questionnaires for pain DETECT and IBD-fatigue scales meant that data for these questionnaires could not be analysed for the overall (pain DETECT) or clinic (IBD-fatigue) populations. The pain DETECT questionnaire would have informed the literature on the prevalence and the nature of IBD pain and neuropathic pain. Further research should endeavour to use this questionnaire in IBD-populations to understand the nature of pain in IBD with the aim of potentially facilitating appropriate treatment options based on patient stratification. Use of the PHQ-9 to measure depression resulted in safety issues in the cross-sectional study, as it was used without a protocol in place to manage participants who had high scores on the suicidal ideation question. When this did occur, a protocol was developed individually with participating sites and participants who had expressed suicidal ideation were flagged to the relevant IBD team. This highlighted the need for a suicide risk protocol to be developed for the feasibility study.

Lastly, other investigations of clinical factors related to pain in IBD were not possible due to budget and time constraints within the PhD. For example, the inclusion of a measure on gut microbiome was considered by the thesis author, to contribute to emerging research around pain, psychological outcomes and gut microbiome in gut-brain interactions (Bonaz & Bernstein, 2013; Gracie et al., 2018; Pusceddu & Gareau, 2018; Oligschlaeger et al., 2019). However, upon initial meetings with researchers, the complexity and time to analyse gut microbiome data meant this was not feasible within this PhD. However, for future studies, recruiting from banks of IBD patients, such as the IBD BioResource (www.ibdbioresource.nihr.ac.uk), further research studies in IBD-pain will be able to
extract and explore relevant data on clinical factors, such as genetic screening and gut microbiome profiling.

9.6.3 Qualitative study

The qualitative study of fourteen individuals with IBD and pain included a mixture of genders, age and IBD diagnoses, largely through use of maximum variation purposive sampling. The topic guide used in interviews was reviewed by patients with IBD and was reported to be relevant and clear to facilitate in-depth interviews. However, limiting factors were that interviews were carried out by the thesis author, who may have been biased in their previous reading of IBD-pain and background in Health Psychology. However, the important process of reflexivity and peer-review coding, discussed in Chapter 6 Section 6.6, aimed to minimise limitations around interpretation bias in interviewing, data analysis and coding.

One way of strengthening data analysis of qualitative interviews would have been further input from PPI, as the analytic process was carried out by the thesis author and two nursing students, and therefore could have been biased toward clinical understanding or experience. One recommended method for qualitative studies is returning transcripts to interviewees to confirm that findings accurately represented experiences and views shared in interviews. However, as discussed in the published article (Section 6.2), this was not carried out as it was felt this may lead to incompatibility between interviewees who had not read all the transcripts and thus did not have a richer understanding of experiences of multiple individuals with IBD-pain.

9.6.4 Feasibility study

The feasibility study tested an online CBT-based intervention, which was considered a novel and dynamic mode of delivery compared to a paper-based/booklet intervention. For example, this allowed the intervention to be interactive, personalised and to use a messaging platform to contact the intervention facilitator, rather than being limited to phone call communication. However, the use of a discussion forum (suggested by PPI) for all participants on IBD-BOOST could have improved a sense of engagement and social support and may be considered for future online interventions for symptom management or psychological outcomes in IBD. Illustrations, audio and video clips were utilised to optimise engagement, adoption of self-management techniques and understanding of intervention content. The ‘red flags’ screening, to check that pain experienced by potential recruits was not attributable to indications of severe active disease or disease-related complications, was developed by
expert clinicians in IBD and was considered feasible to use in screening procedures and clear for participants to complete. A PHQ-9 protocol was in place to risk assess harm/suicidal intentions (Appendix D.3.1), which was carried out by the thesis author. This included providing participants, who had answered positively to particular items on suicidal intention/action in the risk assessment, with a template letter that they could send to their GP to arrange an appointment regarding their mental health (Appendix D.3.2). Participants who expressed suicidal thoughts, but not intentions (and thus not high or imminent risk) were provided with external resources, such as links to Mind and Samaritan hotlines.

Self-report questionnaires used in the feasibility study that differed from the cross-sectional study in Chapter 5 included a gastrointestinal-specific questionnaire of anxiety (Visceral Sensitivity Index, VSI) (Labus et al., 2004) instead of the GAD-7 (Spitzer et al., 2006). The rationale behind this was due to significant associations and a mediating role of the VSI identified in a recently published CBT trial for IBS (Windgassen et al., 2019), and its overarching greater focus on gut-related anxiety which was thought to be more appropriate for individuals with IBD. Secondly, a BAS-related measure of resilience (Connor-Davidson Resilience Scale (CD-RISC) (Campbell-Sills & Stein, 2007)) was included in the feasibility study, rather than the Mental Health Continuum Short-Form (measuring mental well-being) used in the cross-sectional study. This was selected due to its increasing use in IBD populations, including a major study at the University of Edinburgh investigating how environmental factors and gut microorganisms affect IBD disease activity (PREDICCT) https://www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies/ukcrc-studies/predicct, and research demonstrating the modifying effects on the CD-RISC from interventions (Leppin et al., 2014). However, the use of the CD-RISC over other measures of resilience or positive affect (e.g. Satisfaction with Life Scale) could be flagged as a limitation of the feasibility study, given that the intervention resulted in no changes to the CD-RISC score. Alternatively, one could argue that the null findings were attributed to the fact that the intervention wasn’t focused in positive psychological techniques. Further work should aim to investigate the concept of resilience in IBD and its relationship with positive psychology and chronic symptom management.

The feasibility study was a single-arm study and did not include either a waitlist control or active control group. Originally, it was considered that the IBD-pain intervention would be tested against a non-IBD tailored chronic pain programme. This is called the Pain Management Plan (Lewin, 2010) and is utilised in pain management programmes across NHS chronic pain services (discussed in Section 7.2.6).
However, during the intervention development phase for this thesis and IBD-BOOST, the Pain Management Plan was used as a helpful resource (with the authors permission) to guide inclusion of content and exercises. Therefore, there was considerable overlap between the two interventions, while use of a waitlist control was not feasible due the time constraints of the thesis. It was also argued that the inclusion of a control group would be more informative at a piloting rather than feasibility stage of intervention testing and thus was not imperative (Whitehead et al., 2014). However, inclusion of a control group, whether a non-tailored pain management intervention, a psychoeducational leaflet on chronic pain or indeed a waitlist control may have yielded interesting comparative findings in the feasibility study. Other limitations considered for this study, as discussed in Chapter 8, were the lack of interviews conducted with individuals who engaged in few or no intervention sessions. Capturing the experiences of these individuals would have contributed to a better understanding of barriers to engagement and other aspects of the feasibility and acceptability. A final limitation was the possible restriction that delivering the pain intervention through the IBD-BOOST study online platform may have entailed. There was considerable overlap in the draft intervention protocol for this thesis and the IBD-BOOST study (both presented in Chapter 7 Section 7.3.1), yet the pain intervention included ‘core’ sessions covering content on fatigue and urgency, as well as pain. Furthermore, intervention techniques more equally targeting BIS and BAS, as presented in the logic model, may have resulted in improvements in BAS as well as reductions in BIS. However, as stated in Section 7.3.1, the overlap in psychosocial processes evident between pain, fatigue and urgency in IBD was a key contributing factor towards the decision to amalgamate intervention content and delivery of the thesis intervention through IBD-BOOST.

9.7 Recommendations for future research

The findings from this thesis lead to a number of implications for future research. An overarching limitation of included studies was lack of longitudinal design in the cross-sectional study or longer-term follow-up data collection in the feasibility study. The cross-sectional study received ethics approval for one and two-year follow up on psychosocial factors associated with pain, which are to be collected and analysed outside of the PhD. Longitudinal research can be a powerful tool to demonstrate the long-term impact of psychosocial factors on pain severity, pain-related interference or development of chronic pain. Additionally, in the context of ‘positive psychogastroenterology’, assessing patients longitudinally, such as at the point of diagnosis, can allow the role of risk and protective factors to be
investigated, thus guiding possible implementation of early intervention to reduce development of chronic symptoms or psychological comorbidity (Keefer et al., 2018). Investigation of other emotional, cognitive and behavioural processes that may be pertinent in the context of IBD-pain is recommended, such as psychosocial factors identified in IBS and chronic pain associated with other long-term conditions. Additionally, as discussed in Section 9.6.1, further research on the role of social and other environmental factors are warranted, such as social support and reinforcement behaviours. Future work can enable more comprehensive investigation of the BIS/BAS model, such as psychosocial factors outside executive control, for example implicit attentional bias and measures of sensitivity to reward or punishment. Moreover, testing the BIS/BAS model and comparisons between groups of primary chronic pain and disease-related chronic pain would enable further investigation of the possible moderating effect of biological factors in the relationship between BIS/BAS activation and pain perception. Use of self-report measures to assess psychological and pain processing holds the possibility of social desirability bias or memory recall. However, self-reported measures selected for this thesis were selected based on their validity and previous extensive use in pain, IBD or psychological studies.

No validated self-report was used to measure impact of pain on dietary behaviours; four items were included in the cross-sectional study and assessed for intra-correlations and reliability. Nonetheless, findings from the cross-sectional and qualitative study and recent research identified in the updated systematic review, have collectively revealed the significant impact that IBD-pain has on diet and satisfaction with food. Content on diet was brief in the intervention for IBD-pain, due to the lack of conclusive evidence on dietary approaches in IBD or pain management. However, nested qualitative interviews in the feasibility study further indicated individuals' needs for understanding the relationship between diet and pain and dietary-related practical managements strategies to implement. A better understanding of the role of diet in IBD was included in the top 10 research questions, set by patients and clinicians, in the James Lind Alliance setting (Hart et al., 2017). Since then, qualitative and quantitative research has demonstrated the negative impact of IBD on food-related quality of life (Hughes et al., 2015; Czuber-Dochan et al., 2019a; Czuber-Dochan et al., 2019b). As discussed in Section 9.3.2, a recent RCT comparing the effects of a low FODMAP versus sham diet demonstrated the positive reducing effects of low FOMAP on bloating and flatulence in quiescent IBD, however no significant difference was detected for pain between diet groups (Cox et al., 2019). Clearly, future
quantitative, qualitative and interventional research is needed to develop a better understanding of pain, diet and psychological factors in IBD, including the possible mediating role of the gut microbiome.

Finally, the feasibility study conducted had a small sample size of 20 individuals with IBD-pain. Although primarily aimed to test the feasibility and acceptability of the intervention, future research with a larger sample size will increase the power of studies and be able to demonstrate potential efficacy of psychosocial interventions for IBD-pain.

9.8 Implications for clinical practice

Thesis findings also have implications for clinical practice. Chapter 1 demonstrated the current challenges around management and assessment of pain, and lack of psychological services available for people with IBD. The cross-sectional study demonstrated the high proportion of patients using opioid medication (18.5%) to manage pain and meeting the classification for chronic pain (40.3%). As discussed in Chapter 1 Section 1.8.3, pharmacological pain management in IBD is challenging and inconclusive area in clinical practice, as many approaches are associated with risk or disease-exacerbating side effects and thus are not recommended for long-term use. The qualitative study demonstrates the lack of information or guidance around pain management strategies, leading to many individuals developing their own personal short and long-term coping strategies to manage pain. The qualitative study also highlights the issues around overemphasising a diagnosis of IBS-IBD in chronic pain patients with IBD, as not all treatment approaches used in IBS will alleviate symptoms for people with IBD. These findings demonstrate the need for clinicians to support and communicate effectively with patients. Thorough consideration of perpetuating biopsychosocial factors will enable more appropriate treatment options for patients and a better understanding of their pain.

The identification of negative and positive psychosocial factors associated with IBD-pain and preliminary efficacy of a self-management intervention demonstrated in this thesis shed light on non-pharmacological approaches for chronic IBD-pain, and the value these can have on reducing distress and improving quality of life and self-efficacy. Equally, as stated in Chapter 1 Section 1.8.3, unfolding research shows promising avenues for novel pharmacological therapeutic methods for IBD-pain, such as targeting calcium processing channels (Picard et al., 2019). Adjunct use of pharmacological and non-pharmacological approaches may be a powerful combination in providing patients with short and long-term strategies to feel more in control of their pain.
The cross-sectional study also demonstrated the prevalence of pain severity and pain-related interference, using a validated and comprehensively used pain measure, rather than reliance on sub-measures, single items, or use of a visual or numerical analogue scale. While these single item measures are widely used and well-regarded in pain (Hjermstad et al., 2011; Safikhani et al., 2018; Chiarotto et al., 2019), assessment of pain severity and related disability is recommended for clinical practice to guide further discussion and treatment options for patients. The high correlation between self-reported disease activity indices, such as the HBI and SCCAI, with psychological distress, reinforces the use of separate validated pain measures to assess pain, as well as the inclusion of subjective and objective clinical markers when assessing functional symptoms in IBD (Colombel et al., 2019).

Acknowledging the limited resources available for face to face psychological services in IBD, the feasibility study also demonstrated the value of online, therapist-supported psychological intervention. Indeed, e-health is a rapidly growing area of IBD care (as well as in other long-term conditions) and can foster self-management, patient autonomy and more efficient communicative methods with one’s clinical team (Knowles & Mikocka-Walus, 2014; Stiles-Shields & Keefer, 2015; Jackson et al., 2016; Walsh & Travis, 2018). Thesis findings provide a contribution to this growing field, in advocating the use of an online intervention for symptom management and quality of life in IBD. As funding for psychological services remains limited for patients with IBD (IBD Standards Group, 2013), future research and clinical work should strive to build an understanding of psychosocial factors in chronic IBD-symptoms.

9.9 Thesis author reflections

This has been a fascinating, enjoyable and dynamic PhD. Before embarking on the PhD, my knowledge of IBD was limited, yet I was able to bring my academic understanding of Health Psychology and biopsychosocial theory to explore chronic pain in IBD and develop a deeper insight into the disease, symptom burden and overall patient experience. Researching IBD has exposed me to the limited psychological support for patients and made me a strong advocate for increasing access to psychological services in IBD. To learn more about treatment and pathophysiology in IBD, I attended a weekly multidisciplinary team (MDT) meeting with the local IBD team throughout my PhD. This also provided me with the opportunity to develop relationships with the IBD team, recruit at the hospital for
my cross-sectional study and voice the psychological aspects of IBD in MDT meetings. One of my proudest achievements during my PhD studentship was collaborating with the local IBD team; combining my research knowledge with their clinical insight to develop a psychological screening service for IBD patients and a successful business case for a full-time Clinical Psychologist embedded with the IBD team. Since then, I have been involved in writing grant applications to CCUK for further research in IBD-pain and taken up an honorary assistant psychologist post with the IBD Clinical Psychologist, co-facilitating a group-based ACT weekly intervention for patients with IBD experiencing anxiety, depression or chronic symptoms. Here I continue to observe, first-hand, the need and appreciation for psychological support in IBD.

Alongside developing skills in dissemination and writing through publications and conference presentations, the PhD has also stretched my ability to conceptualise and critique psychological theories of chronic pain. I look forward to seeing and contributing to the unfolding evidence-base for the BIS/BAS theory of chronic pain, with its strengths and important implications, including supporting research on positive psychological interventions and ‘treatment matching’ in chronic pain. Following the PhD, I will work full-time on the IBD-BOOST study as a research associate, where I will be able to provide my understanding and knowledge of IBD-pain and intervention development in the large RCT study. I will also gain the opportunity to learn more about fatigue and urgency in IBD as well as develop my skills of working in an RCT and training IBD nurses in CBT techniques. Longer-term, I hope to strengthen my clinical skills by undertaking a doctorate in Clinical Psychology.

9.10 Thesis conclusions
This PhD has provided an important and unique contribution to the literature on IBD-pain. Thesis findings have identified emotional, cognitive and behaviours processes associated with pain in IBD, including risk and protective psychosocial factors. Targeting these in a tailored CBT-based self-management intervention for IBD-pain has demonstrated positive effects on improving quality of life and reducing psychological distress, as well as demonstrating the feasibility and acceptability of an online intervention for IBD-pain to be tested in a larger scale RCT. The PhD has provided the opportunity for the BIS/BAS model of chronic pain to be tested in a disease-specific chronic pain population and investigate the effects of a psychological intervention on reducing and improving the BIS and BAS, respectively. Tailoring the BIS/BAS model for chronic IBD-pain builds on previous conceptual models
of IBD-pain and provides implications for future research on treatment targets. Through systematically reviewing previous literature and quantitative and qualitative research, this PhD has demonstrated the significant impact that pain has on individual’s psychological and physical functioning. Use of the MRC framework guidance in developing complex health interventions ensured that a rigorous methodology was used to develop a tailored self-management for IBD-pain, including use of theory and patient and public involvement. Extensive stakeholder input through collaborating with the larger NIHR-funded RCT study of IBD-BOOST, has allowed for the intervention to be personalised and guided by expert opinion from both patients and clinicians, as well as the dynamic mode of delivery through being delivered online. The final study demonstrated the feasibility and acceptability of the intervention and preliminary effects on reducing psychological distress and improving quality of life. Future research should strive to further investigate psychosocial processes within IBD-chronic pain and use larger sample sizes to test the effects and effectiveness of psychological intervention in IBD.
References


Eluri, S., Cross, R. K., Martin, C., Weinfurt, K. P., Flynn, K. E., Long, M. D., ... & Kappelman, M. D. (2018). Inflammatory bowel diseases can adversely impact domains of sexual function such as satisfaction with sex life. Digestive diseases and sciences, 63(6), 1572-1582.


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## Appendix A Systematic review

A1) Systematic review checklist (page numbers correspond to manuscript submitted to journal)

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
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<tr>
<td><strong>TITLE</strong></td>
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<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
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<tr>
<td><strong>ABSTRACT</strong></td>
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<td>Structured summary</td>
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<td>Provide a structured summary including, as applicable: background; objectives;</td>
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<td>data sources; study eligibility criteria, participants, and interventions; study</td>
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<td>appraisal and synthesis methods; results; limitations; conclusions and</td>
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<td>implications of key findings; systematic review registration number.</td>
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<tr>
<td><strong>INTRODUCTION</strong></td>
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<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>4-8</td>
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<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to</td>
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<td>participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
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<td><strong>METHODS</strong></td>
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<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web</td>
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<td>address), and, if available, provide registration information including</td>
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<td>registration number.</td>
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<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report</td>
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<td>characteristics (e.g., years considered, language, publication status) used as</td>
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<td>criteria for eligibility, giving rationale.</td>
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<td>Information sources</td>
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<td>Describe all information sources (e.g., databases with dates of coverage,</td>
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<td>contact with study authors to identify additional studies) in the search and</td>
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<td>date last searched.</td>
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<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including</td>
<td>Table 2</td>
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<td>any limits used, such that it could be repeated.</td>
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<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included</td>
<td>8-9</td>
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<td>in systematic review, and, if applicable, included in the meta-analysis).</td>
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<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms,</td>
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<td>independently, in duplicate) and any processes for obtaining and confirming data</td>
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<td>from investigators.</td>
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<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding</td>
<td>9</td>
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<td>sources) and any.</td>
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<tr>
<td>Topic</td>
<td>Section</td>
<td>Description</td>
<td>Notes</td>
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<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>9-10 (QA)</td>
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<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>NA</td>
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<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.</td>
<td>NA</td>
</tr>
</tbody>
</table>
A2) Publication supplementary materials

Supplementary Table 1
<table>
<thead>
<tr>
<th>Author, country recruited from</th>
<th>Study Design</th>
<th>Population (IBD N, comparator, age, % M/F)</th>
<th>Pain measure</th>
<th>Key psychosocial and additional clinical/sociodemographic findings</th>
<th>Quality rating</th>
<th>Definition of disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Boye et al. (2008) Norway, Germany Gastroenterology university clinics</td>
<td>Cross-sectional</td>
<td>UC 55, CD 54 Mean age: CD 38.2, UC 39.3 CD 72% F, UC 66% F</td>
<td>Short Form-36 (SF-36) bodily pain</td>
<td>High internal locus of control associated with higher pain-related quality of life in CD ($r = 0.332$). ($B = 1.2$ (SE = 0.5), $p = 0.04$) Neuroticism, conventionality, hostility/aggression and alexithymia not associated with pain-related quality of life. Personality remained significant in (first model of) regression analyses ($p = 0.01$) however overall model with control variables non-significant. Additional: Clinical activity index a significant predictor of pain in UC patients ($B = -3.8$ (1.0), $p = .001$).</td>
<td>High</td>
<td>Harvey Bradshaw Index (CD) &gt;4 Modified version of clinical activity index (UC) &gt;4</td>
</tr>
<tr>
<td>2. Boyle et al. (unpublished), Ireland Specialist IBD clinics in two health centres</td>
<td>Cross-sectional</td>
<td>UC 91, CD 106 ID 3 Mean age: 41 55% M</td>
<td>Brief Pain Inventory</td>
<td>Mean scores in the SAD-21 for anxiety, depression and stress were significantly greater in pain reporters. SAD-21 mean scores (pain vs non-pain reporters): Anxiety (4.6 versus 1.9, $p &lt;0.001$) Depression (5.6 versus 2.6, $p&lt;0.001$) Stress (7.0 versus 4.1, $p&lt;0.001$) Pain was reported by 58% of patients.</td>
<td>Medium</td>
<td>Physician assessment of biochemical endoscopic, histologic and radiologic parameters</td>
</tr>
<tr>
<td>3. Coates et al. (2013) USA Medical Centre Digestive Disease Centre</td>
<td>Cross-sectional</td>
<td>UC 109 Mean age: 45.41 48% F Mean disease duration: 10.0 years</td>
<td>SIBDQ Pain Score (pain frequency) Modified ulcerative colitis disease activity index survey (pain severity)</td>
<td>Patients with higher pain more frequently carried a concurrent diagnosis of a mood disorder. OR 5.76, 95% CI (1.39, 23.89), $p = .02$. 33/322 patients with quiescent IBD reported frequent to constant levels of pain (SIBDQ score ≤4) and were on average younger, more frequency female, more likely to have a co-existing diagnosis of a mood disorder, IBS and a chronic pain syndrome. Additional: In the overall sample, pain ratings were also predicted by elevated ESR, opioid use and presence of a pain syndrome. In participants with quiescent UC, frequent to constant abdominal pain was significantly associated with younger age, female gender, ESR and a co-existing diagnosis of affective spectrum disorder, IBS diagnosis and pain syndrome. Significantly more women (26.4%) than men (16.9%; $p = .02$) described their pain as more frequent.</td>
<td>High</td>
<td>Physician global assessment endoscopic &amp; histologic rating of disease severity, C reactive protein &amp; erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>Mean Age</td>
<td>Disease Distribution</td>
<td>Measure of Pain</td>
<td>Findings</td>
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<tr>
<td>DeBerry et al. (2014)</td>
<td>Cross-sectional</td>
<td>77 UC, 21 healthy controls (HC)</td>
<td>45.0, 52.2</td>
<td>UC 54% F, HC 48% F</td>
<td>VAS McGill Short Form Questionnaire</td>
<td>Patients with UC with pain had significantly higher HADS when compared with controls and patients with UC without pain - UC with pain: 3.7 (0.5), UC no pain: 2.3 (0.3), p &lt; 0.05. Higher depression scores independently predicted pain in UC patients (r &gt; 0.5)</td>
</tr>
</tbody>
</table>

**Additional:** Alongside higher depression scores, VAS of pain significantly correlated with younger age (r = 0.24), increased expression of neurturin (r = 0.33) and decreased expression of transient receptor potential ankyrin 1 in the mucosa (r = 0.22). No correlation between endoscopic, pathology and mucosal expression of IL1b, IL6, IL17 and TNF and pain scores.

| Edman et al. (2017) | Cross-sectional | IBD 82, IBS 132, GERD 188 | 50.1, 55.3 | IBD 76.5% F, IBS 74.2% F, GERD 76.1% F | Self-report numerical rating scale of pain (worst pain and average pain) | Perceived stress significantly positively correlated with average pain (r = 0.32, p < .0001) and worst pain (r = 0.35, p < .01) in the IBD group. |

| Esteve et al. (2013) | Cross-sectional | IBD 128, back pain 141, specialty pain 137 | 37.91, 45.75, 53.20 | IBD 55% F, BP 55% F, SP 56% F | SF-36 bodily pain Pain intensity scale | Across all three groups, pain intensity (and experiential avoidance) correlated with pain fear avoidance (beta = .19, p <.05) |

In IBD patients specifically, pain acceptance significantly positively correlated with resilience (beta = .37) and negatively correlated with negative mood (beta = -.34). |

| Fuller-Thompson & Sulman (2006) | Cross-sectional (population survey) | IBD 3076 | Mean age: (CCHS) within non/depressed 50.5/43.2, (NPHS) within non/depressed 49.5/41.1 | Pain items in survey questionnaire: (usually no pain, discomfort or pain prevents no activities VS pain prevents few activities, some activities, most activities) Pain intensity of pain (none, mild, moderate, severe) | Respondents whose activities were limited by pain (depressed = 35.1% vs non-depressed = 58.4%, p <.001) and who were in severe pain were much more likely to be depressed. Those who reported that activities were prevented by pain were significantly more depressed (OR = 1.71, 95% CI (1.32, 2.23), p <.001). |

In NPHS non/depressed (%): no pain = 61.2 vs 48.6 mild pain = 9.2 vs 10 moderate pain = 21.3 vs 21 severe pain = 8.3 vs 20.5 |

In the NPHS survey, respondents with IBD or a similar bowel disorder who experienced moderate or severe pain were more likely to be depressed if they did not have a confidant (p <0.05) |
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>IBD (NR)</th>
<th>Pain in survey questionnaire</th>
<th>Anxiety and depression</th>
<th>Mean Age</th>
<th>Medium Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. Fuller-Thompson et al. (2015) [7], Canada</td>
<td>Cross-sectional</td>
<td>IBD 269</td>
<td>Mean: NR % F NR</td>
<td>Anxiety was predicted by chronic pain (OR 2.43, 95% CI 1.14, 5.18)</td>
<td>NR</td>
<td>None – self-report of diagnosis</td>
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<tr>
<td>2012 Canadian Community Health Survey Mental Health</td>
<td></td>
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<td>Pain items included in survey:</td>
<td>Among all control variables, chronic pain explained the relationship between IBD and GAD the most, followed by a history of ACEs (adverse childhood experiences) (OR model = 2.83 vs OR model = 2.28).</td>
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<td>47, Canada</td>
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<td>Pain items in survey questionnaire:</td>
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<td>4. Fuller-Thompson et al. (2015) [7], Canada</td>
<td>Cross-sectional</td>
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<td>47, Canada</td>
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<tr>
<td>9. Goodhand et al. (2012) [40], UK</td>
<td>Cross-sectional</td>
<td>UC 103, CD 101, HC 124</td>
<td>Pain items included in survey questionnaire:</td>
<td>Chi-squared analyses showed a significant association between abdominal pain and HADS-A scores in CD patients.</td>
<td>UC 41.2, CD 42.8, HC 28.7, UC 59% F, CD 57% F, HC 29% F</td>
<td>High Clinical Colitis Activity Index &gt; 2 with a Baron’s sigmoidoscopic score &gt; 1.4 (UC)</td>
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<td>UC/CD patients volunteered in other research studies</td>
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<td>40, UK</td>
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<tr>
<td>10. Moisset et al. (2017) [42], France</td>
<td>Cross-sectional</td>
<td>UC 73, CD 129</td>
<td>Pain items included in survey questionnaire:</td>
<td>Anxiety was significantly associated with probable migraine: Multivariate (Selected) OR, 95% CI: 6.77 [2.24–19.53], 2nd quartile vs. 1st quartile 1.36 [0.60–3.08], 3rd quartile vs. 1st quartile</td>
<td>UC 42.6, CD 38.8, UC 41.1% F, CD 63.6% F</td>
<td>High Crohn’s Disease Activity Index (CDAI)</td>
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<td>IBD Unit of Clermont-Ferrand University Hospital</td>
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<td>42, France</td>
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<td>3.44 [1.30–9.09], 4th quartile vs. 1st quartile</td>
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<tr>
<td>11. Moisset et al. (2017) [42], France</td>
<td>Cross-sectional</td>
<td>UC 73, CD 129</td>
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<td>42, France</td>
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<td>3.44 [1.30–9.09], 4th quartile vs. 1st quartile</td>
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</table>
Additional: Female gender and younger age were significant associated with probable migraine. Prevalence of migraine (41%, OR 2.56) and chronic pain with a neuropathic component (11.3% vs 6.9%) was higher in the IBD cohort compared to the general population. More frequent pain reported in CD than UC.

Disease activity significantly associated with abdominal pain but not overall pain, probable migraine or joint pain.

11. Morrison et al. (2013)2 Australia
Specialist IBD outpatient clinic in Melbourne
Cross-sectional
UC 54, CD 66
Median age: 42
40% F
Median disease duration: 7
von Korff Pain Intensity and Disability questionnaire.

Coping strategies correlations with von Korff pain intensity Spearman’s r, (p value): catastrophizing 0.62 (.001), ignoring sensations -0.41 (.007), praying and hoping 0.42 (.006), cognitive coping/suppression -0.23, (0.15), helplessness 0.55 (.001), diverting attention 0.3 (.053).

Pain attitudes/beliefs correlations with von Korff pain intensity: pain control belief 0.3 (0.051), disability -0.5 (.001), harm -0.26 (0.1), emotion 0 (1.0), medication belief -0.42 (.006), solicitude -0.048 (0.76), medical cure belief 0.12 (0.47).

Independent and significant associations with moderate-severe pain:
(OR, 95% CI, p value):
Catastrophising tendency (34.69, 2.97-228, .003)
Depression (1.8, 1.02-3.17, .04)
Medication belief score (.05, .005-.55, .01)
Active disease (HBI/SCCAI) (48.54,1.62-1455, .03)

High
Harvey Bradshaw Index ≥5
Simple Clinical Colitis Activity Index ≥5
Physician global assessment (80% concordance with DAI scores)

12. Odes et al. (2017)3, Israel
Gastroenterology departments at 5 university-affiliated hospitals
Website recruitment ‘The
Cross-sectional
CD 594
Mean age: 38.6
57.6 % F
Disease duration: 11.05
Harvey Bradshaw Index Short Inflammatory Bowel Disease Questionnaire (SIBDQ) SF-36 bodily pain

Higher pain scores significantly correlated with psychological stress, dysfunctional coping strategies, poor family relationships, abstinence, presenteeism, productivity loss and activity impairments and all WPAI sub-measures.
(Severe pain):
Internet sample: (HBI, SF-36, SIBDQ) OR (p value):
Emotion focused coping: 0.96, (0.56) 1.02 (0.81) 0.97 (0.62)
Problem focused coping: 1.14 (0.19) 1.23 (0.10) 0.88 (0.21) Dysfunctional coping: 1.02 (0.76) 1.03 (0.73) 1.11 (0.14)

High
Patient Harvey-Bradshaw Index (P-HBI)
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample Description</th>
<th>Measures</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Israel Foundation for Crohn’s Disease and Ulcerative Colitis’</td>
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<tr>
<td>13. Schwarz et al. (1993)42, USA</td>
<td>Cross-sectional</td>
<td>IBD 46, IBS 121 Mean age: 41.7 63% F</td>
<td>Daily symptom diary (0-4 scale)</td>
<td>Pain/tenderness significantly correlated with all psychological measures excluding STAI-trait:</td>
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<td>pain and depression r=.474 (p&lt;.001)</td>
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<td>pain and state anxiety r=.362 (p&lt;.005)</td>
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<td>pain and trait anxiety r=.310</td>
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<td>pain and psychosomatic symptoms r=.655 (p&lt;.001)</td>
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<tr>
<td>14. Sirois &amp; Wood (2017)45, UK</td>
<td>Longitudinal</td>
<td>144 IBD, 163 arthritis Mean age: IBD 38.3, arthritis 46.9, IBD 77.8% F, arthritis 91.6% F</td>
<td>Bowel Symptoms sub-scale (Inflammatory Bowel Disease Questionnaire)</td>
<td>Univariate analyses: T1 pain significantly positively correlated with T2 depressive symptoms, T2 pain, perceived stress and helplessness, and negatively correlated with T1 self-rated health measured by SF-36 (all p &lt;.01). T2 pain significantly correlated with T1 pain and perceived stress (all p &lt;.01).</td>
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<td>Multivariate analysis:</td>
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<td></td>
<td>In hierarchical regression of longitudinal association between gratitude with T2 depressive symptoms, T2 pain was a significant controlling factor in step 1 (demographic and clinical factors) (p &lt;.05), step 2 (illness cognitions and psychological thriving) (p &lt;.01) and step 3 (gratitude) (p &lt;.01).</td>
</tr>
<tr>
<td>15. Tripp et al. (unpublished), Canada</td>
<td>Cross-sectional</td>
<td>Paper 1: UC 75, CD 140, 7 UC &amp; CD, 83 HC Mean age: 46.11 Mean disease duration: 13.55</td>
<td>Short Form McGill Pain Questionnaire Pain body Diagram</td>
<td>Paper 1: Pain phenotype:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1= abdominal only</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1-2 = additional comorbid sites</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3+ = additional comorbid sites.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenotype 1 showed the lowest scores for catastrophising, depression and QoL compared to others.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>All IBD pain phenotype groups reported more pain catastrophising and depressive symptoms than controls (F(3, 273)=26.22 p&lt;.001 and F(3, 277) = 36.02, p &lt;.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Patients with IBD abdominal pain reported significantly less pain catastrophising (&lt;.01) than IBD patients with 1-2/3+ pain locations. CD exhibited greater levels of</td>
</tr>
</tbody>
</table>
| Tripp et al. (unpublished) Canada | Paper 2: | Pain associated with illness-focused coping ($r = .7$), pain catastrophising ($r = .52$), wellness-focused coping ($r = .35$), depressive symptoms ($r = .68$) and perceived social support $- .26$). 
Illness-focused coping and pain catastrophizing partially mediate the relationship between pain and HR-QoL & The use of IFBC and pain catastrophising is related to reductions in health-related QoL. Greater helplessness was associated with pain and subsequently poorer emotional HRQoL ($Z = -2.22$, $p = .03$). Guarding was associated with pain as well as poorer social and emotional HRQoL ($Z = -2.38$, $p < .01$ and $Z = -2.04$, $p = .04$, respectively). |
Systematic review: Supplementary Table 2.

Table of excluded studies

<table>
<thead>
<tr>
<th>No.</th>
<th>Study reference</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Abdalla et al. (2017)</td>
<td>Pain not reported separately, no psychosocial factor associated with pain</td>
</tr>
<tr>
<td>2.</td>
<td>Benhayon et al. (2013)</td>
<td>IBD population &lt; 18 years, no psychosocial factor associated with pain</td>
</tr>
<tr>
<td>3.</td>
<td>Berrill et al. (2013)</td>
<td>Pain not reported separately</td>
</tr>
<tr>
<td>4.</td>
<td>Berrill et al. (2014)</td>
<td>Pain with IBS composite measure</td>
</tr>
<tr>
<td>5.</td>
<td>Bor et al. (2015)</td>
<td>Unobtainable (from library)</td>
</tr>
<tr>
<td>6.</td>
<td>Borges et al. (2014)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>8.</td>
<td>Camilleri (2006)</td>
<td>No IBD population, study design not eligible</td>
</tr>
<tr>
<td>9.</td>
<td>Chedid et al. (2014)</td>
<td>Unobtainable from author</td>
</tr>
<tr>
<td>10.</td>
<td>Crane &amp; Martin (2004)</td>
<td>No exclusive pain outcome (only pain coping inventory)</td>
</tr>
<tr>
<td>12.</td>
<td>Fikree et al. (2015)</td>
<td>No psychosocial factor associated with pain measured/pain not reported exclusively</td>
</tr>
<tr>
<td>14.</td>
<td>Gerrits et al. (2014)</td>
<td>Results reported for gastrointestinal conditions rather than IBD separately</td>
</tr>
<tr>
<td>15.</td>
<td>Graff L.A et al. (2006)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>16.</td>
<td>Horst et al. (2014)</td>
<td>Pain within disease activity composite measure (SCAI)</td>
</tr>
<tr>
<td>17.</td>
<td>Hotokezaka et al. (2010)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>18.</td>
<td>Iglesias et al. (2009)</td>
<td>Age 16-20 years, no measure of pain and associated psychosocial factor with pain</td>
</tr>
<tr>
<td>19.</td>
<td>Jelsness-Jørgensen et al. (2014)</td>
<td>Pain within IBS composite score</td>
</tr>
<tr>
<td>20.</td>
<td>Kaufman et al. (2014)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>22.</td>
<td>Litcher-Kelly &amp; Hymowitz, (2011).</td>
<td>No exclusive pain measure, no psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>23.</td>
<td>Lix et al. (2008)</td>
<td>No exclusive pain measure/Pain-related anxiety and pain catastrophising only</td>
</tr>
<tr>
<td>24.</td>
<td>Lores et al. (2016)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>25.</td>
<td>Magro et al. (2009)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>26.</td>
<td>Mahadev et al. (2011)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>27.</td>
<td>Maunder et al. (1997)</td>
<td>No psychosocial factor associated with pain</td>
</tr>
<tr>
<td>28.</td>
<td>McCormick et al. (2010)</td>
<td>IBD population &lt;18 years</td>
</tr>
<tr>
<td>29.</td>
<td>Miller et al. (2014)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>30.</td>
<td>Mizrahi et al. (2012)</td>
<td>No psychosocial factor associated with pain at baseline of intervention</td>
</tr>
<tr>
<td>31.</td>
<td>Palm et al. (2005)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>32.</td>
<td>Rivers et al. (2013)</td>
<td>Unobtainable from author</td>
</tr>
<tr>
<td>33.</td>
<td>Rivers et al. (2015)</td>
<td>Study design not eligible, no psychosocial factor associated with pain (associated factor of autonomic dysfunction)</td>
</tr>
<tr>
<td>34.</td>
<td>Rubio et al. (2014)</td>
<td>Pain measure not eligible - onset of pain/rectal distension</td>
</tr>
<tr>
<td>35.</td>
<td>Schoultz et al. (2013)</td>
<td>No psychosocial factor associated with pain measured at baseline of intervention</td>
</tr>
<tr>
<td>36.</td>
<td>Seres et al. (2008)</td>
<td>No psychosocial factor associated with pain measured/Pain and quality of life</td>
</tr>
<tr>
<td>37.</td>
<td>Shaw &amp; Ehrlich (1987)</td>
<td>No psychosocial factor associated with pain measured at baseline of intervention</td>
</tr>
<tr>
<td>38.</td>
<td>Singh et al. (2011)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>39.</td>
<td>Smolen &amp; Topp (2001)</td>
<td>No pain outcome/ no psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>40.</td>
<td>Song et al. (1993)</td>
<td>Pain measure not eligible - pain pressure threshold</td>
</tr>
<tr>
<td>41.</td>
<td>Song et al. (1993)</td>
<td>Pain measure not eligible/unobtainable from library</td>
</tr>
<tr>
<td>42.</td>
<td>Sweis et al. (2014)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td></td>
<td>Reference</td>
<td>Findings</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>44</td>
<td>Trindade et al. (2016)</td>
<td>Full text unobtainable from author</td>
</tr>
<tr>
<td>45</td>
<td>Tripp et al. (2016)</td>
<td>Full text unobtainable from author</td>
</tr>
<tr>
<td>46</td>
<td>van der Have et al. (2015)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>47</td>
<td>Volz et al. (2016)</td>
<td>No psychosocial factor associated with pain at baseline of intervention</td>
</tr>
<tr>
<td>48</td>
<td>Yanartas et al. (2016)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bodily pain associated with antidepressant treatment</td>
</tr>
<tr>
<td>49</td>
<td>Zeitz et al. (2016)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>50</td>
<td>Zeitz et al. (2015)</td>
<td>No psychosocial factor associated with pain measured</td>
</tr>
<tr>
<td>51</td>
<td>Zoltan &amp; Ferenc (2007)</td>
<td>No pain measure</td>
</tr>
</tbody>
</table>
Appendix B Cross-sectional study

B1) Publication Supplementary Materials

Table S1. Means and standard deviations of pain general and pain-specific psychological variables in clinic and online-recruited cohorts

<table>
<thead>
<tr>
<th>Psychosocial measure (mean, SD)</th>
<th>Clinic (n = 82)</th>
<th>Online (n= 161)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General psychosocial measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>8.54 (6.38)</td>
<td>11.90 (6.38)</td>
<td>p &lt; .001*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.43 (5.94)</td>
<td>8.81 (5.82)</td>
<td>p = .089</td>
</tr>
<tr>
<td>Stress</td>
<td>21.56 (7.36)</td>
<td>23.70 (7.86)</td>
<td>p = .043*</td>
</tr>
<tr>
<td>Mental well-being</td>
<td>43.23 (16.03)</td>
<td>36.65 (15.38)</td>
<td>p = .003*</td>
</tr>
<tr>
<td><strong>Pain-specific measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain self-efficacy</td>
<td>37.97 (15.07)</td>
<td>30.05 (15.32)</td>
<td>p &lt; .001*</td>
</tr>
<tr>
<td>Pain catastrophizing</td>
<td>14.91 (12.85)</td>
<td>20.32 (12.80)</td>
<td>p = .002*</td>
</tr>
<tr>
<td>Pain fear avoidance</td>
<td>11.51 (5.58)</td>
<td>12.40 (5.33)</td>
<td>p = .23</td>
</tr>
<tr>
<td>Symptom focusing</td>
<td>12.42 (5.69)</td>
<td>12.92 (5.99)</td>
<td>p = .53</td>
</tr>
<tr>
<td>Embarrassment avoidance</td>
<td>8.91 (7.06)</td>
<td>11.11 (6.72)</td>
<td>p = .019*</td>
</tr>
<tr>
<td>All or nothing behaviour</td>
<td>7.36 (5.02)</td>
<td>11.21 (5.25)</td>
<td>p &lt; .001*</td>
</tr>
<tr>
<td>Avoidance resting behaviour</td>
<td>10.68 (6.46)</td>
<td>14.76 (7.27)</td>
<td>p &lt; .001*</td>
</tr>
<tr>
<td>Pain acceptance</td>
<td>28.88 (5.05)</td>
<td>26.26 (4.83)</td>
<td>p &lt; .001*</td>
</tr>
</tbody>
</table>

*Statistically significant at p<.05
Table S2. Univariate independent samples t-tests of difference in mean pain severity and pain-related interference according to sociodemographic and clinical predictor variables in the pain cohort (n = 243)

<table>
<thead>
<tr>
<th>Sociodemographic</th>
<th>BPI severity</th>
<th>BPI interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>-0.68</td>
<td>-1.20, -0.16</td>
</tr>
</tbody>
</table>

Clinical

<table>
<thead>
<tr>
<th>Variable</th>
<th>MD</th>
<th>95% CI</th>
<th>MD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis CD</td>
<td>0.37</td>
<td>-0.13, 0.88</td>
<td>0.23</td>
<td>-0.54, 1.00</td>
</tr>
<tr>
<td>Previous surgery</td>
<td>-0.70</td>
<td>-1.24, -0.16</td>
<td>-0.53</td>
<td>-1.33, 0.25</td>
</tr>
<tr>
<td>Anti-depressant use</td>
<td>-0.58</td>
<td>-1.17, 0.026</td>
<td>-1.12</td>
<td>-2.01, -0.23</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>-0.78</td>
<td>-1.53, -0.024</td>
<td>-1.14</td>
<td>-2.27, -0.098</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>0.56</td>
<td>0.02, 1.09</td>
<td>-0.74</td>
<td>-0.06, 1.54</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>-1.07</td>
<td>-2.37, 0.23</td>
<td>-2.44</td>
<td>-4.48, -0.41</td>
</tr>
<tr>
<td>Budesonide</td>
<td>-0.44</td>
<td>-1.58, 0.70</td>
<td>-0.46</td>
<td>-2.23, 1.31</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>0.85</td>
<td>-0.88, 2.58</td>
<td>1.68</td>
<td>-0.90, 4.27</td>
</tr>
<tr>
<td>Other 5-ASA</td>
<td>0.03</td>
<td>-0.49, 0.57</td>
<td>-0.13</td>
<td>-0.93, 0.66</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>0.29</td>
<td>-0.80, 1.38</td>
<td>0.55</td>
<td>-1.09, 2.20</td>
</tr>
<tr>
<td>Infliximab</td>
<td>0.67</td>
<td>-0.29, 1.64</td>
<td>1.10</td>
<td>-0.34, 2.54</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>-0.15</td>
<td>-0.79, 0.48</td>
<td>-0.12</td>
<td>-1.07, 0.83</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>0.11</td>
<td>-0.92, 1.13</td>
<td>-0.49</td>
<td>-2.02, 1.04</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>0.21</td>
<td>-1.38, 1.80</td>
<td>0.61</td>
<td>-1.75, 2.99</td>
</tr>
</tbody>
</table>

Table S3. Univariate one-way between groups ANOVAs of differences in pain severity and pain-related interference according to sociodemographic and clinical predictor variables in the overall pain cohort (n=243)

<table>
<thead>
<tr>
<th>Sociodemographic</th>
<th>Pain Severity</th>
<th>Pain-related interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>F(13, 242) = 1.379, p = .17</td>
<td>F(13, 242) = 1.075, p = .38</td>
</tr>
<tr>
<td>Educational status</td>
<td>F(5, 236) = 2.772, p = .019</td>
<td>F(5, 236) = 1.512, p = .19</td>
</tr>
<tr>
<td>Employment status</td>
<td>F(5, 237) = 4.176, p = .001</td>
<td>F(5, 237) = 3.490, p = .005</td>
</tr>
<tr>
<td>Relationship status</td>
<td>F(4, 230) = 1.418, p = .23</td>
<td>F(4, 230) = 1.282, p = .28</td>
</tr>
</tbody>
</table>

Clinical

| Smoking status             | F(2,242) = 6.63, p = .002 | F(2,242) = 6.07, p = .003 |

345
### Table S4. Pearson correlations between pain, psychological and clinical factors in overall pain cohort (n = 243)

<table>
<thead>
<tr>
<th>Pain Severity</th>
<th>Pain-related interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.109</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>.060</td>
</tr>
<tr>
<td>No of. disease flares in prior 2 yrs</td>
<td>.265**</td>
</tr>
<tr>
<td>Faecal calprotectin (n = 43)</td>
<td>-.069</td>
</tr>
<tr>
<td>HBI</td>
<td>.558**</td>
</tr>
<tr>
<td>SCCAI</td>
<td>.482**</td>
</tr>
<tr>
<td>IBS Severity Score</td>
<td>.664**</td>
</tr>
<tr>
<td>Pain Self-Efficacy</td>
<td>-.457**</td>
</tr>
<tr>
<td>Pain Catastrophising</td>
<td>.453**</td>
</tr>
<tr>
<td>Fear Avoidance</td>
<td>.356**</td>
</tr>
<tr>
<td>Symptom Focusing</td>
<td>.267*</td>
</tr>
<tr>
<td>Embarrassment Avoidance</td>
<td>.379**</td>
</tr>
<tr>
<td>All or Nothing Behaviour</td>
<td>.222**</td>
</tr>
<tr>
<td>Damage Beliefs</td>
<td>.309**</td>
</tr>
<tr>
<td>Avoidance resting behaviour</td>
<td>.328**</td>
</tr>
<tr>
<td>Pain acceptance</td>
<td>-.139*</td>
</tr>
<tr>
<td>Depression</td>
<td>.433**</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.254**</td>
</tr>
<tr>
<td>Stress</td>
<td>.250**</td>
</tr>
<tr>
<td>Mental well-being</td>
<td>-.372**</td>
</tr>
</tbody>
</table>
INVESTIGATING PAIN IN INFLAMMATORY BOWEL DISEASE

PARTICIPANT INFORMATION SHEET

Information Sheet - Survey

Study name: Investigate-Pain (IRAS no. 226323), Chief Investigator: Professor Christine Norton, Principal Investigator: Dr Peter Irving

Lead Researcher Louise Sweeney

Invitation to participate

We would like to invite you to participate in this research project organised by researchers at King’s College London and funded by Crohn’s and Colitis UK. The research is looking at pain in Inflammatory Bowel Disease (IBD). The research will involve a number of studies aiming to improve our understanding of different types of pain in IBD, in the aim of developing ways to help individuals manage their pain better. To do this, we are interested in collecting information from individuals with IBD who do and do not experience pain.

To help you decide if you would like to participate, please read the information sheet below. If you have any questions or would like any further information about the study, please ask the lead researcher, Louise Sweeney (louise.sweeney@kcl.ac.uk or telephone: 07745565349).

What is the purpose of the study?

Pain is experienced by many people with IBD, but currently there are not clear reasons why people experience ongoing pain, even in periods of remission. A team of researchers at King’s College London, including academics and specialist nurses, is carrying out a research study to find out more about pain in IBD and certain factors that may be contributing to pain. If you do not experience pain related to your IBD, we are still interested in hearing of your story and experiences.

What would taking part involve?

1. You will be asked to sign a consent form which the researcher will give to you, to make sure you have read this information sheet and are happy to take part.
2. The researcher will then give you a questionnaire booklet which should take approximately 20-30 minutes to complete. You can complete this either straight away and return to the researcher, or take the questionnaire booklet home with you to complete later and then send back to the researcher in the pre-stamped envelope that will be given to you.

3. As part of routine care, your clinician will ask you to provide a stool sample in your own time. This can be returned in person to clinic or directly to the laboratory for testing in a pre-addressed medical packaging envelope. This will allow for assessment of current inflammatory levels. Results of these levels will be retrieved by a member of the research team. A member of the research team will contact you after 1 week from recruitment to check this has been sent or follow up with any issues you may have.

4. In a section of the questionnaire pack, you will be asked if you are interested to take part in phase 2 of the study, which will involve a researcher speaking with you individually in audio-recorded interviews. If you tick this box, you will be asked to provide contact details so that the researcher can contact you to arrange a suitable date and location to meet to carry out interviews – these are expected to last 30-60 minutes. You do not have to take part in both phases of the study.

5. The questionnaire packs will be sent out again to you via post/email at 6 months, 12 months and 24 months after the first questionnaire booklet for follow up information. You will not need to provide a stool sample at these later stages.

What will happen to the samples I give?

The stool sample you provide will be analysed by trained scientists at a hospital laboratory. Your results will be noted for your next appointment with your clinician. Results will also be retrieved by the research team for study purposes. This information will be kept confidential and will be used to help the research team identify potential things (e.g. levels of inflammation) which might be contributing to pain levels.

Do I have to take part?

No, you do not have to take part and you are under no obligation to do so. You can speak with the researcher if you would like more information before making your decision. Deciding not to take part will not have any impact on the care you receive at the hospital.

What are the benefits of taking part?

There are no direct benefits to you from taking part. However, participants will be providing information about the factors that might be related to pain in IBD which will help researchers to gain a better idea of what’s going on. This information will then be used to help researchers come up with a way to help individuals manage their pain more effectively in the future.

What are the possible disadvantages of taking part?

There are no anticipated risks in taking part in the study. You may feel a little distressed when completing questionnaires as some of them require to you to answer about your feelings and thoughts in relation to your IBD, any pain you may be experiencing and your daily functioning. You may withdraw from the study at any time if you change your mind about taking part.
The study team is very experienced in the field of IBD and familiar with many of the issues you may be concerned about. All team members are experienced in offering reassurance to, and caring for, people in clinical settings and during research projects, and will support you at all stages of the study. You can get further support from the Crohn’s & Colitis UK (CCUK) Helpline (Supportive Listening Service), which is available Mon-Fri, 1pm – 3.30pm, and 6.30pm – 9pm, except Bank Holidays in England. (0845 1303344 or 0121 7379931).

**What about confidentiality and anonymity?**

Participation in the study will be kept strictly confidential. All participants will be assigned a participant number, and all personal information and data will be referred to by your participant number rather than your name. Responses to questionnaires will only be accessible to the research team. All consent/assent forms, questionnaires and interview recordings/transcripts will be stored securely and confidentially in a locked filing cabinet in the research office in King’s College London. We may use quotes from interviews however no identifiable personal information will be presented. If you decide to withdraw from the study, we would like to retain the information that has been collected to that point for study purposes. Personal data will be stored for up to five years following recruitment for follow-up research purposes.

**What will you do with the results of the study?**

Participants’ data will be analysed and written up with the intention of submission for publication in a scientific journal. The study will also be written up as part of the lead researcher’s PhD thesis in Health Studies Research. The results will contribute to the development of a self-management treatment to help people with IBD to manage their pain better. A summary of the results will also be made available to read from the Crohn’s and Colitis UK (CCUK) website https://www.crohnsandcolitis.org.uk/ or participants are invited to contact the lead researcher directly to receive the results of the study.

**What if there is a problem?**

If you are concerned about any aspect of the study or wish to make a complaint, please contact Louise Sweeney (louise.sweeney@kcl.ac.uk) or another member of the research team (Professor Christine Norton by email: christine.norton@kcl.ac.uk or telephone: +44 (0) 20 7848 3864).

If you have a complaint, you should talk to a member of the research team who will do their best to answer your questions. If you remain unhappy, you may be able to make a formal complaint through the NHS complaints procedure. Details can be obtained through the Guy’s and St Thomas’ Patient Advisory Liaison Service (PALS) on 0207 1887188. Address: PALS, KIC, Ground floor, North Wing, St Thomas’ Hospital, Westminster Bridge Road, London, SE1 7EH. This study is sponsored by King’s College London University and Guy’s & St Thomas’ Foundation NHS Trust. The sponsor will at all times maintain adequate insurance in relation to the study independently.

Details can be obtained through Patient Advisory Liaison Services (PALS) at the participating hospitals.

**Who is organising and funding the study?**

The research is organised by King’s College London and is being carried out by a PhD student, Louise Sweeney, who is researching pain in IBD. The study has been reviewed by Proportionate Review Sub-committee of the London - Surrey Borders Research
Ethics Committee Ethics Committee and has granted ethical approval on 15/09/2017. The project is being funding by a PhD Studentship awarded by Crohn’s and Colitis UK, and is being supervised by Professor Christine Norton, Professor Rona Moss-Morris and Dr Wladzia Czuber-Dochan.

Any questions about the study should be directed to either to the PhD Researcher on the team or the Chief Investigator:

**PhD Researcher**
Louise Sweeney  
Rm 1.32 24 James Clerk Maxwell Building  
57 Waterloo Road London  
SE1 8WA  
Tel: +07745 565349  
Email: louise.sweeney@kcl.ac.uk

**Chief investigator**
Professor Christine Norton  
Professor of Nursing  
Rm 2.24 James Clerk Maxwell Building  
57 Waterloo Road London SE1 8WA  
Tel: +44 (0) 20 7848 3864  
Email: christine.norton@kcl.ac.uk

Please keep this information sheet for your own records.
CONSENT FORM - Survey

Name of Researcher: Louise Sweeney

1. I confirm that I have read the information sheet dated 09.10.17, version 1.1 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. 

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from King’s College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I understand that the information collected about me will be used to support other ethically approved research in the future, and may be shared anonymously with other researchers.

5. I understand that any information that I provide will be presented anonymously.

6. I consent to the research team accessing the results of my stool sample.

7. I understand that I may be contacted regarding completion of follow-up questionnaires.

8. I agree to take part in the above study.

<table>
<thead>
<tr>
<th>Name of Participant</th>
<th>Date</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Person taking consent</th>
<th>Date</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
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</tbody>
</table>
ID: .................................................................

Date: ............................................................

Investigating pain in inflammatory bowel disease

Study Questionnaire Booklet

A team of researchers at King’ College London is investigating pain in inflammatory bowel disease (IBD). We would like to invite you to read and complete the following questionnaire booklet. Some questions will ask about your overall well-being and functioning and others will specifically ask about any pain you may be experiencing. Some of the questions may seem repetitive, but they have been selected from standard questionnaires and we would be thankful if you could complete the relevant sections. Collecting this information will help us to gain a better understanding of pain in IBD and inform the development of a self-management treatment program for IBD patients with pain.

If you do not suffer from pain or if the pain you have is not directly related to your IBD, we are still interested in hearing of your story and experiences. You will be directed to skip over some sections if they are not relevant to you.

If you have any questions, do not hesitate to get in contact with the research team. On behalf of King’s College London, thank you for taking part in this research.

Section A: To be completed by the Participant

Section B: To be complete by the Clinician

Lead researcher: Louise Sweeney (email: louise.sweeney@kcl.ac.uk)

Study conducted by: King’s College London

Study Funded by: Crohn’s & Colitis UK
# Section A: to be completed by the Participant

## Demographic and Clinical Data Questionnaire

Please tick the appropriate boxes relevant to you.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gender</td>
<td>[ ] Female</td>
</tr>
<tr>
<td>2. Age (at last birthday) in years:</td>
<td></td>
</tr>
<tr>
<td>3. Confirmed diagnosis of IBD</td>
<td>[ ] Crohn’s Disease</td>
</tr>
<tr>
<td>4. Date of IBD diagnosis</td>
<td></td>
</tr>
<tr>
<td>6. Education level</td>
<td>[ ] No formal qualifications</td>
</tr>
</tbody>
</table>
| 7. Relationship status | □ Married /Civil partnership  
□ Living with a partner  
□ Widowed  
□ Divorced/Separated  
□ Single |
| 8. Current employment status | □ Employed full-time  
□ Employed part-time  
□ Full or part-time education  
□ Full-time domestic responsibilities  
□ Retired  
□ Unemployed |
| 9. Smoking history | □ Current smoker  
□ Previous smoker  
□ Non-smoker |
| 10. Previous surgery for IBD (either Crohn’s disease or ulcerative colitis) | □ Yes  
□ No |
| If Yes, Number of surgeries | ________________ |

<table>
<thead>
<tr>
<th>Date of surgery</th>
<th>Location/type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Current stoma  
□ Yes  
□ No
<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Number of IBD flares (active disease) in the last 2 years</td>
<td>0 1 2 3 4 5+ Ongoing disease activity without remission over the last 2 years</td>
</tr>
<tr>
<td>12. Date of last IBD flare (active disease) (start-end)</td>
<td></td>
</tr>
<tr>
<td>13. Severity of symptoms during last period of active disease</td>
<td>Not applicable Mild Moderate Severe</td>
</tr>
<tr>
<td>14. Currently on antidepressants</td>
<td>Yes No If Yes, which one(s):</td>
</tr>
<tr>
<td>15. Current medications for IBD (please tick):</td>
<td>Dose How often?</td>
</tr>
<tr>
<td>☐ Sulfasalazine</td>
<td></td>
</tr>
<tr>
<td>☐ Other 5-ASA (Pentasa, Octasa, Asacol, Mesalazine, Mezavant, Salofalk)</td>
<td></td>
</tr>
<tr>
<td>☐ Azathioprine</td>
<td></td>
</tr>
<tr>
<td>☐ Mercaptopurine</td>
<td></td>
</tr>
<tr>
<td>☐ Infliximab (Remicade, Remsima, Flixabi)</td>
<td></td>
</tr>
<tr>
<td>☐ Adalimumab (Humira)</td>
<td></td>
</tr>
<tr>
<td>☐ Vedolizumab (Entyvio)</td>
<td></td>
</tr>
<tr>
<td>☐ Golimumab (Simponi)</td>
<td></td>
</tr>
<tr>
<td>☐ Methotrexate</td>
<td></td>
</tr>
<tr>
<td>☐ Allopurinol</td>
<td></td>
</tr>
<tr>
<td>☐ Prednisolone</td>
<td></td>
</tr>
<tr>
<td>☐ Budesonide</td>
<td></td>
</tr>
<tr>
<td>☐ Other .........................................................................................</td>
<td></td>
</tr>
<tr>
<td>☐ None</td>
<td></td>
</tr>
</tbody>
</table>
QUESTIONS ABOUT YOUR PAIN

Please answer the following questions and provide a tick in the appropriate boxes relevant to you.

1. Do you experience pain related to your IBD?
2. Do you experience pain when you have periods of active disease?
3. Do you experience pain when you are in a period of remission?
4. Is the pain you experience mostly related to your IBD?
5. If you have had an operation(s) for your IBD, for how long did you experience pain after?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Sometimes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Always</td>
<td>Frequently</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Not sure</td>
</tr>
<tr>
<td>No pain</td>
<td>Up to 6 weeks</td>
<td>Up to 6 months</td>
</tr>
</tbody>
</table>

If other, or the pain you have experienced post-surgery has varied, please specify:

……………………………………………………………………………………………………………………………………………………………

6. In an average week, how frequently do you experience pain?

| 0 days | 1-2 days | 3-5 days | Every day |

7. Please tick any pain-related conditions you have (if any):
   - Low back pain
   - Migraine/Headache
   - Arthritis
   - Fibromyalgia
   - Other (please specify): __________________________________________________________

8. Have you suffered from pain every day for 3 months within the last 6 months? Yes No

9. Do you use any alternative therapies for your pain? E.g. acupuncture, homeopathy Yes No

Please list these: …………………………………………………………………………………………………………………………………

10. Do you use any self-management techniques for your pain? E.g. exercise, hot water bottle.

Please list these …………………………………………………………………………………………………………………………………

Please turn over.
11. Using the body diagram, please tick the boxes where you feel pain, if any (please tick more than one if applicable):

1. Face
2. Neck
3. Shoulder/chest R
4. Shoulder/chest L
5. Upper arm/elbow R
6. Upper arm/elbow L
7. Lower arm/wrist R
8. Lower arm/wrist L
9. Palm of hand R
10. Palm of hand L
11. Chest/bottom of rib cage R
12. Chest/bottom of rib cage L
13. Side of abdomen R
14. Side of abdomen L
15. Pelvis/bladder
16. Thigh/knee R
17. Thigh/knee L
18. Calf (front) R
19. Calf (front) L
20. Top of foot R
21. Top of foot L
22. Head (back)
23. Neck (back)
24. Upper shoulder/spine L
25. Upper shoulder/spine R
26. Upper arm/elbow (back) L
27. Upper arm/elbow (back) R
28. Lower arm/wrist (back) L
29. Lower arm/wrist (back) R
30. Top of hand/fingers L
31. Top of hand/fingers R
32. Upper back/scapula region L
33. Upper back/scapula region R
34. Lower back L
35. Lower back R
36. Pelvis/buttocks L
37. Pelvis/buttocks R
38. Thigh/knee (back) L
39. Thigh/knee (back) R
40. Calf (back) L
41. Calf (back) R
42. Bottom of foot L
43. Bottom of foot R

Please turn over.
12. Please rate your pain by marking a tick in the box that best describes your pain at its **WORST** in the last 24 hours.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain as bad as you can imagine</td>
</tr>
</tbody>
</table>

13. Please rate your pain by marking the box that best describes your pain at its **LEAST** in the last 24 hours.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain as bad as you can imagine</td>
</tr>
</tbody>
</table>

14. Please rate your pain by marking the box that best describes your pain on **AVERAGE**.

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<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<tbody>
<tr>
<td>No pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain as bad as you can imagine</td>
</tr>
</tbody>
</table>

15. Please rate your pain by marking the box that describes how much pain you have **RIGHT NOW**.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Pain as bad as you can imagine</td>
</tr>
</tbody>
</table>

16. Please list any medications you are taking to control your pain (if applicable):

<table>
<thead>
<tr>
<th>Pain medications</th>
<th>Dose</th>
<th>How many times per day?</th>
<th>How long have you been taking this medication?</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

17. In the last 24 hours, how much relief have pain treatments or medications provided? Please mark the box below the percentage that most shows how much **relief** you have received.

<table>
<thead>
<tr>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
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</tr>
</tbody>
</table>
18. Please mark a ☑ in the box of the number that describes how, during the past 24 hours, pain has interfered with your:

<table>
<thead>
<tr>
<th></th>
<th>Does not interfere</th>
<th>Completely interferes</th>
</tr>
</thead>
<tbody>
<tr>
<td>General activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking ability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal work (includes both work outside the home and housework)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relations with other people</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enjoyment of life</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

19. Please mark the picture the best describes your pain:

- Persistent pain with slight fluctuations
- Persistent pain with pain attacks
- Pain attacks without pain between them
- Frequent pain attacks with pain between them

20. Does your pain spread to other regions of your body? Yes ☐ No ☐

Please mark the box with a ☑ to the answer which is most applicable to you:

- Do you suffer from a burning sensation (e.g. stinging nettles) in the areas you have pain?
- Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electric tingling)?
- Is light touching (clothing, a blanket) in this area painful?
- Do you have sudden pain attacks in the area of your pain, like electric shocks?
- Do you suffer from a sensation of numbness in the areas you have pain? (In relation to your answer on page 6, Q.5)
QUESTIONS ABOUT YOUR SYMPTOMS

Please circle the number which best indicates your answer to the following questions:

1. How severe has your abdominal (tummy) pain been over the last 10 days?
   
   0             1              2              3              4              5             6             7              8              9            10
   No pain       Not very severe     Quite severe     Severe     Very severe

2. On how many of the last 10 days did you get pain? ...........................................

3. How severe has your abdominal distension (bloating, swollen or tight) been over the last 10 days?
   
   0             1             2             3             4             5             6             7             8             9            10
   No pain       Not very severe    Quite severe    Severe    Very severe

4. How satisfied have you been with your bowel habit (frequency, ease, etc) over the last ten days?
   
   0             1             2             3             4             5             6             7             8             9            10
   Very happy    Quite happy    Unhappy    Very unhappy

5. How much have your symptoms been affecting/interfering with your life in general over the last ten days?
   
   0             1             2             3             4             5             6             7             8             9            10
   Not at all    Not much    Quite a lot    Completely

IF YOU DO NOT SUFFER FROM PAIN, PLEASE TURN TO PAGE 16.
GENERAL FUNCTIONING AND PAIN

Please answer the following questions in the context of when you experience pain.

Please rate how confident you are that you can do the following things, at present, despite the pain. To indicate your answer, please circle one of the numbers on the scale under each item, where 0 = not confident at all and 6 = completely confident.

1. I can still enjoy things, despite the pain.

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident

2. I can do most of the household chores (e.g. tidying-up, washing dishes etc), despite the pain.

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident

3. I can socialise with my friends or family members as often as I used to do, despite the pain.

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident

4. I can cope with my pain in most situations.

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident

5. I can do some form of work, despite the pain. (“work” includes housework, paid and unpaid work).

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident

6. I can still do many of things I enjoy doing, such as hobbies or leisure activity, despite pain.

   0  1  2  3  4  5  6
   Not at all  Completely
   confident  confident
7. I can cope with my pain without medications.

0 1 2 3 4 5 6

Not at all Completely
confident confident

8. I can still accomplish most of my goals in life, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident

9. I can live a normal lifestyle, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident

10. I can gradually become more active, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident
THOUGHTS AND FEELINGS ABOUT YOUR PAIN

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are statements describing different thoughts and feelings that may be associated with pain. Please tick the appropriate box which best describes the thoughts and feelings you have when you experience pain.

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>To a slight degree</th>
<th>To a moderate degree</th>
<th>To a great degree</th>
<th>All the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I worry all the time about whether the pain will end</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I feel like I can’t go on</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. It’s terrible and I think it’s never going to get any better</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4. It’s awful and I feel that it overwhelms me</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. I feel I can’t stand it anymore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. I become afraid that the pain will get worse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. I keep thinking of other painful events</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. I anxiously want the pain to go away</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. I can’t seem to keep it out of my mind</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. I keep thinking about how much it hurts</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>11. I keep thinking about how badly I want the pain to stop</td>
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<tr>
<td>12. There’s nothing I can do to reduce the intensity of the pain</td>
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<tr>
<td>13. I wonder whether something serious may happen</td>
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</tbody>
</table>
THOUGHTS AND BEHAVIOURS IN RESPONSE TO YOUR PAIN

Please indicate how much you agree or disagree with the following statements about when you experience pain by ticking the appropriate box.

<table>
<thead>
<tr>
<th>Views about your pain</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neither agree nor disagree</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I am afraid that I will make my pain worse if I exercise</td>
<td></td>
<td></td>
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<tr>
<td>2. My pain would be relieved if I were to exercise</td>
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<tr>
<td>3. Avoiding unnecessary activities is the safest thing I can do to prevent my pain from worsening</td>
<td></td>
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<tr>
<td>4. The severity of my pain must mean there is something serious going on in my body</td>
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<tr>
<td>5. Even though I experience pain, I don’t think it is actually harming me</td>
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<tr>
<td>6. When I experience pain, my body is telling me that there is something seriously wrong</td>
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<tr>
<td>7. Physical activity makes my pain worse</td>
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<tr>
<td>8. Doing less helps my pain</td>
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<tr>
<td>9. Pain is a signal that I am damaging myself</td>
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<tr>
<td>10. I am afraid I will have more pain if I am not careful</td>
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<tr>
<td>11. I should avoid exercise when I have pain</td>
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<tr>
<td>12. When I experience pain, I think about it constantly</td>
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<tr>
<td>13. I worry when I am experiencing pain</td>
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<tr>
<td>14. When I am experiencing pain it is difficult for me to think of anything else</td>
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<tr>
<td>15. I think a great deal about my pain</td>
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<tr>
<td>16. My pain is always at the back of my mind</td>
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<tr>
<td>17. I spend a lot of time thinking about my pain</td>
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<tr>
<td>18. I am embarrassed about my pain</td>
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<tr>
<td>19. I worry that people will think badly of me because of my pain</td>
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<tr>
<td>20. The embarrassing nature of my pain prevents me from doing things</td>
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<tr>
<td>21. I avoid social situations because I am scared my pain will get out of control</td>
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<tr>
<td>22. I am ashamed of my pain</td>
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</tr>
</tbody>
</table>
23. My pain has the potential to make me look foolish in front of other people

<table>
<thead>
<tr>
<th>Managing your pain</th>
<th>Never</th>
<th>Sometimes</th>
<th>Quite often</th>
<th>Very often</th>
<th>All the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>24. I stay in bed to control my pain</td>
<td></td>
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<tr>
<td>25. When I experience pain, I rest</td>
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<tr>
<td>26. I tend to avoid activities which make my pain worse</td>
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<tr>
<td>27. I tend to nap during the day to control my pain</td>
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<tr>
<td>28. I tend to overdo things when I’m energetic</td>
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<tr>
<td>29. I find myself rushing to get things done before I crash</td>
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<tr>
<td>30. I tend to overdo things and then rest up for a while</td>
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<tr>
<td>31. I tend to do a lot on a good day and rest on a bad day</td>
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<tr>
<td>32. I sleep when I’m tired in order to control my pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>33. I avoid making social arrangements in case I’m not up to it</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>34. I avoid exerting myself in order to control my pain</td>
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<tr>
<td>35. I’m a bit all or nothing when it comes to doing things</td>
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<tr>
<td>36. I avoid stressful situations</td>
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</tbody>
</table>

37. Which of the following best describes the nature of your symptoms - please tick one:

<table>
<thead>
<tr>
<th>My symptoms are physical</th>
<th>My symptoms are mainly physical</th>
<th>Both physical and psychological factors are involved in my symptoms</th>
<th>My symptoms are mainly psychological</th>
<th>My symptoms are psychological in nature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

Please turn over.
LIVING WITH PAIN

Please rate the truth of each statement as it applies to you by ticking a box.

1. I am getting on with the business of living no matter what level my pain is.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>

2. Keeping my pain level under control takes first priority whenever I’m doing something.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>

3. Although things have changed, I am living a normal life despite my pain.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>

4. Before I can make any serious plans, I have to get some control over my pain.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>

5. I lead a full life even though I experience pain.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>

6. When my pain increases, I can still take care of my responsibilities.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
</table>
7. I avoid putting myself in situations where my pain might increase.

<table>
<thead>
<tr>
<th>Never true</th>
<th>Very rarely true</th>
<th>Seldom true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>Almost always true</th>
<th>Always true</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

8. My worries and fears about what my pain will do to me are true.

YOUR EATING PATTERNS

We are also interested in hearing of the effects pain has on your eating and food-related behaviours. Please tick the appropriate box for the following questions about your eating patterns related to your pain.

<table>
<thead>
<tr>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I avoid certain food or drink which I know makes my pain worse</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2. I skip meals or eating to avoid worsening my pain</td>
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<tr>
<td>3. I tend to not eat out or eat socially because of the risk of making my pain worse</td>
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<tr>
<td>4. My eating patterns have changed because of my pain</td>
<td></td>
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</tbody>
</table>

Please note any comments of how your eating patterns have changed as a result of pain (if applicable):

........................................................................................................................................................................................................
........................................................................................................................................................................................................

Please turn over.
**GENERAL MOOD AND FUNCTIONING**

Over the last 2 weeks, how often have you been bothered by the following problems? Please use a ☑ to indicate your answer.

<table>
<thead>
<tr>
<th></th>
<th>Feeling nervous anxious or on edge</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>2</td>
<td>Not being able to stop or control worrying</td>
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<tr>
<td>3</td>
<td>Worrying too much about different things</td>
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<tr>
<td>4</td>
<td>Trouble relaxing</td>
<td></td>
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<tr>
<td>5</td>
<td>Being so restless that it is hard to sit still</td>
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<tr>
<td>6</td>
<td>Becoming easily annoyed or irritable</td>
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<tr>
<td>7</td>
<td>Feeling afraid as if something awful might happen</td>
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<tr>
<td>8</td>
<td>Little interest or pleasure in doing things</td>
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<tr>
<td>9</td>
<td>Feeling down, depressed, or hopeless</td>
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<tr>
<td>10</td>
<td>Trouble falling or staying asleep, or sleeping too much</td>
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<tr>
<td>11</td>
<td>Feeling tired or having little energy</td>
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<tr>
<td>12</td>
<td>Poor appetite or overeating</td>
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<tr>
<td>13</td>
<td>Feeling bad about yourself – or that you are a failure or have let yourself or your family down</td>
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<tr>
<td>14</td>
<td>Trouble concentrating on things, such as reading the newspaper or watching television</td>
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<tr>
<td>15</td>
<td>Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual</td>
<td></td>
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<tr>
<td>16</td>
<td>Thoughts that you would be better off dead or hurting yourself in someway</td>
<td></td>
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</tbody>
</table>

17. If you ticked off any problems, how difficult have these problems made it for you to do your work, take of things at home, or get along with other people?

<table>
<thead>
<tr>
<th></th>
<th>Not at all difficult</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
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</thead>
<tbody>
<tr>
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</tbody>
</table>

368
STRESS QUESTIONNAIRE

Please answer the following questions about your feelings and thoughts during the last month. Please use a ☑ to indicate your answer.

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost never</th>
<th>Sometimes</th>
<th>Fairly often</th>
<th>Very often</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In the last month, how often have you been upset because of something that happened unexpectedly?</td>
<td></td>
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<tr>
<td>2. In the last month, how often have you felt that you were unable to control the important things in your life?</td>
<td></td>
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<tr>
<td>3. In the last month, how often have you felt nervous and ‘stressed’?</td>
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<tr>
<td>4. In the last month, how often have you felt confident in your ability to handle your personal problems?</td>
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<tr>
<td>5. In the last month, how often have you felt that things were going your way?</td>
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<tr>
<td>6. In the last month, how often have you found that you could not cope with all the things that you had to do?</td>
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<tr>
<td>7. In the last month, how often have you been able to control irritations in your life?</td>
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<tr>
<td>8. In the last month, how often have you felt that you were on top of things?</td>
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<tr>
<td>9. In the last month, how often have you been angered because of things that were outside of your control?</td>
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<tr>
<td>10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?</td>
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</tbody>
</table>

Please turn over.
GENERAL WELL-BEING

Please answer the following questions about how you have been feeling during the past month. Place a ☑ in the box that best represents how often you have experienced or felt the following:

<table>
<thead>
<tr>
<th>During the past month, how often do you feel….</th>
<th>Never</th>
<th>Once or twice</th>
<th>About once a week</th>
<th>About 2 or 3 times a week</th>
<th>Almost every day</th>
<th>Every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Happy</td>
<td></td>
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<tr>
<td>2. Interested in life</td>
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<tr>
<td>3. Satisfied with life</td>
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<tr>
<td>4. That you had something important to contribute to society</td>
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<tr>
<td>5. That you belonged to a community (like a social group or your neighbourhood)</td>
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<tr>
<td>6. That our society is becoming a better place for people like you</td>
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<tr>
<td>7. That people are basically good</td>
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<tr>
<td>8. That the way our society works makes sense to you</td>
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<tr>
<td>9. That you like most parts of your personality</td>
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<tr>
<td>10. Good at managing the responsibilities of your daily life</td>
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<tr>
<td>11. That you had warm and trusting relationships with others</td>
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<tr>
<td>12. That you had experiences that challenged you to grow and become a better person</td>
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</tr>
<tr>
<td>13. Confident to think or express your own ideas and opinions</td>
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</tr>
<tr>
<td>14. That your life has a sense of direction or meaning to it</td>
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</tr>
</tbody>
</table>
LEVELS OF FATIGUE

We are interested in knowing more about your fatigue or ‘tiredness’ levels.

Please circle one number for each question about your levels of fatigue:

<table>
<thead>
<tr>
<th>Question</th>
<th>No fatigue</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is your fatigue level right NOW</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>What was your HIGHEST fatigue level in the past two weeks</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>What was your LOWEST fatigue level in the past two weeks</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>What was your AVERAGE fatigue level in the past two weeks</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>How much of your waking time have you felt fatigued in the past two weeks</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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</table>

Would you be interested in taking part in an interview for the next phase of this research?

Yes ☐ No ☐

If you are happy to be contacted about the next phase of the study, please provide your name, telephone and email contact details below:

Name: ......................................................................................................................................................

Phone: ........................................................................................................................................................

Email: ..........................................................................................................................................................

Would you be interested in taking part an online self-management intervention study for this research?

Yes ☐ No ☐

Thank you for completing this questionnaire.
**SECTION B: TO BE COMPLETED BY THE CLINICIAN**

**Disease Activity Index (DAI)**

**CROHN’S DISEASE:** Harvey Bradshaw Index (Harvey and Bradshaw 1980)

<table>
<thead>
<tr>
<th>A. General well-being</th>
<th>Please select one...</th>
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</thead>
<tbody>
<tr>
<td>Very well</td>
<td>□</td>
</tr>
<tr>
<td>Slightly below par</td>
<td>□</td>
</tr>
<tr>
<td>Poor</td>
<td>□</td>
</tr>
<tr>
<td>Very poor</td>
<td>□</td>
</tr>
<tr>
<td>Terrible</td>
<td>□</td>
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<table>
<thead>
<tr>
<th>B. Abdominal pain</th>
<th>Please select one...</th>
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<tbody>
<tr>
<td>None</td>
<td>□</td>
</tr>
<tr>
<td>Mild</td>
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</tr>
<tr>
<td>Moderate</td>
<td>□</td>
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<td>Severe</td>
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| C. Number of liquid stools per day | ...................................................... |

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<thead>
<tr>
<th>D. Abdominal mass</th>
<th>Please select one...</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
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</tr>
<tr>
<td>Dubious</td>
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</tr>
<tr>
<td>Definite</td>
<td>□</td>
</tr>
<tr>
<td>Definite and tender</td>
<td>□</td>
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<table>
<thead>
<tr>
<th>E. Complications</th>
<th>Please tick all that currently apply...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painful joints/arthritis</td>
<td>□</td>
</tr>
<tr>
<td>Anal fissure/fistula/abscess</td>
<td>□</td>
</tr>
<tr>
<td>Mouth ulcers</td>
<td>□</td>
</tr>
<tr>
<td>Skin nodules or ulcers [including pyoderma &amp; erythema nodosum]</td>
<td>□</td>
</tr>
<tr>
<td>Eye pain or inflammation (red eyes)</td>
<td>□</td>
</tr>
<tr>
<td>Liver problems [e.g. primary sclerosing cholangitis]</td>
<td>□</td>
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**ULCERATIVE COLITIS:** SIMPLE CLINICAL COLITIS ACTIVITY INDEX (Walmsley et al 1998)

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<thead>
<tr>
<th>A. Bowel frequency (day)</th>
<th>Please indicate the number of bowel movements during the day</th>
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<tbody>
<tr>
<td>1-3</td>
<td>□</td>
</tr>
<tr>
<td>4-6</td>
<td>□</td>
</tr>
<tr>
<td>7-9</td>
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<tr>
<td>More than 9</td>
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<table>
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<th>C. Urgency of defecation</th>
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<tr>
<td>No hurry</td>
<td>□</td>
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<tr>
<td>Hurry</td>
<td>□</td>
</tr>
<tr>
<td>Immediately</td>
<td>□</td>
</tr>
<tr>
<td>Incontinence</td>
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<table>
<thead>
<tr>
<th>E. General well-being</th>
<th>Please select one...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very well</td>
<td>□</td>
</tr>
<tr>
<td>Slightly below par</td>
<td>□</td>
</tr>
<tr>
<td>Very poor</td>
<td>□</td>
</tr>
<tr>
<td>Terrible</td>
<td>□</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Bowel frequency (night)</th>
<th>Please indicate the number of bowel movements during the night</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>□</td>
</tr>
<tr>
<td>1-3</td>
<td>□</td>
</tr>
<tr>
<td>4-6</td>
<td>□</td>
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</table>

<table>
<thead>
<tr>
<th>D. Blood in stool</th>
<th>Please select one...</th>
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<tbody>
<tr>
<td>None</td>
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<tr>
<td>Trace</td>
<td>□</td>
</tr>
<tr>
<td>Occasionally frank [visible, obvious]</td>
<td>□</td>
</tr>
<tr>
<td>Usually frank</td>
<td>□</td>
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</table>

<table>
<thead>
<tr>
<th>F. Extracolonic features</th>
<th>Please tick all that apply currently...</th>
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<tr>
<td>Anal fissure/fistula/abscess</td>
<td>□</td>
</tr>
<tr>
<td>Mouth ulcers</td>
<td>□</td>
</tr>
<tr>
<td>Skin nodules or ulcers [including pyoderma &amp; erythema nodosum]</td>
<td>□</td>
</tr>
<tr>
<td>Eye pain or inflammation (red eyes)</td>
<td>□</td>
</tr>
<tr>
<td>Liver problems [e.g. primary sclerosing cholangitis]</td>
<td>□</td>
</tr>
</tbody>
</table>
B.2.4 Ethical approval (REC & HRA): quantitative and qualitative study

London - Surrey Borders Research Ethics Committee
Research Ethics Committee (REC) London Centre
Skipton House
80 London Road
London
SE1 0LH

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

15 September 2017

Professor Christine Norton
57 Waterloo Road
London
SE1 8WA

Dear Professor Norton

Study title: Living with chronic abdominal pain in IBD: a PhD studentship developing and feasibility testing IBD pain management interventions

REC reference: 17/LO/1527

HRA project ID: Z56323

The Proportionate Review Sub-committee of the London - Surrey Borders Research Ethics Committee reviewed the above application on 13 September 2017.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact hra.studyregistration@nhs.net outlining the reasons for your request. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.
Letter of HRA Approval

Study title: Living with chronic abdominal pain in IBD: a PhD studentship developing and feasibility testing IBD pain management interventions
IRAS project ID: 226323
REC reference: 17/LO/1527
Sponsor: King’s College London

I am pleased to confirm that HRA Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. Please read Appendix B carefully, in particular the following sections:

- Participating NHS organisations in England – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities.
- Confirmation of capacity and capability - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria) - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details
21 November 2017

Miss Louise Sweeney
84 Morning Lane
London
E9 6NA

Dear Miss Sweeney

Study title: Living with chronic abdominal pain in IBD: a PhD studentship developing and feasibility testing IBD pain management interventions

REC reference: 17/LO/1527
Amendment number: SA01
Amendment date: 13 October 2017
IRAS project ID: 226323

Approval was sought for changes to the questionnaires, patient recruitment, follow up procedures and Sample Collection change.

The above amendment was reviewed at the meeting of the Sub-Committee held on 25 October 2017.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

A Research Ethics Committee established by the Health Research Authority
## B.2.5 Full correlations of pain and psychosocial factors in cross-sectional study

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<td>8) Symptom Focusing</td>
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<td>10) All or Nothing Behaviour</td>
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<td>15) Anxiety</td>
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Appendix C Qualitative study

C1) Draft thematic maps

Understanding & Communication
- Socio/cultural with HIV: assessment of pain, working together, prioritising symptoms
- Social support: awareness, disclosure
- Own understanding & perceived causes of pain: diet, stress, bodily processes
- RE: community: sharing of experiences, learning from others

Management/Coping
Practical Management
- Diet
- Exercise & stretching
- Reminding/Activity
- Clothing, Heat
- Medications (H/3), balance

Psychological Management
- Monitoring/Learning
- Safety/Control
- Distraction
- Concealment
- Holistic strategies: meditation, CBT

Needs
- Wanting to exercise
- HCP accessibility
- More information & guidance
- Psychological support
- A quick fix

Impact
- Physiological: stress, performance, attendance
- Emotional: mood, fear of surgery, pain signals reminder, future concerns, ambivalence/chaos, pain as reminder, lack of confidence
- Functional/Physical: feeling aged, daily routine, mobility, exercise/Activity
- Social: guilt, lack of commitment/canceling plans, not going out

Resilience
- Acceptance vs denial
- Personalisation/Tolerance
- Optimism
- Acceptance
- Social; social support & social modulation
- Adjustment

Symptom Patterns
- Nature of pain
  - Location, sensation, timeline
  - Unpredictability, uncontrollability
- Pain & flares
- Associated symptoms
  - Fatigue
  - Urgency
  - Various cycles
  - Managing more than one symptom

Breaking the cycle
- Home seen as trap
- Get up and go
- Changing focus to something else

Health and activity levels
- Fatigue, pain and poor health barrier to exercise
- Reduced exercise increases pain and stiffness
- Feeling old and broken
- Wanting to exercise but lack of confidence with interaction of symptoms

Unrelenting nature
- Mentally distracting
- Building tolerance (yet barrier to communication)
- “bite the bullet” Grin and bear it
- Dull/dull/tiring, nagging
- Constant awareness vs bothersome

Cycles of anxiety
- Pain as a warning signal
  - creates stress and panic
- Stress increases risk of flare
- Side effects of EBD and pain medication

Poor communication and understanding
- Commitment/embarrassment of disease resulting in poor understanding/awareness
- Poor understanding resulting in perceived stigma e.g. work colleagues
- Therapy alleviating this
### Sources of solutions
- Oneself – learning and monitoring
- Others with IBD
- Working with healthcare professionals
- Friends/family with medical background

### Search for a solution
- Lack of understanding of causes of pain barrier to finding a solution
- Preoccupation
- Frustration, anger, avoidance, submission
- Vs acceptance, resilience, motivation

### Solutions from experience

#### What is considered a solution?
- No pain at all
- ‘Being well’
- Control
- Managing mental health
- Consistency/predictability
- Having a plan or protocol
- Ability to communicate

#### Types of solutions
- Immediate relief – heat, stretching, toilet safety
- Maintenance – diet, sleep, exercise, rest
- Indirect solutions – social support, distraction, work, motivations
- Sustainable solutions
- Evidence-based solutions
Okay, it should be recording. Okay, excellent. So, can I ask you to just confirm your diagnosis of your IBD?

It’s ulcerative colitis.

Okay. And can you, let me start, you experience in relation to your IBD, the pain is quite, can be accurate in the time.

Right. I don’t think, it certainly used to be all of my mid-section. And I get perianal, I don’t know if that’s the whole colon, it’s permanent. So, I think there’s a relation to where the intestine join, because of where the more kind of acute in more sort if it seems to be, I don’t know, if it’s just occasional, and it’s seen pain I experience frequently, some sort day-to-day, every day, a kind of dull pain is say the abdomen which I had it as if as 2 get worse with time, there’s a relation you know, acute sometimes I’ll have need to go to the then that pain, it’s in my general tendency.

And that’s because it doesn’t feel a lot worse or, yep, like to say my walking sometimes if I’m touching the it’s a chronic pain. And so that would be a kind of, and that’s, and that’s heater, more, would you say when you have this underlying dull kind of chronic ache you talk about. But then when it’s it’s, it becomes that kind of sharp pain.

Just more uncomfortable, so kind of deeper pain. So it means, for example, I find it tight, you know. And tight. So, for me, the on the waist like, it hurts, it hurts to have anything right part, and then a looser bottom where it’s not flat. It puts pressure, and it exacerbates the pain.

So, you say it’s kind of around the abdomen area? Which is the area just in that...
I get other pains. And in terms of, I sometimes get pain in my legs, which I would describe as kind of growing pains – like I still have a thirty-six-year-old woman. I think they’re less frequent than I used to get them, and I think it’s associated with when I’m especially tired. I also get pain in my feet sometimes. So I’m going through a process of investigation in the rheumatology department, whether I’ve got some sort of inflammatory process that happens similar to gout, it’s not a confirmed diagnosis. And it tends to be a localised pain, kind of between the joints of my toes. Or the underside of my foot, which will be really sharp and perhaps it will be associated with a little bit of inflammation. And it will be difficult for me to walk. I would be kind of hobbling for about a week. And it just goes away then as quickly as it came on.

So, that’s a lot more intense?

Yes. Yes, exactly.

And so, earlier on you were saying when you have the more acute stab pain kind of pain, you can associate that with either an urgency to then to go to the toilet or something you might have eaten. And then you’re saying the sort of more dull period, you associated with fatigue, great fatigue. Have you noticed generally that your pain correlates with other symptoms related to your ulcerative colitis?

No, I think that’s generally hard, because I can – well, I would say, sorry, bloating, the pain seems to get worse with bloating. And I think I’m a bit more bloated generally when I’m in pain. So there seems to be some relationship between pain and bloating. And it gets worse when I’m gassy. So, you know, if it feels sort of like trapped wind in my gut, then it will kind of change the nature of my pain, it will be more crampy. And more acute or sharper, I guess. But I don’t think it’s necessarily correlated with increased frequency and going to the washroom or worse diarrhoea. I kind of never usually have normal bowel movements anyway. I usually have some degree of diarrhoea. But, I don’t think they have anything like, because I’ve had worse experiences of ulcerative colitis in the past or, you know, flares, and I remember when it was like, you know, waking up in the night and needing to go to the washroom, having more concerns about urgency, that sort of thing. I don’t have those problems now, although I have pain now where I didn’t used to, you know, earlier on in my disease.

And in terms of, you said, you seemed to say that when you have a flare, do you think you are able to recognise the particular sort of sensations of pain when it’s bringing on a flare? Do you feel you’re able to sort of dissociate that type of pain sensation compared to when you’re in remission?

I don’t know. I’m entirely confident in being able to distinguish the two. But, I think my pain gets worse, and I get nauseated when I’m having a flare and my bowels get worse. I think that’s the only distinction for me. And I don’t know that it’s a flare, you know, as according to my gastroenterologist, that it happens to have these faecal calprotectin testing done. So it’s – I find it very difficult to identify a flare, because of my normal sort of low grade, you know, bad bowels and pain and fatigue and bloating, because I experience that all the time. I very rarely don’t experience that.

And what do you think then, what are you kind of thinking then when you have this dull ache, when you aren’t aware that you’re in a flare, kind of what are the thoughts that are going through your head when you have that kind of constant abdominal discomfort?

I just think about I feel I’m going to have the pain forever – for the rest of my life, but also every day, all the time, all day. And you know, history has shown that that’s not the case, but I feel like I have, over the years, the last number of years, my episodes of having no pain and fewer and further between than when I do have pain. So I do worry a lot about the impact of how my ability to work, because I feel like I’m always struggling to get over it and...
Unrelenting and impacting nature of the pain in my knee and ankle.

Notable pain is there, but it is not bothersome.

Worrying and warning signal pain dependent on location of joint, eg. back, joint.

In you're in actual pain, a sign of a possible underlying issue. Having a pain in your knee is severe, and it can't really progress quickly.

Relief and maintenance of activity to push myself forward in the day and help with fatigue.

Dietary maintenance to abd, pain.

A bit about the pain is tolerable, it's been like this for a bit longer.

The kind of pain that I'm in, I don't have any pain relief medication, and the pain seems to be related to my liver and kidney.

Treatment of the severe/disagreement.

Objective:

I mean you're talking about kind of correlating with blood test results and iron levels and things. Have you seen that something correlates with other symptoms that you have related to your Crohn's?

Yes, sorry, I should probably have put that in. It's alright.
<table>
<thead>
<tr>
<th>Tolerance</th>
<th>Acceptance</th>
<th>Feeling defeated</th>
<th>Putting up a fight</th>
<th>Reading a threshold</th>
<th>Unrelenting nature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Learning to tolerate and the adverse effects of this</td>
<td>Making peace</td>
<td>Beaten down/emotional impact</td>
<td>Catching early</td>
<td>Tolerance</td>
<td>Mentally draining</td>
</tr>
<tr>
<td>I think probably with me, I'm not very patient with myself. I'm quite patient with other people. But when it comes to me, I sort of - I mean, on the positive side, you lose weight with Crohn's. You lose weight, you get healthy. You know, I guess you just have to embrace it is what it is. And try and find a way to make it fit into your life.</td>
<td>&quot;I mean, on the positive side, you lose weight with Crohn's. You lose weight, you get healthy. You know, I guess you just have to embrace it is what it is. And try and find a way to make it fit into your life.&quot;</td>
<td>&quot;At one stage I was noting what I'd ate the day before, what kind of supplements I'd been taking. But yes, it is quite a lot of the end. And it was just for personal use really. And in the end, I just gave up.&quot;</td>
<td>&quot;Yes, I wonder if this tolerance is like when - at the beginning, when I first had it - that was too much, you know what I mean. Whereas, where I have smaller bouts now than what I used to. Sometimes, even if I get it twice in a week, a little, a little bout, I can tolerate it, you know what I mean?&quot;</td>
<td>&quot;Yes, I wonder if this tolerance is like when - at the beginning, when I first had it - that was too much, you know what I mean. Whereas, where I have smaller bouts now than what I used to. Sometimes, even if I get it twice in a week, a little, a little bout, I can tolerate it, you know what I mean?&quot;</td>
<td>&quot;The pain has a, has a massive, massive impact on the rest of your senses, you know. And it's because it's so unremitting, I think. And it's not even - there are times when it's not occurring and you are moving about and you're getting on with your day. But it is still there, you know, yes, it's just unremitting. (Interview 13)&quot;</td>
</tr>
<tr>
<td>And I think generally I'm probably at a three most of the time. I feel like I've kind of got this sort of rumbling</td>
<td>Yes, I just tend to get on with it, at the moment. I try to, you know, to just accept it.</td>
<td>&quot;...and I find, when I'm in pain, I feel helpless and my mood is low, I feel apathetic. I have quite strong anhedonia. I don't want to do anything. I have the hassle, not deriving any pleasure from doing what I usually would have made me happy with what I'm doing&quot;</td>
<td>&quot;&quot;You have to look at what you've been through and you look at the pain and you look at how it affects you psychologically. And how it affects your self-esteem and there's so many areas, you know, that you know, it's...&quot;</td>
<td>&quot;I just try to get on with it. And ignore it. I think I've got quite a high pain threshold, which probably helps.&quot;</td>
<td>&quot;So I do worry a bit about the impact of how my ability to work, because I feel like I'm always struggling to get over it and, not for it to go away. (1)&quot;</td>
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<td>And I think generally I'm probably at a three most of the time. I feel like I've kind of got this sort of rumbling</td>
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<td>&quot;...and I find, when I'm in pain, I feel helpless and my mood is low, I feel apathetic. I have quite strong anhedonia. I don't want to do anything. I have the hassle, not deriving any pleasure from doing what I usually would have made me happy with what I'm doing&quot;</td>
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C3) Interview reflections

Qualitative Interviews

Format

- Check participant has read the information sheet
- Give participant opportunity to ask any questions
- Ask participant to sign and date the consent form
- Check the participant is happy for the interview to be recorded, and state that they are free to withdraw at any time, or the interview can be stopped.
- Confirm their diagnosis of their IBD

Reflections on interviews

Interview 1 - 6/03/18
This interviewee had very extensive knowledge in Psychology (having previously completed a PhD in Psychology) and was about my age. This was an interesting first interview - I wanted to ensure that I was asking the questions with enough open and non-leading terms, but seeing as my interviewee had extensive knowledge and insight into pain and mental health, I felt like I wanted to explore everything and it was hard to stay on track. As the participant was my age, I was aware during the interview to not be too conversational and casual, but rather to stay as the role of the researcher; open, professional, active listener, etc.

I could tell I was nervous during this interview, as I wouldn’t allow enough of a pause between the interviewee’s responses, and sometimes would cut them off. I learnt that this was especially difficult when carrying out an interview over the phone, as it is harder to observe when the interviewee is still thinking or about to add to their previous point. I acknowledged that I needed to slow my pace down for subsequent interviews. As this participant was also describing all the types of pain management interventions they had previously tried, including counselling and CBT, I remember feeling despondent and worried that our intervention wouldn’t be able to help. However, the participant sent me a very positive email following the interview thanking me for our research efforts and to keep her posted.

Interview 2 – 07/03/18
During this interview, I was much better at allowing the participant to speak much more freely in this interview and wasn’t so interrupting. However, I observed during my interview, and from looking at the transcript, that the clarity in my question asking was still lacking. I sometimes overcomplicated my question, rather than just saying ‘does it impact you in any other areas of your life?’ I would waffle, including at one point saying, ‘sorry, let me start that again’. It’s important that I still remember to ask my questions slowly and clearly, to help ease the interviewee and make the conversation flow better.

I was also aware that, despite the topic guide, this participant participants frequently raised a topic that I had planned to ask later in the interview, and so I learnt through this interview how to be flexible and structured when asking and responding to questions to the answers. I was also good in this interview at referring back to things the participant had said earlier to explore another area of the conversation. This seemed a natural way of moving the conversation around, and I observed how helpful some note taking during the interview was to allow this to happen.

Interview 3 – 08/03/18
I remember this interview being particularly saddening. I was interviewing my participant face to face on this occasion and they were telling me how much their pain had disrupted their confidence to physically exercise, how they were struggling with depression and how they were in a dispute with their work for exacerbating their stress and not being understanding of their IBD. I felt on some occasions that I wanted to say something reassuring or positive to make my interviewee feel better. I was able to express empathy and validation, but also wanted to explore other areas in which the pain was having an impact.
### COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

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<tbody>
<tr>
<td><strong>Personal characteristics</strong></td>
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<tr>
<td>Interviewer/facilitator</td>
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<td>Which author/s conducted the interview or focus group?</td>
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<tr>
<td>Credentials</td>
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<td>What were the researcher’s credentials? E.g. PhD, MD</td>
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<tr>
<td>Occupation</td>
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<td>What was their occupation at the time of the study?</td>
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<tr>
<td>Gender</td>
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<td>Was the researcher male or female?</td>
<td>4</td>
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<tr>
<td>Experience and training</td>
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<td>What experience or training did the researcher have?</td>
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<td><strong>Relationship with participants</strong></td>
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<tr>
<td>Relationship established</td>
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<td>Was a relationship established prior to study commencement?</td>
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<tr>
<td>Participant knowledge of the interviewer</td>
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<td>What did the participants know about the researcher? e.g. personal goals, reasons for doing the research</td>
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<td>Interviewer characteristics</td>
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<td>What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic</td>
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<tr>
<td>Domain 2: Study design</td>
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<tr>
<td><strong>Theoretical framework</strong></td>
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<tr>
<td>Methodological orientation and Theory</td>
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<td>What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis</td>
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<tr>
<td><strong>Participant selection</strong></td>
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<tr>
<td>Sampling</td>
<td>10</td>
<td>How were participants selected? e.g. purposive, convenience, consecutive, snowball</td>
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<tr>
<td>Method of approach</td>
<td>11</td>
<td>How were participants approached? e.g. face-to-face, telephone, mail, email</td>
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<tr>
<td>Sample size</td>
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<td>How many participants were in the study?</td>
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<tr>
<td>Non-participation</td>
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<td>How many people refused to participate or dropped out? Reasons?</td>
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<td><strong>Setting</strong></td>
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<td>Setting of data collection</td>
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<td>Where was the data collected? e.g. home, clinic, workplace</td>
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<tr>
<td>Presence of nonparticipants</td>
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<td>Was anyone else present besides the participants and researchers?</td>
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<td>Domain 3: analysis and findings</td>
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<td><strong>Data analysis</strong></td>
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<td>How many data coders coded the data?</td>
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<td>Description of the coding tree</td>
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<td>Did authors provide a description of the coding tree?</td>
<td>No but thematic map presented pg. 30 &amp; Figure 1</td>
</tr>
<tr>
<td>Derivation of themes</td>
<td>26</td>
<td>Were themes identified in advance or derived from the data?</td>
<td>5</td>
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<tr>
<td>Software</td>
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<td>What software, if applicable, was used to manage the data?</td>
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<td>Participant checking</td>
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<td>Did participants provide feedback on the findings?</td>
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<td><strong>Reporting</strong></td>
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<tr>
<td>Quotations presented</td>
<td>29</td>
<td>Were participant quotations presented to illustrate the themes/findings?</td>
<td>6-19</td>
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<tr>
<td>Was each quotation identified? e.g. participant number</td>
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<tr>
<td>Data and findings consistent</td>
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<td>Was there consistency between the data presented and the findings?</td>
<td>6-10</td>
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<tr>
<td>Clarity of major themes</td>
<td>31</td>
<td>Were major themes clearly presented in the findings?</td>
<td>pg. 30 &amp; Figure 1</td>
</tr>
<tr>
<td>Clarity of minor themes</td>
<td>32</td>
<td>Is there a description of diverse cases or discussion of minor themes?</td>
<td>Sub-themes</td>
</tr>
</tbody>
</table>

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

*reasons for lack of inclusion stated in Response to reviewer’s comments document with supporting reference*
INVESTIGATING PAIN IN INFLAMMATORY BOWEL DISEASE
PARTICIPANT CONSENT FORM

CONSENT FORM – Interviews

Name of Researcher: Louise Sweeney

1. I confirm that I have read the information sheet dated 09.10.17, version 1.1 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from King’s College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I understand that the information collected about me will be used to support other ethically approved research in the future, and may be shared anonymously with other researchers.

5. I understand that interviews will be audio-recorded and transcribed for analysis.

6. I understand that any information that I provide will be presented anonymously.

7. I agree to take part in the above study.

__________________________  ______________________  ________________
Name of Participant          Date                        Signature

__________________________  ______________________  ________________
Name of Person taking consent  Date                        Signature
Appendix D Feasibility study

D1) Study documents
D.1.1 Participant information sheet

Managing Pain in IBD study
PARTICIPANT INFORMATION SHEET

Study name: Managing Pain in IBD Chief Investigator: Professor Christine Norton
Lead Researcher: Louise Sweeney

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Invitation to participate

We would like to invite you to participate in this research project organised by researchers at King’s College London and funded by Crohn’s and Colitis UK. The study will involve testing a self-management intervention for pain in IBD, which has been known to be helpful in managing pain associated with other long-term conditions.

To help you decide if you would like to participate, please read the information sheet below. If you have any questions or would like any further information about the study, please ask the lead researcher, Louise Sweeney (louise.sweeney@kcl.ac.uk or telephone: +44 (0) 20 7848 3625)

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What is the purpose of the study?

Pain is experienced by many people with IBD, but currently there are not clear reasons why people experience ongoing pain, even in periods of remission. Pain can have a significant impact on patient’s quality of life, and we know from our research that pain does not always relate to disease activity and other clinical results. There are interventions which have shown to be effective for people experiencing chronic pain, both in primary chronic pain conditions (low back pain, migraine) and pain associated with other longterm conditions such as multiple sclerosis and rheumatoid arthritis. A team of researchers at King’s College London, including academics and specialist nurses, is carrying out a research study to test an online self-management intervention for pain in IBD. This self-management intervention is based on cognitive behavioural therapy (CBT) principles, taking place over a 9-week period.

What would taking part involve?

1. If you fulfil pre-screening questions and eligibility criteria and agree to take part, you will be asked to sign a consent form which the researcher will send to you, to make sure you have read this information sheet, have any questions and would like to take part.

2. You will be asked to fill out a questionnaire prior to starting the intervention. This can be sent via email or post, depending on your preference. This questionnaire will include questions about your disease, medications, pain, quality of life, thoughts about pain and mood and will help us show whether these factors change during the course of the programme. The questionnaire will take about 20-30 minutes to complete. Your data will be archived safely and held for 10 years in accordance with sponsor requirements.

3. A stool sample kit will be posted to you, so that the study can collect a measure of your current inflammatory levels. You will be asked to provide a stool sample in your own time.
and post it directly to the laboratory for testing. The research team will be sent the results of your sample confidentially by the laboratory. The results can also be sent to you if you would like the research team to do so. You will also be reimbursed £5 when you receive your stool sample kit.

4. You will be sent a unique ID log in to access the online 9-week programme. You will be asked to log in each week to complete a session, which will take approximately 30-60 minutes to complete and include some tasks. You will have a 30-minute telephone/skype discussion with the intervention facilitator at Week 1, following your first session. You will then be able to contact the intervention facilitator through the website in a messaging format, if you have any questions or anything you would like to raise throughout the intervention.

5. You will be asked to complete a questionnaire after completing the intervention at Week 9 so that we can see if the programme has made a difference and what your views are about it. This can be sent via post or email depending on your preference. You will not need to provide a stool sample at this later stage.

6. You may be invited once the programme has finished for an interview. The researcher will ask you to talk about your experiences of the programme, to get a detailed understanding of the potential usefulness of the intervention. You do not have to decide about taking part in the interviews now. If you decide to take part in the self-management programme, we will ask you later if you are interested in also being interviewed. Even if you are interested in being interviewed, you may not be selected if more other people offer to take part than we need.

What does the programme involve?

After agreeing to take part and completing the informed consent form, you will be sent a questionnaire at baseline which will ask about your IBD, pain, mood and thoughts. After completing this you will receive a unique log in ID to gain access to the website to begin the online intervention. The intervention is based on cognitive behavioural therapy (CBT). CBT is an evidence based psychological treatment. It is a way of helping people solve problems and improve the way we think and feel by learning new methods of coping and problem solving.

It is based on 2 principles:

- Our thoughts and feelings are connected to our behaviours, moods and physical experiences and to the events in our lives.
- The perception of an event affects our emotional, behavioural and physiological responses to that event.

The intervention will take place over 9-weeks and will require you to complete weekly sessions online and some complete some tasks. Sessions in the intervention include Understanding Pain in IBD, Managing Stress and Emotions, Increasing Activity and Exercise and Social Support and Communication. After completing Session 1, you will have a telephone conversation with the intervention facilitator, where you will review the session and ask any questions. You will then be able to contact the intervention facilitator through the website in a messaging format, if you have any questions or anything you would like to raise throughout the intervention. You will have access to all your usual care. You can choose a time of day that suits you to speak with the intervention facilitator.

What is in the stool sample kit that I will receive in the post?

The stool sample pack will include:

1. A stool sample pot to place your sample in
2. An outer shell case to secure the pot in
3. A sample request form for you to complete the highlighted areas (date, time, study ID)
4. A pre-stamped pre-addressed medical envelope to place your sample and sample request form in.
5. £5 reimbursement for participating in the study and sending your stool sample
What will happen to the samples I give?

The stool sample you provide will be analysed by trained scientists at a hospital laboratory. Your results will be retrieved by the research team for the study and will be given to you should you request it. This information will be kept confidential and will be used to help the research team assess your current level of inflammation which will help inform the results of the study. The results can also be sent to you if you would like the research team to do so.

Do I have to take part?

No, you do not have to take part and you are under no obligation to do so. You can speak with the researcher if you would like more information before making your decision. Deciding not to take part will not have any impact on the care you receive at hospital.

What will happen if I agree to take part, and am selected for the interview following the programme?

One of the researchers (Louise Sweeney) will contact you via telephone or Skype, according to your preference, to interview you at a time and date which suits you. Louise draw on your experience in taking part in the study to guide your interview, including what you found helpful or difficult, what you would change, whether you feel your pain symptoms have or have not improved, and how you feel about the results.

Louise has completed other IBD studies. She will be empathetic and understanding and will encourage you to talk about your experiences in whichever way you feel most comfortable to do so. Before the interview begins, Louise will ask for your written consent, ensuring that you understand what you are being asked to do and that you agree to take part. The interview will be recorded on a digital audio device and typed up later.

What are the benefits of taking part?

The intervention will aim to help individuals adopt skills and techniques to manage their pain and IBD better. There is no guarantee that the intervention will eliminate participants pain completely. If the intervention works, this will inform a larger trial being conducted by researchers at King’s College London, looking at an online CBT self-management programme for pain, fatigue and urgency in IBD. If the intervention is not feasible or does not work, we will know what we need to do more research on to develop other ways of helping people with pain in IBD. If you have requested it, we will send you a summary report of the findings when the study is completed.

What are the possible disadvantages of taking part?

There may be a small risk of you becoming a little distressed when you complete the study questionnaires, working through the sessions, when you are talking to the facilitator about your pain or when you are being interviewed, because reflecting on your thoughts and emotions related to your IBD and pain could be upsetting. You may withdraw from the study at any time if you change your mind about taking part.

The study team is very experienced in the field of IBD and familiar with many of the issues you may be concerned about. All team members are experienced in offering reassurance to, and caring for, people in clinical settings and during research projects, and will support you at all stages of the study. You can get further support from the Crohn’s & Colitis UK (CCUK) Helpline (Supportive Listening Service), which is available Mon-Fri, 1pm – 3.30pm, and 6.30pm – 9pm, except Bank Holidays in England. (0845 1303344 or 0121 7379931). For mental health support, others sources include the charity Mind Phone: 0300 123 3393 (Mon-Fri, 9am-6pm) Website: www.mind.org.uk or Samaritans Phone: 116 123 (free 24-hour helpline) Website: www.samaritans.org.uk. Alternative options to seek help for your physical and mental health include contacting your local IBD service at your local hospital, contacting your GP or calling the NHS nonemergency number on 111 (24 hours a day) www.nhs.uk.

What about confidentiality and anonymity?

Participation in the study will be kept strictly confidential. All participants will be assigned a participant number, and all personal information and data will be referred to by your participant number rather than your name. Responses to questionnaires will only be accessible to the research team. All consent/assent forms, questionnaires and interview recordings/transcripts will be stored securely and confidentially in a locked filing cabinet in the research office in King’s College London. We may use
quotes from interviews however no identifiable personal information will be presented. Personal data will be stored for up to five years following recruitment for follow-up research purposes.

What will happen if I want to withdraw from this study?
You are free to withdraw yourself from the study at any time without giving a reason. You will have up to one week after being recruited into the study to request withdrawal of identifiable information. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

What will you do with the results of the study?
Participants’ data will be analysed and written up with the intention of submission for publication in a scientific journal. The study will also be written up as part of the lead researcher’s PhD thesis in Health Studies Research. The results will also inform a large study looking at the management of pain, fatigue and urgency in IBD. A summary of the results will also be made available to read from the Crohn’s and Colitis UK (CCUK) website [https://www.crohnsandcolitis.org.uk/](https://www.crohnsandcolitis.org.uk/) or participants are invited to contact the lead researcher directly to receive the results of the study.

Who is organising and funding the study?
The research is organised by King’s College London and is being carried out by a PhD student, Louise Sweeney, who is researching pain in IBD. The study has been reviewed by KCL PNM Research Ethics Subcommittee. The project is being funded by a PhD Studentship awarded by Crohn’s and Colitis UK, and is being supervised by Professor Christine Norton, Professor Rona Moss-Morris and Dr Wladzia Czuber-Dochan.

---

What do I need to do to take part?

1. Read the participant information sheet
2. Sign the consent form
3. Receive a stool sample kit in the post
4. Complete your pre-intervention questionnaire
5. Start the 9 Week programme
6. Complete the Week 9 questionnaire
7. Post your sample to the laboratory in the pre-stamped envelope
8. You will have telephone/skype/contact with the facilitator at Week 1 following your first session

Further information and contact details:
If the study has harmed you in any way or you have any questions about the study, please contact either the PhD Researcher on the team or the Chief Investigator:

**PhD Researcher**  
Louise Sweeney  
Rm 1.32 James Clerk Maxwell Building  
57 Waterloo Road London SE1 8WA  
Tel: +44 (0) 20 7848 3625  
Email: louise.sweeney@kcl.ac.uk

**Chief Investigator**  
Professor Christine Norton  
Professor of Nursing  
Rm 2.25 James Clerk Maxwell Building  
57 Waterloo Road London SE1 8WA  
Tel: +44 (0) 20 7848 3864  
Email: christine.norton@kcl.ac.uk
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. New (over the last 2 weeks) severe pain in your stomach (upper abdomen) which may or may not be much worse after eating?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes:</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1a: Has this been present for 3 months or more?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1b: Have you spoken to a doctor or nurse about this pain?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1c: Have you had any investigations for this pain?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1d: Has any cause been diagnosed for this pain? If so, what?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Regular or persistent vomiting over the past 2 weeks</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3. Unintentional rapid weight loss of 5kg (10 pounds) or more (over 2-3 months) without trying to lose weight</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. New (over the past 2 weeks) inability to eat anything except a very soft diet because solid food causes pain</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. Sudden new onset of constipation plus inability to pass gas (flatus) and a very distended abdomen over the past 2 weeks</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If yes:</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5a: Has this been present for 3 months or more?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5b: Have you spoken to a doctor or nurse about this pain?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5c: Have you had any investigations for this pain?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5d: Has any cause been diagnosed for this constipation? If so, what?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. New (over the past 2 weeks) symptoms of passing dark black (treacle-like) stools which has NOT been investigated</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7. Fevers (high temperature, except for an obvious reason, such as the ‘flu’) over the past 2 weeks which has NOT been investigated</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>8. New rectal bleeding (more than a few drops) over the past 2 weeks which has NOT been investigated</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Pain Questionnaire

Please mark a X in the box of the number that describes how, during the past 24 hours, pain has interfered with your:

<table>
<thead>
<tr>
<th>Does not interfere</th>
<th>Completely interferes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

General activity

Mood

Walking ability

Normal work (includes both work outside the home and housework)

Relations with other people

Sleep

Enjoyment of life
D.1.3. Participant eligibility screening form

Patient Eligibility Screening Form – Managing Pain in IBD study

FOR RESEARCHER TO COMPLETE

REMAS: XXXXXX

Participant study no.: ...........................................

Date: ..........................................

**Inclusion criteria** (please tick the boxes) for potentially eligible participant:

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have they received a definitive diagnosis of Crohn’s disease or ulcerative colitis from a medical professional/gastroenterologist</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Have they been diagnosed for at least 6 months?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are they aged 16 or over?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Do they have a sufficient command of spoken and written English to understand the study documentation and procedures</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Have they suffered from chronic or intermittent pain for at least 3 months or more?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Do they score of mean pain interference at ≥4 (Brief Pain Inventory) (Cleeland &amp; Ryan, 1994) (pre-screening eligibility questionnaire)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

If ALL the answers to the inclusion criteria are YES please screen against the exclusion criteria below.

**Exclusion criteria** (please tick the boxes)

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are they unable to provide informed consent (e.g. due to reduced mental capacity)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are they currently recruited into a clinical trial/pharmacological intervention?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Have they undergone a course of Cognitive Behavioural Therapy for pain within the previous 6 months?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are they currently receiving formal psychotherapy or active psychological treatment?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Do they have indications of severe disease/disease-related complication (sub-acute obstruction) indicated by ‘red flags’ (pre-screening eligibility questionnaire)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

If ALL the answers to the exclusion criteria are NO please now consider this participant for the research project to Managing Pain in IBD study.
PARTICIPANT CONSENT FORM

CONSENT FORM – INTERVENTION

REMAS Number: HR-18/19-8806

Name of Researcher: Louise Sweeney. Please initial box.

1. I confirm that I have read the information sheet dated 22.01.19, version V1.2 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that I will be asked to complete a questionnaire before starting the intervention and following the intervention and I agree to do this.

3. I understand that I may be approached for an interview about my experience in the study.

4. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

5. I understand that data collected during the study may be looked at by individuals from King’s College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.

6. I understand that the information collected about me will be used to support other ethically approved research in the future and may be shared anonymously with other researchers.

7. I understand that any information that I provide will be presented anonymously.

8. I consent to the research team accessing the results of my stool sample.
9. I agree to take part in the above study.

<table>
<thead>
<tr>
<th>Name of Participant</th>
<th>Date</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Person taking consent</th>
<th>Date</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CONTACT DETAILS

EMAIL: ____________________________

ADDRESS: ____________________________

POSTCODE: ____________________________

TELEPHONE NUMBER: ____________________________

RESULTS OF FAECAL CALPROTECTIN TO BE SENT TO THIS PARTICIPANT?

Yes ☐

No ☐
Managing Pain in IBD study

Pre-Intervention Questionnaire

A team of researchers at King’ College London is investigating pain in inflammatory bowel disease (IBD). We would like to invite you to read and complete the following questionnaire booklet. Some questions will ask about your overall well-being and functioning and others will specifically ask about any pain you may be experiencing. Some of the questions may seem repetitive, but they have been selected from standard questionnaires and we would be thankful if you could complete the relevant sections.

If you have any questions, do not hesitate to get in contact with the research team. On behalf of King’s College London, thank you for taking part in this research.

Lead researcher: Louise Sweeney (email: louise.sweeney@kcl.ac.uk)
Study conducted by: King’s College London
Study Funded by: Crohn’s & Colitis UK
Demographic and Clinical Data Questionnaire

Please tick the appropriate boxes relevant to you.

<table>
<thead>
<tr>
<th>16. Gender</th>
<th>□ Female □ Male</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>17. Age (at last birthday) in years:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>18. Confirmed diagnosis of IBD</th>
<th>□ Crohn’s Disease □ Ulcerative Colitis</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>19. Year of IBD diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>..........................................................</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>20. Choose one option that best describes your ethnic group or background</th>
</tr>
</thead>
</table>

**White**
- □ English/Welsh/Scottish/Northern Irish/British
- □ Irish
- □ Gypsy or Irish Traveller
- □ Any other white background, please describe:
  ..........................................................................................

**Mixed/Multiple ethnic groups**
- □ White and Black Caribbean
- □ White and Black African
- □ White and Asian
- □ Any other Mixed/Multiple ethnic background, please describe:
  ..........................................................................................

**Asian/Asian British**
- □ Indian
- □ Pakistani
- □ Bangladeshi
- □ Chinese
- □ Any other Asian background, please describe
  ..........................................................................................

**Black/African/Caribbean/Black British**
- □ African
- □ Caribbean
- □ Any other Black/African/Caribbean background, please describe
  ..........................................................................................

**Other ethnic group**
21. Education level

- No formal qualifications
- Vocational qualifications (e.g. NVQ)
- School level qualifications (e.g. GCSE, O Level, CSE)
- Advanced School level qualifications (e.g. A Level, Scottish Highers)
- University degree (e.g. BSc, BA)
- Postgraduate degree (e.g. MSc, PhD)

22. Relationship status

- Married /Civil partnership
- Living with a partner
- Widowed
- Divorced/Separated
- Single

23. Current employment status

- Employed full-time
- Employed part-time
- Full or part-time education
- Full-time domestic responsibilities
- Retired
- Unemployed

24. Smoking history

- Current smoker  Cigarettes/day:_______________
- Previous smoker
- Non-smoker

25. Previous surgery for IBD (either Crohn's disease or ulcerative colitis)

- Yes
- No

If Yes, Number of surgeries  ________________

<table>
<thead>
<tr>
<th>Date of surgery</th>
<th>Location/type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Question</td>
<td>Options</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Current stoma</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>Current ileo-anal pouch</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>26. Number of IBD flares (active disease) in the last 2 years</td>
<td>□ 0 □ 1 □ 2 □ 3 □ 4 □ 5+ □ Ongoing disease activity without remission over the last 2 years</td>
</tr>
<tr>
<td>27. Last IBD flare (MM/YY)</td>
<td></td>
</tr>
<tr>
<td>28. Severity of symptoms during last period of active disease</td>
<td>□ Not applicable □ Mild □ Moderate □ Severe</td>
</tr>
<tr>
<td>29. Currently on antidepressants</td>
<td>□ Yes □ No □ If Yes, which one(s): □</td>
</tr>
<tr>
<td>30. Current medications for IBD (please tick):</td>
<td>Dose □ How often?</td>
</tr>
<tr>
<td>□ Sulfasalazine</td>
<td></td>
</tr>
<tr>
<td>□ Other 5-ASA (Pentasa, Octasa, Asacol, Mesalazine, Mezavant, Salofalk)</td>
<td></td>
</tr>
<tr>
<td>□ Azathioprine</td>
<td></td>
</tr>
<tr>
<td>□ Mercaptopurine</td>
<td></td>
</tr>
<tr>
<td>□ Infliximab (Remicade, Remsima, Flixabi)</td>
<td></td>
</tr>
<tr>
<td>□ Adalimumab (Humira)</td>
<td></td>
</tr>
<tr>
<td>□ Vedolizumab (Entyvio)</td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Quantity</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Golimumab (Simponi)</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td></td>
</tr>
<tr>
<td>Allopurinol</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
</tr>
<tr>
<td>Budesonide</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
QUESTIONS ABOUT YOUR PAIN

19. Using the body diagram, please tick the boxes where you feel pain, if any (please tick more than one if applicable):

45. Face
46. Neck
47. Shoulder/chest R
48. Shoulder/chest L
49. Upper arm/elbow R
50. Upper arm/elbow L
51. Lower arm/wrist R
52. Lower arm/wrist L
53. Palm of hand R
54. Palm of hand L
55. Chest/bottom of rib cage R
56. Chest/bottom of rib cage L
57. Side of abdomen R
58. Side of abdomen L
59. Pelvis/bladder
60. Thigh/knee R
61. Thigh/knee L
62. Calf (front) R
63. Calf (front) L
64. Top of foot R
65. Top of foot L
66. Head (back)
67. Neck (back)
68. Upper shoulder/spine L
69. Upper shoulder/spine R
70. Upper arm/elbow (back) L
71. Upper arm/elbow (back) R
72. Lower arm/wrist (back) L
73. Lower arm/wrist (back) R
74. Top of hand/fingers L
75. Top of hand/fingers R
76. Upper back/scapula region L
77. Upper back/scapula region R
78. Lower back L
79. Lower back R
80. Pelvis/buttocks L
81. Pelvis/buttocks R
82. Thigh/knee (back) L
83. Thigh/knee (back) R
84. Calf (back) L
85. Calf (back) R
86. Bottom of foot L
87. Bottom of foot R

Please turn over.
20. Please rate your pain by marking a tick in the box that best describes your pain at its **WORST** in the last 24 hours.

<table>
<thead>
<tr>
<th>No pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pain as bad as

21. Please rate your pain by marking the box that best describes your pain at its **LEAST** in the last 24 hours.

<table>
<thead>
<tr>
<th>No pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

Pain as bad as

22. Please rate your pain by marking the box that best describes your pain on **AVERAGE**.

<table>
<thead>
<tr>
<th>No pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pain as bad as

23. Please rate your pain by marking the box that describes how much pain you have **RIGHT NOW**.

<table>
<thead>
<tr>
<th>No pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
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<td></td>
</tr>
</tbody>
</table>

Pain as bad as

24. Please list any medications you are taking to control your pain (if applicable):

<table>
<thead>
<tr>
<th>Pain medications</th>
<th>Dose</th>
<th>How many times per day?</th>
<th>How long have you been taking this medication?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

25. In the last 24 hours, how much relief have pain treatments or medications provided? Please mark the box below the percentage that most shows how much **relief** you have received.

<table>
<thead>
<tr>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
26. Please mark a ☑️ in the box of the number that describes how, during the past 24 hours, pain has interfered with your:

<table>
<thead>
<tr>
<th></th>
<th>Does not interfere</th>
<th>Completely interferes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
<tr>
<td>General activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking ability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal work (includes both work outside the home and housework)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relations with other people</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enjoyment of life</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
QUALITY OF LIFE QUESTIONNAIRE

The following questions ask about your bowel problem and how it affected your life over the last two weeks. Please tick one answer for each of the questions. If you are unsure about how to answer any questions, just give the best answer you can. Do not spend too much time answering, as your first thoughts are likely to be the most accurate.

1. On how many days over the last two weeks have you had loose or runny bowel movements?
   - None
   - On one or two days only
   - On three to seven days
   - On eight to fourteen days (ie more than every other day)

2. On how many days over the last two weeks have you felt tired?
   - None
   - On one or two days only
   - On three to seven days
   - On eight to fourteen days (ie more than every other day)

3. On how many days over the last two weeks have you felt frustrated?
   - No, not at all
   - Yes, some of the time
   - Yes, most of the time
   - Yes, all of the time

4. In the last two weeks, has your bowel condition prevented you from carrying out your work or other normal activities?
   - No, not at all
   - Yes, for one or two days
   - Yes, for three to seven days
   - Yes, for eight to fourteen (ie more than every other day)

5. On how many days over the last two weeks have you opened your bowels more than three time a day?
   - No, not at all
   - Yes, on one or two days
   - Yes, on three to seven days
Yes, on eight to fourteen (ie more than every other day)

6. **On how many days over the last two weeks have you felt full of energy?**

- No, not at all
- Yes, on one or two days
- Yes, on three to seven days
- Yes, on eight to fourteen (ie more than every other day)

7. **In the last two weeks have you been worried about being admitted to hospital because of your bowel problem?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

8. **In the last two weeks did your bowel condition prevent you from going out socially?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time
- Does not apply to me

9. **On how many days over the last two weeks have your bowels opened accidentally?**

- None
- On one or two days only
- On three to seven days
- On eight to fourteen (ie more than every other day)

10. **On how many days over the last two weeks have you felt generally unwell?**

- None
- On one or two days only
- On three to seven days
- On eight to fourteen (ie more than every other day)

11. **In the last two weeks have you felt the need to keep close to a toilet?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time
12. In the last two weeks, has your bowel condition affected your leisure or sports activities?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time
- Does not apply to me

13. On how many days over the last two weeks have you felt pain in your abdomen?

- None
- On one or two days only
- On three to seven days
- On eight to fourteen days (ie more than every other day)

14. On how many nights over the last two weeks have you been unable to sleep well (days if you are a shift worker)?

- None
- On one or two nights only
- On three to seven nights
- On eight to fourteen nights (ie more than every other night)

15. In the last two weeks have you felt depressed?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

16. In the last two weeks have you had to avoid attending events where there was no toilet close at hand?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

17. On how many days over the last two weeks, have you had a problem with large amounts of wind?

- None
- On one or two days only
on three to seven days
on eight to fourteen days (ie more than every other day)

18. On how many days over the last two weeks have you felt off your food?

none
on one or two days only
on three to seven days
on eight to fourteen days (ie more than every other day)

19. Many patients with bowel problems have worries about their illness. How often during the last two weeks have you felt worried?

No, not at all
Yes, some of the time
Yes, most of the time
Yes all of the time

20. On how many days over the last two weeks has your abdomen felt bloated?

none
on one or two days only
on three to seven days
on eight to fourteen days (ie more than every other day)

21. In the last two weeks have you felt relaxed?

No, not at all
Yes, some of the time
Yes, most of the time
Yes, all of the time

22. On how many days over the last two weeks have you noticed blood with your bowel movements?

none
on one or two days only
on three to seven days
on eight to fourteen days (ie more than every other day)

23. In the last two weeks have you been embarrassed by your bowel problem?

No, not at all
Yes, some of the time
Yes, most of the time
Yes, all of the time
24. On how many days over the last two weeks have you wanted to go back to the toilet immediately after you thought you had emptied your bowels?

- none
- on one or two days only
- on three to seven days
- on eight to fourteen days (ie more than every other day)

25. In the last two weeks have you felt upset?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

26. On how many days over the last two weeks have you had to rush to the toilet?

- none
- on one or two days only
- on three to seven days
- on eight to fourteen days (ie more than every other day)

27. In the last two weeks have you felt angry as a result of your bowel problem?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

28. In the last two weeks, has your sex life been affected by your bowel problem?

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time
- Does not apply to me

29. On how many days over the last two weeks have you felt sick?

- none
- on one or two days only
- on three to seven days
- on eight to fourteen days (ie more than every other day)
30. **In the last two weeks have you felt irritable?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

31. **In the last two weeks have you felt lack of sympathy from others?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

32. **In the last two weeks have you felt happy?**

- No, not at all
- Yes, some of the time
- Yes, most of the time
- Yes, all of the time

*Please turn over.*
GENERAL FUNCTIONING AND PAIN

Please answer the following questions in the context of when you experience pain.

Please rate how confident you are that you can do the following things, at present, despite the pain. To indicate your answer, please circle one of the numbers on the scale under each item, where 0 = not confident at all and 6 = completely confident.

11. I can still enjoy things, despite the pain.

0 1 2 3 4 5 6
Not at all Completely
certain

12. I can do most of the household chores (e.g. tidying-up, washing dishes etc), despite the pain.

0 1 2 3 4 5 6
Not at all Completely
certain

13. I can socialise with my friends or family members as often as I used to do, despite the pain.

0 1 2 3 4 5 6
Not at all Completely
certain

14. I can cope with my pain in most situations.

0 1 2 3 4 5 6
Not at all Completely
certain

15. I can do some form of work, despite the pain. (“work” includes housework, paid and unpaid work).

0 1 2 3 4 5 6
Not at all Completely
certain

16. I can still do many of the things I enjoy doing, such as hobbies or leisure activity, despite pain.

0 1 2 3 4 5 6
Not at all Completely
certain
17. I can cope with my pain without medications.

0 1 2 3 4 5 6

Not at all Completely
confident confident

18. I can still accomplish most of my goals in life, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident

19. I can live a normal lifestyle, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident

20. I can gradually become more active, despite the pain.

0 1 2 3 4 5 6

Not at all Completely
confident confident
THOUGHTS AND FEELINGS ABOUT YOUR PAIN

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are statements describing different thoughts and feelings that may be associated with pain. Please tick the appropriate box which best describes the thoughts and feelings you have when you experience pain.

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>To a slight degree</th>
<th>To a moderate degree</th>
<th>To a great degree</th>
<th>All the time</th>
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</thead>
<tbody>
<tr>
<td>1. I worry all the time about whether the pain will end</td>
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<td>2. I feel like I can’t go on</td>
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<td>3. It’s terrible and I think it’s never going to get any better</td>
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<td>4. It’s awful and I feel that it overwhelms me</td>
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<td>5. I feel I can’t stand it anymore</td>
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<td>6. I become afraid that the pain will get worse</td>
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<td>7. I keep thinking of other painful events</td>
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<td>8. I anxiously want the pain to go away</td>
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<td>9. I can’t seem to keep it out of my mind</td>
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<td>10. I keep thinking about how much it hurts</td>
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<tr>
<td>11. I keep thinking about how badly I want the pain to stop</td>
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<td>12. There’s nothing I can do to reduce the intensity of the pain</td>
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<td>13. I wonder whether something serious may happen</td>
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</table>
THOUGHTS AND BEHAVIOURS IN RESPONSE TO YOUR PAIN

Please indicate how much you agree or disagree with the following statements about when you experience pain by ticking the appropriate box.

<table>
<thead>
<tr>
<th>Views about your pain</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neither agree nor disagree</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I am afraid that I will make my pain worse if I exercise</td>
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<td>2. My pain would be relieved if I were to exercise</td>
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<td>3. Avoiding unnecessary activities is the safest thing I can do to prevent my pain from worsening</td>
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<td>4. Physical activity makes my pain worse</td>
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<td>5. Doing less helps my pain</td>
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<td>6. I should avoid exercise when I have pain</td>
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<tr>
<td>Managing your pain</td>
<td>Never</td>
<td>Sometimes</td>
<td>Quite often</td>
<td>Very often</td>
<td>All the time</td>
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<tr>
<td>7. I stay in bed to control my pain</td>
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<tr>
<td>8. When I experience pain, I rest</td>
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<tr>
<td>9. I tend to avoid activities which make my pain worse</td>
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<tr>
<td>10. I tend to nap during the day to control my pain</td>
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<tr>
<td>11. I tend to overdo things when I’m energetic</td>
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<tr>
<td>12. I find myself rushing to get things done before I crash</td>
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<tr>
<td>13. I tend to overdo things and then rest up for a while</td>
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<tr>
<td>14. I tend to do a lot on a good day and rest on a bad day</td>
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<tr>
<td>15. I sleep when I’m tired in order to control my pain</td>
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<td>16. I avoid making social arrangements in case I’m not up to it</td>
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<tr>
<td>17. I avoid exerting myself in order to control my pain</td>
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<td>18. I’m a bit all or nothing when it comes to doing things</td>
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<tr>
<td>19. I avoid stressful situations</td>
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</tbody>
</table>
GENERAL MOOD AND FUNCTIONING

Over the past 2 weeks, how often have you been bothered by the following problems? Please use a ☐ to indicate your answer.

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
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<tr>
<td>2. Feeling down, depressed, or hopeless</td>
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<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
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<tr>
<td>4. Feeling tired or having little energy</td>
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<tr>
<td>5. Poor appetite or overeating</td>
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<tr>
<td>6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down</td>
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<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
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<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual</td>
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<tr>
<td>9. Thoughts that you would be better off dead or hurting yourself in someway</td>
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</tbody>
</table>

10. If you ticked off any problems, how difficult have these problems made it for you to do your work, take of things at home, or get along with other people?

Please turn over.
Below are statements that describe how some people respond to symptoms or discomfort in their belly or lower abdomen. These may include pain, diarrhoea, constipation, bloating or sense of urgency.

Please answer ‘how strongly you agree or disagree’ with each of these statements, AS THEY RELATE TO YOU. Answer all the statements as honestly and thoughtfully as you can.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Agree</th>
<th>Moderately Agree</th>
<th>Mildly Agree</th>
<th>Moderately Disagree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>I worry that whenever I eat during the day, bloating and distension in my belly will get worse</td>
<td></td>
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<tr>
<td>12.</td>
<td>I get anxious when I go to a new restaurant</td>
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<tr>
<td>13.</td>
<td>I often worry about problems in my belly</td>
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<tr>
<td>14.</td>
<td>I have a difficult time enjoying myself because I cannot get my mind off of discomfort in my belly</td>
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<tr>
<td>15.</td>
<td>I often fear that I won’t be able to have a normal bowel movement</td>
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<tr>
<td>16.</td>
<td>Because of fear of developing abdominal discomfort, I seldom try new foods</td>
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<td>17.</td>
<td>No matter what I eat, I will probably feel uncomfortable</td>
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<td>18.</td>
<td>As soon as I feel abdominal discomfort I begin to worry and feel anxious</td>
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<tr>
<td></td>
<td>Strongly Agree</td>
<td>Moderately Agree</td>
<td>Mildly Agree</td>
<td>Moderately Disagree</td>
<td>Strongly Agree</td>
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<tr>
<td>19. When I enter a place I haven’t been before, one of the first things I do is look for a bathroom</td>
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<tr>
<td>20. I am constantly aware of the feelings I have in my belly</td>
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<tr>
<td>21. I often feel discomfort in my belly could be a sign of serious illness</td>
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<tr>
<td>22. As soon as I awake, I worry that I will have discomfort in my belly during the day</td>
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<tr>
<td>23. When I feel discomfort in my belly, it frightens me</td>
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<tr>
<td>24. In stressful situations, my belly bothers me a lot</td>
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<tr>
<td>25. I constantly think about what is happening inside my belly</td>
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</tbody>
</table>
For each item, please mark an “x” in the box below that best indicates how much you agree with the following statements as they apply to you over the last month. If a particular situation has not occurred recently, answer according to how you think you would have felt.

<table>
<thead>
<tr>
<th></th>
<th>Not true at all</th>
<th>Rarely true</th>
<th>Sometimes true</th>
<th>Often true</th>
<th>True nearly all the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>15. I am able to adapt when changes occur</td>
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<tr>
<td>16. I can deal with whatever comes my way</td>
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<tr>
<td>17. I try to see the humorous side of things when I am faced with problems</td>
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<tr>
<td>18. Having to cope with stress can make me stronger</td>
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<tr>
<td>19. I tend to bounce back after illness, injury, or other hardships.</td>
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<tr>
<td>20. I believe I can achieve my goals, even when there are obstacles</td>
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<td>22. I am not easily discouraged by failure</td>
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<td>23. I think of myself as a strong person when dealing with life’s challenges and difficulties</td>
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<tr>
<td>24. I am able to handle unpleasant or painful feelings like sadness, fear and anger.</td>
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</table>
Thank you for completing this questionnaire.

Please post it in the enclosed envelope to: Louise Sweeney, Room 1.32, James Clerk Maxwell Building, 57 Waterloo Road, London, SE1 8WA
D.1.6 Post-Intervention Questionnaire (same as pre-intervention questionnaire minus demographic items plus additional below items)

**Intervention Follow-Up Questionnaire**

Based on your experience of completing the intervention, please complete the following questions. Please respond to the questions as honestly as possible. Your answers will help us to interpret the results of the intervention and develop more effective interventions for the future.

1. **How many of the sessions did you complete?**
   - 9 sessions
   - 5-7 sessions
   - 3-5 sessions
   - 0 sessions

2. **How many contacts (telephone/skype/email) did you have with the facilitator?**
   - More than 4 contacts
   - 3 contacts
   - 1-3 contacts
   - 0 contact

3. **By what mode did you contact the facilitator?**
   - Telephone
   - Email
   - Skype

4. **Would you have preferred to have the sessions face to face (coming to the hospital for the sessions) instead of via telephone/Skype/email? Please tick one answer only**
   - Yes
   - No
5. Did you complete the Homework Sheets at the end of each session in the manual? Please tick one answer only

Yes [ ]

No [ ]

6. How much time per week did you spend completing the intervention (including: reading through the manual, talking to the therapist, completing tasks and homework sheets?) Please tick one answer only

More than 90 minutes [ ]

60-90 minutes [ ]

30-59 minutes [ ]

Less than 30 minutes [ ]

7. Do you intend to continue using some of the techniques you have used in the intervention? Please circle a number which best corresponds to your views

0 1 2 3 4 5 6 7 8 9 10

Definitely will

8. Overall were you satisfied with the intervention? Please circle a number which best corresponds to your views

0 1 2 3 4 5 6 7 8 9 10

Not satisfied

9. Do you have any other comments? Please write in the space provided below.

..........................................................................................................................................................

..........................................................................................................................................................
# ACCEPTIBILITY OF THE INTERVENTION

How positive do you feel about the intervention?

0  1  2  3  4  5  6  7  8  9  10

**Not positive**

How much of an effort was the intervention?

0  1  2  3  4  5  6  7  8  9  10

**No effort**

To what extent did you perceive the intervention to be effective?

0  1  2  3  4  5  6  7  8  9  10

**Not effective**

To what extent did you find the intervention a helpful approach for managing your pain?

0  1  2  3  4  5  6  7  8  9  10

**Not at all**

To what extent did you understand the workings of the intervention?

0  1  2  3  4  5  6  7  8  9  10

**Not at all**

How confident did you feel to participate in the sessions and tasks in the intervention?

0  1  2  3  4  5  6  7  8  9  10

**Not at all**

To what extent was the intervention costly for you? (i.e. time given up doing other things)

0  1  2  3  4  5  6  7  8  9  10

**Not at all**

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CONSENT FORM – INTERVIEWS

Name of Researcher: Louise Sweeney. Please initial box

1. I confirm that I have read the information sheet dated 26.11.18, version 1.0 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I agree to my interview being audio-recorded, and understand that this recording will be transcribed by a third party (professional) transcriber if needed.

3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

4. I understand that data collected during the study, may be looked at by individuals from King’s College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.

5. I understand that the information collected about me will be used to support other ethically approved research in the future and may be shared anonymously with other researchers.

6. I understand that any information that I provide will be presented anonymously.

7. I understand that even if I withdraw from the above study or lose mental capacity to continue taking part and am withdrawn by the study team, the data collected from me up until that time will be used in analysing the results, unless I specify not to do so. I understand that I will not be able to withdraw data from the study after the analysis of the data.

8. I agree to take part in the interview phase of the study.

Please continue onto the next page to complete this document.
Name of Participant __________________________  Date __________________________  Signature __________________________

Name of Person taking consent __________________________  Date __________________________  Signature __________________________
## NESTED INTERVIEWS TOPIC GUIDE

**Study title:** Managing Pain in IBD study  
**REMAS number:**

<table>
<thead>
<tr>
<th>Questions</th>
<th>Prompts</th>
</tr>
</thead>
</table>
| Tell me about your IBD                                                  | What type of IBD do you have?  
How long have you had IBD for?  
What are the main symptoms of your IBD?  
Which medications are you taking for your IBD?                         |
| Tell me about your experience of the intervention                       | How has the intervention been for you?  
Can you tell me more about that?  
Can you tell me what you liked about the intervention?  
Can you tell me what you didn’t like about the intervention?          |
| Tell me about your experiences of and views on the sessions and homework tasks | Tell me about your experiences of carrying out the activities in the sessions  
Tell me about your experiences of carrying out the homework tasks?     |
| Tell me about your experiences of and views on the support from the facilitator | What did you find helpful from your discussions with the facilitator?  
What would you have liked to gain more of from your discussions with the facilitator? |
| How useful was the intervention for you?                                | Which parts of the intervention were most helpful and why?  
Which parts of the intervention were least helpful and how can these be improved? |
| How do you think the intervention could be improved?                    | How do you think the format could be changed (changes in number of sessions, modality of delivery, manual format, language)?  
How could the delivery of the intervention be improved?  
What information was missing from the manual?  
What additional information could be included?  
Are there any parts of the intervention that you would like to continue using?  
Do you have ideas of other ways in which pain in IBD could be managed that were not included in this intervention? |
| Final comments                                                           | Is there anything else you would like to add or talk about? |
D.2) Ethics approval (REMAS)

D.2.1 Ethics approval

Miss Louise Sweeney
22 January 2019

Dear Louise

Reference Number: HR-18/19-8806

Study Title: Managing Pain in IBD study

Review Outcome: Approved pending amendments/clarifications

Thank you for submitting amendments to your application. However, there is an issue to be resolved before full approval is granted. This is specified below:

1. Section C9 and Information Sheet: The Committee is of the view that participants should be allowed a period of time to request the removal of identifiable data. This need only be for a period of a week or two. The Information Sheet should clarify that it will not be possible to remove data that is not identifiable.

In order to amend the application, you will simply need to log on onto REMAS and modify the existing application. Once again, your academic supervisor will be required to provide verification. The amended application will be reviewed by Chair’s action rather than by the full Committee.

The submission of your amended application must be accompanied by a cover letter outlining the changes you have made in response to each of the Committee’s requests. For ease of completion we recommend that you cut and paste the feedback table from your outcome letter into your cover letter and respond to each point individually. The cover letter should be attached as a Supporting Document in section I9 of your application. Failure to attach a cover letter to your resubmitted application will result in your application being marked as ‘Invalid’ and returned to you by the Research Ethics Office prior to review.

If for some reason you choose not to proceed with this research ethics application, please inform the Research Ethics Office.

Please note that research involving human participants must not commence until full ethical approval has been granted.

Yours sincerely,

Mr James Patterson
Senior Research Ethics Officer

For and on behalf of

Chair
PNM Research Ethics Subcommittee

Cc: Professor Christine Norton
D.2.2 Approval of minor amendment

Miss Louise Sweeney
18 December 2018

Dear Louise,

Reference Number: HR-18/19-8806

Study Title: Managing Pain in IBD study

Review Outcome: Approved pending amendments/clarifications

Thank you for submitting the above application for ethical approval. Your application has been reviewed and has been approved pending amendments. You are now required to address a number of issues before full approval is granted. These are specified in the feedback table below. Please respond to each point raised by the Committee and amend your application form, and appendices, accordingly.

In order to amend the application, you will simply need to log on onto REMAS and modify the existing application. Once again, your academic supervisor will be required to provide verification. The amended application will be reviewed by Chair’s action rather than by the full Committee.

The submission of your amended application must be accompanied by a cover letter outlining the changes you have made in response to each of the Committee’s requests. For ease of completion we recommend that you cut and paste the feedback table from your outcome letter into your cover letter and respond to each point individually. The cover letter should be attached as a Supporting Document in section I9 of your application. Failure to attach a cover letter to your resubmitted application will result in your application being marked as ‘Invalid’ and returned to you by the Research Ethics Office prior to review.

If for some reason you choose not to proceed with this research ethics application, please inform the Research Ethics Office.

Please note that research involving human participants must not commence until full ethical approval has been granted.

Yours sincerely,

Mr James Patterson
Senior Research Ethics Officer

For and on behalf of

Dr Karen Gillett, Joint Chair
PNM Research Ethics Subcommittee

Cc: Professor Christine Norton

Major Issues (will require substantial consideration by the applicant before approval can be granted)

Minor Issues related to application (the reviewer should identify the relevant section number before each comment)

1. Section C6: The £5 you intend to offer as an incentive should be accounted for.

2. Section C9 and Information Sheet: The Committee is of the view that participants should be allowed a period of time to subsequently withdraw their data.

3. Section E5: Provide a departmental postal address for the location at which research data will be stored during and after the study.
4. Section E9 and Consent Form: Please ensure that statements about the future use of participants' data are consistent.

5. Section H6: Submit your approach letter to the gatekeeper

6. Pre-intervention questionnaire: Please use Office for National Statistics (ONS) categories of ethnicity.

**Minor Issues related to recruitment documents**

7. Information Sheet:
   i. Provide information about the £5 incentive. ii. Remove the paragraph titled 'What if there is a problem?'
   iii. The Committee recommends that you do not use a mobile number unless it is one dedicated for the purposes of the study.
   iv. Insert the paragraph beginning with 'If this study has harmed you in any way...' before the contact details for your academic supervisor. This is required for insurance purposes.

8. Advertisement document: If possible, the College logo should be displayed.

9. The Committee believes that £5 may not be sufficient incentive for participants in this study. Therefore, you may wish to consider offering entry into a prize draw instead which would allow you to offer one or more bigger prizes as an incentive.
D3) D.3.1 PHQ-9 risk assessment protocol

PROTOCOL FOR ASSESSING AND REPORTING RISK IN RESEARCH

The following principles and procedures govern risk assessment and reporting.

**General procedures**

Whenever any significant risk is identified a risk assessment should be completed and (counter signed) by the chief investigator and/or nominated deputy as soon after the assessment as possible.

Any significant, but not imminent risk should be reported to the person’s GP by the participant and, if appropriate, other health care professionals, as soon as is reasonably possible.

Any imminent risk should lead to the immediate involvement of the appropriate emergency health services. The chief investigator must ensure that Research Associates, Assistants, and Students are fully informed and competent to follow the procedures.

When the chief investigator is away they should ensure appropriate cover is arranged for any risk issues that might arise in their absence.

**Exploring Risk**

There are seven questions to be used following any indication of risk from responses to interview questions or any other sources. We define risk as any report of suicide/self harm ideation.

Ask the Exploring Risk in Research Interviews questions below and then look at answers from the sheet to determine the level of risk, A, B, or C.

**Exploring Risk in Item 9 on PHQ 9 with a score of 1 or more**

**THOUGHTS**

“I see that you’ve said / you mentioned that........

These are thoughts / feelings that people suffering from depression often have, but it’s important to make sure you are receiving the right kind of support. So if it’s OK, I would now like to ask you some more questions that will explore these feelings in a little more depth.”

**PLANS**

1. Have you made any actual plans to end your life? Yes / No
If **yes** – details

---

### ACTIONS

2. Have you made any actual preparations to kill yourself?  
   **Yes / No**  
   If **yes** – details

3. Have you ever attempted suicide in the past?  
   **Yes / No**  
   If **yes** – details

---

### PREVENTION

4. Is there anything stopping you killing or harming yourself at the moment?  
   **Yes / No**  
   If **yes** – details

5. Do you feel that there is any immediate danger that you will harm or kill yourself?  
   **Yes / No**  
   Details:
Researcher Risk Protocol

Look at answers from the sheet to determine the level of risk, A, B1, or C:

**Actions by Researcher/Facilitator**

All answers ‘no’ apart from Q4 ‘yes’:

- **A**

  I can see that things have been very difficult for you, but it seems to me these thoughts about death are not ones you would act on – would this be how you see things? (if they say yes) I would advise you to make an appointment to see your GP to talk about these feelings and I will provide you with a template letter to your GP to inform them of our discussions.

  Sign post participant to Samaritans help line and send participant letter ‘GP risk letter v1 21/11/2018.’

- **B1**

  Things seem to be very hard for you right now and I think it would help if you were to speak to your GP about these feelings. I will provide you with a letter to send to your GP to tell them that we have spoken and that you have been having some troubling thoughts. I would also advise you to make an appointment to see your GP to talk about these feelings.

  Sign post participant to Samaritans help line and send participant letter ‘GP risk letter v1 21/11/2018.’

‘Yes’ for any **one** of Qs 1-3; plus ‘yes’ for Q4 and ‘no’ for Q5

- **B1**

  Things seem to be very hard for you right now and I think it would help if you were to speak to your GP about these feelings. I will provide you with a letter to send to your GP to tell them that we have spoken and that you have been having some troubling thoughts. I would also advise you to make an appointment to see your GP to talk about these feelings.

  Sign post participant to Samaritans help line and send participant letter ‘GP risk letter v1 21/11/2018.’
Action to take in the case of immediate risk:

Participant needs immediate help – do not leave them alone. Ask participant to stay on the line why you arrange suitable care. Follow the chain of supervisory contact (only one contact needed from 1-3) and enact immediate risk procedure (point 4):

**Christine Norton**
Telephone: 
Email: Christine.norton@kcl.ac.uk

**Rona Moss-Morris**
Telephone: 0207 188 0178
Email: rona.moss-morris@kcl.ac.uk

**Wladzia Czuber-Dochan**
Telephone: 020 7848 3531
Email: wladzia.czuber-dochan@kcl.ac.uk

Then follow the chain of contact below:

- Call ambulance

*Risk assessment to be carried out by:*
(Lead Researcher: Louise Sweeney louise.sweeney@kcl.ac.uk)
(Facilitator: Georgia Moffatt georgia.moffatt@kcl.ac.uk)
3.2 GP letter provided to participants if flagged in PHQ-9 risk assessment

COINCIDE GP Risk Letter – to be sent after risk assessment

Surgery Address

Date

Dear Doctor _____________

Notification of suicide ideation from questionnaire completed as part of the Manging Pain in IBD Study

Patient Name:--------------------------- DOB: ....../....../.........

I am writing to notify you that I have reported thoughts of suicide ideation on a questionnaire as part of a research study.

As part of the assessment I was asked to fill out a PHQ-9, as you know this questionnaire asks if the patient has had “Thoughts that you would be better off dead or of hurting yourself in some way” (Question 9). My response to this was that in the past 2 weeks he/she has had these thoughts several days/more than half the days/nearly every day. As a result of this the research team contacted me to discuss this further and if I would like to take any action.

I feel I would benefit from talking to you about these thoughts. I would like to arrange to make an appointment to come and see you to discuss this further.

The clinical management remains your responsibility, but it is part of the study’s research team protocol to inform you of any risks disclosed to the research so that you can take account of me in our care plan.

Yours sincerely,

Name of participant
MANAGING AND UNDERSTANDING PAIN IN IBD

THIS SESSION WILL COVER:

- What is IBD-pain?
- Acute and chronic pain in IBD: what’s the difference?
- Factors associated with IBD-pain
- Taking a closer look at your vicious cycle of pain
- Common questions around pain in IBD
- Summary

Remember to complete your symptom graph by rating the impact of your most bothersome symptom; go to your symptom graph (page 236) in My Activities at the back of the manual now.

This session may take around 30-45 minutes to complete

WHAT IS IBD-PAIN?

Pain is a commonly experienced symptom of IBD. Most people with IBD will experience some level of pain during flares. Some also report pain when they are not in a flare. Pain that persists without inflammation for more than 3 months or on and off for 6 months is defined as chronic pain.

Pain is most frequently reported in the abdomen area, but people with IBD can also experience pain in their joints, lower back, skin and eyes. Pain can vary from an ongoing discomfort to short bursts of stabbing pain.
FREQUENCY OF IBD-PAIN

When and how frequently people experience pain can also vary.

“I get it first thing in the morning and pretty much as soon as I wake up.”

“…consistent, certainly since I came out of hospital.”

“It can be every day then stop for a while.”

“It can be an ongoing ache that can last from a minute to five minutes and would normally clear on its own accord.”

“But that’s a very continuous, same-level pain or ache for the entire time.”

“The other a short sharp pain which only last seconds.”

“It can vary, as it can be lots, can be a very small amount and it’s completely random. It has no relation to if the problem is getting worse, if it’s getting better, it can happen at any time of the day.”

Pain can be unpredictable, so it can be difficult to know what is going on and what to do to reduce the pain. You may also find it hard to balance the use of pain medications.

You may also feel like your healthcare professionals give you lots of different advice. This makes it tricky to know which the best option for you is. Having a better understanding of factors associated with your pain will make you feel more confident and motivated to manage your pain effectively.

ACUTE AND CHRONIC PAIN: WHAT’S THE DIFFERENCE?

It is very common to experience acute pain in IBD, such as when you are having a flare. Chronic pain occurs when you still experience pain even when your disease is in remission. This type of pain can be triggered and maintained by both physical and mental factors.

Managing your well-being, such as changing unhelpful emotions and thoughts and reducing your levels of stress can help to reduce the intensity of the pain and impact it has on your life.
Acute pain system

Acute pain is triggered by a specific harmful event or stimulus. In IBD this can be inflammation or an obstruction in the bowel. Acute pain is expected to go away after the source of pain has been effectively treated (e.g., treated by steroids, biologics, surgery).

In acute pain, nerve fibres take the pain message from the site of damage as fast as possible through the spinal cord to the pain centres in the brain. These fast nerve fibres are called ‘A’ fibres. The nerve fibres need to send messages quickly for the body to do something immediately, e.g., remove a hand from a hot pan.

This is a survival mechanism to protect the body. You can think of the acute pain system as being like dialling straight through to the emergency services for immediate action.

Chronic pain system

The chronic pain system is different to the acute pain system. It sends messages very slowly and repeatedly to several pain centres in the brain. To send messages it uses slow nerve fibres called ‘C’ fibres.

The brain may interpret these pain messages to mean that the problem (e.g., inflammation) is still happening and is not over. Alternatively, the nerve fibres may develop a ‘memory’ for pain experiences and continue to send pain messages even when there is no current inflammation or damage. This is like a light switch being broken and the lightbulb staying on.

The ‘C’ fibre nerve endings can become very sensitive to movement, hot and cold sensations and chemical changes. Sometimes if the pain area is touched or moved, it sends off many pain messages to the brain.

In IBD, overactive pain messages may be sent during normal digestive activity, such as food moving through the digestive tract. The nerves seem to increase the pain feelings or intensity or cause other sensations like numbness or tingling.

FACTORS ASSOCIATED WITH PAIN

Pain can be difficult to manage. Like the other two symptoms that we talk about in BOOST (fatigue and urgency), pain can be triggered and maintained by many different factors. In Session 1, we explained how biological, psychological and social factors can contribute to your IBD symptoms. In this session, we will cover factors associated with pain in more detail.

No single factor explains why you experience pain and how it varies.

Pain in IBD can be a result of:

- Medical factors
- Maintaining factors (what we do, the way we think, how we feel)
- The environment
We will discuss each of these one by one and then review your vicious cycle of pain.

**MEDICAL FACTORS RELATED TO PAIN**

**Medical factors associated with acute abdominal pain**

*Read through the points below to learn about the medical factors associated with acute abdominal pain.*

**Inflammation**

Inflammation of the intestinal wall or at another site of disease (e.g., around the back passage) occurs during a flare of IBD and this can lead to a constant and dull type of pain, or at times to a more sharp and severe pain.

**Complications of your IBD**

Pain can also be associated with complications from your IBD. For example, obstruction (blockages) in the bowel or narrowing of digestive tract (strictures) can be associated with severe pain.

Inflammation, blockages and strictures can lead to abdominal distension or bloating. They cause substances such as gases or fluids to accumulate in the abdomen and cause it to expand. This can result in pain or discomfort and feeling bloated.

**Bowel movements**

Inflammation can also affect the movement of the bowel, typically causing the bowel to move faster thus resulting in diarrhoea. This leads to contents moving through the bowel more quickly after a meal, which leads to more irritation of the bowel. This results in pain. Irregular bowel movements can also stimulate the stretch receptors in the bowel which then lead to pain.

**Medical factors associated with chronic abdominal pain**

Over time, pain in the abdomen can become chronic or persistent. This means that you may still experience pain even when you are in remission and endoscopic and blood results are normal.

*Read through the points to learn about the medical factors associated with chronic abdominal pain.*

**Low levels of inflammation**

An ongoing but low level of inflammation in the digestive tract which is not picked up by clinical tests.
Highly sensitive pain fibres

Your gut can become highly sensitive (hypersensitive) to bowel contents and movement in the digestive tract. This may be because of having a flare or multiple flares over time. This means that you may also feel discomfort or pain even in circumstances where there is no damage or flare.

Pain pathways in the brain

Pain and emotions are processed in the same part of the brain. As mentioned in Session 1, scientists say ‘neurons that fire together, wire together’. This means that the physical connections in your brain strengthen if you concentrate on specific sensations. You may understandably have a range of unhelpful thoughts and emotions when you are in pain. If you focus a lot on the pain or feel highly anxious and stressed when in pain this can strengthen the pain signal, making your experience more intense.

Read through other types of pain that you may experience with your IBD.

Joint pain

Pain in IBD is most commonly experienced in the abdominal region, but many people also report experiencing pain in their joints. Joint pain can be a result of IBD-associated rheumatic disease such as arthritis. Joint pain can also be a side effect of certain medicines, such as prednisolone or other steroid drugs.

Widespread pain

A small number of IBD patients will experience widespread pain across their body that comes with tingling or burning sensations. These may be more characteristic of nerve (neuropathic) pain or chronic pain syndromes such as fibromyalgia. Patients that experience both pain associated with IBD and other pain syndromes such as fibromyalgia or chronic migraine may have more of a central pain syndrome. This means that the brain is processing and exaggerating pain signals in the absence of harmful stimuli.

MAINTAINING FACTORS AND IBD-PAIN

Throughout BOOST, we have discussed how what we do, the way we think and how we feel can have an impact on pain.
What we do

If you have had severe pain for a long time, you may have tried to manage it by resting more and avoiding or reducing activity. You might then push yourself to do as much as possible when you are feeling better and decide to rest more when your pain gets worse.

In Session 2 (page 30), we talked about the importance of maintaining a consistent pattern of activity, exercise and eating. We also covered different patterns of activity in response to symptoms, including boom or bust, overactivity and underactivity. Moreover, we discussed fear avoidance, where over time your ability to exercise or carry out certain movements, positions or activities may have become difficult, due to fear that doing this action may worsen your pain.

In Session 3 (page 56), we covered how to adopt helpful sleep habits and maintain a consistent pattern of sleeping. Both these sessions are helpful for managing pain and maybe worth revisiting. We will also focus on specific behaviours relevant to pain later in this session.
The way we think

It is easy for a chronic illness to bring on unhelpful ideas and thoughts, which in turn influence the way you make sense of your symptoms. Unhelpful thoughts can trap you in a vicious cycle where the more pain you experience, the more unhelpful thoughts you have. The more you believe them, the more pain you have. In this session we will look at thoughts specific to pain and things you can do to reduce pain.

“I just became so worried that my bowel was going to perforate or that something really bad was going to happen. And then that made me more conscious of the pain and then the pain was getting worse because I was stressed and my body was going into overdrive.”

“It makes me exceptionally anxious when I experience a pain that I’ve never had before, which is tricky with this disease, because every day I’m learning something new about it and every day I have a new sort of pain.”

In Sessions 4a and 4b (pages 76-100), we explained how to identify unhelpful thoughts and how to come up with alternatives.

How we feel

Stress and specific mood states can make pain worse. They can also affect how you cope.

“Medicine will get you so far but if you are not happy then no amount of medication can help with that.”

“I certainly know that the symptoms that I get now are very much stress related, if I’m particularly stressed then the pains will start to materialise perhaps a day or two later.”

In Session 5, we considered how stress and unhelpful emotions can trigger, maintain or worsen your pain and ways to cope with stress and manage emotions related to your symptoms.

You may want to revisit some of these sessions, according to what affects your pain the most. Specifically, you may find it useful to revisit some of the tasks associated with them. Many of the exercises in the programme take time to become part of your routine. We will guide you on what tasks you can choose to revisit throughout the rest of this session.
ENVIRONMENT AND IBD-PAIN

Stress

Having continuous or unpredictable pain can be frustrating and challenging. Not seeing a clear pattern between your pain and your disease activity can be confusing. Not having clear answers or options from your healthcare professionals can leave you feeling disheartened. These aspects of chronic pain in IBD can all increase your levels of stress.

Stress can also arise from other aspects of life, whether this includes your work, daily routines or others around you. Sometimes you may also have uncontrollable stressors, such as how your illness progresses. It is important to recognise when stresses in life are controllable or uncontrollable.

Others around you

Stress can be caused by other people, such as work colleagues, family or relationships. Other people may say unhelpful or inappropriate things to you. This may be because they do not understand what IBD is or what you are going through or may be too worried about you.

“It can be frustrating because they know what’s happening, but they don’t know to the extent. As in, they know I’m in pain, but they don’t understand how much pain I am in.”

“I didn’t really share it with anybody. So I wouldn’t really share the pain side of things, because I’d have to explain what was like the bigger picture.”

“I think they know, I’ve told them the condition and the name of the disease. But I don’t think that they fully appreciate what you are physically going through.”

“I think also people don’t necessarily understand. I think that’s another big deal, because you can’t see it.”

You may also find that symptoms can have an impact on your social life, where you have to limit your social activities as a result of your pain.

“My social life has really taken a blow because I’m a bit scared to do things in case the pain comes back and I’m not sort of in my own safe environment.”

“I have cancelled a lot of social things to the point where I think some of my friends don’t bother asking me to things anymore.”

“When I ring and have to cancel because I would just, feel too unwell, or couldn’t bear, kind of going out, because I think actually that’s something that happens when I’m in pain, I feel quite depressed”
Having a good social support network is really important with helping you manage your pain. In Session 6 (page 130), we covered how to optimise your social support and communication with others about your symptoms and IBD.

Take a break

Feel free to take a break if you need it.

YOUR VICIOUS CYCLE OF IBD-PAIN

In Session 1, you created your *vicious cycle* of symptoms, where you identified behaviours, thoughts and emotions in relation to the symptom that impacted you the most. Now that you have completed all the core sessions of BOOST, we are going to look back on your vicious cycle.

*If in Session 1, you identified pain as your most burdensome symptom* and had completed your vicious cycle using pain as the symptom, you may want to reflect on what you have already written and **add additional relevant behaviours, thoughts and emotions in the pain-specific vicious cycle diagram in My Activities – My Vicious Cycle for Session 1, page 237.** Go to My Activities – My Vicious Cycle (Session 1) now and make changes to the vicious cycle you had filled out during Session 1. Here are some prompts to help you think:

- Are there any other behaviours or ways you respond when you are in pain?
- Are there any other thoughts you experience when you’re in pain?
- Are there any other ways you feel when you are in pain?

*If in Session 1, you identified fatigue or urgency as your most burdensome symptom* and had completed your vicious cycle using fatigue or urgency as the symptom, **you can now create a vicious cycle for pain.** Using the vicious cycle you previously completed for fatigue or urgency as an example, fill out the blank pain-specific vicious cycle in My Activities – Vicious Cycle (Pain Specific Session, page 241) to represent your behaviours, thoughts and emotions in relation to pain. Go to My Activities – My Vicious Cycle (Pain Specific Session) now and fill out a new vicious cycle in relation to pain.

This vicious cycle is useful because it separates medical and environmental factors that trigger pain, from other factors more under our control that maintain and worsen pain.

We will now take a closer look at behaviours, thoughts and emotions in the context of pain specifically. We will go through the different aspects one by one and guide you in identifying ways in which you can make small but important changes to help you manage your pain.

You may want to focus on one of the aspects (behaviours, thoughts or emotions) according to what you think may make the biggest difference to you right now. We will also encourage you to set new
goals in relation to these aspects at the end of the session. If a section is not relevant to you, you can skip to the next section.

TAKING A CLOSER LOOK AT BEHAVIOURS IN YOUR VICIOUS CYCLE OF PAIN

If you feel this section is not relevant for you, please skip to Taking a closer look at thoughts in your vicious cycle of pain.

As we explained in Session 1, our behaviours, thoughts and emotions are all linked. The things we do in response to pain (our behaviours) can affect the way we think and feel about the pain.

As we covered in Session 2, when you are in pain you may feel you want to curl up into a ball and avoid engaging in work or social activities. This is a natural and understandable response to pain. However, long periods of rest can result in muscle stiffness, sore joints and reduced strength, contributing to more bodily pain.

Look back at the unhelpful behaviours you identified in response to pain when you filled out your pain-specific vicious cycle (page 241). Read through the questions below to see which strategies you could use to overcome any unhelpful behaviours you identified.

Do you find that your levels of activity vary day to day depending on your pain?

If your activity levels vary depending on your pain, you may find you have periods of boom and bust where you get through as much as you can and then crash at the end of the day. Once you get into the boom or bust cycle it can be difficult to get out of it.

By starting to set activity level goals that you can achieve consistently, you create a basis from which to gradually increase the amount you are able to do and improve how you feel. Initially, you can start by stabilising your activity pattern and scheduling a consistent level of activity that you are able to do on both good and bad days.
Think of Alex.

Alex has a very busy job. Often when he comes home from work he finds his level of pain is very high. On these days he crashes and spends the evening on the sofa sleeping or watching TV.

In contrast, on the days in which his pain levels are lower, he pushes himself to go for a run for an hour, clean the house and cook elaborate meals. He ends up not having any time to relax until he goes to bed. When he wakes up the next morning he finds himself too sore to go to work.

Alex realises that his boom or bust activity pattern is making his pain worse in the long run. So he decides to set himself some goals aiming for consistency.

Instead of doing running, cleaning and cooking all in one day he decides to spread these tasks throughout the week.

He also decides to schedule some time during the day in which he can do some relaxation exercises.

These are Alex’s SMART goals for Week 1:

“This week I will:
- Leave work at 5pm on Tuesdays and Thursdays and go for a 20-minute run.
- Clean the house for 1 hour on Saturday
- Cook meals for the week on Monday night
- Sit and do some relaxation exercises 10-minutes at lunch every day”

At first, he feels like he is less active than before. But this is just because his activity is more spread out throughout the week. As he develops a consistent, daily pattern of activity he is then able to build up on the amount he can do each week without crashing.

These are Alex’s SMART goals for exercise in the following weeks:

- Week 2: “I will leave work at 5pm on Tuesdays and Thursdays and go for a 25-minute run.”
- Week 3: “I will leave work at 5pm on Tuesdays and Thursdays and go for a 30-minute run.”
- Week 4: “I will leave work at 5pm on Tuesdays and Thursdays and go for a 30-minute run. I will also go for a 45-minute walk on Sunday morning.”

Have you found that over time you have become generally less active because of your pain?

If you generally become less active because of your pain, you may find that you have periods of underactivity. Avoiding activity over time can result in muscle stiffness, lethargy, disability and reduced strength. These can all contribute to worsening symptoms.

Avoiding activities and the unhelpful thoughts that come with them can also lower our mood. The more we avoid actions, the more we may build up a fear of engaging them in the future.
Increasing your activity very gradually can help your body gain back some of its fitness and make you feel less pain in the long term. It is important to make these changes slowly, so that your body can adapt.

**Think of Alex.**

Alex wants to get back into being more physically active. In the long term, his goal is to be able to do 150 minutes of activity per week, in line with the NHS physical activity guidelines. However, trying to do this straightaway is not feasible and would worsen his pain as he has done very little after two bad flares of his IBD.

So, Alex decides to set smaller, short-term weekly goals in relation to walking. Because he knows consistency is important, he sets his initial goal, to what he can do even on a bad day.

From here he decides to monitor and increase the amount he does gradually, which allows him to reach his long-term goal in time, whilst letting his body adapt. Throughout he maintains one key role – he either goes up a little each week or if it has been a very bad week stays the same.

**This is Alex's SMART goal for Week 1:**

“This week I will go for a 10-minute walk before dinner on Tuesday and Friday.”

Thinking about his progress, Alex finds that the 10-minute walk is doable, but he would not feel comfortable walking for any longer. Therefore, he keeps the time the same but adds in a walk on one more day for week 2.

**These are Alex's SMART goals for exercise in the following weeks:**

- Week 2: “I will go for a 10-minute walk before dinner on Tuesday, Thursday and Saturday this week.”
- Week 3: “I will go for a 10-minute walk before dinner on Monday, Wednesday, Friday and Sunday this week.”
- Week 4: “I will go for a 15-minute walk before dinner on Tuesday, Thursday and Saturday this week.”

By setting goals and thinking about his progress, Alex is able to change the goal a little bit each week. Seeing the improvement and having control over the activity also helps with confidence and motivation to manage his pain.

**What are your goals for building a consistent pattern of activity?**

To help you, we have broken down the goal into 3 parts:
What will you do:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

When:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

How often:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

☐ If you might like to add building a consistent pattern of activity as a goal, tick this box.

If you ticked the box, go to your My Goals for the Pain Specific Session (page 253) and write down your goals related to building a consistent pattern of activity.

**TAKING A CLOSER LOOK AT THOUGHTS IN YOUR VICIOUS CYCLE OF PAIN**

If you feel this section is not relevant for you, please skip to Taking a closer look at emotions in your vicious cycle of pain

The way in which we think about pain can affect the way we feel and behave in relation to our pain. For example, you may find that when you experience pain, you have unhelpful thoughts, which make you feel upset and more likely to avoid social activities. Look at the examples in the thought record. The percentages (%) indicate how much the person believes the thought to be true.
<table>
<thead>
<tr>
<th>Date</th>
<th>Situation</th>
<th>Feeling</th>
<th>Unhelpful Thought</th>
<th>Alternative Thought</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 June</td>
<td>My partner got annoyed at me for not wanting to go out for dinner</td>
<td>Angry</td>
<td>My partner should understand what I am going through with my pain and know what I need <em>(should)</em></td>
<td>It is hard for others to really understand what it is like to have IBD pain. Perhaps if I had tried to explain what it is like he would not have gotten annoyed</td>
</tr>
<tr>
<td></td>
<td>Tummy feeling painful so lay down on the couch at home to watch TV instead of going for a walk</td>
<td>Very worried</td>
<td>I am sure this is the start of a new flare. I couldn’t get through another one. I had better just rest up as this will prevent it getting worse <em>(catastrophising)</em></td>
<td>I have pain a lot and most of the time it isn’t linked to a flare unless there are other bad symptoms too. Exercise can sometimes help pain a bit, so a walk may be good as I will focus more on my tummy if I lie down on the couch</td>
</tr>
</tbody>
</table>

### Think of Alex.

Alex wants to take up more exercise as he has lost confidence because of his pain.

His housemate Chris goes to Pilates at their local gym every Monday, so he decides to join him. Alex’s aim is to improve his stretching, strength and flexibility gradually. He enjoys his first class, despite finding the abdominal exercises very hard and it puts him in a good mood.

He works even harder in the second class, only to wake up with some pain in his abdomen and lower back. He has never experienced this type of pain before and his mind starts to wander, “I should never have started that Pilates class”, “now I will definitely need surgery again”, “I should stay in bed to control this pain”, “I will never be able to work with this pain so I will just stay in bed.”
Once you have read the scenario, try to weigh up the evidence by answering the following questions.

1. **How else could Alex interpret what has happened?**

   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

2. **Is Alex just focusing on the negative aspect of the situation? How?**

   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

3. **Is Alex expecting the worst (catastrophising)? How?**

   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

4. **Is Alex trying to predict the future? How?**

   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________
   ___________________________________________________________

**Did you manage to find alternative ways for Alex to think about the situation?**

If you found the exercise difficult, read the following to see some possible answers to the questions above.

1. **How else could Alex interpret what has happened?**

   Alex had not engaged in exercise for a while as he had lost confidence with his pain. Feeling a bit of pain or fatigue after exercise is normal. His joints, muscles and ligaments may have become stiff over time because of inactivity. The stiffness may have been causing him to feel aches, pain and fatigue after his Pilates class.

2. **Is Alex just focusing on the negative aspect of the situation?**

   Yes, Alex is worrying that the pain he is experiencing could mean that he needs surgery. It is normal to experience pain and aches after exercise. He is basing his judgement on the last class, without thinking about the first class which he enjoyed.

3. **Is Alex expecting the worst (catastrophising)?**
Yes, Alex is catastrophising because he is thinking that he now needs surgery without considering that his Pilates class could have made him feel aches and pain around his abdomen and back. He does not consider that these aches may pass once his body has recovered from the exercise.

4. Is Alex trying to predict the future?
Yes, Alex is trying to predict the future. He does not know if he will need surgery again and jumping to conclusions about surgery has only made Alex anxious and worried. This may make him less confident to attend future Pilates classes which he had been enjoying.

How likely do you think these alternative ways of thinking are?

__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________

COMING UP WITH ALTERNATIVE THOUGHTS

Look back at the unhelpful thoughts you identified in response to pain when you filled out your pain-specific vicious cycle. You can find this at the back of the manual (page 241).

Select one of the unhelpful thoughts you identified and write it here:

__________________________________________________________________________________
__________________________________________________________________________________

1. Briefly describe a situation where you might have been thinking that thought or something similar.

__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________

2. What evidence do you have in support of this thought?

__________________________________________________________________________________
__________________________________________________________________________________
__________________________________________________________________________________

3. What evidence do you have that this thought may not be true?

__________________________________________________________________________________
__________________________________________________________________________________
4. Is there a more positive aspect to the situation you are ignoring? If so write it here.

__________________________________________________________________________________

__________________________________________________________________________________

5. Now look through your answers. Can you think of some alternative thoughts?

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________

If you have found this exercise particularly relevant to you, you might find it helpful to complete your alternative thoughts record in My Tasks for Session 4b (page 100) again.

☐ If you might like to add completing an alternative thought record again as a goal, tick this box.

If you ticked the box, go to your My Goals for Pain Specific Session (page 253) and write down your goals related to completing an alternative thought record again.

Take a break

Feel free to take a break if you need it.

TAKING A CLOSER LOOK AT EMOTIONS IN YOUR VICIOUS CYCLE OF PAIN

If you feel this section is not relevant for you, please skip to IBD-pain and medication

It is natural and understandable that you may be feeling different emotions such as worry, frustration or anger because of your pain. This can be caused by some of the thoughts you may have associated with your pain (this pain will never go away) or some of the ways you respond behaviourally to your pain (staying in bed all day and not being able to attend a friend’s birthday).

Some of the ways you can manage these emotions include finding ways to express your emotions (in person or in writing) and gradually exposing yourself to activities that cause you anxiety. You can
also find ways to manage stress, including engaging in some mindfulness or relaxation exercises (see Session 5 page 104, or the recordings on the memory stick).

Expressing emotions

Talking about your feelings to people you trust makes it easier to manage the difficult emotions caused by your pain. However, many people keep their emotions to themselves. They may feel embarrassed or uncomfortable about showing them. They may fear negative judgement from others, or that they will be a burden to other people. Some people also have difficulty identifying what they are feeling.

Think of Alex.

Alex often cancels dates he has made with his friends at the last minute because of his pain.

However, he has never told his friends that the reason why he cancels is because of his anxiety and embarrassment about his pain getting out of control. He is afraid that his friends won’t understand his pain and the way he feels about it.

Soon his friends start to feel rejected and don’t understand why Alex has stopped spending time with them.

One evening Alex confides in his friend Kate about his pain and embarrassment. His friend tells him she is relieved to hear this is the reason Alex has been cancelling their dates. She was worried Alex had been losing interest in their friendship and had been wondering if she should stop phoning to make arrangements.

Kate also realises how awful it must be for Alex to feel this anxious end embarrassed about his pain. She asks if there is anything she can do to help him feel less anxious when going out with friends.

Writing about your feelings

A researcher in Texas, James Pennebaker, has shown that writing about how you feel about difficult experiences can help relieve distress and improve health. Writing about how you feel is a good way to understand and process the information. It can also help you get your thoughts in order before you talk to someone about how you feel.
Read the box below to know more about how to try this strategy for yourself.

- At first, try to write for between 15-20 minutes, every day for three days.
- Write about what is bothering you at the moment and what makes you feel distressed. Try to explore your feelings and thoughts, both generally and specific to pain.
- You can write about the same thing every day or choose to write about different things.
- Don’t worry about spelling or grammar – nobody will be looking at what you write and it’s purely an outlet for yourself. You can choose to keep what you write, or you can throw it away (if you choose to keep it, think about where to store it privately).
- Find yourself a comfortable and private space to write.
- It is likely that writing about your feelings may make you feel upset or distressed initially. This is completely normal. By processing these feelings you can start to accept these normal reactions and understand the meaning behind them.
- If you find writing about your feelings helpful, then you can choose to do so more often.

Exposure

It is understandable to avoid situations that make you anxious. In addition to letting people know when you feel anxious, one way of increasing your tolerance of feeling anxious or fearful is through a process of exposure. Exposure means gradually re-introducing experiences that may have been avoided because they cause anxious feelings.

If you can gradually reintroduce situations to your life that provoke anxiety, it can increase your tolerance of the symptoms of pain themselves. You will start to feel more confident in dealing with unpredictable situations or symptoms.

Of course, if the exposure feels a bit much you can always break your initial goal into smaller parts to make it more manageable.

Think of Alex.

Alex’s doctor has encouraged him to do more aerobic exercise. Alex has joined a gym and he keeps setting a day for his first session – each time something holds him back.

He realises, deep down, that he is worried that going to the gym will make his pain worse.
He decides to write a list of activities at the gym that he is worried about and number them from most worrying to least worrying.

Here is his list:

1. Running on the treadmill.
2. Lifting weights.
3. Using the cross-trainer.
4. Walking on the treadmill.
5. Having a swim in the pool.

He then goes to the gym and tries the least worrying activity (number 5) – swimming in the pool for 20 minutes. He does that for a 2 weeks until it no longer bothers him.

Then he tackles the next easiest, 15 minutes of walking on the treadmill. Soon this doesn’t worry him. He goes on like this until he can use all of the equipment at the gym without feeling anxious about his pain.

раф

Think of a recent event when you felt emotional about your pain and write it below:

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________

How could you try and manage the situation?

Before you come up with ways in which you could manage difficult emotions in relation to your pain, these are some example goals for Alex’s situation.

- When Alex feels anxious about going out to the movies, he will call one of his friends for a chat before leaving home.
- When Alex feels stressed by a hectic week, he will set aside some time to invite one of his friends for a drink at his place.
- When Alex feels frustrated, he will set aside some time in the evening to write about how he feels.

Now you can set your own goal. To help you, we have broken down the goal into 3 parts:

What will you do:

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________

When:

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________

How often:

__________________________________________________________________________________

__________________________________________________________________________________

__________________________________________________________________________________
If you might like to add working on better managing emotions (talking to others and/or writing about feelings) as a goal, tick this box.

*If you ticked the box, go to your My Goals for Pain Specific Session (page 253) and write down your goals related to working on better managing emotions.*

If managing emotions in relation to your pain is particularly important for you, you might find it helpful to do more of the mindfulness and relaxation exercises in My Tasks for Session 5 (page 125).

If you might like to add practicing mindfulness and relaxation exercises as a goal, tick this box.

*If you ticked the box, go to your My Goals for Pain Specific Session (page 253) and write down your goals related to practicing mindfulness and relaxation exercises.*

**IBD-PAIN AND MEDICATION**

Pain medications for IBD can include the following:

- **Paracetamol** – this is a most mild type of pain medication. Some people find use of paracetamol helpful for their pain.
- **Ibuprofen and other NSAIDS (non-steroidal anti-inflammatory drugs)** – these can be effective for reducing pain and associated inflammation related to arthritis or joint pain. For abdominal pain, use of ibuprofen or other NSAIDS have been shown to increase the risk of bringing on a flare and so requires medical advice.
- **Antidepressants** – at low doses, these can have independent effects on pain apart from treating psychiatric issues such as major depressive disorder.
- **Gabapentin and Pregabalin** – these are prescribed for nerve (neuropathic) pain conditions as they work by dampening down the pain signals from the nerves. They are a good treatment for hypersensitivity and chronic pain. However, their use for abdominal pain is less well established.
- **Opioids** – these are the strongest class of pain medication. These are not recommended for long-term pain management as they can over time increase pain severity because of further gastrointestinal complications.

*It is very important that you speak to your doctor or nurse about any questions you have regarding pain medications and to work together to find out what pain medications may be suitable for you.*
COMMON QUESTIONS AROUND PAIN IN IBD

Read the boxes about communication and assessment of pain in IBD.

“Why is it difficult for doctors to understand my problem?”

It is difficult for others to truly understand your pain. It can seem invisible. Healthcare professionals cannot measure pain. They can measure inflammation in the gut and carry out procedures to look at the gut, but they cannot see or feel the pain itself.

“What does having IBS in IBD mean?”

Your healthcare professionals may have told you that your pain in remission could be due to irritable bowel syndrome (IBS). IBS is a gastrointestinal condition with very similar symptoms to IBD (abdominal pain, diarrhoea, fatigue, bloating). Though in IBS there is no clear evidence of inflammation or damage to the gastrointestinal tract. IBS may be caused by:

- Undetectable levels of inflammation
- Your gut becoming highly sensitive to stimuli and movement, or being activated in the absence of stimuli
- Changes in the way that your gut moves

A diagnosis of IBS can sometimes be frustrating as you may not know how this can help you manage your pain. If your healthcare professional has suggested it may be ‘IBS in IBD’, then ask about your treatment options and what people with IBS find useful.

Treatment can include medicines (antispasmodics such as Buscopan), anti-depressants, dietary soothing techniques (peppermint) and strict dietary regimes (low FODMAP). Cognitive behavioural therapy (CBT) is also one of the recommended treatment approaches for IBS.

In BOOST we have integrated key techniques used in CBT such as changing unhelpful thoughts, relaxation exercises or increasing your activity levels. So, these techniques may be useful for your IBS as well as your IBD.

“Why don’t people take my pain seriously?”

It can sometimes feel as if your pain is not being taken seriously. Most healthcare professionals will believe that it is very distressing and disabling for you. Family, friends and healthcare professionals will often be frustrated at not being able to change things for you.

You could write down a list of questions to ask your healthcare professionals more about the pain and your body’s pain systems. You may also want to use the information in this session to help your family and friends understand more about pain systems, the difficulties caused by pain and how they affect your pain.
MANAGING AND UNDERSTANDING PAIN IN IBD: GOAL SETTING

Throughout the session you have identified some pain-specific goals, relating to your behaviours, thoughts and emotions, you may want to work on. It is important to set clear weekly goals to improve your pain management and to monitor your progress.

Go to your My Goals for the Pain Specific Session section at the back of the manual (page 253) to view your pain-specific goals you identified.

Other goals you might want to set may be related to:
- Developing a more consistent pattern of activity
- Increasing your activity levels
- Developing alternative thoughts related to pain using a thought record
- Managing stressful situations by practicing mindfulness exercises, talking to someone or writing down what you are feeling

Now have a go at setting your goals and add these to the goals table in My Activities – My Goals for the Pain Specific Session (page 253).
Well done, you have finished the Managing and Understanding Pain in IBD session!

We have covered a lot on pain in IBD. In this session, you have learned that:

- Pain is a very common symptom of IBD and can be experienced in both periods of flaring and remission.
- There are two pain systems, acute and chronic. Acute pain occurs when there is damage or inflammation occurring, and pain signals are sent instantly to the brain. Chronic pain involves a slower pain messaging system and occurs when pain messages are being sent to the brain when there is no damage or identifiable levels of inflammation.
- Pain in IBD is associated with biological, psychological (behaviours, thoughts and emotions) and environmental factors.

If you have completed all the symptom-specific sessions you wanted to work on, please remember to do the summary session, Summary and Maintaining Improvement on page 224, before finishing the programme.